National Collaborating Centre for Women's and Children's Health

Feverish illness in children

assessment and initial management in children younger than 5 years

Clinical Guideline

May 2007

Funded to produce guidelines for the NHS by NICE

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assessment and initial management in children younger than 5 years

National Collaborating Centre for Women's and Children's Health

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Stakeholder organisations

Action for Sick Children
Acute Care Collaborating Centre
Addenbrookes NHS Trust
Airedale General Hospital – Acute Trust
Anglesey Local Health Board

Aspirin Foundation
Association of Child Psychotherapists
Association of Medical Microbiologists
Association of Paediatric Emergency Medicine
Association of the British Pharmaceuticals Industry (ABPI)
Barking Havering & Redbridge Acute Trust
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British National Formulary (BNF)
British Psychological Society
British Society for Antimicrobial Chemotherapy
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Hampshire Partnership NHS Trust
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Healthcare Commission
Heart of England NHS Foundation Trust
Herpes Viruses Association
Hertfordshire Partnership NHS Trust
Hospital Infection Society
Infection Control Nurses Association of the British Isles
Institute of Biomedical Science
King's College Acute Trust
Leeds Teaching Hospitals NHS Trust
Leukaemia Research Fund
Liverpool PCT
Luton and Dunstable Hospital NHS Trust
Maidstone and Tunbridge Wells NHS Trust
Medicines and Healthcare products Regulatory Agency (MHRA)
Medway NHS Trust

Meningitis Research Foundation
Meningitis Trust
Mental Health Collaborating Centre
Mid Essex Hospitals NHS Trust
Mid Staffordshire General Hospitals NHS Trust
Milton Keynes PCT
National Childbirth Trust
National Collaborating Centre for Cancer
National Collaborating Centre for Nursing and Supportive Care (NCC-NSC)
National Collaborating Centre for Primary Care
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National Patient Safety Agency
National Public Health Service – Wales
National Reyes Syndrome Foundation of the UK
National Youth Advocacy Service
Neonatal & Paediatric Pharmacists Group (NPPG)
Newcastle PCT
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NHS Pathways
NHS Quality Improvement Scotland
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NICE – Implementation Consultant – Region SW
NICE – Implementation Consultant – Region East
NICE – Implementation Consultant – Region NW & NE
NICE – Implementation Consultant – Region West Midlands
NICE – R&D for information
North Eastern Derbyshire PCT
North Lincolnshire PCT
North Tees and Hartlepool Acute Trust
North West London Hospitals NHS Trust
Northwick Park and St Mark's Hospitals NHS Trust
Paracetamol Information Centre
Patient and Public Involvement Programme (PPIP) for NICE
PERIGON (formerly the NHS Modernisation Agency)
Princess Alexandra Hospital NHS Trust
Prodigy
Queen Mary's Hospital NHS Trust (Sidcup)
Reckitt Benckiser Healthcare (UK) Ltd
Regional Public Health Group – London
Rotherham PCT
Royal Bolton Hospitals NHS Trust
Royal College of General Practitioners
Royal College of General Practitioners Wales
Royal College of Nursing
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Royal College of Pathologists
Royal College of Physicians of London
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Royal Liverpool Children's Hospital
Royal Pharmaceutical Society of Great Britain
Royal Society of Medicine
Royal United Hospital Bath NHS Trust
Royal West Sussex Trust
Sandwell & West Birmingham NHS Trust
Scottish Intercollegiate Guidelines Network (SIGN)
Sedgefield PCT
Sheffield Children's Hospital Trust
Sheffield PCT
Society for Academic Primary Care

South Birmingham PCT
South East Sheffield PCT
South Huddersfield and Central Huddersfield PCTs
South Yorkshire Ambulance Service NHS Trust
Specialist Advisory Committee on Antimicrobial Resistance (SACAR)
Staffordshire Ambulance HQ
Staffordshire Moorlans PCT
Stockport PCT
Sussex Ambulance Services NHS Trust
Tameside and Glossop Acute Trust
Tameside and Glossop PCT
UK Specialised Services Public Health Network
UKCPA – Infection Management Group
University College London Hospitals (UCLH) Acute Trust
University Hospital Lewisham NHS Trust
University of Bristol
University of Southampton
Welsh Assembly Government
Welsh Scientific Advisory Committee (WSAC)
Wirral Hospital Acute Trust
Wyre Forest Primary Care Trust

Abbreviations

AHA	American Heart Association
ANC	absolute neutrophil count
AOR	adjusted odds ratio
CI	confidence interval
CNS	central nervous system
CRP	C-reactive protein
CRT	capillary refill time
CSF	cerebrospinal fluid
ED	emergency department
EL	evidence level (level of evidence)
ER	emergency room
ESR	erythrocyte sedimentation rate
FWS	fever without (apparent) source
GDG	Guideline Development Group
GP	general practitioner
HES	Hospital Episode Statistics
hpf	high power field
HSE	herpes simplex encephalitis
HTA	Health technology appraisal
ICU	intensive care unit
ITU	intensive therapy unit
IV	intravenous
LR	likelihood ratio
LRTI	lower respiratory tract infection
MCD	meningococcal disease
MHRA	Medicines and Healthcare products Regulatory Agency
NCC-WCH	National Collaborating Centre for Women's and Children's Health
NHS	National Health Service
NICE	National Institute for Health and Clinical Excellence
NNT	number needed to treat
NPV	negative predictive value
NSAIDs	nonsteroidal anti-inflammatory drugs
OPD	outpatient department
OR	odds ratio
PCT	procalcitonin
PGE_2	prostaglandin E2
PPIP	Patient and Public Involvement Programme
PPV	positive predictive value
QALY	quality-adjusted life year
RCT	randomised controlled trial
ROC	receiver operating characteristic
RR	relative risk; respiratory rate
RSV	respiratory syncytial virus
SBI	serious bacterial illness/infection
SD	standard deviation
SIGN	Scottish Intercollegiate Guidelines Network
SpO_2	transcutaneous oxygen saturation
SR	systematic review
temp.	temperature
TRIP	Turning Research into Practice
UTI	urinary tract infection
UK	United Kingdom
WBC	white blood cell count
WHO	World Health Organization
YOS	Yale Observation Score
YIOS	Young Infant Observation Score

Glossary of terms

Absolute risk	Measures the probability of an event or outcome occurring (e.g. an adverse reaction to the drug being tested) in the group of people under study. Studies that compare two or more groups of patients may report results in terms of the **absolute risk reduction**.
Absolute risk reduction (ARR)	The ARR is the difference in the risk of an event occurring between two groups of patients in a study – for example, if 6% of patients die after receiving a new experimental drug and 10% of patients die after having the old drug treatment then the ARR is 10% – 6% = 4%. Thus by using the new drug instead of the old drug 4% of patients can be prevented from dying. Here the ARR measures the risk reduction associated with a new treatment. See also **absolute risk**.
Acute sector	Hospital-based health services which are provided on an inpatient, day case or outpatient basis.
Acute trust	A trust is an NHS organisation responsible for providing a group of healthcare services. An acute trust provides hospital services (but not mental health hospital services, which are provided by a mental health trust).
Allied health professionals	Healthcare professionals other than doctors and nurses directly involved in the provision of health care. Includes several groups such as physiotherapists, occupational therapists and dietitians. (Formerly known as professions allied to medicine or PAMs.)
Ambulatory care	All types of health services provided to patients who are not confined to a hospital bed as inpatients during the time services are rendered. Examples relevant to this guideline would include attendance to a walk-in centre or paediatric assessment unit, or the provision of care by paediatric community nurses.
Antipyretic interventions	Procedures or medications used with the intent of reducing body temperature in patients with fever. The term includes physical cooling methods and antipyretic medication. Paracetamol and ibuprofen are the drugs commonly used for this purpose in the UK.
Applicability	The extent to which the results of a study or review can be applied to the target population for a clinical guideline.
Appraisal of evidence	Formal assessment of the quality of research evidence and its relevance to the clinical question or guideline under consideration, according to predetermined criteria.
ARR	See **absolute risk reduction**.
Bacteraemia	The presence of bacteria in the blood. In this condition the bacteria are not causing an infection in the bloodstream (cf. **septicaemia**).
Best available evidence	The strongest research evidence available to support a particular guideline recommendation.
Bias	Influences on a study that can lead to invalid conclusions about a treatment or intervention. Bias in research can make a treatment look better or worse than it really is. Bias can even make it look as if the treatment works when it actually does not. Bias can occur by chance or as a result of **systematic errors** in the design and execution of a study. Bias can occur at various stages in the research process, e.g. in the collection, analysis, interpretation, publication or review of research data. For examples see **selection bias**, **performance bias**, **information bias**, **confounder or confounding factor**, **publication bias**.
Blinding or masking	The practice of keeping the investigators or subjects of a study ignorant of the group to which a subject has been assigned. For example, a clinical trial in which the participating patients or their doctors are unaware of whether they (the patients) are taking the experimental drug or a **placebo** (dummy treatment). The purpose of 'blinding' or 'masking' is to protect against bias. See also **double-blind study**, **single-blind study**, **triple-blind study**.

Capillary refill time (CRT) — A test performed on physical examination in which the skin is pressed until blanched by the clinician's finger and the time taken for the skin to return to its previous colour is measured. Capillary refill time (CRT) can be measured peripherally (on the extremities) or centrally (on the chest wall). A prolonged CRT may be a sign of circulatory insufficiency (e.g. shock) or dehydration.

Case–control study — A study that starts with the identification of a group of individuals sharing the same characteristics (e.g. people with a particular disease) and a suitable comparison (**control**) group (e.g. people without the disease). All subjects are then assessed with respect to things that happened to them in the past, e.g. things that might be related to getting the disease under investigation. Such studies are also called **retrospective** as they look back in time from the outcome to the possible causes.

Case report (or case study) — Detailed report on one patient (or case), usually covering the course of that person's disease and their response to treatment.

Case series — Description of several cases of a given disease, usually covering the course of the disease and the response to treatment. There is no comparison (**control**) group of patients.

Causal relationship — Describes the relationship between two **variables** whenever it can be established that one causes the other. For example, there is a causal relationship between a treatment and a disease if it can be shown that the treatment changes the course or outcome of the disease. Usually **randomised controlled trials** are needed to ascertain causality. Proving cause and effect is much more difficult than just showing an association between two variables. For example, if it happened that everyone who had eaten a particular food became sick, and everyone who avoided that food remained well, then the food would clearly be associated with the sickness. However, even if leftovers were found to be contaminated, it could not be proved that the food caused the sickness – unless all other possible causes (e.g. environmental factors) had been ruled out.

CCT — See **controlled clinical trial**.

CER — Control event rate. See **event rate**.

Cerebrospinal fluid (CSF) — The watery fluid that surrounds the brain and spinal cord. Samples of CSF can be obtained by **lumbar puncture**.

Checklist — See **study checklist**.

Chemical dot thermometer — A thermometer consisting of cells embedded in a plastic strip in which the cells contain a combination of chemicals that change colour in response to changes in temperature. Also known as a chemical phase-change thermometer.

Chest indrawing — The indrawing of the lower chest wall.

Clinical audit — A **systematic** process for setting and monitoring standards of clinical care. Whereas 'guidelines' define what the best clinical practice should be, 'audit' investigates whether best practice is being carried out. Clinical audit can be described as a cycle or spiral. Within the cycle there are stages that follow a systematic process of establishing best practice, measuring care against specific criteria, taking action to improve care, and monitoring to sustain improvement. The spiral suggests that as the process continues, each cycle aspires to a higher level of quality.

Clinical effectiveness — The extent to which a specific treatment or intervention, when used under *usual or everyday conditions*, has a beneficial effect on the course or outcome of disease compared with no treatment or other routine care. (Clinical trials that assess effectiveness are sometimes called management trials.) Clinical 'effectiveness' is not the same as **efficacy**.

Clinical governance — A framework through which NHS organisations are accountable for both continually improving the quality of their services and safeguarding high standards of care by creating an environment in which excellence in clinical care will flourish.

Clinical impact — The effect that a guideline recommendation is likely to have on the treatment, or treatment outcomes, of the **target population**.

Clinical importance — The importance of a particular guideline recommendation to the clinical management of the **target population**.

Clinical question — This term is sometimes used in guideline development work to refer to the questions about treatment and care that are formulated in order to guide the search for research evidence. When a clinical question is formulated in a precise way, it is called a **focused question**.

Clinical trial — A research study conducted with patients which tests out a drug or other intervention to assess its effectiveness and safety. Each trial is designed to answer scientific questions and to find better ways to treat individuals with a specific disease. This general term encompasses **controlled clinical trials** and **randomised controlled trials**.

Clinician — A qualified healthcare professional providing patient care, e.g. doctor, nurse, physiotherapist.

Cluster — A group of patients, rather than an individual, used as the basic unit for investigation. See also **cluster design**, **cluster randomisation**.

Cluster design — Cluster designs are those where research subjects are not sampled or selected independently, but in a group. For example, a clinical trial where patients in a general practice are allocated to the same intervention; the general practice forming a cluster. See also **cluster** and **cluster randomisation**.

Cluster randomisation — A study in which groups of individuals (e.g. patients in a GP surgery or on a hospital ward) are randomly allocated to treatment groups. Take, for example, a smoking cessation study of two different interventions – leaflets and teaching sessions. Each GP surgery within the study would be randomly allocated to administer one of the two interventions. See also **cluster** and **cluster design**.

Cochrane Collaboration — An international organisation in which people find, appraise and review specific types of studies called **randomised controlled trials**. The Cochrane Database of Systematic Reviews contains regularly updated reviews on a variety of health issues and is available electronically as part of the **Cochrane Library**.

Cochrane Library — The Cochrane Library consists of a regularly updated collection of evidence-based medicine databases including the Cochrane Database of Systematic Reviews (reviews of **randomised controlled trials** prepared by the **Cochrane Collaboration**). The Cochrane Library is available on CD-ROM and the internet.

Cohort — A group of people sharing some common characteristic (e.g. patients with the same disease), followed up in a research study for a specified period of time.

Cohort study — An **observational study** that takes a group (cohort) of patients and follows their progress over time in order to measure outcomes such as disease or mortality rates and make comparisons according to the treatments or interventions that patients received. Thus, within the study group, subgroups of patients are identified (from information collected about patients) and these groups are compared with respect to outcome, e.g. comparing mortality between one group that received a specific treatment and one group that did not (or between two groups that received different levels of treatment). Cohorts can be assembled in the present and followed into the future (a 'concurrent' or '**prospective**' cohort study) or identified from past records and followed forward from that time up to the present (a 'historical' or '**retrospective**' cohort study). Because patients are not randomly allocated to subgroups, these subgroups may be quite different in their characteristics and some adjustment must be made when analysing the results to ensure that the comparison between groups is as fair as possible.

Combined modality — Use of different treatments in combination (e.g. surgery, chemotherapy and radiotherapy used together for cancer patients).

Commercial 'in confidence' material — Information (e.g. the findings of a research project) defined as 'confidential' as its public disclosure could have an impact on the commercial interests of a particular company. (Academic 'in confidence' material is information (usually work produced by a research or professional organisation) that is pending publication.)

Co-morbidity — Co-existence of a disease or diseases in the people being studied in addition to the health problem that is the subject of the study.

Confidence interval (CI)

A way of expressing certainty about the findings from a study or group of studies, using statistical techniques. A confidence interval describes a range of possible effects (of a treatment or intervention) that are consistent with the results of a study or group of studies. A wide confidence interval indicates a lack of certainty or precision about the true size of the clinical effect and is seen in studies with too few patients. Where confidence intervals are narrow they indicate more precise estimates of effects and a larger sample of patients studied. It is usual to interpret a '95%' confidence interval as the range of effects within which we are 95% confident that the true effect lies.

Confounder or confounding factor

Something that influences a study and can contribute to misleading findings if it is not understood or appropriately dealt with. For example, if a group of people exercising regularly and a group of people who do not exercise have an important age difference then any difference found in outcomes about heart disease could well be due to one group being older than the other rather than due to the exercising. Age is the confounding factor here and the effect of exercising on heart disease cannot be assessed without adjusting for age differences in some way.

Consensus development conference

A technique used for the purpose of reaching an agreement on a particular issue. It involves bringing together a group of about ten people who are presented with evidence by various interest groups or experts who are not part of the decision-making group. The group then retires to consider the questions in the light of the evidence presented and attempts to reach a consensus. See also **Consensus methods**.

Consensus methods

A variety of techniques that aim to reach an agreement on a particular issue. Formal consensus methods include **Delphi** and **nominal group techniques**, and **consensus development conferences**. In the development of clinical guidelines, consensus methods may be used where there is a lack of strong research evidence on a particular topic.

Considered judgement

The application of the collective knowledge of a guideline development group to a body of evidence, to assess its applicability to the **target population** and the strength of any recommendation that it would support.

Consistency

The extent to which the conclusions of a collection of studies used to support a guideline recommendation are in agreement with each other. See also **homogeneity**.

Control event rate (CER)

See **event rate**.

Control group

A group of patients recruited into a study that receives no treatment, a treatment of known effect, or a **placebo** (dummy treatment), in order to provide a comparison for a group receiving an experimental treatment, such as a new drug.

Controlled clinical trial (CCT)

A study testing a specific drug or other treatment involving two (or more) groups of patients with the same disease. One (the experimental group) receives the treatment that is being tested, and the other (the comparison or **control group**) receives an alternative treatment, a **placebo** (dummy treatment) or no treatment. The two groups are followed up to compare differences in outcomes to see how effective the experimental treatment was. A CCT where patients are randomly allocated to treatment and comparison groups is called a **randomised controlled trial**.

Cost–benefit analysis

A type of **economic evaluation** where both costs and benefits of healthcare treatment are measured in the same monetary units. If benefits exceed costs, the evaluation would recommend providing the treatment.

Cost-effectiveness

Value for money. A specific healthcare treatment is said to be 'cost-effective' if it gives a greater health gain than could be achieved by using the resources in other ways.

Cost-effectiveness analysis

A type of **economic evaluation** comparing the costs and the effects on health of different treatments. Health effects are measured in 'health-related units', for example, the cost of preventing one additional heart attack.

Cost–utility analysis

A special form of **cost-effectiveness analysis** where health effects are measured in **quality-adjusted life years**. A treatment is assessed in terms of its ability to both extend life and to improve the quality of life.

C-reactive protein (CRP)	A plasma protein that circulates in increased amounts during inflammation and after tissue damage. Measurement of CRP in blood samples is widely used as a marker of infection or inflammation.
Cross-sectional study	The observation of a defined set of people at a single point in time or time period – a snapshot. (This type of study contrasts with a **longitudinal study**, which follows a set of people over a period of time.)
Data set	A list of required information relating to a specific disease.
Decision analysis	Decision analysis is the study of how people make decisions or how they *should* make decisions. There are several methods that decision analysts use to help people to make better decisions, including **decision trees**.
Decision tree	A decision tree is a method for helping people to make better decisions in situations of uncertainty. It illustrates the decision as a succession of possible actions and outcomes. It consists of the probabilities, costs and health consequences associated with each option. The overall effectiveness or overall cost-effectiveness of various actions can then be compared.
Declaration of interest	A process by which members of a working group or committee 'declare' any personal or professional involvement with a company (or related to a technology) that might affect their objectivity e.g. if their position or department is funded by a pharmaceutical company.
Delphi method	A technique used for the purpose of reaching an agreement on a particular issue, without the participants meeting or interacting directly. It involves sending participants a series of postal questionnaires asking them to record their views. After the first questionnaire, participants are asked to give further views in the light of the group feedback. The judgements of the participants are statistically aggregated, sometimes after weighting for expertise. See also **consensus methods**.
Delphi statement	A statement of the advised course of action in relation to a particular clinical topic, based on the collective views of a body of experts by using the **Delphi** technique.
DGH	District general hospital (non-teaching hospital).
Diagnostic study	A study to assess the effectiveness of a test or measurement in terms of its ability to accurately detect or exclude a specific disease.
Dominance	A term used in **health economics** describing when an option for treatment is both less clinically effective and more costly than an alternative option. The less effective and more costly option is said to be 'dominated'.
Double-blind study	A study in which neither the subject (patient) nor the observer (investigator/clinician) is aware of which treatment or intervention the subject is receiving. The purpose of blinding is to protect against bias.
Economic evaluation	A comparison of alternative courses of action in terms of both their costs and consequences. In **health economic** evaluations the consequences should include health outcomes.
EER	Experimental event rate – see **event rate**.
Effectiveness	See **clinical effectiveness**.
Efficacy	The extent to which a specific treatment or intervention, under *ideally controlled conditions* (e.g. in a laboratory), has a beneficial effect on the course or outcome of disease compared with no treatment or other routine care.
Elective	A term for clinical procedures that are regarded as advantageous to the patient but not urgent.
Empirical	Based directly on experience (observation or experiment) rather than on reasoning alone.
Encephalitis	Inflammation of the substance of the brain. It is usually caused by infection with viruses (e.g. herpes simplex virus).
Epidemiology	The study of diseases within a population, covering the causes and means of prevention.

Event rate	The proportion of patients in a group for whom a specified health event or outcome is observed. Thus, if out of 100 patients, the event is observed in 27, the event rate is 0.27 or 27%. **Control event rate (CER)** and **experimental event rate (EER)** are the terms used in control and experimental groups of patients, respectively.
Evidence based	The process of systematically finding, appraising and using research findings as the basis for clinical decisions.
Evidence-based clinical practice	Evidence-based clinical practice involves making decisions about the care of individual patients based on the best research evidence available rather than basing decisions on personal opinions or common practice (which may not always be evidence based). Evidence-based clinical practice therefore involves integrating individual clinical expertise and patient preferences with the best available evidence from research.
Evidence level (EL)	A code (e.g. 1++, 1+) linked to an individual study, indicating where it fits into the **hierarchy of evidence** and how well it has adhered to recognised research principles. Also called **level of evidence**.
Evidence table	A table summarising the results of a collection of studies which, taken together, represent the evidence supporting a particular recommendation or series of recommendations in a guideline.
Exclusion criteria	See **selection criteria**.
Experimental event rate (EER)	See **event rate**.
Experimental study	A research study designed to test whether a treatment or intervention has an effect on the course or outcome of a condition or disease – where the conditions of testing are to some extent under the control of the investigator. **Controlled clinical trials** and **randomised controlled trials** are examples of experimental studies.
Experimental treatment	A treatment or intervention (e.g. a new drug) being studied to see whether it has an effect on the course or outcome of a condition or disease.
External validity	The degree to which the results of a study hold true in non-study situations, for example in routine clinical practice. May also be referred to as the **generalisability** of study results to non-study patients or populations.
Extrapolation	The application of research evidence based on studies of a specific population to another population with similar characteristics.
Extremities	Medical term for the hands and feet.
Febrile convulsion	A fit caused by high body temperature in young children. Uncomplicated febrile convulsions are not associated with epilepsy in later life or other neurological complications.
Fever	For the purposes of this guideline, fever was defined as 'an elevation of body temperature above the normal daily variation'. See Section 1.6 for more information on this definition.
Fever without (apparent) source (FWS)	The condition in which a patient has a fever but no obvious cause or focus of infection can be found on physical examination.
Focal neurological signs	Findings on physical examination that are caused by lesions in a particular area of the central nervous system. Examples include weakness of a limb or a cranial nerve palsy. These signs suggest that a given disease process is focal rather than diffuse.
Focal seizures	An epileptic seizure that originates from one part of the brain. Symptoms depend on which part of the brain is affected. Typically, one part of the body or one side of the body will develop convulsive movements. Focal (or partial) seizures can also include sensory disturbances, such as smelling or hearing things that are not there. In an uncomplicated focal seizure, consciousness is not lost. However, focal seizures can progress to involve the whole brain in a generalised seizure in which consciousness will be lost.
Focus group	A **qualitative research** technique. It is a method of group interview or discussion of 6–12 people focused around a particular issue or topic. The method explicitly includes and uses the group interaction to generate data.

Focused question — A study question that clearly identifies all aspects of the topic that are to be considered while seeking an answer. Questions are normally expected to identify the patients or population involved, the treatment or intervention to be investigated, what outcomes are to be considered, and any comparisons that are to be made. For example, do insulin pumps (intervention) improve blood sugar control (outcome) in adolescents with type 1 diabetes (population) compared with multiple insulin injections (comparison)? See also **clinical question**.

Fontanelle — A membrane-covered gap or soft spot between the skull bones on the vertex of an infant's skull. A bulging fontanelle can be a sign of meningitis.

Forest plot — A graphical display of results from individual studies on a common scale, allowing visual comparison of results and examination of the degree of **heterogeneity** between studies.

Funnel plot — Funnel plots are simple scatter plots on a graph. They show the treatment effects estimated from separate studies on the horizontal axis against a measure of sample size on the vertical axis. **Publication bias** may lead to asymmetry in funnel plots.

Generalisability — The extent to which the results of a study hold true for a population of patients beyond those who participated in the research. See also **external validity**.

Gold standard — A method, procedure or measurement that is widely accepted as being the best available.

Grey literature — Reports that are unpublished or have limited distribution, and are not included in bibliographic retrieval systems.

Grunting — A deep guttural breathing sound that can represent respiratory distress in infants and young children.

Guideline — A systematically developed tool that describes aspects of a patient's condition and the care to be given. A good guideline makes recommendations about treatment and care, based on the best research available, rather than opinion. It is used to assist clinician and patient decision making about appropriate health care for specific clinical conditions.

Guideline recommendation — Course of action advised by the guideline development group on the basis of their assessment of the supporting evidence.

Health economics — A branch of economics that studies decisions about the use and distribution of healthcare resources.

Health technology — Health technologies include medicines, medical devices such as artificial hip joints, diagnostic techniques, surgical procedures, health promotion activities (e.g. the role of diet versus medicines in disease management) and other therapeutic interventions.

Health technology appraisal (HTA) — A health technology appraisal, as undertaken by NICE, is the process of determining the clinical and cost-effectiveness of a **health technology**. NICE health technology appraisals are designed to provide patients, health professionals and managers with an authoritative source of advice on new and existing health technologies.

Herpes simplex infections — A group of acute infections caused by herpes simplex virus type 1 or type 2 that is characterised by the development of one or more small fluid-filled vesicles with a raised erythematous base on the skin or mucous membrane. Occasionally the viruses can cause more serious infections such as encephalitis in young children.

Heterogeneity — Or lack of **homogeneity**. The term is used in **meta-analyses** and **systematic reviews** when the results or estimates of effects of treatment from separate studies seem to be very different – in terms of the size of treatment effects or even to the extent that some indicate beneficial and others suggest adverse treatment effects. Such results may occur as a result of differences between studies in terms of the patient populations, outcome measures, definition of **variables** or duration of follow-up.

Hierarchy of evidence — An established hierarchy of study types, based on the degree of certainty that can be attributed to the conclusions that can be drawn from a well-conducted study. Well-conducted **randomised controlled trials** (RCTs) are at the top of this hierarchy. (Several large statistically significant RCTs which are in agreement represent stronger evidence than say one small RCT.) Well-conducted studies of patients' views and experiences would appear at a lower level in the hierarchy of evidence.

Homogeneity — This means that the results of studies included in a **systematic review** or **meta-analysis** are similar and there is no evidence of **heterogeneity**. Results are usually regarded as homogeneous when differences between studies could reasonably be expected to occur by chance. See also **consistency**.

HTA — See **Health technology appraisal**.

Leucocyte count — The number of white blood cells per unit volume in venous blood. A differential leucocyte count measures the relative numbers of the different types of white cell.

Ill appearance — An ill-looking child is an overall impression the assessing healthcare professional can make when presented with a child. This impression is formed not only from objective measurements but also from subjective feelings about how the child looks/reacts. If a healthcare professional's subjective instinct is to describe the child as ill looking then the child is most likely at high risk of serious illness. Healthcare professionals should be confident to follow their impressions of a child's wellbeing.

Inclusion criteria — See **selection criteria**.

In-depth interview — A **qualitative research** technique. It is a face-to-face conversation between a researcher and a respondent with the purpose of exploring issues or topics in detail. It does not use pre-set questions, but is shaped by a defined set of topics or issues.

Infant — A child that is under the age of 12 months.

Information bias — Pertinent to all types of study and can be caused by inadequate questionnaires (e.g. difficult or biased questions), observer or interviewer errors (e.g. lack of **blinding**), response errors (e.g. lack of **blinding** if patients are aware of the treatment they receive) and measurement errors (e.g. a faulty machine).

Intention-to-treat (ITT) analysis — An analysis of a clinical trial where patients are analysed according to the group to which they were initially randomly allocated, regardless of whether or not they had dropped out, fully complied with the treatment, or crossed over and received the alternative treatment. Intention-to-treat analyses are favoured in assessments of **clinical effectiveness** as they mirror the non-compliance and treatment changes that are likely to occur when the treatment is used in practice.

Internal validity — Refers to the integrity of the study design.

Intervention — Healthcare action intended to benefit the patient, for example drug treatment, surgical procedure, psychological therapy, etc.

Interventional procedure — A procedure used for diagnosis or treatment that involves making a cut or hole in the patient's body, entry into a body cavity or using electromagnetic radiation (including X-rays or lasers). The National Institute for Health and Clinical Excellence (NICE) has the task of producing guidance about whether specific interventional procedures are safe enough and work well enough for routine use.

Kawasaki disease — A condition consisting of prolonged fever, a rash, changes to the extremities and mucous membranes, and enlargement of lymph glands in the neck. The exact cause is unknown but the condition is thought to be caused by a microbiological toxin. Kawasaki disease can cause aneurysms in the coronary arteries unless it is treated promptly.

Level of evidence — See **evidence level**.

Literature review — A process of collecting, reading and assessing the quality of published (and unpublished) articles on a given topic.

Longitudinal study — A study of the same group of people at more than one point in time. (This type of study contrasts with a **cross-sectional study** which observes a defined set of people at a single point in time.)

Lumbar puncture — A procedure in which cerebrospinal fluid is obtained by inserting a hollow needle into the space between vertebrae in the lumbar region of the spine. The procedure is used to diagnose meningitis and encephalitis.

Masking — See **blinding**.

Meningitis — Inflammation of the meninges, the membranes that lie between the surface of the brain and the inside of the skull. Meningitis is usually caused by infection with bacteria or viruses. Bacterial meningitis is a serious condition associated with appreciable mortality and significant neurological complications.

Meningococcal disease — Any of a number of infections caused by the bacterium *Neisseria meningitidis* (also known as the meningococcus). In young children meningococcal disease usually manifests as septicaemia, meningitis or a combination of the two. Meningococcal septicaemia is the leading infectious cause of death in childhood in the UK.

Meta-analysis — Results from a collection of independent studies (investigating the same treatment) are pooled, using statistical techniques to synthesise their findings into a single estimate of a treatment effect. Where studies are not compatible, for example because of differences in the study populations or in the outcomes measured, it may be inappropriate or even misleading to statistically pool results in this way. See also **systematic review** and **heterogeneity**.

Methodological quality — The extent to which a study has conformed to recognised good practice in the design and execution of its research methods.

Methodology — The overall approach of a research project, for example the study will be a **randomised controlled trial**, of 200 people, over 1 year.

Multicentre study — A study where subjects were selected from different locations or populations, for example a cooperative study between different hospitals or an international collaboration involving patients from more than one country.

Nasal flaring — An enlargement of the nostrils during breathing. Nasal flaring can indicate that increased work is required for breathing.

Negative predictive value (NPV) — The proportion of people with a negative test result who do not have the disease (where not having the disease is indicated by the gold standard test being negative).

Neonate — A newly born child aged up to and including 28 days.

NHS Direct — NHS Direct is a service that provides 24 hour confidential health advice and information. NHS Direct can help people who are feeling ill, are unsure what to do, would like to find out more about a condition or treatment, or need details of local health services. The service can be accessed by:

- visiting www.nhsdirect.nhs.uk
- going to NHS Direct Interactive on digital satellite TV (by pressing the interactive button on the remote control)
- calling 0845 4647.

NNH — Number needed to harm. See **number needed to treat**.

NNT — See **number needed to treat**.

Nominal group technique — A technique used for the purpose of reaching an agreement on a particular issue. It uses a variety of postal and direct contact techniques, with individual judgements being aggregated statistically to derive the group judgement. See also **consensus methods**.

Non-experimental study — A study based on subjects selected on the basis of their availability, with no attempt having been made to avoid problems of bias.

Non-paediatric practitioner — The term non-paediatric practitioner refers to a healthcare professional who has not had specific training and does not have recognised expertise in the management of children and their illnesses (cf. **paediatric specialist**). The term is mainly used to refer to healthcare professionals working in primary care but it may also apply to healthcare professionals in many general emergency departments.

Non-systematic review — See **review**.

Number needed to treat (NNT)

This measures the impact of a treatment or intervention. It states how many patients need to be treated with the treatment in question in order to prevent an event which would otherwise occur. For example, if the NNT = 4, then four patients would have to be treated to prevent one bad outcome. The closer the NNT is to 1, the better the treatment is. Analogous to the NNT is the number needed to harm (NNH),which is the number of patients that would need to receive a treatment to cause one additional adverse event. For example, if the NNH = 4, then four patients would have to be treated for one bad outcome to occur.

Objective measure

A measurement that follows a standardised procedure that is less open to subjective interpretation by potentially biased observers and study participants.

Observation

Observation is a research technique used to help understand complex situations. It involves watching, listening to and recording behaviours, actions, activities and interactions. The settings are usually natural, but they can be laboratory settings, as in psychological research.

Observational study

In research about diseases or treatments, this refers to a study in which nature is allowed to take its course. Changes or differences in one characteristic (e.g. whether or not people received a specific treatment or intervention) are studied in relation to changes or differences in other(s) (e.g. whether or not they died), without the intervention of the investigator. There is a greater risk of **selection bias** than in **experimental studies**.

Odds ratio (OR)

Odds are a way of representing probability, especially familiar for betting. In recent years odds ratios have become widely used in reports of clinical studies. They provide an estimate (usually with a **confidence interval**) for the effect of a treatment. Odds are used to convey the idea of 'risk' and an odds ratio of 1 between two treatment groups would imply that the risks of an adverse outcome were the same in each group. For rare events the odds ratio and the **relative risk** (which uses actual risks and not odds) will be very similar. See also **relative risk**, **risk ratio**.

Off-label prescribing

When a drug or device is prescribed outside its **specific indication**, to treat a condition or disease for which it is not specifically licensed.

Osteomyelitis

Infection of bone and bone marrow. Osteomyelitis is usually caused by bacteria. It can cause a chronic infection and disability if not treated appropriately.

Outcome

The end result of care and treatment and/or rehabilitation. In other words, the change in health, functional ability, symptoms or situation of a person, which can be used to measure the effectiveness of care/treatment/rehabilitation. Researchers should decide what outcomes to measure before a study begins; outcomes are then assessed at the end of the study.

***P* value**

If a study is done to compare two treatments then the *P* value is the probability of obtaining the results of that study, or something more extreme, if there really was no difference between treatments. (The assumption that there really is no difference between treatments is called the 'null hypothesis'.) Suppose the *P* value was $P = 0.03$. What this means is that if there really was no difference between treatments then there would only be a 3% chance of getting the kind of results obtained. Since this chance seems quite low we should question the validity of the assumption that there really is no difference between treatments. We would conclude that there probably is a difference between treatments. By convention, where the value of *P* is below 0.05 (i.e. less than 5%) the result is seen as statistically significant. Where the value of *P* is 0.001 or less, the result is seen as highly significant. *P* values just tell us whether an effect can be regarded as statistically significant or not. In no way do they relate to how big the effect might be, for which we need the **confidence interval**.

Paediatric specialist

The term paediatric specialist refers to a healthcare professional who has had specific training or has recognised expertise in the management of children and their illnesses. Examples include paediatricians, or healthcare professionals working in children's emergency departments.

PCT

See **primary care trust**.

Peer review Review of a study, service or recommendations by those with similar interests and expertise to the people who produced the study findings or recommendations. Peer reviewers can include professional and/or patient/carer representatives.

Performance bias Systematic differences in care provided apart from the intervention being evaluated. For example, if study participants know they are in the **control group** they may be more likely to use other forms of care, people who know they are in the experimental group may experience **placebo effects**, and care providers may treat patients differently according to what group they are in. **Masking** (**blinding**) of both the recipients and providers of care is used to protect against performance bias.

Pilot study A small scale 'test' of the research instrument. For example, testing out (piloting) a new questionnaire with people who are similar to the population of the study, in order to highlight any problems or areas of concern, which can then be addressed before the full-scale study begins.

Placebo Placebos are fake or inactive treatments received by participants allocated to the **control group** in a clinical trial that are indistinguishable from the active treatments being given in the experimental group. They are used so that participants are ignorant of their treatment allocation in order to be able to quantify the effect of the experimental treatment over and above any **placebo effect** due to receiving care or attention.

Placebo effect A beneficial (or adverse) effect produced by a **placebo** and not due to any property of the placebo itself.

Point estimate A best single estimate (taken from research data) for the true value of a treatment effect or other measurement. For example, researchers in one clinical trial take their results as their best estimate of the real treatment effect – this is their estimate at their point in time. The precision or accuracy of the estimate is measured by a **confidence interval**. Another clinical trial of the same treatment will produce a different point estimate of treatment effect.

Positive predictive value (PPV) The proportion of people with a positive test result who have the disease (where having the disease is indicated by the 'gold' standard test being positive).

Power See **statistical power**.

Primary care Health care delivered to patients outside hospitals. Primary care covers a range of services provided by GPs, nurses and other healthcare professionals, dentists, pharmacists and opticians.

Primary care trust (PCT) A primary care trust is an NHS organisation responsible for improving the health of local people, developing services provided by local GPs and their teams (called **primary care**) and making sure that other appropriate health services are in place to meet local people's needs.

Probability How likely an event is to occur, for example how likely a treatment or intervention will alleviate a symptom.

Procalcitonin A precursor of the hormone calcitonin that is released into the bloodstream in response to infection or inflammation. Proclacitonin can be measured in blood samples and it is currently under development as a potential test for the detection of serious infections.

Prognostic factor Patient or disease characteristics, for example age or **co-morbidity**, that influence the course of the disease under study. In a randomised trial to compare two treatments, chance imbalances in **variables** (prognostic factors) that influence patient outcome are possible, especially if the size of the study is fairly small. In terms of analysis these prognostic factors become **confounding factors**. See also **prognostic marker**.

Prognostic marker A **prognostic factor** used to assign patients to categories for a specified purpose – for example for treatment, or as part of a clinical trial – according to the likely progression of the disease. For example, the purpose of randomisation in a clinical trial is to produce similar treatment groups with respect to important prognostic factors. This can often be achieved more efficiently if randomisation takes place within subgroups defined by the most important prognostic factors. Thus if age was very much related to patient outcome then separate randomisation schemes would be used for different age groups. This process is known as stratified random allocation.

Prospective study

A study in which people are entered into the research and then followed up over a period of time with future events recorded as they happen. This contrasts with studies that are **retrospective**.

Protocol

A plan or set of steps that defines appropriate action. A research protocol sets out, in advance of carrying out the study, what question is to be answered and how information will be collected and analysed. Guideline implementation protocols set out how guideline recommendations will be used in practice by the NHS, both at national and local levels.

Publication bias

Studies with statistically significant results are more likely to get published than those with non-significant results. **Meta-analyses** that are exclusively based on published literature may therefore produce biased results. This type of bias can be assessed by a **funnel plot**.

Qualitative research

Qualitative research is used to explore and understand people's beliefs, experiences, attitudes, behaviour and interactions. It generates non-numerical data, for example a patient's description of their pain rather than a measure of pain. In health care, qualitative techniques have been commonly used in research documenting the experience of chronic illness and in studies about the functioning of organisations. Qualitative research techniques such as **focus groups** and **in-depth interviews** have been used in one-off projects commissioned by guideline development groups to find out more about the views and experiences of patients and carers.

Quality-adjusted life years (QALYs)

A measure of health outcome that looks at both length of life and quality of life. QALYs are calculated by estimating the years of life remaining for a patient following a particular care pathway and weighting each year with a quality of life score (on a zero to one scale). One QALY is equal to 1 year of life in perfect health, or 2 years at 50% health, and so on.

Quantitative research

Research that generates numerical data or data that can be converted into numbers, for example clinical trials or the national Census that counts people and households.

Quasi-experimental study

A study designed to test whether a treatment or intervention has an effect on the course or outcome of disease. It differs from a **controlled clinical trial** and a **randomised controlled trial** in that:

- the assignment of patients to treatment and comparison groups is not done randomly, or patients are not given equal probabilities of selection, or
- the investigator does not have full control over the allocation and/or timing of the intervention, but nonetheless conducts the study as if it were an experiment, allocating subjects to treatment and comparison groups.

Random allocation or randomisation

A method that uses the play of chance to assign participants to comparison groups in a research study, for example, by using a random numbers table or a computer-generated random sequence. Random allocation implies that each individual (or each unit in the case of **cluster randomisation**) being entered into a study has the same chance of receiving each of the possible interventions.

Randomised controlled trial (RCT)

A study to test a specific drug or other treatment in which people are randomly assigned to two (or more) groups, with one (the experimental group) receiving the treatment that is being tested and the other (the comparison or **control group**) receiving an alternative treatment, a **placebo** (dummy treatment) or no treatment. The two groups are followed up to compare differences in outcomes to see how effective the experimental treatment was. (Through randomisation, the groups should be similar in all aspects apart from the treatment they receive during the study.)

Relative risk (RR)

A summary measure that represents the ratio of the risk of a given event or outcome (e.g. an adverse reaction to the drug being tested) in one group of subjects compared with another group. When the 'risk' of the event is the same in the two groups the relative risk is 1. In a study comparing two treatments, a relative risk of 2 would indicate that patients receiving one of the treatments had twice the risk of an undesirable outcome than those receiving the other treatment. Relative risk is sometimes used as a synonym for **risk ratio**.

Reliability	Reliability refers to a method of measurement that consistently gives the same results. For example, someone who has a high score on one occasion tends to have a high score if measured on another occasion very soon afterwards. With physical assessments it is possible for different clinicians to make independent assessments in quick succession – and if their assessments tend to agree then the method of assessment is said to be reliable.
Remote assessment	An assessment carried out when the patient is geographically remote from the assessor such that physical examination is not possible.
Retrospective study	A retrospective study deals with the present/past and does not involve studying future events. This contrasts with studies that are **prospective**.
Review	Summary of the main points and trends in the research literature on a specified topic. A review is considered non-systematic unless an extensive literature search has been carried out to ensure that all aspects of the topic are covered and an objective appraisal made of the quality of the studies.
Risk ratio	Ratio of the risk of an undesirable event or outcome occurring in a group of patients receiving experimental treatment compared with a comparison (**control**) group. The term **relative risk** is sometimes used as a synonym for risk ratio.
Royal Colleges	In the UK medical/nursing world, the term Royal Colleges, as for example in 'The Royal College of …', refers to organisations that usually combine an educational standards and examination role with the promotion of professional standards.
Safety netting	The provision of support for patients in whom the clinician has some uncertainty as to whether the patient has a self-limiting illness and is concerned that their condition may deteriorate. Safety netting may take a number of forms, such as dialogue with the patient or carer about symptoms and signs to watch for, advice about when to seek further medical attention, review after a set period, and liaising with other healthcare services.
Sample	A part of the study's **target population** from which the subjects of the study will be recruited. If subjects are drawn in an unbiased way from a particular population, the results can be generalised from the sample to the population as a whole.
Sampling	Refers to the way participants are selected for inclusion in a study.
Sampling frame	A list or register of names that is used to recruit participants to a study.
Scottish Intercollegiate Guidelines Network (SIGN)	SIGN was established in 1993 to sponsor and support the development of evidence-based clinical guidelines for the NHS in Scotland.
Secondary care	Care provided in hospitals.
Selection bias	Selection bias has occurred if: • the characteristics of the **sample** differ from those of the wider population from which the sample has been drawn, or • there are systematic differences between comparison groups of patients in a study in terms of prognosis or responsiveness to treatment.
Selection criteria	Explicit standards used by guideline development groups to decide which studies should be included and excluded from consideration as potential sources of evidence.
Semi-structured interview	**Structured interviews** involve asking people pre-set questions. A semi-structured interview allows more flexibility than a structured interview. The interviewer asks a number of open-ended questions, following up areas of interest in response to the information given by the respondent.
Sensitivity	In diagnostic testing, sensitivity refers to the chance of having a positive test result given that you have the disease. 100% sensitivity means that all those with the disease will test positive, but this is not the same the other way around. A patient could have a positive test result but not have the disease – this is called a 'false positive'. The sensitivity of a test is also related to its **negative predictive value** (true negatives) – a test with a sensitivity of 100% means that all those who get a negative test result do not have the disease. To fully judge the accuracy of a test, its **specificity** must also be considered.
Septic	Affected by bacterial infection; hence septic shock, septic arthritis, etc.

Septicaemia A serious medical condition in which there is rapid multiplication of bacteria in the bloodstream and in which bacterial toxins are present in the blood. Septicaemia is usually fatal unless treated promptly with parenteral antibiotics.

Shock A pathological condition that can suddenly affect the haemodynamic equilibrium, usually manifested by failure to perfuse or oxygenate vital organs.

Sign A finding on physical examination of a patient that provides the clinician with an objective indication of a particular diagnosis or disorder (cf. **symptom**).

SIGN See **Scottish Intercollegiate Guidelines Network**.

Single-blind study A study in which *either* the subject (patient/participant) *or* the observer (clinician/investigator) is not aware of which treatment or intervention the subject is receiving.

Specific indication When a drug or a device has a specific remit to treat a specific condition and is not licensed for use in treating other conditions or diseases.

Specificity In diagnostic testing, specificity refers to the chance of having a negative test result given that you do not have the disease. 100% specificity means that all those without the disease will test negative, but this is not the same the other way around. A patient could have a negative test result yet still have the disease – this is called a 'false negative'. The specificity of a test is also related to its **positive predictive value** (true positives) – a test with a specificity of 100% means that all those who get a positive test result definitely have the disease. To fully judge the accuracy of a test, its **sensitivity** must also be considered.

Standard deviation A measure of the spread, scatter or variability of a set of measurements. Usually used with the mean (average) to describe numerical data.

Statistical power The ability of a study to demonstrate an association or causal relationship between two **variables**, given that an association exists. For example, 80% power in a clinical trial means that the study has a 80% chance of ending up with a ***P* value** of less than 5% in a statistical test (i.e. a statistically significant treatment effect) if there really was an important difference (e.g. 10% versus 5% mortality) between treatments. If the statistical power of a study is low, the study results will be questionable (the study might have been too small to detect any differences). By convention, 80% is an acceptable level of power.

Structured interview A research technique where the interviewer controls the interview by adhering strictly to a questionnaire or interview schedule with pre-set questions.

Study checklist A list of questions addressing the key aspects of the research methodology that must be in place if a study is to be accepted as valid. A different checklist is required for each study type. These checklists are used to ensure a degree of consistency in the way that studies are evaluated.

Study population People who have been identified as the subjects of a study.

Study quality See **methodological quality**.

Study type The kind of design used for a study. **Randomised controlled trials**, **case–control studies** and **cohort studies** are all examples of study types.

Subject A person who takes part in an experiment or research study.

Survey A study in which information is systematically collected from people (usually from a sample within a defined population).

Symptom A patient's report of an abnormal feeling or sensation that provides the clinician with a subjective indication of a particular diagnosis or disorder (cf. **sign**).

Systematic Methodical, according to plan; not random.

Systematic error Refers to the various errors or biases inherent in a study. See also **bias**.

Systematic review A review in which evidence from scientific studies has been identified, appraised and synthesised in a methodical way according to predetermined criteria. May or may not include a **meta-analysis**.

Systemic Involving the whole body.

Tachypnoea Abnormally rapid respiratory rate.

Target population	The people to whom guideline recommendations are intended to apply. Recommendations may be less valid if applied to a population with different characteristics from the participants in the research study, for example in terms of age, disease state or social background.
Tepid sponging	A traditional treatment for fever in which the patient is undressed and sponged with lukewarm water that is then allowed to evaporate.
Tertiary centre	A major medical centre providing complex treatments that receives referrals from both primary and secondary care. Sometimes called a tertiary referral centre. See also **primary care** and **secondary care**.
Triangulation	Use of three or more different research methods in combination; principally used as a check of validity. The more the different methods produce similar results, the more valid the findings.
Triple-blind study	A study in which the statistical analysis is carried out without knowing which treatment patients received, in addition to the patients and investigators/ clinicians being unaware which treatment patients were getting.
Trust	A trust is an NHS organisation responsible for providing a group of healthcare services. An acute trust provides hospital services. A mental health trust provides most mental health services. A **primary care trust** buys hospital care on behalf of the local population, as well as being responsible for the provision of community health services.
Tympanic thermometer	A thermometer that is inserted into the external ear canal and measures the temperature of blood vessels in the tympanic membrane (eardrum) by detecting infrared radiation.
Validity	Assessment of how well a tool or instrument measures what it is intended to measure. See also **external validity**, **internal validity**.
Variable	A measurement that can vary within a study, for example the age of participants. Variability is present when differences can be seen between different people or within the same person over time, with respect to any characteristic or feature that can be assessed or measured.

1 Introduction

1.1 Feverish illness in children

Feverish illness in young children usually indicates an underlying infection of some kind and, as such, the condition is a cause of concern for parents and carers. The condition is also a diagnostic challenge for healthcare professionals, and infectious diseases remain a major cause of childhood mortality and morbidity in the UK. As a result, there is a perceived need to improve the recognition, evaluation and immediate treatment of feverish illnesses in children.

Incidence and prevalence

Feverish illness is very common in young children. Figure 1.1 shows the proportions of children from a birth cohort of all infants born in one English county (Avon) whose parents either reported a high temperature or presented to a doctor for this reason.[1] It can be seen that a high temperature is reported by nearly 40% of parents of children aged under 6 months, and in over 60% of children in the other age ranges between 6 months and 5 years. Between 20% and 40% of children in the various age ranges are taken to a doctor because of fever, with the highest proportions presenting between the ages of 6 and 18 months. It has been estimated that an average of eight infective episodes occur in otherwise healthy children during the first 18 months of life.[2]

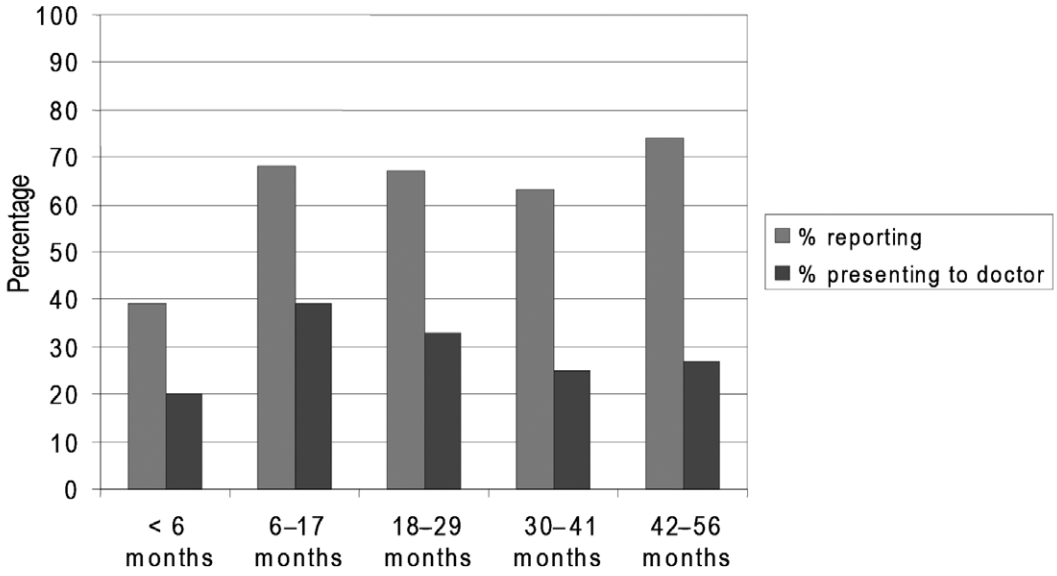

Figure 1.1 Proportions of children reporting and presenting to doctors with high temperature by age range; data from Hay[1]

The prevalence of feverish illness in children is reflected by statistics from primary care. Fever is probably the most common reason for a child to be taken to the doctor. In a study of 1% of the national child population, the mean general practice (GP) consultation rate was 3.7 per child per year and almost double that rate for children aged under 4 years. Infections and respiratory disorders made up over 40% of the consultations.[3] In the fourth national study of morbidity in general practice, which included nearly 10 000 children, the annual consultation rates for infections were 60% of the population aged less than 12 months, 36% aged 1–4 years and 20% aged 5–15 years.[4] Not surprisingly, fever in children is also a common reason for seeking health advice

out of hours. In one service, 34% of calls concerned children under 5 years of age.[5] Fever was a concern in 52% of calls about children aged under 12 months and in 64% of calls about children aged 1–5 years.

Feverish illness is also one of the most common reasons for children to be seen in hospital emergency departments and it is a leading cause of admission to children's wards. In a study from an emergency department in Nottingham, 32% of the 120 000 annual total attendances were for children.[6] Febrile illness was the second most common medical reason for attendance, accounting for 20% of such cases. On children's wards, at least 48% of admissions are associated with infection. Most of these infections present with a feverish illness with or without other symptoms such as breathing difficulty, fit, rash or cough. Feverish illness is second only to breathing difficulty as the most common presenting problem leading to acute hospital admission in childhood.[7]

Issues for healthcare professionals

Feverish illness in young children is a diagnostic challenge for healthcare professionals because it is often difficult to identify the cause. In most cases, the illness is due to a self-limiting virus infection and the child will recover quickly without intervention. However, fever may also be the presenting feature of serious bacterial illnesses such as meningitis, septicaemia, urinary tract infections and pneumonia. Estimates of the incidence of these and other serious infections are given in Table 1.1. Although there is quite a large variation in the estimated incidences according to the source of data, it appears that up to 1% of children aged 0–5 years may have one of these infections each year.

In some children with fever there will be symptoms and signs that suggest a particular infection, such as an inflamed eardrum in a child with otitis media or a non-blanching rash in a child with meningococcal septicaemia. When these features are identified, the diagnosis can be established relatively easily and the child can be treated appropriately. There will remain a significant number of children, however, who have no obvious cause of fever despite careful assessment and investigation. These children with fever without apparent source (FWS), are a particular concern to healthcare professionals because it is especially difficult to distinguish between simple viral illnesses and life-threatening bacterial infections in this group.[8] In general, FWS tends to be a problem in young children, and the younger the child the more difficult it is to establish a diagnosis and assess the severity of illness. Because of these problems, a number of diagnostic and management strategies have been developed for feverish illness without obvious source in young children.[9]

To further complicate the problem of assessment and diagnosis, the clinical picture often changes rapidly in young children. The condition of young children with serious illness may deteriorate

Table 1.1 Estimated incidence of serious infections in children aged 0–5 years in the UK; data from Hospital Episode Statistics (HES)

Diagnosis group	Incidence (per 100 000)	
	HES data	Published data
Pneumonia	664	92[a]
Septicaemia	388	20–50[b]
Urinary tract infection	333	
Meningitis	30.2	
Septic arthritis	9.25	3.75–5.0
Osteomyelitis	6.17	2.9
Other bacterial infection	0.66	
Encephalitis	3.65	0.8[c]
Kawasaki disease[d]	10.2	8.1
Total	1445	

[a] Pneumococcal pneumonia.
[b] Meningococcal septicaemia.
[c] Herpes simplex encephalitis.
[d] Kawasaki disease is not a confirmed infectious disease but it is believed to be caused by a microbiological toxin.

within hours of onset but, on the other hand, an ill-appearing child with a viral illness may make a rapid recovery. Thus, another challenge for healthcare professionals is to determine when to observe the child for a period of time, and when to investigate and begin treatment.

Most healthcare professionals are aware that infectious diseases were, and remain, an important cause of mortality and morbidity in childhood. In the past hundred years there have been impressive reductions in childhood mortality. The infant mortality rate in the UK, for example, has fallen from 20% to 0.5% since 1890. Much of this improvement has been due to public health measures, and immunisation against infectious disease has increasingly been an important factor. In recent years, the reduction in childhood mortality has changed only a little. In other countries, mortality rates have continued to fall and some European countries now have childhood mortality rates that are 30–40% lower than that of the UK. These figures suggest that more can be done to reduce childhood mortality in this country.

Figure 1.2 shows that infection is a major cause of mortality in children aged 0–5 years. There are over 100 deaths from infection in children aged 1–12 months each year in England and Wales. In the first year of life, infection is second only to congenital defects as a cause of death. In children aged 1–4 years there are around 30 deaths from infection per year of life, and infection is the most common cause of death in this age group.

It is possible that the childhood mortality rate in the UK could be reduced to a figure in line with other European countries if the proportion due to infections could be reduced. Immunisation will probably play an important part in this process. For example, the new pneumococcal conjugate vaccine, which was introduced into the UK schedule in 2006, has led to a dramatic reduction in invasive disease due to *Streptococcus pneumoniae* in other countries.[10] However, it is likely that improved recognition, evaluation and treatment of febrile illnesses in children could also lead to a reduction in mortality from infectious disease. For instance, a recent national study investigated deaths from meningococcal disease, which is the leading cause of mortality from infectious diseases in children.[11] The researchers found that mortality from meningococcal disease is often associated with late identification, sub-optimal treatment and other deficiencies in health care.

There is some concern that there is considerable variation in the provision of care for children with feverish illnesses across the UK. At present there are no national guidelines on the management of such children and practice has developed in different ways in different areas. For example, in many paediatric units it is common practice to observe febrile children for several hours while assessment takes place, but in other units it is not. In some situations there is evidence that differences in practice can affect outcome. For example, this could be construed from

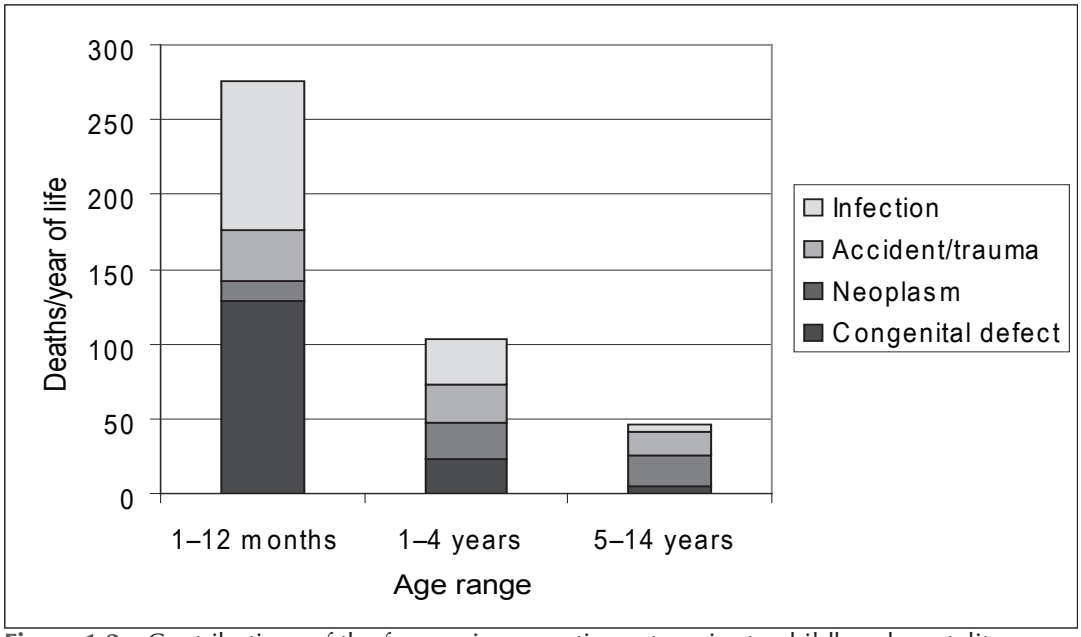

Figure 1.2 Contributions of the four major causative categories to childhood mortality, England and Wales, 2004; neonatal deaths and deaths due to perinatal events have been excluded; data from the Department of Health, courtesy of R MacFaul

the above-mentioned study of meningococcal disease.[11] It is also known that the outcome from infectious diseases can be associated with the degree of affluence or deprivation of the area in which children live. Another study of meningococcal disease has shown that the mortality rate from the disease for children in the most deprived areas is three times that of children from the most affluent areas of the UK.[12] The case mortality rates are also significantly higher in children from deprived areas. Differences in childhood mortality rates due to health inequality are well recognised, and it is an objective of a Public Service Agreement issued by the Department of Health in 2001 that the gap in infant mortality between different social groups should be reduced by 10%, by 2010. Addressing differences in the management of febrile illnesses in young children may be one way of helping to achieve this target.

Parental concern

It is clear that febrile illnesses continue to have a considerable impact on childhood mortality and morbidity. This impact is reflected in the concerns of parents and carers. Kai conducted a survey of parents' responses to acute illness in their children and found that fever, cough and the possibility of meningitis were parents' primary concerns when their children became acutely ill.[13] The parents were often worried that an illness might herald potential harm. In the case of fever this included the development of meningitis or fits, or permanent impairment of some kind, such as brain damage or even death. Parents were also concerned that the presence of fever itself could damage their children. This concern, which can lead to what has been described as fever phobia,[14] is quite widespread and tends to increase with the height of temperature. In scientific terms, fever is a natural response to infection and is not harmful in itself. It is the underlying infection that has the potential to cause harm. Indeed, there are some theoretical grounds to suggest that fever is beneficial in the body's response to infection. In any event, it is clear that parents and carers could receive more useful advice about feverish illness from healthcare professionals. This could include information about detecting potential serious infections and how to manage fever.

Need for guidance

It is a requirement of the Children's National Service Framework that all ill children should have access to high-quality, cost-effective, evidence-based care.[15] From the above, it can be seen that there is a need for evidence-based guidance to inform healthcare professionals about how to judge whether a child who presents with a fever is likely to develop a serious illness. Healthcare professionals also need advice to support their decision on whether to observe the child, to perform diagnostic tests, to start treatment such as antibiotics or to refer onwards for specialist care. The guidance would also usefully include advice on the best ways to detect fever, the management of fever itself, and what to inform parents and carers who have made contact with the health services. The guidance should be applicable to primary and secondary care and should take account of the number of agencies that are involved in giving health care and advice to parents and carers. It is also important that parental preferences, as well as the child's best interests in terms of health outcomes, should be taken into account when considering the various options for investigation and treatment.

1.2 Aim of the guideline

This guideline has been designed for the assessment and initial management of children aged up to 5 years who present to health services with a feverish illness. In accordance with the remit received from the Department of Health and Welsh Assembly Government, the guideline includes:

- assessment of severity of illness, including how to measure and interpret height of fever
- clinical management in primary care, including investigations, use of antibiotics and when to refer for specialist care
- initial assessment by paediatric specialists, including appropriate investigation and initial treatment.

The guideline also includes suggested advice that can be given to parents and carers following an encounter with a healthcare professional.

What is covered

a) the accuracy of different measurements of body temperature, including the methods and sites, and how to interpret the height of fever
b) in a child presenting with fever, identification of signs and symptoms that would help to establish the possible diagnoses and focus for infection
c) in a child presenting with fever, identification of clinical signs and symptoms that would help to predict the severity of the child's illness
d) identification of which clinical signs and symptoms would direct the healthcare professional to carry out further investigations, what these investigations should include and how to interpret them
e) when a child presenting with a fever should be started on treatment (for example antipyretics and/or antibiotics) to try to improve their condition or manage their illness
f) thresholds for referral:
   - what clinical signs or symptoms can be used to identify young children who should be referred
   - what additional factors should be taken into consideration when deciding whether or not to admit a young child to hospital
   - which clinical signs or symptoms should be used to identify young children who should be referred directly to intensive care
g) what advice should be given to parents and carers following the child's initial assessment by the healthcare professional, including the use of antipyretic drugs and other cooling methods.

What is not covered

a) management after a specific diagnosis has been made
b) management beyond initial stabilisation
c) feverish illness in children already admitted to hospital
d) children with a pre-existing co-morbidity for which the presentation of fever is already covered by an established management plan by their specialist team, for example those with cystic fibrosis or immunosuppression
e) children presenting with recurring and/or persistent fever
f) management of febrile convulsions
g) children with tropical diseases.

1.3 For whom is the guideline intended?

This clinical guideline is intended for use by all healthcare professionals who are involved in the care or management of young children with feverish illnesses. The guideline is intended for use in the full range of healthcare settings provided for children with acute illnesses, including both primary and secondary care. For the purposes of this guideline, primary care includes services such as NHS Direct, where the assessment of the child may not include a physical examination. The term specialist paediatric care has been used to define services where the child will be cared for and managed by trained paediatric staff. For the most part, the term refers to hospital paediatric departments and specialist children's emergency departments.

1.4 Who has developed the guideline?

The guideline was developed by a multi-professional and lay working group (the Guideline Development Group or GDG) convened by the National Collaborating Centre for Women's and Children's Health (NCC-WCH). The membership included:

- four paediatric consultants
- two general practitioners
- two children's nurses
- one emergency department paediatric specialist
- one NHS Direct representative
- one pharmacist

- two carer representatives
- one paediatric specialist registrar.

Staff from the NCC-WCH provided methodological support for the guideline development process, undertook systematic searches, retrieval and appraisal of the evidence, health economics modelling and wrote successive drafts of the guideline.

All GDG members' interests were recorded on a declaration form provided by NICE. The form covered consultancies, fee-paid work, shareholdings, fellowships and support from the healthcare industry.

1.5 Other relevant documents

- *Urinary Tract Infection in Children* (publication expected August 2007).

1.6 Definitions and care pathway

At the first stage of the guideline development process, the GDG recognised that it was necessary to have a definition of fever and also to decide what outcomes they would look for in terms of serious illness. A care pathway was used to identify patient flows and key decision points which informed the development of clinical questions.

Definitions used in the guideline

It was necessary for the GDG to define certain terms that could be used as inclusion or exclusion criteria for the guideline and literature searches.

Definition of fever

The GDG considered several definitions of fever that have been used in the scientific literature. The GDG was aware that normal body temperature varies within and between individuals. It was also recognised that the measurement of body temperature can vary with the site of measurement and type of thermometer used. Accordingly, it was acknowledged that any definition of fever based on a fixed body temperature would be arbitrary. It was therefore decided to use a well-recognised physiological definition.[16] For the purposes of this guideline, fever was thus defined as 'an elevation of body temperature above the normal daily variation'.

It was also decided that the entry point into the guideline would be a child presenting to health services with a measured or perceived fever. It was recognised that not all parents and carers have access to thermometers and it was considered appropriate that the definition and entry point allow the inclusion of children who are deemed to have a fever, with or without the use of a thermometer.

Despite agreeing on the above definition, the GDG recognised that other definitions of fever are used in most of the scientific studies that appear in the literature searches and evidence tables. For these studies, the inclusion criteria typically defined a fixed body temperature such as ≥ 38 °C or higher.

Definition of serious illness

Much of this guideline is devoted to identifying children with serious illnesses from among the many who present to healthcare professionals with a fever. The GDG recognised that it would be necessary to have a definition of serious illness to be used as an outcome measure in literature searches, etc. In addition to mortality and morbidity, it was agreed that a list of diagnoses that represented serious illnesses was needed. For the purposes of this guideline, serious illness is defined as 'an illness with fever that could cause death or disability if there were a delay in diagnosis and treatment'.

The GDG also considered which diagnoses would fulfil this definition and, after consulting the literature, the following list of terms and diagnoses was included in literature searches:

- bacterial infection
- serious bacterial infection

- meningitis
- septicaemia
- bacteraemia
- pneumonia
- urinary tract infection
- septic arthritis
- osteomyelitis
- Kawasaki disease
- encephalitis (herpes simplex).

Care pathway

The GDG designed an outline care pathway early in the development process to explore how a child with feverish illness might access, and be dealt with by, the health services. The resulting pathway is shown in Figure 1.3. The pathway starts with a child at home with fever, and the pathway and guideline come into effect when parents or carers decide to access the health services. The figure also illustrates a number of other concepts that were crucial to the guideline development process. More detailed clinical questions evolved from the pathway and the pathway was modified at the end of the development process to incorporate the recommendations derived from the updated clinical questions.

It was recognised that children with fever may currently be assessed by healthcare professionals who either have or do not have recognised training and/or expertise in the management of children and childhood diseases. In this guideline, professionals with specific training and/or expertise are described as paediatric specialists and they are said to be working in specialist care. Those without specific training and/or expertise are described as non-paediatric practitioners although it is acknowledged that such practitioners may be managing children and their illnesses on a regular basis. Non-paediatric practitioners are said to be working in non-specialist care.

For most children with feverish illness, the initial contact will be in non-specialist care. These contacts will mostly be in primary care but some non-specialist contacts may also be made in secondary care, for example in a general emergency department. A minority of these patients will then be referred on to specialist care, for example in a paediatric assessment unit.

The GDG recognised that assessments of children with feverish illness can take place in three main situations. These are represented by the shaded boxes on the care pathway in Figure 1.3. Broadly, assessments can take place in two ways in non-specialist care. The first is a traditional face-to-face encounter where the child undergoes a full clinical assessment, including history and physical examination. This usually occurs in general practice but it could equally occur in a walk-in centre or a hospital emergency department. Alternatively, the first point of contact could be with what has been described as a remote assessment. This is where the child is assessed by a healthcare professional who is unable to examine the child because the child is geographically remote from the assessor. Remote assessments are becoming increasingly important in the health service and they are used both in and out of normal working hours. Examples include NHS Direct and other telephone advice services. In some circumstances, although the child is not geographically remote from the assessor, it may not fall within the scope of practice for a particular healthcare professional to carry out a physical examination of the child, for example a pharmacist. In these circumstances, the healthcare professional may choose to follow the remote assessment guidance rather than the face-to-face guidance that takes into account signs found on physical examination. In specialist care, the clinical assessment will be undertaken by individuals trained in the care of sick children and the assessment may take place in a paediatric assessment unit, on a children's ward or in a dedicated paediatric emergency department.

The care pathway demonstrates a number of possible outcomes from each type of encounter with the health services. From a remote assessment, parents and carers will either be advised how to care for their child at home with appropriate advice as to when to seek further attention, or they will be advised to bring the child in for a formal clinical assessment. For the small number of children who have symptoms suggestive of an immediately life-threatening illness, the parents or carers will be advised to take the child for an immediate specialist assessment, for example by calling an ambulance. From a clinical assessment in non-specialist care, a child may again be returned home with appropriate advice. Alternatively, the child may be discharged with a 'safety

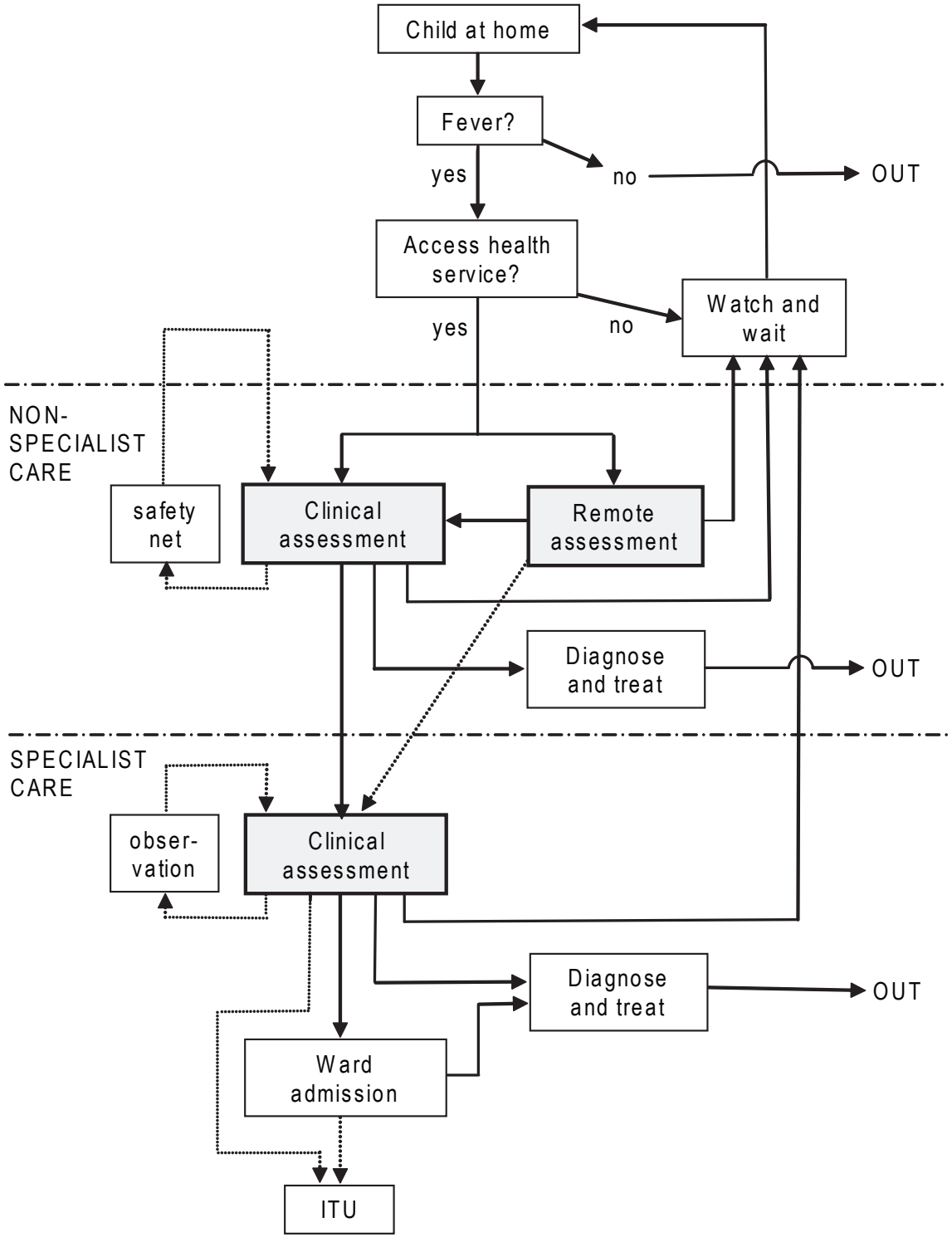

Figure 1.3 Care pathway for feverish illness in children

net' that ensures that the child has some kind of clinical review or planned further contact with the health services (see Chapter 6). If the child is considered to be sick or potentially at risk of serious illness, the child will be referred to specialist care. In many cases, a firm diagnosis will be made by the non-paediatric practitioner and the child will be managed and treated accordingly. In these circumstances, the child progresses beyond the scope of this guidance and it is expected that the child would be treated according to relevant national or local guidelines.

In specialist care, a diagnosis may also be made promptly and the child will also leave the remit of this guideline. Some children will be discharged with advice. Others will require immediate admission to the children's ward and a minority will require intensive care (ITU). This will leave a group of children in whom there is uncertainty as to whether they require admission or not. Increasingly, these children are observed for a number of hours on an assessment unit and then re-evaluated. It is hoped that this practice can help distinguish children with serious illnesses from those with self-limiting conditions.

1.7 Guideline development methodology

This guideline was commissioned by NICE and developed in accordance with the guideline development process outlined in the NICE *Guidelines Manual*.[17]

Literature search strategy

Initial scoping searches were carried out to identify relevant guidelines (local, national, international) produced by other development groups. The reference lists in these guidelines were checked against subsequent searches to identify missing evidence.

Systematic searches to answer the clinical questions formulated and agreed by the GDG were carried out using the following databases via the OVID platform: MEDLINE (1966 onwards), Embase (1980 onwards), Cumulative Index to Nursing and Allied Health Literature (1982 onwards) and PsycINFO (1967 onwards). The most recent search conducted for the three Cochrane databases (Cochrane Central Register of Controlled Trials, Cochrane Database of Systematic Reviews, and the Database of Abstracts of Reviews of Effects) was Quarter 3, 2006. Searches to identify economic studies were undertaken using the above databases and the NHS Economic Evaluations Database (NHS-EED).

Relevant published evidence to inform the guideline development process and answer the clinical questions was identified by systematic search strategies. The clinical questions are shown in the relevant sections. Additionally, stakeholder organisations were invited to submit evidence for consideration by the GDG, provided it was relevant to the clinical questions and of equivalent or better quality than evidence identified by the search strategies. GDG members also contributed evidence under the same conditions.

Search strategies combined relevant controlled vocabulary and natural language in an effort to balance sensitivity and specificity. Both generic and specially developed methodological search filters were used appropriately. Unless advised by the GDG, searches were not date specific.

There was no systematic attempt to search grey literature (conferences, abstracts, theses and unpublished trials). Hand searching of journals not indexed on the databases was not undertaken. Ongoing trials were identified and the principal investigators asked to share their research proposals and outcomes, if available.

Although search strategies were devised for children under the age of 5 years, evidence beyond this age group was considered when no other evidence was available for children under 5 years. Refer to the evidence tables outlining these studies on the accompanying CD-ROM.

Searches were updated and re-run 6–8 weeks before the stakeholder consultation, thereby ensuring that the latest relevant published evidence was included in the database. Any evidence published after this date was not included. For the purposes of updating this guideline, 1 September 2006 should be considered the starting point for searching for new evidence.

Further details of the search strategies, including the methodological filters used, are provided on the accompanying CD-ROM.

Synthesis of clinical effectiveness evidence

The NICE *Guidelines Manual* was largely abided by. However, because this is a symptom-based guideline with un-established methodology, the methodology used is stated where it was not covered in the NICE *Guidelines Manual*. Evidence relating to clinical effectiveness was reviewed using established guides[17–24] and classified using the established hierarchical system shown in Table 1.2.[24] This system reflects the susceptibility to bias that is inherent in particular study designs.

The type of clinical question determines the highest level of evidence that may be sought. In assessing the quality of the evidence, each study receives a quality rating coded as '++', '+' or '–'. For issues of therapy or treatment, the highest possible evidence level (EL) is a well-conducted systematic review or meta-analysis of randomised controlled trials (RCTs; EL = 1++) or an individual RCT (EL = 1+). Studies of poor quality are rated as '–'. Usually, studies rated as '–' should not be used as a basis for making a recommendation, but they can be used to inform recommendations. For issues of prognosis, the highest possible level of evidence is a cohort study (EL = 2) since this is the most appropriate methodology to address prognosis. There are no specific ELs for prognosis and therefore all the prognostic studies were rated according to Table 1.2.

For each clinical question, the highest available level of evidence was selected. Where appropriate, for example if a systematic review, meta-analysis or RCT existed in relation to a question, studies of a weaker design were not included. Where systematic reviews, meta-analyses and RCTs did not exist, other appropriate experimental or observational studies were sought, such as diagnostic studies, which examined the performance of the clinical test if the efficacy of the test was required (see Table 1.3). Where an evaluation of the effectiveness of the test in the clinical management of patients and the outcome of disease was required, evidence from RCTs or cohort studies was used.

The system in Table 1.2 covers studies of treatment effectiveness. However, it is less appropriate for studies reporting diagnostic tests of accuracy. In the absence of a validated hierarchy for this type of test, NICE suggests levels of evidence that take into account the factors likely to affect the validity of these studies (see Table 1.3).

Prognostic studies

A substantial part of the evidence for this guideline was derived from prognostic studies. It is worth noting that there is very limited research on prognostic studies and on methods for assessing their quality. The NICE *Guidelines Manual* currently contains virtually no advice on how to assess such studies. These limitations were recognised from the outset and the NICE methodology was adapted to account for these deficiencies, as outlined in Table 1.3.

Table 1.2 Levels of evidence for intervention studies[17]

Level	Source of evidence
1++	High-quality meta-analyses, systematic reviews of randomised controlled trials (RCTs) or RCTs with a very low risk of bias
1+	Well-conducted meta-analyses, systematic reviews of RCTs or RCTs with a low risk of bias
1–	Meta-analyses, systematic reviews of RCTs or RCTs with a high risk of bias
2++	High-quality systematic reviews of case–control or cohort studies; high-quality case–control or cohort studies with a very low risk of confounding, bias or chance and a high probability that the relationship is causal
2+	Well-conducted case–control or cohort studies with a low risk of confounding, bias or chance and a moderate probability that the relationship is causal
2–	Case–control or cohort studies with a high risk of confounding, bias or chance and a significant risk that the relationship is not causal
3	Non-analytical studies (for example case reports, case series)
4	Expert opinion, formal consensus

Table 1.3 Levels of evidence for studies of the accuracy of diagnostics tests[17]

Level	Type of evidence
Ia	Systematic reviews (with homogeneity)[a] of level-1 studies[b]
Ib	Level-1 studies[b]
II	Level-2 studies[c]; systematic reviews of level-2 studies
III	Level-3 studies[d]; systematic reviews of level-3 studies
IV	Consensus, expert committee reports or opinions and/or clinical experience without explicit critical appraisal; or based on physiology, bench research or 'first principles'

[a] Homogeneity means there are no or minor variations in the directions and degrees of results between individual studies that are included in the systematic review.

[b] Level-1 studies are studies that use a blind comparison of the test with a validated reference standard (gold standard) in a sample of patients that reflects the population to whom the test would apply.

[c] Level-2 studies are studies that have only one of the following:
- narrow population (the sample does not reflect the population to whom the test would apply)
- use a poor reference standard (defined as that where the 'test' is included in the 'reference', or where the 'testing' affects the 'reference')
- the comparison between the test and reference standard is not blind
- case–control studies.

[d] Level-3 studies are studies that have at least two or three of the features listed above.

For searching, a highly sensitive evidence-based prognostic study search strategy developed by McMaster University was adopted. Searches for this evidence utilised a prognostic search filter by Wilczynski *et al*.[25] full details of the search strategy are provided on the accompanying CD-ROM.

The search identified 3151 prognostic studies. After filtering double references, 300 different abstracts were screened for inclusion.

Studies were appraised using the checklist for cohort studies in Appendix D of the NICE *Guidelines Manual*, and the evidence level was allocated using the hierarchy described in Table 1.2. According to this system, the best quality evidence would usually be of evidence level 2 because RCTs are not usually used to address questions of prognosis. Prospective cohort studies are generally the preferred type of study. Lower evidence level studies were included on an individual basis if they contributed information that was not available in the higher evidence level studies but yielded important information to inform the GDG discussions for formulating recommendations.

Delphi consensus

In areas where important clinical questions were identified but no substantial evidence existed, a two-round Delphi consensus method was used to derive recommendations that involved the participation of over 50 clinicians, parents and carers from appropriate stakeholder organisations. The participants rated a series of statements developed by the GDG using a scale of 1–9 (1 being strongly disagree, 9 being strongly agree). Consensus was defined as 75% of ratings falling in the 1–3 or 7–9 categories. Results and comments from each round were discussed by the GDG and final recommendations were made according to predetermined criteria. Full details of the consensus process are presented in Appendix A.

For economic evaluations, no standard system of grading the quality of evidence exists. Economic evaluations that are included in the review have been assessed using a quality assessment checklist based on good practice in decision-analytic modelling.[26] Evidence was synthesised qualitatively by summarising the content of identified papers in evidence tables and agreeing brief statements that accurately reflected the evidence. Quantitative synthesis (meta-analysis) was not performed in this guideline due to methodological and statistical heterogeneity of the studies identified.

Summary results and data are presented in the guideline text. More detailed results and data are presented in the accompanying evidence tables. Where possible, dichotomous outcomes are presented as relative risks (RRs) with 95% confidence intervals (CIs), and continuous outcomes are presented as mean differences with 95% CIs or standard deviations (SDs). Moreover, RRs

were also calculated as positive predictive values (PPV)/(1 – negative predictive value (NPV)) in diagnoses and prognoses when appropriate.

The quality of cohort studies was appraised based on Appendix B in the NICE *Guideline Manual*, and Appendix F for diagnostic studies.

Health economics

The aim of the economic input into the guideline was to inform the GDG of potential economic issues relating to fever in children. The health economist helped the GDG by identifying topics within the guideline that might benefit from economic analysis, reviewing the available economic evidence and, where necessary, conducting economic analysis. Where published economic evaluation studies were identified that addressed the economic issues for a clinical question, these are presented alongside the clinical evidence. However, this guideline addressed only assessment and initial management of fever in children. Economic evaluation requires assessment of healthcare resources (costs) alongside health outcomes, preferably quality-adjusted life years (QALYs). Since clinical outcomes of treatment were outside the scope of the guideline, it was anticipated that the economic literature that addressed the guideline questions would be very limited.

Apart from the review of the literature, additional health economic analysis was undertaken for specific questions in the guideline which the GDG identified as requiring economic evaluation. Specifically, health economic analysis was undertaken on the cost of thermometers, and the cost-effectiveness of specific investigations in specialist care (C-reactive protein versus procalcitonin). Additional economic models were developed to assess the impact of changing the pattern of referrals to secondary care but the lack of data prevented any meaningful analysis and conclusions to be drawn from this.

For the analysis that was undertaken, clinical data reported in the guideline were used, and UK cost data were collected. The perspective adopted is the NHS and cost data are reported for 2005/06.

Health economic analysis carried out as part of the guideline development is presented within the relevant clinical chapter, with readers being referred forward to appendices which provide more detailed explanation of methods and results.

Health economic statements are made in the guideline in sections where the use of NHS resources is considered.

Forming recommendations

For each clinical question, the recommendations were derived from the evidence statements presented to the GDG as summaries from the studies reviewed . The link between the evidence statements and recommendation were made explicit in the translation of the evidence statement. The GDG agreed the final recommendation through informal consensus. In the first instance, informal consensus methods were used by the GDG to agree evidence statements and recommendations. Additionally, in areas where important clinical questions were identified but no substantial evidence existed, formal consensus methods were used to identify current best practice (see the section above). Shortly before the consultation period, five to ten key priorities were selected using a nominal group technique for implementation (details available at the NCC-WCH). To avoid giving the impression that higher grade recommendations are of higher priority for implementation, NICE no longer assigns grades to recommendations.

External review

This guideline has been developed in accordance with the NICE guideline development process. This has included giving registered stakeholder organisations the opportunity to comment on the scope of the guideline at the initial stage of development and on the evidence and recommendations at the concluding stage. This involved reviewing by two independent reviewers as part of NICE's external expert review process for its guidelines. The developers have carefully considered all of the comments during the stage of the consultation by registered stakeholders and expert external reviewers and validation by NICE.

Schedule for updating the guideline

Clinical guidelines commissioned by NICE are published with a review date 4 years from date of publication. Reviewing may begin earlier than 4 years if significant evidence that affects guideline recommendations is identified sooner. The updated guideline will be available within 2 years of the start of the review process.

2 Summary of recommendations

2.1 Key priorities for implementation (key recommendations)

Detection of fever

In children aged 4 weeks to 5 years, healthcare professionals should measure body temperature by one of the following methods:

- electronic thermometer in the axilla
- chemical dot thermometer in the axilla
- infrared tympanic thermometer (3.2.2)

Reported parental perception of a fever should be considered valid and taken seriously by healthcare professionals. (3.3)

Clinical assessment of the child with fever

Children with feverish illness should be assessed for the presence or absence of symptoms and signs that can be used to predict the risk of serious illness using the traffic light system (Table 4.1). (4.4)

Healthcare professionals should measure and record temperature, heart rate, respiratory rate and capillary refill time as part of the routine assessment of a child with fever. (4.5.2)

Management by remote assessment

Children with any 'red' features but who are not considered to have an immediately life-threatening illness should be urgently assessed by a healthcare professional in a face-to-face setting within 2 hours. (5.3)

Management by the non-paediatric practitioner

If any 'amber' features are present and no diagnosis has been reached, healthcare professionals should provide parents or carers with a 'safety net' or refer to specialist paediatric care for further assessment. The safety net should be one or more of the following:

- providing the parent or carer with verbal and/or written information on warning symptoms and how further health care can be accessed (see Chapter 9)
- arranging further follow-up at a specified time and place
- liaising with other healthcare professionals, including out-of-hours providers, to ensure direct access for the child if further assessment is required. (6.3)

Oral antibiotics should not be prescribed to children with fever without apparent source. (6.5.1)

Management by the paediatric specialist

Infants younger than 3 months with fever should be observed and have the following vital signs measured and recorded:

- temperature
- heart rate
- respiratory rate. (7.3)

Children with fever without apparent source presenting to paediatric specialists with one or more 'red' features should have the following investigations performed:

- full blood count
- blood culture
- C-reactive protein
- urine testing for urinary tract infection.* (7.4.1)

The following investigations should also be considered in children with 'red' features, as guided by the clinical assessment:

- lumbar puncture in children of all ages (if not contraindicated)
- chest X-ray irrespective of body temperature and white blood cell count (WBC)
- serum electrolytes and blood gas. (7.4.1)

Antipyretic interventions

Antipyretic agents do not prevent febrile convulsions and should not be used specifically for this purpose. (8.3)

2.2 Summary of recommendations

Chapter 3 Thermometers and the detection of fever

The oral and rectal routes should not routinely be used to measure the body temperature of children aged 0–5 years. (3.2.1)

In infants under the age of 4 weeks, body temperature should be measured with an electronic thermometer in the axilla. (3.2.2)

In children aged 4 weeks to 5 years, healthcare professionals should measure body temperature by one of the following methods:

- electronic thermometer in the axilla
- chemical dot thermometer in the axilla
- infrared tympanic thermometer. (3.2.2)

Healthcare professionals who routinely use disposable chemical dot thermometers should consider using an alternative type of thermometer when multiple temperature measurements are required. (3.2.2)

Forehead chemical thermometers are unreliable and should not be used by healthcare professionals. (3.2.2)

Reported parental perception of a fever should be considered valid and taken seriously by healthcare professionals. (3.3)

Chapter 4 Clinical assessment of the child with fever

First, healthcare professionals should identify any immediately life-threatening features, including compromise of the airway, breathing or circulation, and decreased level of consciousness. (4.3)

Children with feverish illness should be assessed for the presence or absence of symptoms and signs that can be used to predict the risk of serious illness using the traffic light system (Table 4.1). (4.4)

Children with the following symptoms or signs should be recognised as being in a high-risk group for serious illness:

- unable to rouse or if roused does not stay awake
- weak, high-pitched or continuous cry
- pale/mottled/blue/ashen

* See *Urinary Tract Infection in Children*, NICE clinical guideline (publication expected August 2007).

- reduced skin turgor
- bile-stained vomiting
- moderate or severe chest indrawing
- respiratory rate greater than 60 breaths/minute
- grunting
- bulging fontanelle
- appearing ill to a healthcare professional. (4.5.1)

Children with any of the following symptoms should be recognised as being in at least an intermediate-risk group for serious illness:

- wakes only with prolonged stimulation
- decreased activity
- poor feeding in infants
- not responding normally to social cues/no smile
- dry mucous membranes

Table 4.1 Traffic light system for identifying risk of serious illness. Children with fever and *any* of the symptoms or signs in the 'red' column should be recognised as being at high risk. Similarly, children with fever and any of the symptoms or signs in the 'amber' column and none in the 'red' column should be recognised as being at intermediate risk. Children with symptoms and signs in the 'green' column and none in the 'amber' or 'red' columns are at low risk. The management of children with fever should be directed by the level of risk.

	Green – low risk	Amber – intermediate risk	Red – high risk
Colour	• Normal colour of skin, lips and tongue	• Pallor reported by parent/carer	• Pale/mottled/ashen/blue
Activity	• Responds normally to social cues • Content/smiles • Stays awake or awakens quickly • Strong normal cry/not crying	• Not responding normally to social cues • Wakes only with prolonged stimulation • Decreased activity • No smile	• No response to social cues • Appears ill to a healthcare professional • Does not wake or if roused does not stay awake • Weak, high-pitched or continuous cry
Respiratory		• Nasal flaring • Tachypnoea: RR > 50 breaths/minute, age 6–12 months RR > 40 breaths/minutes, age > 12 months • Oxygen saturation ≤ 95% in air • Crackles	• Grunting • Tachypnoea: RR > 60 breaths/minute • Moderate or severe chest indrawing
Hydration	• Normal skin and eyes • Moist mucous membranes	• Dry mucous membranes • Poor feeding in infants • CRT ≥ 3 seconds • Reduced urine output	• Reduced skin turgor
Other	• None of the amber or red symptoms or signs	• Fever for ≥ 5 days	• Age 0–3 months, temperature ≥ 38 °C • Age 3–6 months, temperature ≥ 39 °C
		• Swelling of a limb or joint • Non-weight bearing/not using an extremity	• Non-blanching rash • Bulging fontanelle • Neck stiffness • Status epilepticus • Focal neurological signs • Focal seizures
		• A new lump > 2 cm	• Bile-stained vomiting

CRT = capillary refill time; RR = respiratory rate.

- reduced urine output
- a new lump larger than 2 cm
- pallor reported by parent or carer
- nasal flaring. (4.5.1)

Children who have all of the following features, and none of the high- or intermediate-risk features, should be recognised as being in a low-risk group for serious illness:

- strong cry or not crying
- content/smiles
- stays awake
- normal colour of skin, lips and tongue
- normal skin and eyes
- moist mucous membranes
- normal response to social cues. (4.5.1)

Healthcare professionals should measure and record temperature, heart rate, respiratory rate and capillary refill time as part of the routine assessment of a child with fever. (4.5.2)

Healthcare professionals examining children with fever should be aware that a raised heart rate can be a sign of serious illness, particularly septic shock. (4.5.2)

A capillary refill time of 3 seconds or longer should be recognised as an intermediate-risk group marker for serious illness ('amber' sign). (4.5.2)

Healthcare professionals should measure the blood pressure of children with fever if the heart rate or capillary refill time is abnormal and the facilities to measure blood pressure are available. (4.5.2)

Height of body temperature alone should not be used to identify children with serious illness. However, children in the following categories should be recognised as being in a high-risk group for serious illness:

- children younger than 3 months with a temperature of 38 °C or higher
- children aged 3–6 months with a temperature of 39 °C or higher. (4.5.3)

Duration of fever should not be used to predict the likelihood of serious illness. (4.5.3)

Children with fever should be assessed for signs of dehydration. Healthcare professionals should look for:

- prolonged capillary refill time
- abnormal skin turgor
- abnormal respiratory pattern
- weak pulse
- cool extremities. (4.5.4)

Healthcare professionals should look for a source of fever and check for the presence of symptoms and signs that are associated with specific diseases (see Table 4.4). (4.6.1)

Meningococcal disease should be considered in any child with fever and a non-blanching rash, particularly if any of the following features are present:

- an ill-looking child
- lesions larger than 2 mm in diameter (purpura)
- a capillary refill time of 3 seconds or longer
- neck stiffness. (4.6.2)

Meningitis should be considered in a child with fever and any of the following features:

- neck stiffness
- bulging fontanelle
- decreased level of consciousness
- convulsive status epilepticus. (4.6.4)

Healthcare professionals should be aware that classical signs of meningitis (neck stiffness, bulging fontanelle, high-pitched cry) are often absent in infants with bacterial meningitis. (4.6.4)

Herpes simplex encephalitis should be considered in children with fever and any of the following features:

- focal neurological signs
- focal seizures
- decreased level of consciousness. (4.6.5)

Pneumonia should be considered in children with fever and any of the following signs :

- tachypnoea (respiratory rate greater than 60 breaths/minute, age 0–5 months; greater than 50 breaths/minute, age 6–12 months; greater than 40 breaths /minute, age older than 12 months)
- crackles in the chest
- nasal flaring
- chest indrawing
- cyanosis
- oxygen saturation of 95% or less when breathing air. (4.6.6)

Table 4.4 Summary table for symptoms and signs suggestive of specific diseases

Diagnosis to be considered	Symptoms and signs in conjunction with fever
Meningococcal disease	Non-blanching rash, particularly with one or more of the following: • an ill-looking child • lesions larger than 2 mm in diameter (purpura) • capillary refill time of ≥ 3 seconds • neck stiffness
Meningitis	Neck stiffness Bulging fontanelle Decreased level of consciousness Convulsive status epilepticus
Herpes simplex encephalitis	Focal neurological signs Focal seizures Decreased level of consciousness
Pneumonia	Tachypnoea (RR > 60 breaths/minute, age 0–5 months; RR > 50 breaths/minute, age 6–12 months; RR > 40 breaths/minute, age > 12 months) Crackles in the chest Nasal flaring Chest indrawing Cyanosis Oxygen saturations ≤ 95%
Urinary tract infection	Vomiting Poor feeding Lethargy Irritability Abdominal pain or tenderness Urinary frequency or dysuria Offensive urine or haematuria
Septic arthritis	Swelling of a limb or joint Not using an extremity Non-weight bearing
Kawasaki disease	Fever for more than 5 days and at least four of the following: • bilateral conjunctival injection • change in mucous membranes • change in the extremities • polymorphous rash • cervical lymphadenopathy

RR = respiratory rate.

Urinary tract infection should be considered in any child younger than 3 months with fever.* (4.6.7)

Urinary tract infection should be considered in a child aged 3 months and older with fever and one or more of the following:*

- vomiting
- poor feeding
- lethargy
- irritability
- abdominal pain or tenderness
- urinary frequency or dysuria
- offensive urine or haematuria. (4.6.7)

Septic arthritis/osteomyelitis should be considered in children with fever and any of the following signs:

- swelling of a limb or joint
- not using an extremity
- non-weight bearing. (4.6.8)

Kawasaki disease should be considered in children with fever that has lasted longer than 5 days and who have four of the following five features:

- bilateral conjunctival injection
- change in mucous membranes in the upper respiratory tract (e.g. injected pharynx, dry cracked lips or strawberry tongue)
- change in the extremities (e.g. oedema, erythema or desquamation)
- polymorphous rash
- cervical lymphadenopathy. (4.6.9)

Healthcare professionals should be aware that, in rare cases, incomplete/atypical Kawasaki disease may be diagnosed with fewer features. (4.6.9)

When assessing a child with feverish illness, healthcare professionals should enquire about recent travel abroad and should consider the possibility of imported infections according to the region visited. (4.7)

Chapter 5 Management by remote assessment

Healthcare professionals performing a remote assessment of a child with fever should seek to identify symptoms and signs of serious illness and specific diseases as described in Chapter 4 and summarised in Tables 4.1 and 4.4. (5.3)

Children whose symptoms or combination of symptoms suggest an immediately life-threatening illness (see Chapter 4) should be referred immediately for emergency medical care by the most appropriate means of transport (usually 999 ambulance). (5.3)

Children with any 'red' features but who are not considered to have an immediately life-threatening illness should be urgently assessed by a healthcare professional in a face-to-face setting within 2 hours. (5.3)

Children with 'amber' but no 'red' features should be assessed by a healthcare professional in a face-to-face setting. The urgency of this assessment should be determined by the clinical judgment of the healthcare professional carrying out the remote assessment. (5.3)

Children with 'green' features and none of the 'amber' or 'red' features can be managed at home with appropriate advice for parents and carers including advice on when to seek further attention from the healthcare services (see Chapter 9). (5.3)

* See *Urinary Tract Infection in Children*, NICE clinical guideline (publication expected August 2007).

Chapter 6 Management by the non-paediatric practitioner

Management by a non-paediatric practitioner should start with a clinical assessment as described in Chpater 4. Healthcare practitioners should attempt to identify symptoms and signs of serious illness and specific diseases as summarised in Tables 4.1 and 4.4. (6.2)

Children whose symptoms or combination of symptoms and signs suggest an immediately life-threatening illness (see Chapter 4) should be referred immediately for emergency medical care by the most appropriate means of transport (usually 999 ambulance). (6.3)

Children with any 'red' features but who are not considered to have an immediately life-threatening illness should be referred urgently to the care of a paediatric specialist. (6.3)

If any 'amber' features are present and no diagnosis has been reached, healthcare professionals should provide parents or carers with a 'safety net' or refer to specialist paediatric care for further assessment. The safety net should be one or more of the following:

- providing the parent or carer with verbal and/or written information on warning symptoms and how further health care can be accessed (see Chapter 9)
- arranging further follow-up at a specified time and place
- liaising with other healthcare professionals, including out-of-hours providers, to ensure direct access for the child if further assessment is required. (6.3)

Children with 'green' features and none of the 'amber' or 'red' features can be managed at home with appropriate advice for parents and carers, including advice on when to seek further attention from the healthcare services (see Chapter 9). (6.3)

Children with symptoms and signs suggesting pneumonia who are not admitted to hospital should not routinely have a chest X-ray. (6.4)

Urine should be tested on children with fever as recommended in *Urinary Tract Infection in Children*.* (6.4)

Oral antibiotics should not be prescribed to children with fever without apparent source. (6.5.1)

Children with suspected meningococcal disease should be given parenteral antibiotics at the earliest opportunity (either benzylpenicillin or a third-generation cephalosporin). (6.5.2)

Chapter 7 Management by the paediatric specialist

Management by the paediatric specialist should start with a clinical assessment as described in Chapter 4. The healthcare professional should attempt to identify symptoms and signs of serious illness and specific diseases as summarised in Tables 4.1 and 4.4. (7.2)

Infants younger than 3 months with fever should be observed and have the following vital signs measured and recorded:

- temperature
- heart rate
- respiratory rate. (7.3)

Infants younger than 3 months with fever should have the following investigations performed:

- full blood count
- blood culture
- C- reactive protein
- urine testing for urinary tract infection*
- chest X-ray only if respiratory signs are present
- stool culture, if diarrhoea is present. (7.3)

Lumbar puncture should be performed on the following children (unless contraindicated):

- infants younger than 1 month
- all infants aged 1–3 months who appear unwell
- infants aged 1–3 months with white blood cell count (WBC) less than 5×10^9/litre or greater than 15×10^9/litre. (7.3)

* See *Urinary Tract Infection in Children*, NICE clinical guideline (publication expected August 2007).

When indicated, a lumbar puncture should be performed without delay and, whenever possible, before the administration of antibiotics. (7.3)

Parenteral antibiotics should be given to:

- infants younger than 1 month
- all infants aged 1–3 months who appear unwell
- infants aged 1–3 months with WBC less than 5×10^9/litre or greater than 15×10^9/litre. (7.3)

When parenteral antibiotics are indicated for infants less than 3 months of age, a third-generation cephalosporin (e.g. cefotaxime or ceftriaxone) should be given plus an antibiotic active against listeria (e.g. ampicillin or amoxicillin). (7.3)

Children with fever without apparent source presenting to paediatric specialists with one or more 'red' features should have the following investigations performed:

- full blood count
- blood culture
- C-reactive protein
- urine testing for urinary tract infection.* (7.4.1)

The following investigations should also be considered in children with 'red' features, as guided by the clinical assessment:

- lumbar puncture in children of all ages (if not contraindicated)
- chest X-ray irrespective of body temperature and white blood cell count (WBC)
- serum electrolytes and blood gas. (7.4.1)

Children with fever without apparent source presenting to paediatric specialists who have one or more 'amber' features should have the following investigations performed unless deemed unnecessary by an experienced paediatrician.

- urine should be collected and tested for urinary tract infection*
- blood tests: full blood count, C- reactive protein and blood cultures
- lumbar puncture should be considered for children younger than 1 year
- chest X-ray in a child with a fever greater than 39 °C and white blood cell count (WBC) greater than 20×10^9/litre. (7.4.1)

Children who have been referred to a paediatric specialist with fever without apparent source and who have no features of serious illness (that is, the 'green' group), should have urine tested for urinary tract infection* and be assessed for symptoms and signs of pneumonia. (7.4.1)

Routine blood tests and chest X-rays should not be performed on children with fever who have no features of serious illness (that is, the 'green' group). (7.4.1)

Febrile children with proven respiratory syncytial virus or influenza infection should be assessed for features of serious illness. Consideration should be given to urine testing for urinary tract infection.* (7.4.2)

In children aged 3 months or older with fever without apparent source, a period of observation in hospital (with or without investigations) should be considered as part of an assessment to help differentiate non-serious from serious illness. (7.4.3)

When a child has been given antipyretics:

- healthcare professionals should not rely on a decrease or lack of decrease in temperature after 1–2 hours to differentiate between serious and non-serious illness
- children in hospital with 'amber' or 'red' features should be reassessed after 1–2 hours. (7.4.4)

Children with fever and shock presenting to specialist paediatric care or an emergency department should be:

- given an immediate intravenous fluid bolus of 20 ml/kg; the initial fluid should normally be 0.9% sodium chloride
- actively monitored and given further fluid boluses as necessary. (7.5)

* See *Urinary Tract Infection in Children*, NICE clinical guideline (publication expected August 2007).

Children with fever presenting to specialist paediatric care or an emergency department should be given immediate parenteral antibiotics if they are:

- shocked
- unrousable
- showing signs of meningococcal disease. (7.5)

Immediate parenteral antibiotics should be considered for children with fever and reduced levels of consciousness. In these cases symptoms and signs of meningitis and herpes simplex encephalitis should be sought (see Table 4.4). (7.5.3)

When parenteral antibiotics are indicated, a third-generation cephalosporin (e.g. cefotaxime or ceftriaxone) should be given, until culture results are available. For children younger than 3 months, an antibiotic active against listeria (e.g. ampicillin or amoxicillin) should also be given. (7.5.3)

Children with fever and symptoms and signs suggestive of herpes simplex encephalitis should be given intravenous aciclovir. (7.5.4)

Oxygen should be given to children with fever who have signs of shock or oxygen saturation (SpO_2) of less than 92% when breathing air. (7.5.5)

Treatment with oxygen should also be considered for children with an SpO_2 of greater than 92%, as clinically indicated. (7.5.5)

In a child presenting to hospital with a fever and suspected serious bacterial infection, requiring immediate treatment, antibiotics should be directed against *Neisseria meningitidis, Streptococcus pneumoniae, Escherichia coli, Staphylococcus aureus* and *Haemophilus influenzae* type b. A third-generation cephalosporin (e.g. cefotaxime or ceftriaxone) is appropriate, until culture results are available. For infants younger than 3 months, an antibiotic active against listeria (e.g. ampicillin or amoxicillin) should be added. (7.6)

Healthcare professionals should refer to local treatment guidelines when rates of bacterial antibiotic resistance are significant. (7.6)

In addition to the child's clinical condition, healthcare professionals should consider the following factors when deciding whether to admit a child with fever to hospital:

- social and family circumstances
- other illnesses that affect the child or other family members
- parental anxiety and instinct (based on their knowledge of their child)
- contacts with other people who have serious infectious diseases
- recent travel abroad to tropical/subtropical areas, or areas with a high risk of endemic infectious disease
- when the parent or carer's concern for their child's current illness has caused them to seek healthcare advice repeatedly
- where the family has experienced a previous serious illness or death due to feverish illness which has increased their anxiety levels
- when a feverish illness has no obvious cause, but the child remains ill longer than expected for a self-limiting illness. (7.7)

If it is decided that a child does not need to be admitted to hospital, but no diagnosis has been reached, a safety net should be provided for parents and carers if any 'red' or 'amber' features are present. The safety net should be one or more of the following:

- providing the parent or carer with verbal and/or written information on warning symptoms and how further health care can be accessed (see Chapter 9)
- arranging further follow-up at a specified time and place
- liaising with other healthcare professionals, including out-of-hours providers, to ensure direct access for the child if further assessment is required. (7.7)

Children with 'green' features and none of the 'amber' or 'red' features can be managed at home with appropriate advice for parents and carers, including advice on when to seek further attention from the healthcare services (see Chapter 9). (7.7)

Children with fever who are shocked, unrousable or showing signs of meningococcal disease should be urgently reviewed by an experienced paediatrician and consideration given to referral to paediatric intensive care. (7.8)

Children with suspected meningococcal disease should be given parenteral antibiotics at the earliest opportunity (either benzylpenicillin or a third-generation cephalosporin). (7.9).

Children admitted to hospital with meningococcal disease should be under paediatric care, supervised by a consultant and have their need for inotropes assessed. (7.9)

Chapter 8 Antipyretic interventions

Tepid sponging is not recommended for the treatment of fever. (8.2.1)

Children with fever should not be underdressed or over-wrapped. (8.2.1)

The use of antipyretic agents should be considered in children with fever who appear distressed or unwell. Antipyretic agents should not routinely be used with the sole aim of reducing body temperature in children with fever who are otherwise well. The views and wishes of parents and carers should be taken into consideration. (8.2.2).

Either paracetamol or ibuprofen can be used to reduce temperature in children with fever. (8.2.2)

Paracetamol and ibuprofen should not be administered at the same time to children with fever. (8.2.3)

Paracetamol and ibuprofen should not routinely be given alternately to children with fever. However, use of the alternative drug may be considered if the child does not respond to the first agent. (8.2.3)

Antipyretic agents do not prevent febrile convulsions and should not be used specifically for this purpose. (8.3)

Chapter 9 Advice for home care

Parents or carers should be advised to manage their child's temperature as described in Chapter 8. (9.2)

Parents or carers looking after a feverish child at home should be advised:

- to offer the child regular fluids (where a baby or child is breastfed the most appropriate fluid is breast milk)
- how to detect signs of dehydration by looking for the following features:
  - sunken fontanelle
  - dry mouth
  - sunken eyes
  - absence of tears
  - poor overall appearance
- to encourage their child to drink more fluids and consider seeking further advice if they detect signs of dehydration
- how to identify a non-blanching rash
- to check their child during the night
- to keep their child away from nursery or school while the child's fever persists but to notify the school or nursery of the illness. (9.2)

Following contact with a healthcare professional, parents and carers who are looking after their feverish child at home should seek further advice if:

- the child has a fit
- the child develops a non-blanching rash
- the parent or carer feels that the child is less well than when they previously sought advice
- the parent or carer is more worried than when they previously sought advice
- the fever lasts longer then 5 days
- the parent or carer is distressed, or concerned that they are unable to look after their child. (9.3)

2.3 Research recommendations

Measuring temperature in young babies: tympanic versus axilla electronic versus axilla chemical dot versus temporal artery. (3.2.2)

A study to confirm normal ranges for heart rate at various body temperatures and to determine whether children with heart rates outside these ranges are at higher risk of serious illness. (4.5.2.1)

There is a need for a prospective study to assess the prognostic value of symptoms such as limb pain and cold hands and feet that have been identified as possible early markers of meningococcal disease. (4.6.2)

The GDG recommends that a UK study is undertaken to determine the validity of symptoms reported on remote assessment for children with fever. (5.3)

The GDG recommends that research is carried out on referral patterns between primary and secondary care for children with fever, so the health economic impact of this and future guidelines can be estimated. (6.3)

The GDG recommends that a UK study of the performance characteristics and cost-effectiveness of procalcitonin versus C-reactive protein in identifying serious bacterial infection in children with fever without apparent source be carried out. (7.4.1)

The GDG recommends that studies are conducted in primary care and secondary care to determine whether examination or re-examination after a dose of antipyretic medication is of benefit in differentiating children with serious illness from those with other conditions. (7.4.4)

The GDG recommends that studies are conducted on the effectiveness of physical methods of attempting to reduce fever, for example lowering ambient temperature, fanning and cold oral fluids. (8.2.1)

Efficacy and cost-effectiveness studies are required which measure symptom relief associated with fever relief. (8.2.2)

The GDG recommends that a study is conducted on the effectiveness and safety of alternating doses of paracetamol and ibuprofen in reducing fever in children who remain febrile after the first antipyretic. (8.2.3)

3 Thermometers and the detection of fever

3.1 Introduction

Body temperature in children can be measured at a number of anatomical sites using a range of different types of thermometers. Sites used to measure temperature include the mouth, rectum and axilla. The types of thermometers available include mercury-in-glass, electronic, chemical and infrared. Mercury-in-glass thermometers were the traditional type of thermometer used to measure body temperature but they are no longer recommended for use in infants and young children because of the risks of breakage and mercury spillage.[27] Furthermore, UK health and safety regulations require that mercury-containing medical devices should not be used whenever a suitable alternative exists.[28] Mercury-in-glass thermometers will not be considered further in this guideline except as a comparator in diagnostic studies.

Electronic thermometers are widely used by healthcare professionals as an alternative to mercury-in-glass thermometers. Electronic thermometers have the advantages of being accurate and very quick to use but they are often complex and quite expensive pieces of medical equipment. Recently, cheaper compact electronic thermometers have been produced and these are available for use by the public as well as healthcare professionals. Chemical phase-change thermometers measure body temperature by using a combination of chemicals that change colour in response to variations in temperature. These can either be chemical dot thermometers where the chemicals are contained in cells on a plastic stick, or chemical forehead thermometers which consist of a patch of chemicals in a plastic pouch that is placed on the forehead. Chemical dot thermometers are usually designed for single use but reusable types are available. All types of chemical thermometers can be used by the public. In recent years, infrared thermometers have been used more and more frequently. This type of thermometer detects infrared radiation from blood vessels and this is then used to estimate central body temperature. Most thermometers of this type measure temperature at the eardrum (infrared tympanic thermometers) but temporal artery thermometers are now available where temperature is measured on the scalp. Infrared thermometers are quick, non-invasive and simple to use. They are relatively expensive, however.

In this chapter, the different sites and thermometers are compared with regard to their accuracy in measuring true body temperature and their ability to detect fever. In general, the various sites and different types of thermometers are compared in their diagnostic ability against a traditional gold standard. The gold standard is usually a measurement with a mercury-in-glass or electronic thermometer using the mouth in older children and the rectum in young children and infants. This chapter also looks at the ability of parents and carers to detect fever in young children using subjective means such as palpation of the child's brow.

3.2 Thermometers and the site of measurement

Body temperature can be recorded from a number of sites in the body in babies and young children. Traditionally, temperature was taken by the oral route in older children and adults, while the rectal route was used in infants and young children. Alternatives methods include using the axilla or using a tympanic thermometer. These methods are generally considered to not be as accurate as traditional measurement[29,30] but they are often quicker and easier to use in young children.[31] Axillary and tympanic measurements may also be better accepted by children and their carers.[31,32]

3.2.1 Oral and rectal temperature measurements

Clinical questions

How accurate are the different types of thermometer in the measurement of body temperature in young children, and how do they compare in their ability to detect fever?

How accurate are the readings of temperature from different sites of the body in young children, and how do these sites compare in the ability to detect fever?

Narrative evidence

An attempt was made to find evidence of the comparative accuracy of oral and rectal temperature measurements using mercury-in-glass or electronic thermometers. Two EL II studies were found that looked at the diagnostic accuracy of an electronic thermometer embedded in an infant pacifier.[33,34] The studies recruited children of different ages (e.g. 10 days to 24 months[33] to < 2 years[34]). The reported sensitivity was 10% and 63.3%, respectively.

The GDG did not consider these studies to be applicable to UK practice because these thermometers are not available and the evidence for their usefulness is weak.

Evidence summary

The GDG was aware that temperature measurements by the oral and rectal routes were rarely used in young children by healthcare professionals in the UK. These sites are probably the most accurate for temperature measurement but there are concerns about their safety and acceptability. The GDG could not reach a consensus among themselves as to whether these routes should be used and it was therefore decided to use the Delphi technique in an attempt to achieve formal consensus.

Regarding oral thermometers, the following background information and statement was put to the Delphi panel.

Background

In older children and adults, the inside of the mouth is considered to be one of the most accurate sites for the measurement of body temperature. When temperature is measured via the mouth, it is necessary for the thermometer to be held in place under the tongue while the measurement is taken. Most children's nurses are taught that children under the age of 5 years cannot cooperate with this procedure and that inaccurate measurements will be obtained. There are also concerns that some young children will bite the thermometer, and others find the technique uncomfortable or even painful.

Delphi statement 7.2

Healthcare professionals should not routinely use the oral route (mouth) to measure body temperature in children under the age of 5 years. The following responses were obtained from the first round of the Delphi process:

1 to 3	4 to 6	7 to 9	Don't know	Missing	Total	Median
2 (4%)	4 (8%)	44 (85%)	2 (4%)	1	52	9

The statement therefore achieved consensus at the first round of the Delphi technique.

Regarding rectal thermometers, the following background information and statements were put to the Delphi panel. The results from the first round of the Delphi process are also shown.

Background

In this technique, the probe of an electronic thermometer is placed in the rectum (back passage). The rectum is often considered the most accurate site of measurement of body temperature; the rectal route is therefore a reliable way of detecting fever in babies and young children.

Some people find rectal thermometers unacceptable for routine use. In newborn babies there have been reports of injuries including perforation of the bowel after the use of rectal mercury thermometers. Some people are concerned that electronic thermometers could have the same

effect. In newborn babies taking the temperature in the axilla (armpit) is almost as accurate as using the rectal route (back passage).

Delphi statement 7.3
Healthcare professionals should routinely use electronic thermometers by the rectal route (back passage) to measure body temperature in children aged: 0–3 months.

1 to 3	4 to 6	7 to 9	Don't know	Missing	Total	Median
45 (87%)	3 (6%)	3 (6%)	1 (2%)	1	52	1

The statement therefore achieved consensus at the first round of the Delphi technique.

Delphi statement 7.4
Healthcare professionals should not routinely use electronic thermometers by the rectal route (back passage) to measure body temperature in children aged 3 months to 2 years.

1 to 3	4 to 6	7 to 9	Don't know	Missing	Total	Median
46 (88%)	4 (8%)	1 (2%)	1 (2%)	1	52	1

The statement therefore achieved consensus at the first round of the Delphi technique.

Delphi statement 7.5
Healthcare professionals should routinely use electronic thermometers by the rectal route (back passage) to measure body temperature in children aged 2–5 years.

1 to 3	4 to 6	7 to 9	Don't know	Missing	Total	Median
47 (92%)	3 (6%)	0	1 (2%)	1	52	1

The statement therefore achieved consensus at the first round of the Delphi technique.

Delphi evidence summary
There was a lack of evidence on the relative accuracy or ability to detect fever using the oral and rectal routes of temperature measurement. The Delphi panel achieved consensus at the first round on all statements relating to oral and rectal temperature measurements. Eight-five percent of the panel agreed with the statement that the oral route should not be used routinely in young children. On the three statements regarding the rectal route, between 87% and 92% of the panel disagreed with the recommendation that this route should be used routinely. (EL IV)

GDG translation
The GDG considered that the results of the Delphi process indicated strongly that the oral and rectal routes should not be used for routine temperature measurements in infants and young children.

Recommendation on oral and rectal temperature measurements

The oral and rectal routes should not routinely be used to measure the body temperature of children aged 0–5 years.

3.2.2 Measurement of body temperature at other sites

In the event of not recommending temperature measurements by the oral or rectal route, it was necessary for the GDG to recommend an alternative method of measurement. The GDG collected data on axillary measurements using electronic and chemical thermometers, infrared measurements at the tympanic and temporal artery sites, and on forehead crystal thermometers. The GDG looked at evidence on the accuracy and ability to detect fever of these sites and thermometers.

Narrative evidence

Axillary temperature measurement

One EL 2+ SR[29] and 20 prospective studies (two EL Ib,[35,36] ten EL II[37–46] and eight EL III[47–54]) were found. The EL reflects the quality of report but may not necessarily reflect the quality of the studies themselves. Therefore, all the EL III studies were judged to be adequate for inclusion to inform recommendation. There is tremendous methodological heterogeneity among the included studies. For instance, the age of included children varied from 12–48 hours after birth[36] to 6–14 years[48]; the setting also varied from birth registry,[55] paediatric ward,[44] and emergency department[56] to nursery.[43] There is also variation of the device (e.g. mercury[43] or digital[44] thermometry). Owing to the clinical and statistical heterogeneity, it was inappropriate to perform meta-analysis. The findings suggest that, on average, axillary temperature underestimates body temperature by at least 0.5 °C (although the difference between the body temperature may be smaller when a mercury thermometer rather than an electronic one is used). There is also a wide range of variation between individuals. The mean difference between axillary temperature and body temperature varied between 0.09 °C[57] and 1.52 °C,[40] and the SR[29] showed that the upper limit of mean difference was 2 °C if axillary temperature was taken by digital thermometers. Furthermore, the sensitivities for detecting fever ranged from 25%[35] to 98%.[39]

For studies with data specifically looking at neonates, the reported mean differences between rectal and axillary temperature were 0.09 °C (95% CI 0.06 to 0.12 °C),[43] 0.3 °C,[58] and 0.2 °F.[36] There appeared to be a significant correlation between the rectal and axillary temperatures[46,49,36]; no sensitivity and specificity were reported in this subgroup. Moreover, one EL II study[37] reported that in infants younger than 1 month, the difference between the axillary and rectal temperatures varied with age. Least squares linear regression analysis showed that the rectal temperature was equal to the axillary temperature plus 0.2 °C for each week of age up to 5 weeks.

Chemical dot (phase-change) thermometers

Three EL II prospective cohort studies[45,59,60] investigating the diagnostic accuracy of chemical dot thermometers were found. Only the diagnostic accuracy of chemical dot thermometers used in the axilla was looked at. The age and setting of children included varied from 0–102 days in neonatal ICU[60] to 3–36 months admitting to hospitals.[45] The mean difference in axillary temperature between chemical dot and mercury thermometer measurement was 0.32 °C[59] to 0.93 °C.[60] Moreover, the sensitivity ranged between 68%[45] and 92%,[59] with RR of 17.2[59] to detect fever.

Forehead crystal thermometers

Two EL II prospective cohort studies[61,62] and two EL III studies[63,64] investigating the diagnostic accuracy of forehead measurement were found. These studies varied at baseline. For example, one[61] recruited patients aged 0–14 years, the other[62] had children aged 12 days to 17 years. The authors also used different references for comparisons. For example, one study[62] compared forehead temperature with either rectal temperature (< 4 years) or oral temperature (> 4 years) measured by mercury glass thermometer and another[64] oral temperature measured by digital thermometer. The limited data suggest that forehead measurement underestimated body temperature by 1.2 °C on average.

Infrared tympanic thermometers

Two EL II SRs[30,65] and 21 prospective cohort studies (two EL Ib,[66,67] eight EL II[38,40,43,68–72] and ten EL III studies[73–83]) investigating the diagnostic accuracy of tympanic temperature measurement were found. The SR[30] included 4441 children aged 0–16 years. Other prospective cohort studies[38,40,43,66—82] had very different baselines in terms of sampling frame, age, condition of children recruited and method of temperature measurement. For instance, one study[66] recruited children aged 0–18 years from a paediatric clinic, another study[77] recruited injured children aged 1–14 years, and another recruited babies from a well-baby nursery.[69] Based on pooled analysis, tympanic measurement differs on average from body temperature by 0.29 °C.[30] The difference between tympanic temperature and body temperature can be up to 0.74 °C below to 1.34 °C[30] above and this varies with age, mode, environment temperature and devices. Moreover, the pooled estimates of sensitivity and specificity from random effect models were 63.7% (95% CI

55.6% to 71.8%) and 95.2% (93.5% to 96.9%).[30] Refer to the evidence tables on the accompanying CD-ROM for details.

Some studies[67,69] suggested that tympanic thermometers were unreliable in infants under 3 months because of difficulties in ensuring that the probe is correctly positioned in the ear canal. The GDG was unable to achieve consensus on the cut-off point of age using tympanic thermometers and thus this issue was put forward for Delphi consensus. The background information and statement below were put to the Delphi panel.

Background

These thermometers use a probe in the ear canal to measure the temperature of the eardrum. Infrared tympanic thermometers are licensed for use in people of all ages, including babies and young children. Some researchers and many users have suggested that tympanic thermometers may be inaccurate in babies under the age of 3 months because it is difficult to ensure that the probe is correctly positioned. Other researchers have found that tympanic thermometers can be used reliably in children of all ages as long as the user ensures that the ear canal is straight and the probe is pointing at the eardrum. In young babies this is achieved by tugging gently on the outer ear.

Delphi statement 7.1

Infrared tympanic thermometers can be used in babies under the age of 3 months as long as it is ensured that the probe is positioned correctly.

The following responses were obtained from two rounds of the Delphi process.

1 to 3	4 to 6	7 to 9	Don't know	Missing	Total	Median
11 (21%)	8 (15%)	28 (54%)	5 (10%)		52	7

There was no consensus for this statement.

Temporal artery thermometers

Only one EL III prospective cohort study[84] meeting the inclusion criteria investigating the accuracy of temporal artery thermometers was found. The researchers recruited 332 parents with children under 2 years and there were 327 sets of complete data. They found that the temporal artery thermometer detected 81% rectal temperature ≥ 38.0 °C, 88% (89/101) rectal temperature ≥ 38.3 °C.

Evidence summary

Axillary temperature

On average, axillary temperature measurement using an electronic thermometer underestimates body temperature by at least 0.5 °C. There is also a wide range of variation in the difference between axillary and body temperature between individuals. The difference can be as much as 2 °C in some children. In different EL Ib and EL II studies, the axillary route has variable sensitivities for detecting fever compared with the rectal or oral routes (25–89%). (EL II)

In neonates the axillary route appears to be more accurate, with a difference from rectal temperature of around 0.5 °C. (EL II) In the one study to report the ability to detect fever in neonates, the axillary route was reported to have a sensitivity of 98%. (EL II)

Chemical dot thermometers (axillary route)

Three EL II studies that reported on the use of chemical dot thermometers in children were found. Axillary temperatures were measured in all three studies. The studies varied in terms of settings, the ages of children included and the methods of analysis. Only two of the studies assessed ability to detect fever. Given the above limitations, the accuracy of chemical dot thermometers is usually reported to be comparable with other thermometers used in the axilla. In the one study to compare the ability to detect fever against rectal temperature, the sensitivity was 68%. (EL II)

Tympanic temperature (by infrared thermometer)

Tympanic measurement differs on average from body temperature by 0.3 °C. From EL Ib and EL II studies the difference between tympanic temperature and body temperature can be up to 0.74 °C below to 1.34 °C above and this varies with age, mode, environment temperature and device. The sensitivity to detect fever ranged from 51% to 97% in these studies.

Some studies reported that tympanic measurements are difficult or inaccurate in infants under the age of 3 months. Other studies reported that the technique could be used in infants of all ages, including neonates. A statement that tympanic measurements should not be used in infants under the age of 3 months was put to the Delphi panel. Consensus was not attained.

Forehead temperature (by chemical thermometer)

Data on the measurement of forehead temperature is sparse. The limited data suggests that forehead measurement appears to be inaccurate (underestimates body temperature by 1.2 °C on average). (EL II) Forehead thermometers may be poor at detecting fever (sensitivity 27–88%). (EL II)

Temporal artery temperature (by infrared thermometer)

Measurement of temporal artery temperature has not been extensively studied. The available data suggest this technique has fair sensitivity (81%) to detect fever. (EL III)

Health economics

Cost analysis of thermometers was undertaken for this guideline (Appendix B). The analysis was based on the data from hospital setting as regards the annual number of measurements.[85] The results of the analysis are summarised in Table 3.1. The results are discounted to show the present value of costs which accrue in the future (up to 10 years). The analysis showed that the contact/electronic thermometers are the least costly option when staff costs are not included in the analysis. When the staff cost are included, the total cost of electronic/compact, contact/compact electronic and tympanic thermometers are comparable. Contact/electronic thermometers have a high purchase price but the fact that they can be used repeatedly means that they may be less costly per test than the chemical thermometers, which have a low purchase price but can be used only once (or can be reused only a limited number of times). Since the cost per test is dependent on the volume of tests undertaken, chemical thermometers may be a better use of resources than either electronic thermometer in very low volume settings, such as some primary care providers.

GDG translation

The GDG noted that the alternatives to oral and rectal thermometers can all give inaccurate readings and have variable sensitivity in detecting fever. Taking temperatures by the axillary route using an electronic or chemical dot thermometer underestimates body temperature by 0.5 °C on average. Tympanic temperatures measured with an infrared thermometer differ from body temperature by 0.3 °C on average. The GDG noted that these three types of measurements had not been compared with each other and therefore decided that they could not recommend one type

Table 3.1 Estimated 10 year expenditure on thermometers suitable for axillary and tympanic measurement in a large teaching hospital, discounted at 3.5% (see Appendix B for details)

	Chemical (single use)	Chemical (reusable)	Contact/ electronic	Contact/compact electronic	Infrared sensing (tympanic)
Minimum priced model (with staff cost)		£12,260,326	£758,535	£4,137,153	£1,064,403
Maximum priced model (with staff costs)		£688,596	£941,610	£877,437	£732,427
Minimum priced model (without staff costs)	£769,177	£173,260	£834,153	£108,131	£930,102
Maximum priced model (without staff costs)	£2,637,178	£371,899	£673,009	£541,865	£598,126

over another. Data from neonates suggests that axillary measurements are more accurate in this age group and it was therefore decided to recommend this route at that age.

The GDG was aware that some authorities suggest that tympanic measurements are unreliable or impossible to perform in infants under the age of 3 months. The evidence was inconclusive on this issue and when the question was put to the Delphi panel there was no consensus. Accordingly, the GDG felt that they could not suggest age limits on the use of tympanic thermometers. The GDG considered that more research was needed in this area. Moreover, it would be helpful if direct comparisons were made between all of the different thermometers that were recommended for use in young children.

From the health economics estimates, the GDG noted that there was considerable overlap in the estimated costs of most types of thermometers. When staff costs were not included, compact electronic thermometers appeared to be the most cost-effective. The health economics analysis was based on the cost of thermometers in an acute care setting, and the best choice of thermometer may differ across different clinical settings, such as primary care or accident and emergency triage. In the acute care setting analysis, when estimated staff costs were included, the costs of electronic, compact electronic and tympanic thermometers were comparable. Single-use chemical thermometers appeared expensive. This is partly because a new thermometer is needed for each measurement and estimated staff costs are very high because they take longer to read than the other types of thermometers. The model assumes that healthcare professionals are not engaged in other activities while waiting to read the thermometer, which may not reflect actual practice and may therefore overestimate the cost. Furthermore, the GDG noted that the economic model uses an assumption of 18 recordings per admission. The GDG decided that single-use chemical thermometers may be a cost-effective choice in situations where repeated measurements are unlikely to be needed.

On the use of temporal artery thermometers, the GDG considered that there was insufficient evidence at present from which to make a recommendation. The GDG did not believe that forehead crystal thermometers were accurate enough to be recommended for use by healthcare professionals.

Recommendations on thermometers and the site of measurement

In infants under the age of 4 weeks, body temperature should be measured with an electronic thermometer in the axilla.

In children aged 4 weeks to 5 years, healthcare professionals should measure body temperature by one of the following methods:

- electronic thermometer in the axilla
- chemical dot thermometer in the axilla
- infrared tympanic thermometer

Healthcare professionals who routinely use disposable chemical dot thermometers should consider using an alternative type of thermometer when multiple temperature measurements are required.

Forehead chemical thermometers are unreliable and should not be used by healthcare professionals.

Research recommendation on thermometers and the site of measurement

Measuring temperature in young babies: tympanic versus axilla electronic versus axilla chemical dot versus temporal artery.

3.3 Subjective detection of fever by parents and carers

Not all families own a thermometer and parents and carers often attempt to confirm that their child has a fever by subjective means. This is usually done by placing a hand over the child's

forehead or other part of the body surface. Most guidelines and review articles do not refer to subjective methods of detecting fever. The GDG considered it important to determine whether subjective detection of fever is accurate and should be considered a valid entry point into this guideline.

Clinical question

How accurate is the subjective detection of fever by parents and carers compared with the detection of fever with a thermometer?

Narrative evidence

Five EL II studies,[86–90] one EL III prospective cohort study[91] and one EL III research letter[59] investigating the diagnostic accuracy of subjective measurement to detect fever were found. Overall, most of the studies were conducted in resource-poor settings such as Malawi[88] or Zimbabwe[59], the age of children included varied (e.g. 2 days to 48 months[87] to 1 month to 18 years[90]) and the authors used different reference standards (for instance, one compared perceived fever with oral temperature ≥ 37.8 °C or rectal temperature ≥ 38.3 °C measured by either mercury or digital thermometer[86]). The other prospective cohort study[87] used tympanic temperature measured by non-contact tympanic thermometer and rectal temperature by mercury thermometer as standard. The overall finding suggested that parental perceived fever had reasonable diagnostic accuracy with the sensitivity of detection of fever ranging from 74%[86] to 97%[88] and specificity ranging from 19%[88] to 86%[86] in EL II studies. Sensitivities and specificities as high as 94% and 90.6%, respectively, have been reported by EL II studies.[59,91]

Evidence summary

Subjective detection of fever by parents and carers has been relatively well studied but there are no UK studies. The sensitivity of palpation for the detection of fever ranged from 74% to 97%. (EL II). Five of the six studies that quoted specificity gave values between 67% and 91%; the other gave a value of 19%. (EL II)

GDG translation

The GDG noted that, although there had been no direct comparisons, the sensitivity and specificity of detecting fever by palpation were comparable with those reported for axillary and tympanic thermometers. The GDG therefore decided that detection of fever by palpation was probably as good as the other alternatives to oral and rectal temperature measurements. The GDG considered that it was important for these facts to be recognised by healthcare professionals.

Recommendation on subjective detection of fever by parents and carers

Reported parental perception of a fever should be considered valid and taken seriously by healthcare professionals.

4 Clinical assessment of the child with fever

4.1 Introduction

Concerned parents or carers of young children commonly seek access to healthcare services when their child has a fever.

The initial assessment of the feverish child is very important. The majority of children presenting with fever will have either a self-limiting viral condition or an obvious cause for their fever for which specific treatment can be given. A minority will present with fever with no obvious underlying cause, and a small number of these will have a serious illness.

Initial contact may be made remotely (e.g. by telephone) or the child may present directly to a facility where a face-to-face assessment can take place. Wherever the assessment is carried out, the assessor needs to understand the significance of certain symptoms and signs. A careful and thorough assessment should mean that in the majority of cases:

- the child with a potentially serious illness is recognised and managed appropriately
- the child with a minor self-limiting illness is not burdened with unnecessary medical intervention and the parents/carers are supported with appropriate self-care advice.

4.2 Priorities in the clinical assessment of feverish illness in children

Although most children with a fever will have a self-limiting illness, a minority will have a serious or even life-threatening illness. The over-riding priority for healthcare professionals should be to reduce the mortality of children with feverish illness in the UK, which remains higher than many other European countries. The priorities for healthcare professionals should be to:

1. identify any immediately life-threatening features
2. assess the child's likelihood of having a serious illness or self-limiting illness, without necessarily diagnosing any one particular condition
3. determine a source of the illness to direct specific treatment
4. make appropriate management decisions based upon the results of the assessment.

The clinical assessment is similar wherever it takes place and is described in detail in this chapter. Adaptations will need to be made to the assessment if the child cannot be physically examined, but the priorities and principles remain the same. The management of children after assessment, however, will be determined not only by the results of the assessment but also by the facilities available to the healthcare professional (e.g. a nurse consultant on the phone at NHS Direct, a GP in a surgery, or a paediatrician in a hospital). The management is therefore dealt with separately in subsequent chapters.

4.3 Life-threatening features of illness in children

Evidence was sought for symptoms and signs associated with fever which would predict serious illness in young children.

Clinical questions

In children with fever, what signs or combination of symptoms and signs are associated with serious illness or mortality?

Are there any scoring systems that use symptoms and signs in children with fever to predict the risk of serious illness? How accurate are they?

Evidence summary

Although evidence was found to determine risk factors for serious illness (see Section 4.5), none of the features in isolation or combination were strongly associated with death.

GDG translation

The GDG felt that recommending a specific list of life-threatening signs could result in under-recognition of cases if such a list was used in isolation. Healthcare providers are trained to follow the principles of the Resuscitation Council (UK) guidelines for resuscitation: i.e. assessment of airway, breathing, circulation and neurological dysfunction.[92] Although the GDG could not find any prospective comparison of using these priorities with any other resuscitation strategy, they have been developed with widespread consultation and are seen as best practice by all those involved in the acute management of children. The GDG agreed with stakeholder input to reinforce the principles to determine life-threatening features. However, the GDG has not produced a specific list of signs as this could have the result of removing the clinical judgement required to assess whether a child has an immediate threat to life.

Recommendation on life-threatening features of illness in children

First, healthcare professionals should identify any immediately life-threatening features, including compromise of the airway, breathing or circulation, and decreased level of consciousness.

4.4 Assessment of risk of serious illness

4.4.1 Introduction

After assessing the presence or absence of immediately life-threatening features in a child with a fever, the next priority for the healthcare professional should be to make a further risk assessment based on the presenting symptoms and signs. Some symptoms and signs lead towards a diagnosis of a specific illness or focus of infection. Other symptoms and signs are non-specific but may indicate the severity of illness. Healthcare professionals need to be able to detect those children with non-specific features of serious illness as well as be able to consider the working diagnosis for each case. Healthcare professionals also need to know when to be reassured that children have a self-limiting illness whose parents or carers need advice and support rather than specific treatments or admission to hospital.

4.4.2 Traffic light system

The GDG decided to highlight graphically the non-specific features of illness severity and the specific symptoms and signs of serious illnesses in a 'traffic light' table. The 'red' features are the most worrying, followed by the 'amber' features, and the 'green' features are the most reassuring.

The traffic light table is used throughout the rest of the guideline as a basis for making management decisions based on risk rather than diagnosis. Once a working diagnosis has been reached, the child should follow national/local guidance on the management of that specific condition and therefore exit this guideline.

The traffic light table has been developed from many different sources. To ensure the recommendations follow in a logical sequence, the table is provided here *before* the evidence and translations. These are provided in Sections 4.5 and 4.6 of this chapter and the reader is advised to refer back to the table whenever it is mentioned.

Recommendation on assessment of risk of serious illness

Children with feverish illness should be assessed for the presence or absence of symptoms and signs that can be used to predict the risk of serious illness using the traffic light system (Table 4.1).

Table 4.1 Traffic light system for identifying risk of serious illness. Children with fever and *any* of the symptoms or signs in the 'red' column should be recognised as being at high risk. Similarly, children with fever and any of the symptoms or signs in the 'amber' column and none in the 'red' column should be recognised as being at intermediate risk. Children with symptoms and signs in the 'green' column and none in the 'amber' or 'red' columns are at low risk. The management of children with fever should be directed by the level of risk.

	Green – low risk	Amber – intermediate risk	Red – high risk
Colour	• Normal colour of skin, lips and tongue	• Pallor reported by parent/carer	• Pale/mottled/ashen/blue
Activity	• Responds normally to social cues • Content/smiles • Stays awake or awakens quickly • Strong normal cry/not crying	• Not responding normally to social cues • Wakes only with prolonged stimulation • Decreased activity • No smile	• No response to social cues • Appears ill to a healthcare professional • Does not wake or if roused does not stay awake • Weak, high-pitched or continuous cry
Respiratory		• Nasal flaring • Tachypnoea: RR > 50 breaths/minute, age 6–12 months RR > 40 breaths/minutes, age > 12 months • Oxygen saturation ≤ 95% in air • Crackles	• Grunting • Tachypnoea: RR > 60 breaths/minute • Moderate or severe chest indrawing
Hydration	• Normal skin and eyes • Moist mucous membranes	• Dry mucous membranes • Poor feeding in infants • CRT ≥ 3 seconds • Reduced urine output	• Reduced skin turgor
Other	• None of the amber or red symptoms or signs	• Fever for ≥ 5 days	• Age 0–3 months, temperature ≥ 38 °C • Age 3–6 months, temperature ≥ 39 °C
		• Swelling of a limb or joint • Non-weightbearing limb/ not using an extremity	• Non-blanching rash • Bulging fontanelle • Neck stiffness • Status epilepticus • Focal neurological signs • Focal seizures
		• A new lump > 2 cm	• Bile-stained vomiting

CRT = capillary refill time; RR = respiratory rate.

4.5 Non-specific symptoms and signs of serious illness

Evidence was sought for symptoms and signs associated with fever which would predict wellness or serious illness in young children. These symptoms and signs could be non-specific for any feverish illness or be particular to a specific underlying disease. Some features were looked for individually. These included heart rate, capillary refill time (CRT), blood pressure, respiratory rate (RR), height and duration of fever and the assessment of dehydration.

4.5.1 General symptoms and signs of serious illness

Clinical questions

In children with fever, what symptoms or combination of symptoms are associated with serious illness or mortality?

Are there any scoring systems that use symptoms of children with fever to predict the risk of serious illness?

In children with fever, what signs or combination of symptoms and signs are associated with serious illness or mortality?

Are there any scoring systems that use symptoms and signs in children with fever to predict the risk of serious illness? How accurate are they?

In children with fever, what symptoms and signs are associated with self-limiting illness?

In view of the number of different healthcare locations in which the initial assessment can take place, studies that looked just at symptoms alone were reviewed (to assist the remote assessor) and studies that used symptoms and signs were reviewed (to assist the face-to-face assessor).

To determine which clinical features in feverish children are associated with serious illness and which are associated with a non-serious illness, studies looking at children with a variety of symptoms and signs on presentation and followed up to end diagnosis or outcome were sought (prospective cohort studies).

Scoring systems have been developed to try to distinguish seriously ill children from those who have a minor self-limiting illness, based on a combination of objective symptoms and signs. Studies determining the accuracy of these scoring systems were also sought.

Individual symptoms

Four EL 2+[93–96] and one EL 2–[97] prospective cohort studies were found that reported on the relationship between individual symptoms and the likely presence of serious illness. The studies varied widely in terms of setting (for example, primary and secondary care, developed countries and resource-poor countries), methods of analysis, the ages of children included (0–18 years with different exclusion criteria), symptoms described, definitions and prevalence of serious illness. Due to the methodological and hence statistical heterogeneity, it was inappropriate to perform a meta-analysis.

The symptoms in children aged less than 6 months that were associated with serious illness in one or more papers were drowsiness (RR 7.6),[93] decreased activity (RR 5.8),[93] pale on history (RR 4.4),[93] poor feeding (less than half normal amount) (RR 4.4,[93] OR 2.9–6.0[98]), decreased wet nappies (< 4 in 24 hours) (RR 4.1)[93] and bile-stained vomiting (RR 5.1).[93] The RR was calculated based on the reported positive predictive values (PPVs) and negative predictive values (NPVs).

Individual symptoms and signs

Six EL 2+[93–96,98,99] and one EL 2–[97] prospective studies describing the signs and symptoms associated with serious bacterial infection (SBI) were found. There is methodological heterogeneity among the studies. For example, the setting varied from developed countries such as Australia[93] to aggregated data from resource-poor settings.[98] Moreover, the age of children included varied from < 2 months[98] to 3 months to 15 years.[94] The list of signs strongly associated with SBI were:

- being drowsy[93,98]
- moderate/severe chest recession[93,98,99]
- respiratory rate > 60 breaths/minute[97–99]
- nasal flaring[98]
- grunting[98]
- crackles[98]
- lump > 2 cm[93]
- being pale[93]
- not looking well[99]
- bulging fontanelle.[98]

Scoring systems of combinations of symptoms and signs

When searching for scoring systems using combinations of signs and symptoms, only prospective cohort studies recruiting children with fever without apparent source (FWS) were included.

Seven EL 2+[100–104,106,107] and one EL 2–[105] prospective studies were found covering two scoring systems for febrile infants, which used clinical features of patients alone: Yale Observation Scale (YOS, see Table 4.2)[100–105] and the Young Infant Observation Scale (YIOS).[106,107] Other scoring

Table 4.2 The features of the Yale Observation Scale (YOS)

Observation item	Normal = 1	Moderate impairment = 3	Severe impairment = 5
Quality of cry	Strong or none	Whimper or sob	Weak or moaning, high-pitched, continuous cry or hardly responds
Reaction to parent stimulation	Cries brief or no cry and content	Cries on and off	Persistent cry with little response
State variation	If awake, stays awake or if asleep, awakens quickly	Eyes close briefly when awake or awakens with prolonged stimulation	No arousal and falls asleep
Colour	Pink	Pale extremities or acrocyanosis	Pale or cyanotic or mottled or ashen
Hydration	Skin and eyes normal and moist mucous membranes	Skin and eyes normal and mouth slightly dry	Skin doughy or tented and dry mucous membranes and/or sunken eyes
Response to social overtures	Smiles or alerts (consistently)	Brief smile or alert	No smile, anxious, dull; no alerting to social overtures

systems (Rochester[96,108,109] and Philadelphia[96]) use laboratory values as part of the scale and were therefore not included in this section. There is heterogeneity among the studies as the setting varied from developed countries such as the USA to resource-poor settings such as India, and the age of children included ranged from 0–2 months[106] to 3–36 months.[105]

Neither the YOS nor YIOS alone could reliably detect serious illness in infants without missing many cases. The YOS did improve the detection of serious illness in infants when combined with a physician-taken history and examination (sensitivity and NPV improved from 86% to 89–93% and from 85–97% to 96–98%, respectively).[102] All the validation studies found that a low YOS score is associated with well infants. From the validation study of the YOS,[101] in children aged 3 months to 3 years with a score of 6, the NPV is 97.4% for occult bacteraemia.

The symptoms and signs in the YOS associated with being well are:

- strong cry/no cry
- content
- pink
- eyes not sunken/skin normal (hydration)
- if awake stays awake, if asleep is easily roused
- smiles.

When deriving the YOS scoring system, the following symptoms and signs were correlated with serious illness:[100,102]

- weak/high-pitched
- continuous cry
- unable to rouse
- pale/mottled/blue
- sunken eyes/doughy skin
- no smile.

Evidence summary

Individual symptoms and individual symptoms and signs

The evidence from prospective cohort studies demonstrates a number of individual symptoms (i.e. drowsiness, decreased activity, poor feeding, pale, reduced urine output, bile-stained vomiting) and signs (i.e. being drowsy, moderate/severe chest recession, respiratory rate > 60 breaths/minute, nasal flaring, grunting, crackles, lump > 2 cm, being pale, not looking well, bulging fontanelle) that are associated with serious illness in infants and young children. Most of the

evidence is limited to data relating to infants less than 6 months in a secondary care setting. In isolation, none of these symptoms or signs are reliably associated with serious illness.

Scoring systems of combinations of symptoms and signs

Scoring more than 10 using the YOS scoring system after a history and examination may help identify other infants and children at high risk of serious illness.

A YOS of 6 with a well-appearing child makes the presence of a serious illness very unlikely. However, the development of features of serious illness including the symptoms listed on the YOS should prompt further evaluation.

In isolation, none of these symptoms are strongly associated with serious illness. A child identified as 'ill' when assessed by an experienced healthcare professional is likely to have an SBI. To ensure that children with serious illness are recognized early, many children without serious illness will need to be examined.

Health economics

The GDG did not identify any issues where cost-effectiveness issues were a priority for this clinical question.

GDG translation

Individual symptoms and individual symptoms and signs

Prospective cohort studies of children with fever have identified a number of symptoms and signs that are predictive of serious illness. Much of the most reliable data relates to infants up to the age of 6 months. The GDG decided that it was reasonable based on clinical experience to extrapolate the symptoms and signs to older children and use them as part of the assessment of older children with a feverish illness. The GDG is aware that there is currently a large prospective study being conducted in Australia on the predictive values of symptoms and signs in febrile children of all ages. In the UK, a project is in development on the recognition of acute illness in children (Dr R MacFaul, personal communication). It is hoped that the results of these studies will inform future guidance on the assessment of the risk of serious illness in children with feverish illness.

Scoring systems of combinations of symptoms and signs

The features used in the YOS associated with serious illness are validated and show good correlation with those children who go on to develop serious illness in children aged 3 months to 3 years. The GDG felt that these features can be extrapolated for use on children up to the age of 5 years, based on clinical experience and extrapolated to the UK population.

'Traffic light' system

The GDG attempted to summarise the results of risk stratification from the prospective cohort studies and scoring studies in a 'traffic light' system. From the scoring studies, those symptoms and signs that scored only 1 on the YOS were designated 'green'. Those individual symptoms and signs that scored 5 in the YOS were designated 'red', as a child with only one 'red' symptom and all other 'green' symptoms (i.e. scoring 10 in the YOS) was at significant risk of serious illness. Those symptoms and signs that scored 3 in the YOS were designated 'amber', because while a child with a combination of 'amber' symptoms or signs was at significant risk of serious illness, a child with only one 'amber' feature was not at significant risk of serious illness.

From the prospective cohort studies, the GDG assigned 'red', 'amber' or 'green' status to additional symptoms and signs based on their associated risk of serious illness and on clinical experience.

Recommendations on general symptoms and signs of serious illness

Children with the following symptoms or signs should be recognised as being in a high-risk group for serious illness:

- unable to rouse or if roused does not stay awake
- weak, high-pitched or continuous cry
- pale/mottled/blue/ashen
- reduced skin turgor

- bile-stained vomiting
- moderate or severe chest indrawing
- respiratory rate greater than 60 breaths/minute
- grunting
- bulging fontanelle
- appearing ill to a healthcare professional.

Children with any of the following symptoms should be recognised as being in at least an intermediate-risk group for serious illness:

- wakes only with prolonged stimulation
- decreased activity
- poor feeding in infants
- not responding normally to social cues/no smile
- dry mucous membranes
- reduced urine output
- a new lump larger than 2 cm
- pallor reported by parent or carer
- nasal flaring.

Children who have all of the following features, and none of the high- or intermediate-risk features, should be recognised as being in a low-risk group for serious illness:

- strong cry or not crying
- content/smiles
- stays awake
- normal colour of skin, lips and tongue
- normal skin and eyes
- moist mucous membranes
- normal response to social cues.

4.5.2 Common physiological measurements and their predictive values of serious illness

Several other signs were looked for specifically as it was felt they were possible markers of serious illness. These included heart rate, capillary refill time (CRT), blood pressure and respiratory rate.

4.5.2.1 Heart rate

Heart rate is often assumed to be a useful marker of serious illness. For example, it is widely taught to use heart rate as a marker of circulatory insufficiency in shock.[110] However, heart rate is affected by a variety of factors (e.g. age, activity, anxiety, pain, body temperature) as well as the presence or absence of serious illness. A specific search was thus undertaken to look at heart rate in the context of serious illness.

Narrative summary

No evidence was found that provided 'normal values' for heart rate in the population of children under 5 years old. There is one EL 2+ study[111] that compared heart rate in children under 1 year with their body temperature. This study found that for every 1 °C rise in body temperature, the resting heart rate rose by 9.6 beats/minute (Figure 4.1). The GDG is aware that there is an ongoing UK study to determine normal values for resting heart rate in children with fever aged 3 months to 12 years.

There are unvalidated tables of normal resting heart-rate values in young infants and children without fever which are widely taught (Figure 4.2).

Evidence summary

There is a lack of evidence regarding heart rate as a marker of serious illness. Despite this, the GDG felt that heart rate is a potentially important marker of serious illness. The Delphi panel was used to decide whether heart rate should be part of the routine assessment of a child with a fever, because a raised heart rate can be a sign of serious illness, particularly septic shock.

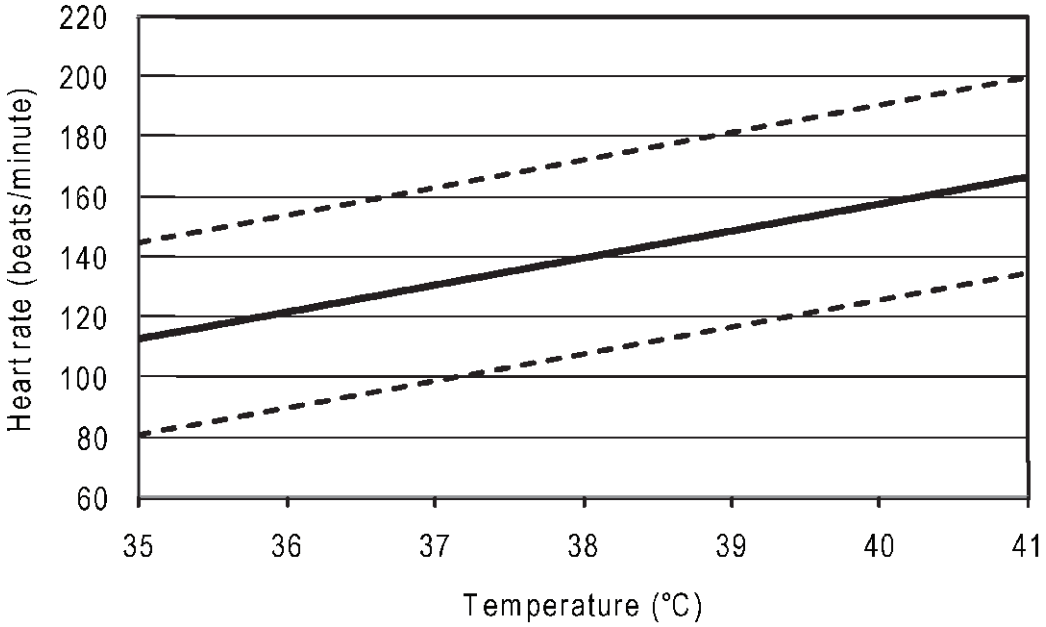

Figure 4.1 Heart rate rise with rising temperature in children less than 1 year old; adapted with permission from Hanna and Greenes[111]

Delphi statement

'Healthcare professionals examining children with fever must measure and record heart rate as part of their routine assessment.'

1 to 3	4 to 6	7 to 9	Don't know	Missing	Total	Median
2 (4%)	8 (15%)	39 (75%)	3 (6%)	1	52	9

Seventy-five percent of the Delphi panel agreed with this statement in round 1 (consensus achieved).

'Healthcare professionals should refer a child for specialist paediatric (children's) care if the resting heart rate is above the expected range for a feverish child.'

1 to 3	4 to 6	7 to 9	Don't know	Missing	Total	Median
2 (4%)	15 (30%)	33 (65%)	1 (2%)	1 (2%)	51	7

This statement did not reach consensus despite adaptations made to the original statement after round 1.

GDG translation

Heart rate was not placed in the 'traffic light' system (see below) as the Delphi panel did not agree that heart rate *per se* should be used as a basis for referral to specialist care. The statement 'healthcare professionals examining children with fever must measure and record heart rate as part of their routine assessment' was adapted and combined with the statement about the physiological parameters that should be documented as part of the assessment (see the end of Section 4.5.2.4). The GDG felt it important to make healthcare professionals aware of the significance of a raised heart rate particularly in septic shock (see the recommendations at the end of Section 4.5.2.4).

The GDG felt that basic physiological parameters in children should be backed up by a better weight of evidence. The GDG is aware that one research project on the predictive value of heart rate and other vital signs in children with fever is currently in progress in the UK (Drs R MacFaul and M Thompson, personal communications) but it is likely that larger studies will be needed to

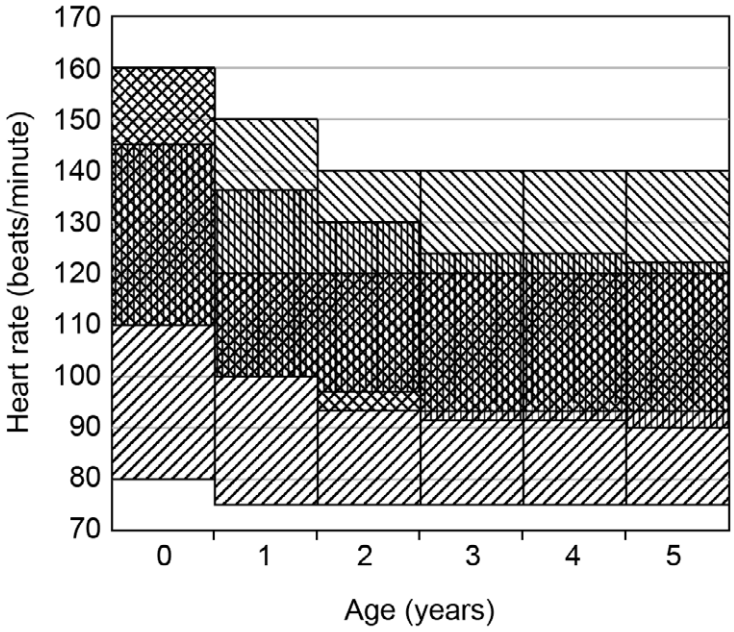

Figure 4.2 Widely quoted values for paediatric heart rates at various ages (left diagonals[288]; right diagonals[289]) and the heart rates of children with minor blunt trauma at various ages (vertical lines[112])

produce definitive results. The GDG therefore recommends that studies are performed to confirm normal ranges for heart rate at various body temperatures and to determine whether children with heart rates outside these ranges are at higher risk of serious illness.

Research recommendation on heart rate

A study to confirm normal ranges for heart rate at various body temperatures and to determine whether children with heart rates outside these ranges are at higher risk of serious illness.

4.5.2.2 Capillary refill time

Narrative summary

Five studies were found investigating the prognostic value of the capillary refill time (CRT) with three EL 2+ prospective studies[113–115] and one EL 2– retrospective study[116] which included children in ICU post-resuscitation, which was excluded owing to the lack of relevance. In addition, there is one EL 2+ SR[117] for signs and symptoms of dehydration which included CRT. Overall, the studies were conducted in a range of settings varying from primary care to intensive care in the UK,[113] the USA[114] and Kenya[115] with different baselines which made meta-analysing inappropriate.

The SR[117] showed that prolonged CRT had sensitivity of 0.60 (95% CI 0.29 to 0.91) and specificity of 0.85 (95% CI 0.72 to 0.98) of detecting 5% dehydration, which made CRT the most specific sign of dehydration. The results from prospective cohort studies showed that there was no significant association of CRT of 3 seconds with meningococcal disease, other significant bacterial illness or white blood cell count (WBC) (statistics not provided).[113] In one prospective cohort study, the receiver operating characteristic (ROC) curve showed that the best performance was obtained when a CRT of 3 seconds was taken to be 'prolonged'; furthermore, a prolonged CRT (> 3 seconds) was associated with a more urgent triage category, the administration of fluid bolus and the length of hospital stay (all $P < 0.05$).[113] Moreover, children with dehydration had prolonged CRT of 2 seconds, with a sensitivity of only 44% for predicting a fluid deficiency of < 5% or more of body weight (other statistics not provided).[114] Overall agreement for CRT was moderate ($k = 0.42$), and was better for normal values (≤ 1 second) ($k = 0.48$) and clearly abnormal values (≥ 4 seconds) ($k = 0.49$).[115]

Furthermore, in a search of the specific signs and symptoms of meningococcal disease, CRT was found to be indicative (the OR of CRT > 3 seconds of having meningococcal disease is 29.4 (95% CI 9.4 to 92.6)[118] in children with a petechial rash. In another SR[117] that included four trials investigating the usefulness of prolonged CRT to indicated dehydration, the findings showed that the pooled sensitivity of prolonged CRT (defined differently in different studies) was 0.60 (95% CI 0.29 to 0.91), with a specificity of 0.85 (95% CI 0.72 to 0.98), for detecting 5% dehydration.

Evidence summary

The authors used different cut-offs of CRT and it appeared that CRT of 2 seconds was a weak predictor of dehydration and serious illness while a CRT ≥ 3 seconds is associated with dehydration and significant illness (e.g. meningococcal disease) in children.

GDG translation

The GDG noted that CRT is quick to carry out and exhibits moderate reproducibility. A statement about measuring CRT was combined with the statement about the physiological parameters which should be documented as part of the assessment (see the end of Section 4.5.2.4). The GDG considered that a CRT of ≥ 3 seconds was an 'amber' sign (see the recommendations at the end of Section 4.5.2.4).

4.5.2.3 Blood pressure

Evidence summary

Blood pressure was not identified as an independent risk factor for serious illness in any of the prospective cohort studies and scoring systems. Low blood pressure was identified as one of several risk factors for adverse outcome in children with meningococcal disease.[119]

GDG translation

The GDG agreed with stakeholder comments that blood pressure should be measured in children with fever who are displaying features of possible serious illness. Blood pressure can be a helpful measurement to monitor children with possible sepsis although low blood pressure is a late feature of septic shock. Other markers such as raised heart rate and prolonged capillary refill time are present earlier and require no special equipment to measure. The GDG concluded that blood pressure should be measured when facilities exist to monitor blood pressure and other markers of inadequate organ perfusion (i.e. shock) are detected (see the recommendations at the end of Section 4.5.2.4).

4.5.2.4 Respiratory rate

Evidence summary

Refer to Sections 4.5.1 (General symptoms and signs of serious illness), 4.5.4 (Assessment of dehydration) and 4.6.6 (Pneumonia) for evidence relating to respiratory rate.

GDG translation

An abnormal respiratory rate has been shown to be a non-specific marker of serious illness, a specific feature of pneumonia and required for the assessment of dehydration. The GDG felt that respiratory rate is therefore an important physiological parameter which needs to be assessed by healthcare professionals. A statement about measuring respiratory rate was combined with the statement about the physiological parameters which should be documented as part of the assessment (see below).

Recommendations on heart rate, capillary refill time, blood pressure and respiratory rate

Healthcare professionals should measure and record temperature, heart rate, respiratory rate and capillary refill time as part of the routine assessment of a child with fever.

Healthcare professionals examining children with fever should be aware that a raised heart rate can be a sign of serious illness, particularly septic shock.

A capillary refill time of 3 seconds or longer should be recognised as an intermediate-risk group marker for serious illness ('amber' sign).

Healthcare professionals should measure the blood pressure of children with fever if the heart rate or capillary refill time is abnormal and the facilities to measure blood pressure are available.

4.5.3 Height and duration of fever and its predictive value of serious illness

When a child with a febrile illness is being assessed, healthcare professionals often ask about the degree and duration of fever. The reason for these questions is that it is often assumed that these variables can be used to help differentiate serious bacterial illnesses from less serious self-limiting viral infections. Regarding the height of recorded fever, it is often thought that there is a higher risk of serious illness with increasing body temperature. Regarding duration of fever, it is sometimes thought that an SBI is more likely with increasing duration of fever. This is on the grounds that viral illnesses will usually resolve spontaneously over a shorter period of time. There is also a converse view that children with serious illness will present to healthcare professionals earlier in the illness because they may have other features that lead parents and carers to suspect the child is seriously unwell.

4.5.3.1 Height of fever

Clinical question

Can the height of body temperature in a young child with fever be used to predict the risk of serious illness or mortality?

Narrative evidence

The literature search was restricted to prospective cohort studies because this would yield the highest quality evidence (EL 2). Twelve prospective cohort studies,[93,95,98,99,120–127] of which three were EL 2–,[124,125,127] were found that reported on the relationship between height of fever and the outcome in terms of serious illness. The studies varied widely in terms of setting (e.g. hospital emergency department or paediatric assessment units in different countries such as Australia,[93] the UK[121] or the USA, and Puerto Rico[120]), ages of children included (e.g. < 28 days[127] to 3–36 months[128]), definition of fever (e.g. rectal temperature ≥ 38 °C or rectal temperature ≥ 39 °C) and outcomes measured. There was also wide variation in the methods of analysis. For these reasons it was not possible or appropriate to pool the data.

Several large EL 2+ studies reported a higher relative risk of SBI with increasing body temperature, with body temperatures ≥ 39 °C in particular being associated with a higher risk. Other studies did not report this association. The sensitivity of a high body temperature to detect SBI is low. With one exception, the sensitivity of a temperature ≥ 39 °C to detect SBI was between 10% and 32%. In developed countries the sensitivity of a temperature ≥ 39 °C to detect SBI was between 10% and 14%. The PPV of a temperature ≥ 39 °C varied between 4% and 40% in developed countries.

Evidence summary

Twelve prospective cohort studies (nine EL 2+ and three EL 2–) that reported on the relationship between height of fever and the outcome in terms of serious illness were found.

Several large EL 2+ studies reported a higher relative risk of SBI with increasing body temperature, with body temperatures ≥ 39 °C in particular being associated with a higher risk. Other EL 2+ studies did not report this association.

Health economics

The GDG did not identify any issues that required a cost-effectiveness analysis for this clinical question.

GDG translation

The GDG noted that most large EL 2+ studies suggest that the risk of serious illness increases with height of fever in young children. Body temperatures ≥ 39 °C in particular were usually

associated with a higher relative risk of SBI. The strongest associations were reported in studies involving children aged less than 6 months. However, the sensitivity and PPV of temperatures ≥ 39 °C were low, which suggests that most cases of serious illness would be missed if height of body temperature was used in isolation to identify children with serious illness. Furthermore, the GDG noted that other features of a child with feverish illness, such as his or her age or an 'ill appearance' were often more predictive.

The GDG concluded that healthcare professionals should be aware that there is an association between height of body temperature and risk of SBI. However, this association is not sufficiently robust to recommend immediate action or referral based on body temperature alone. An exception was made for children aged under 6 months with body temperature ≥ 39 °C because the evidence was strongest for this age group.

In addition, the GDG noted that children aged under 3 months with fever are generally at a higher risk of serious illness (see Section 7.3). The incidence of serious illness in this group, for instance, is over ten times higher than that in older children. The clinical studies that provide the evidence for this age group used a body temperature ≥ 38 °C as the definition of fever. The GDG therefore decided that children aged under 3 months with a body temperature ≥ 38 °C should also be included in the recommendation about risk of serious illness.

Recommendations on height of fever

Height of body temperature alone should not be used to identify children with serious illness. However, children in the following categories should be recognised as being in a high-risk group for serious illness:

- children younger than 3 months with a temperature of 38 °C or higher
- children aged 3–6 months with a temperature of 39 °C or higher.

4.5.3.2 Duration of fever and its predictive value of serious illness

Clinical question

Can the duration of fever in a febrile young child be used to predict the risk of serious illness or mortality?

Narrative evidence

Three EL 2+ prospective studies[126,129,130] that looked at the duration of fever as a risk factor for SBIs in general were found. One of them[129] reported that a duration of fever > 48 hours had an odds ratio of 3.85 (95% CI 1.11 to 13.3) for predicting serious illness. This relationship just reached statistical significance as an independent predictor of SBI. Another prospective cohort study[126] reported that duration of fever was longer in infants with SBIs (26.5 ± 41.5 hours) than those without (18.6 ± 21.7 hours) ($P < 0.01$). Furthermore, in comparison with < 24 hours, duration of fever > 48 hours had an odds ratio of 1.04 (95% CI 0.35 to 3.12) of having SBIs.[130] Of the other two EL 2 studies, one reported that children with SBI had statistically significant longer duration of fever while the other did not.

Two EL 2+ prospective studies[122,123] were also found that looked at the incidence of (predominantly occult) bacteraemia in relation to duration of fever in children with temperature ≥ 39 °C. Both studies reported a higher relative risk of bacteraemia with a shorter duration of fever (RR 1.5[122] to 4.6[123]). The PPVs of a short duration of fever were 4% and 10%.[122,123]

Evidence summary

It was noted that there was a weak association between duration of fever and risk of serious illness from the three studies that looked at SBI in general. There was also an apparently converse association between duration of fever and risk of one particular SBI, namely bacteraemia.

Health economics

The GDG did not identify any issues that required a cost-effectiveness analysis for this clinical question.

GDG translation

The GDG noted a weak association between duration of fever and risk of serious illness from the five studies that looked at SBI in general. They also noted an apparently converse association between duration of fever and risk of one particular SBI, namely bacteraemia. The GDG concluded that the evidence was equivocal and relatively weak in both directions. They concluded that, on the basis of existing evidence, duration of fever could not usefully be included in the list of features that may be used to help predict serious illness.

The GDG was aware that longer durations of fever than those reported in the studies above may be associated with certain serious illnesses. In particular, the GDG noted that a fever lasting 5 days or more is one of the diagnostic criteria for Kawasaki disease. For this reason, it was decided to include a fever lasting 5 days or more as one of the 'amber' features in the traffic light system. A recommendation on the diagnosis of Kawasaki Disease is included in Section 4.6.9.

Recommendation on duration of fever and its predictive value of serious illness

Duration of fever should not be used to predict the likelihood of serious illness

4.5.4 Assessment of dehydration

A number of studies have used degree of dehydration as a marker of serious illness. However, the symptoms and signs used in a number of studies have lacked rigour. The GDG looked for evidence for objective symptoms and signs for dehydration.

Narrative evidence

A recent EL 2+ SR[117] looking at children 1 month to 5 years was found. Although this SR only searched MEDLINE, it was judged to be adequate for inclusion. The authors reviewed 1603 papers, half of which were excluded because of lack of rigour or lack of clarity in outcomes. Of the remainder, only 26 were found to be rigorous enough to meet their criteria. Moreover, in this SR, dehydration was measured using percentage volume lost. They found three studies that evaluated the accuracy of a history of low urine output. A history of low urine output did not increase the likelihood of 5% dehydration (likelihood ratio (LR) 1.3, 95% CI 0.9 to 1.9). The most sensitive signs not requiring particular specialised tests for dehydration were dry mucous membranes, poor overall appearance, and sunken eyes and absent tears (see Table 4.3 for the sensitivities). Prolonged capillary refill time, cool extremities, reduced skin turgor and abnormal respiratory pattern were the most specific individual signs of dehydration.

Evidence summary

It is difficult to detect dehydration in children with fever. Individual symptoms and parental observations are poor predictors of dehydration. Furthermore, history of low urine output does not increase the risk of dehydration. The results showed that prolonged capillary refill time,

Table 4.3 Summary characteristics for clinical findings to detect 5% dehydration[117]

Clinical feature	Sensitivity (95% CI)	Specificity (95% CI)
Prolonged capillary refill time	0.60 (0.29 to 0.91)	0.85 (0.72 to 0.98)
Abnormal skin turgor	0.58 (0.40 to 0.75)	0.76(0.59 to 0.93)
Abnormal respiratory pattern	0.43 (0.31 to 0.55)	0.79(0.72 to 0.86)
Sunken eyes	0.75 (0.62 to 0.88)	0.52 (0.22 to 0.81)
Dry mucous membranes	0.86 (0.80 to 0.92)	0.44 (0.13 to 0.74)
Absent tears	0.63 (0.42 to 0.84)	0.68 (0.43 to 0.94)
Increased heart rate	0.52 (0.44 to 0.60)	0.58 (0.33 to 0.82)
Sunken fontanelle	0.49 (0.37 to 0.60)	0.54 (0.22 to 0.87)
Poor overall appearance	0.80 (0.57 to 1.04)	0.45 (–0.1 to 1.02)
Cool extremities	0.10–0.11 (range)	0.93–1.00 (range)

reduced skin turgor and abnormal respiratory pattern are the most specific individual signs of dehydration.

GDG translation

The GDG recognised that dehydration is a marker of serious illness but there was a lack of evidence to determine the difference between mild, moderate and severe dehydration. The most specific symptoms and signs of dehydration have been highlighted for healthcare professionals to assess to ensure a low false positive rate. The most sensitive symptoms and signs have been highlighted for parents to assess to ensure a low false negative rate (see Chapter 9).

Recommendation on assessment of dehydration

Children with fever should be assessed for signs of dehydration. Healthcare professionals should look for:

- prolonged capillary refill time
- abnormal skin turgor
- abnormal respiratory pattern
- weak pulse
- cool extremities.

4.6 Symptoms and signs of specific serious illnesses

4.6.1 Introduction

The next priority in the assessment of a child with a feverish illness is to determine the underlying source of their illness.

Recommendation on symptoms and signs of specific serious illnesses

Healthcare professionals should look for a source of fever and check for the presence of symptoms and signs that are associated with specific diseases (see Table 4.4).

The guideline is not meant to be a textbook on how to examine a child for all possible infections. However, the scope does include 'identification of signs and symptoms that would help to establish the possible diagnoses and focus for infection'. The GDG focused on those serious illnesses that may have immediate consequences to the child's life expectancy or long-term quality of life.

The GDG looked at those symptoms and signs that are predictive of specific serious illnesses, which are:

- meningitis
- septicaemia
- bacteraemia
- pneumonia
- urinary tract infection
- encephalitis (herpes simplex)
- septic arthritis/osteomyelitis
- Kawasaki disease.

The databases were searched and the highest evidence levels, i.e. prospective cohort studies, were used when evidence was available. Retrospective studies were included when there is a lack of better quality studies. The data were appraised, summarised and translated by the GDG members.

Clinical question

In children with fever, what symptoms and signs or combinations of symptoms and signs are predictive of the specific conditions defined as serious illnesses?

Table 4.4 Summary table for symptoms and signs suggestive of specific diseases

Diagnosis to be considered	Symptoms and signs in conjunction with fever
Meningococcal disease	Non-blanching rash, particularly with one or more of the following: • an ill-looking child • lesions larger than 2 mm in diameter (purpura) • capillary refill time of ≥ 3 seconds • neck stiffness
Meningitis	Neck stiffness Bulging fontanelle Decreased level of consciousness Convulsive status epilepticus
Herpes simplex encephalitis	Focal neurological signs Focal seizures Decreased level of consciousness
Pneumonia	Tachypnoea (RR > 60 breaths/minute, age 0–5 months; RR > 50 breaths/minute, age 6–12 months; RR > 40 breaths/minute, age > 12 months) Crackles in the chest Nasal flaring Chest indrawing Cyanosis Oxygen saturations ≤ 95%
Urinary tract infection	Vomiting Poor feeding Lethargy Irritability Abdominal pain or tenderness Urinary frequency or dysuria Offensive urine or haematuria
Septic arthritis	Swelling of a limb or joint Not using an extremity Non-weight bearing
Kawasaki disease	Fever for more than 5 days and at least four of the following: • bilateral conjunctival injection • change in mucous membranes • change in the extremities • polymorphous rash • cervical lymphadenopathy

RR = respiratory rate.

4.6.2 Meningococcal disease

Narrative evidence and summary

Three EL 2+ prospective population-based studies[94,118,132] to determine the clinical predictors of meningococcal disease in children with a haemorrhagic (non-blanching) rash with or without fever were found. The children's ages ranged from > 1 month[94,118,132] to < 16 years[132] and the population varied from Denmark,[132] and the UK[118] to the USA.[94] The features that helped predict the presence of meningococcal disease were:

- distribution of rash below the superior vena cava distribution (OR 5.1[132])
- presence of purpura – lesions > 2 mm (OR 7.0[132]; 37.2[118])
- neck stiffness (OR 6.9[132])
- capillary refill time > 2 seconds (OR 29.4[118])
- ill appearance (OR 16.7[118])
- CRP > 6 mg/litre.[118,132]

One recent UK-based EL 3 retrospective study[133] was also found that aimed to determine the frequency and time of onset of clinical features of meningococcal disease, to enable clinicians to make an early diagnosis before the individual was admitted to hospital. The researchers found that most children had only non-specific symptoms in the first 4–6 hours, but were close to death by 24 hours. The classic features of haemorrhagic rash, meningism and impaired consciousness developed later (median onset 13–22 hours). In contrast, 72% of children had earlier symptoms (leg pains, cold hands and feet, abnormal skin colour) that first developed at a median time of 8 hours.

GDG translation

The GDG considered a non-blanching rash (petechiae or purpura), neck stiffness and ill appearance on clinical examination as being 'red' features.

The feature of rash below the nipple line was not included in the traffic light table. This is because the sign is more useful in ruling out meningococcal disease if the rash is only found in the superior vena cava distribution rather than ruling the diagnosis in. Capillary refill time was not included for similar reasons and because the traffic light system only refers to clinical findings.

The GDG decided that they could not make a recommendation based on the possible early features of meningococcal disease[133] because of the retrospective nature of the study, the lack of controls and the possibility of recollection bias. The GDG did appreciate the potential benefit of diagnosing meningococcal disease at an early stage and called for further, prospective, research on this subject.

Recommendation on meningococcal disease

Meningococcal disease should be considered in any child with fever and a non-blanching rash, particularly if any of the following features are present:

- an ill-looking child
- lesions larger than 2 mm in diameter (purpura)
- capillary refill time of 3 seconds or longer
- neck stiffness

Research recommendation on meningococcal disease

There is a need for a prospective study to assess the prognostic value of symptoms such as limb pain and cold hands and feet that have been identified as possible early markers of meningococcal disease.

4.6.3 Non-meningococcal septicaemia

No prospective population studies were found which determined the clinical features of non-meningococcal sepsis. Papers on occult pneumococcal bacteraemia were excluded as they only included laboratory screening test data. After searching for retrospective studies in the recent 10 years, there was no study judged to be of good enough quality to base recommendations upon and therefore none have been made.

4.6.4 Meningitis

Two EL 2+ prospective population studies[134,135] and one EL 2– narrative review[136] on determining the symptoms and signs of bacterial meningitis were found. Neck stiffness and a decreased conscious level are the best predictors of bacterial meningitis. However, neck stiffness is absent in 25% of infants under 12 months .[134] (EL 2+) Infants under 6 months of age have a bulging fontanelle in 55% of bacterial meningitis cases.[134] (EL 2+)

A third EL 2+ prospective population study to determine the causes of status epilepticus in children was submitted by the GDG.[137] In this UK study, 17% of children with a first-ever febrile convulsive status epilepticus had bacterial meningitis.

GDG translation

The GDG considered neck stiffness, a bulging fontanelle and a decreased conscious level as being 'red' features. Although the management of febrile convulsions is outside the scope of the guideline the GDG felt it important to highlight the risk of meningitis in children with a prolonged febrile seizure. The GDG also felt it was important to highlight to healthcare professionals that classical features of meningitis are often absent in infants.

Recommendations on meningitis

Meningitis should be considered in a child with fever and any of the following features:

- neck stiffness
- bulging fontanelle
- decreased level of consciousness
- convulsive status epilepticus.

Healthcare professionals should be aware that classical signs of meningitis (neck stiffness, bulging fontanelle, high-pitched cry) are often absent in infants with bacterial meningitis.

4.6.5 Herpes simplex encephalitis

Narrative evidence and summary

Only one EL 3 retrospective case series[138] conducted in Scotland was found which looked at the signs of herpes simplex encephalitis (HSE) in children. Focal neurological signs (89%) and seizures (61%), especially focal seizures, were the most frequent signs of HSE, but also neck stiffness (65%) and a decreased conscious level (52%).

GDG translation

Although the evidence was weak, the GDG felt that it was important to highlight these signs because early treatment of HSE improves outcomes.

The GDG considered neck stiffness, focal neurological signs, partial (focal) seizures and a decreased conscious level as being 'red' features.

Recommendation on herpes simplex encephalitis

Herpes simplex encephalitis should be considered in children with fever and any of the following features:

- focal neurological signs
- focal seizures
- decreased level of consciousness.

4.6.6 Pneumonia

Narrative evidence and summary

Six EL 2+ prospective studies[139–144] that looked at clinical features of pneumonia were found. The study sites varied widely, from the USA,[139,140] the Philippines,[141] India[142] and Jordan[143] to Lesotho.[144] The age included also varied from 2 years[140] to < 6 years.[143]

Respiratory rate is a useful marker of pneumonia. Using age-related respiratory rates for tachypnoea (> 59 breaths/minute in the age group 0–5 months, > 52 breaths/minute in the age group 6–12 months and > 42 breaths/minute in the age group > 12 months) there is a relative risk (RR) of 7.73[140] of having radiological signs of pneumonia. Other overall findings are:

- presence of cough has a sensitivity of 98% and specificity of 70% in children admitted for pneumonia[143]
- crepitations has an RR of 16.2[142]
- cyanosis has a RR of 4.38[142]
- oxygen saturations ≤ 95% have an RR of 3.5[139]
- chest indrawing has an RR of 8.38[142]
- nasal flaring if age < 12 months has an adjusted OR of 2.2)[139]

There are difficulties with all the studies in that the gold standard for diagnosing bacterial pneumonia is not specific as viral pneumonia cannot be confidently excluded on chest X-ray.

GDG translation

None of the signs for pneumonia are diagnostic in isolation. Not all of the signs found in the evidence were appropriate to the UK population. The GDG considered a respiratory rate of > 60 breaths/minute, moderate/severe chest indrawing, 'ashen' or 'blue' skin colour and grunting as being 'red' features. The GDG considered tachypnoea, nasal flaring and oxygen saturations < 95% in air as being 'amber' features.

Recommendation on pneumonia

Pneumonia should be considered in children with fever and any of the following signs:

- tachypnoea (respiratory rate greater than 60 breaths/minute, age 0–5 months; greater than 50 breaths/minute, age 6–12 months; greater than 40 breaths/ minute, age older than 12 months)
- crackles in the chest
- nasal flaring
- chest indrawing
- cyanosis
- oxygen saturation of 95% or less when breathing air.

4.6.7 Urinary tract infection

Refer to the NICE *Urinary Tract Infection in Children* (UTIC) guideline for the summary of evidence and translation.

The recommendations below have been adapted from the NICE UTIC draft guideline as the scope of the two guidelines overlapped. The recommendation for children over 3 months has been altered as the population for whom this guideline applies all have a feverish illness.

Recommendations on urinary tract infection

Urinary tract infection should be considered in any child younger than 3 months with fever.*

Urinary tract infection should be considered in a child aged 3 months and older with fever and one or more of the following:*

- vomiting
- poor feeding
- lethargy
- irritability
- abdominal pain or tenderness
- urinary frequency or dysuria
- offensive urine or haematuria.

4.6.8 Septic arthritis/osteomyelitis

Narrative evidence and summary

One EL 2+ prospective validation US study[145] of a clinical decision rule for a septic hip that recruited 51 children (age not specified) with septic arthritis was found. The study used two clinical features (fever and ability to bear weight on affected limb) and two laboratory features (erythrocyte sedimentation rate (ESR) and white blood cell count (WBC)). These performed well when all the features were available to assess. It was felt that the evidence for using the signs without blood tests was inadequate to base recommendations upon, and thus retrospective studies were searched for. Three EL 3 retrospective studies for osteomyelitis/septic arthritis[146–148] conducted in Taiwan,[146] Malaysia[147] and Nigeria[148] were found. The extra signs detected by retrospective studies were swelling of an affected limb and the limb not being used.

* See *Urinary Tract Infection in Children*, NICE clinical guideline (publication expected August 2007).

GDG translation

Recommendations have only been made for the clinical features, as definitive diagnosis of septic arthritis and/or osteomyelitis is beyond the scope of the guideline. The GDG considered non-weight bearing, swelling of a limb or joint and not using an extremity as being 'amber' features.

Recommendation on septic arthritis/osteomyelitis

Septic arthritis/osteomyelitis should be considered in children with fever and any of the following signs:

- swelling of a limb or joint
- not using an extremity
- non-weight bearing.

4.6.9 Kawasaki disease

Narrative evidence and summary

No prospective studies looking at clinical features that are predictive of Kawasaki disease were found and thus retrospective studies from the past 10 years were searched for.

The two EL 3 retrospective studies[149,150] identified used the American Heart Association (AHA) criteria to determine the diagnosis of Kawasaki disease. These studies went on to look at the frequency of these features in children diagnosed with Kawasaki disease. The findings of these studies did not change the AHA criteria.

The AHA criteria suggested that the diagnosis of Kawasaki disease can be made in children with a history of fever for at least 5 days, plus at least four of the following five signs:

- changes in the extremities, such as erythema of the palms and soles and oedema of the hands and feet
- polymorphous exanthema
- bilateral bulbar conjunctival injection without exudates
- erythema of the lips, tongue and oral cavity
- cervical lymphadenopathy of 1.5 cm in diameter or greater, which is usually unilateral.

Incomplete (atypical) Kawasaki disease is diagnosed with fewer than the suggested criteria above and is seen in younger patients who are more likely to have coronary artery aneurysms if left untreated.

GDG translation

The GDG felt it was important to highlight the need to rule out Kawasaki disease in children who have had fever for 5 days or more. Therefore a fever for 5 days or more is an 'amber' sign. The GDG highlighted the fact that Kawasaki disease, especially in the under 1 year age group, can be present without all of the features listed in the recommendation below.

Recommendation on Kawasaki disease

Kawasaki disease should be considered in children with fever that has lasted longer than 5 days and who have four of the following five features:

- bilateral conjunctival injection
- change in mucous membranes in the upper respiratory tract (e.g. injected pharynx, dry cracked lips or strawberry tongue)
- change in the extremities (e.g. oedema, erythema or desquamation)
- polymorphous rash
- cervical lymphadenopathy.

Healthcare professionals should be aware that, in rare cases, incomplete/atypical Kawasaki disease may be diagnosed with fewer features.

4.7 Imported infections

The management of children with imported infections is beyond the scope of this guideline. However, the GDG recognised that significant numbers of children do enter or return to the UK from overseas each year. Some of these children will have been in countries where tropical and sub-tropical infectious diseases such as malaria and typhoid fever are endemic. Accordingly, the GDG decided to make the recommendation below.

Recommendation on imported infections

When assessing a child with feverish illness, healthcare professionals should enquire about recent travel abroad and should consider the possibility of imported infections according to the region visited.

5 Management by remote assessment

5.1 Introduction

When a concerned parent or carer decides to make contact with a healthcare professional about a feverish child, the initial contact may be by telephone and in these circumstances a remote assessment may be undertaken. In this context, 'remote' refers to the assessment of the child's symptoms carried out by an assessor who is *geographically remote* from the child. It is common practice for remote assessment to be carried out during the out-of-hours period and, similarly, remote assessment may be a prerequisite for patients requesting an urgent in-hours appointment with their GP. Specific advice lines also exist, such as the 0845 4647 service offered by NHS Direct. 999 calls to the ambulance service are similarly assessed in order to determine the urgency of the response required.

The purpose of the remote assessment is to identify the level of care the child needs and to refer to the most appropriate location of care to meet those needs within an appropriate time frame. This process will include the identification of those with potentially life-threatening compromise to airway, breathing, circulation and level of consciousness, those with symptoms suggestive of serious illness and also identification of those children who are most likely to have a self-limiting illness and for whom care at home is the most appropriate option.

The skills and experience of the healthcare professional carrying out the remote assessment will vary and their assessment may or may not be supported by decision support software or other paper-based protocols. Remote assessment can be difficult as the assessor has only the symptoms reported by the caller on which to base the assessment. An additional difficulty, particularly when assessing a small child, is that the quality of information reported by the caller is likely to be variable and may be influenced by parental/carer concern. Symptoms which concern one parent/carer may not concern another and similarly symptoms which concern a parent/carer may not be those which most concern a healthcare professional.

It is essential that listening and critical thinking skills are employed throughout the assessment in order to ensure that all cues are identified and interpreted appropriately. This will include taking into account the level of parental/carer concern, the cause of which may not be easy to pinpoint. At times, however, it will be possible to identify a likely cause of the fever and that being the case the appropriate guidance for that condition should be followed.

In some circumstances the child may not be geographically remote from the assessor but physical examination of the child may not fall within the scope of practice for that healthcare professional. The assessor may thus feel it is more appropriate to follow the remote assessment guidance rather than that for face-to-face assessment which takes into account signs found on physical examination.

5.2 Clinical assessment

It is assumed that children with feverish illnesses undergoing a remote assessment will have a clinical assessment as decribed in Chapter 4. By necessity, the emphasis will be on detecting symptoms rather than physical signs. The first priority is to identify any immediately life-threatening features, including compromise of the airway, breathing, circulation and level of consciousness. Children with feverish illness should then be assessed for the presence or absence of symptoms that predict the risk of serious illness using the traffic light system (see Table 4.1). Finally, the healthcare professional should seek the presence of symptoms that might suggest a particular diagnosis.

5.3 Management according to risk of serious illness

Evidence summary and GDG statement

The GDG sought evidence that might refer particularly to the clinical evaluation of risk of serious illness by remote assessment or might direct management in this situation. No additional studies were found to add to the body of evidence which is described in Chapter 4. None of the studies found were specific to remote assessment or gave an indication of the time frame within which interventions should occur. With the exception of studies concerning the subjective detection of fever by parents and carers (Section 3.3), no studies were found validating symptoms reported by parents or carers on remote assessment.

In line with the evidence presented in Chapter 4, the GDG concluded that children with immediately life-threatening features should receive emergency care. Children with 'red' features should be referred for an urgent face-to-face assessment, preferably within primary care. Those with 'amber' features would also require a face-to-face asessment although usually there would be less urgency. As decribed in Chapter 4, children with 'green' features only are at very low risk of serious illness and can be cared for at home. For children requiring an urgent face-to-face assessment, the GDG felt it was important to define the time frame within which an urgent assessment should be carried out because children with 'red' features are at high risk of having a serious illness. The GDG was unable to achieve consensus among themselves about the time limit for an urgent assessment and this question was therefore put out to formal consensus. The GDG used the Delphi panel to establish the definition of 'urgent' in the context of referral for further assessment.

Delphi consensus

Background

Parents or carers often phone healthcare professionals for advice (e.g. NHS Direct, GP surgery) when their child has a fever.

The GDG has identified a number of symptoms which may indicate SBI (such as meningitis or pneumonia) and should prompt a 999 call. Other symptoms have been identified which warrant an urgent referral for a face-to-face assessment.

Delphi statement 2.1

An urgent face-to-face assessment means that a child should be seen within:

2 hours	6 hours	12 hours	24 hours	Don't know	Total	Median
43 (83%)	5 (10%)	1 (2%)	0	3 (6%)	52	2

In the first round consensus (83%) was reached that an urgent face-to-face assessment means that a child should be seen within 2 hours.

Health economics

The GDG recognised that the requirement for a face-to-face assessment within 2 hours for children with 'red' features may have health economic implications. In particular, the recommendation could be seen as producing an increase in the number of children referred from remote assessment to face-to-face assessment within this timescale. A detailed justification of this recommendation on clinical and health economic grounds was therefore developed. This is included in the guideline as Appendix E. In summary, the GDG concluded that the recommendation on urgent assessment would not represent an uplift in the provision of care for the following reasons:

- Children with 'red' features are at significant risk of serious illness and death.
- The traffic light system would encourage the referral of children with 'red' features for urgent assessment while discouraging the referral of the much larger number of children with 'green' features and most children with 'amber' features.
- 2 hours is an existing standard for referral for face-to-face assessment by out-of-hours providers and NHS Direct.

- Fewer than 3% children undergoing remote assessment are likely to have 'red' features. At present a greater proportion of children with fever undergoing assessment by NHS Direct are referred for urgent consultation.

GDG translation

The GDG recognised that remote assessment of symptoms and signs can be difficult as the quality of the information provided can vary.

However, some children will need an immediate assessment in view of the serious nature of the symptoms or combination of symptoms reported.

Other children will need an urgent face-to-face review by a healthcare professional who can examine the child.

The GDG felt it was not appropriate to identify individual symptoms as immediately life threatening because healthcare professionals will need to make a judgment in individual cases, based on the overall picture described.

As a result of stakeholder feedback and to ensure clarity of the recommendation, the GDG made the decision to combine the recommendation about which children should have an urgent face-to-face assessment and the recommendation about the time frame within which that assessment should take place into a single recommendation.

The GDG recognised that owing to the limitations of remote assessment, some children who are not seriously ill will be referred for urgent face-to-face assessment based on symptoms reported but not subsequently confirmed on examination. Nevertheless, the health economic analysis suggested that the recommendation of a 2 hour limit for urgent assessment could save lives and would not present an undue burden to the health service.

The GDG recognised that there have been no prognostic or validation studies on the predictive value of symptoms reported to remote assessors in children with feverish illness. It was therefore decided to call for research in this area.

Recommendations on management according to risk of serious illness

Healthcare professionals performing a remote assessment of a child with fever should seek to identify symptoms and signs of serious illness and specific diseases as described in Chapter 4 and summarised in Tables 4.1 and 4.4.

Children whose symptoms or combination of symptoms suggest an immediately life-threatening illness (see Chapter 4) should be referred immediately for emergency medical care by the most appropriate means of transport (usually 999 ambulance).

Children with any 'red' features but who are not considered to have an immediately life-threatening illness should be urgently assessed by a healthcare professional in a face-to-face setting within 2 hours.

Children with 'amber' but no 'red' features should be assessed by a healthcare professional in a face-to-face setting. The urgency of this assessment should be determined by the clinical judgment of the healthcare professional carrying out the remote assessment.

Children with 'green' features and none of the 'amber' or 'red' features can be managed at home with appropriate advice for parents and carers, including advice on when to seek further attention from the healthcare services (see Chapter 9).

Research recommendation on management according to risk of serious illness

The GDG recommends that a UK study is undertaken to determine the validity of symptoms reported on remote assessment for children with fever.

6 Management by the non-paediatric practitioner

6.1 Introduction

Parents or carers of young children may seek a face-to-face assessment of their feverish child or be directed to do so following a remote assessment. There are an increasing number of professionals who may make this assessment. These include their GP, a nurse-practitioner in a walk-in centre, a pharmacist or an emergency department doctor. This guideline uses the term non-paediatric practitioner for this group. The setting of the assessment, although important, is less relevant than the experience and training of the healthcare professional undertaking the assessment. For this reason, the GDG has separated recommendations pertaining to the non-paediatric practitioner assessment from those of the paediatric specialist. It has been assumed throughout that both the paediatric specialist and non-paediatric practitioner have the skills required to make a clinical assessment of a feverish child.

The initial face-to-face assessment of the feverish child is very important. The vast majority of children presenting to the non-paediatric practitioner with fever will have a condition that can be diagnosed, assessed and treated appropriately there and then or with simple follow-up arrangements.

In some cases, following assessment, the non-paediatric practitioner may refer the child to paediatric services for an opinion, for further necessary investigations that cannot be carried out in primary care, or for further treatment and care.

Fever without apparent source

A small number of children with fever will present with no obvious underlying source, and a small number of these will have a serious illness requiring further investigation and treatment by a paediatric specialist.

It is not always possible to distinguish serious illness from non-serious illness in the early stages of the condition. Safety netting is therefore vital to ensure that parents/carers and clinician agree when further care should be accessed and how. This may include, but not exclusively, a fixed appointment, formal liaison with other parts of the health system such as out-of-hours providers, or simple advice.

6.1.1 Safety netting

Following a consultation and the making of a provisional diagnosis and management plan, it is good practice for the healthcare professional to consider the following three questions:

- If I am right, what do I expect to happen?
- How will we know if I am wrong?
- What should happen then?

Safety netting is not a new concept.[151] It may take a number of forms, from dialogue with carer/parent about 'amber' and 'red' symptoms and signs they should watch for, review after a set period or liaising with other healthcare services. Good safety netting ensures continuity of care and a provision for possible deterioration of a child.

The GDG was unable to be prescriptive about safety netting since this will be determined by the actual practitioner carrying out the assessment and their professional competences and the range of services available locally. For example, a rural GP might use a different set of safety nets than a nurse working in an urban walk-in centre when dealing with the same child.

The GDG felt that safety netting was particularly important when a child presents with 'amber' features (see below), which were not felt to require automatic referral to secondary care at that time.

6.2 Clinical assessment

It is assumed that children with feverish illnesses presenting to a non-paediatric practitioner will undergo a face-to-face clinical assessment as described in Chapter 4. The first priority is to identify any immediately life-threatening features, including compromise of the airway, breathing, circulation and level of consciousness. Children with feverish illness should then be assessed for the presence or absence of symptoms and signs that predict the risk of serious illness using the traffic light system (see Table 4.1). Finally, the healthcare professional should look for a focus of infection or other symptoms and signs that might suggest a particular diagnosis.

Recommendation on clinical assessment by the non-paediatric practitioner

Management by a non-paediatric practitioner should start with a clinical assessment as described in Chapter 4. Healthcare practitioners should attempt to identify symptoms and signs of serious illness and specific diseases as summarised in Tables 4.1 and 4.4.

6.3 Management according to risk of serious illness

Evidence summary

The GDG was unable to find evidence to direct the management of children with fever in terms of referral to specialist care or care at home according to the risk of serious illness.

GDG statement

After an assessment of a febrile child has been made, the non-paediatric specialist has the following management options:

If a diagnosis has been reached:

- reassurance to parents and carers that this is a self-limiting illness
- explanation, discussion and organising treatment options
- home care advice and safety netting
- refer for specialist paediatric treatment.

If no diagnosis has been reached:

- reassurance to parents and carers that this is probably a self-limiting illness given the absence of significant symptoms or signs
- perform some tests to help determine the diagnosis
- provide a safety net
- refer for specialist paediatric assessment.

A feverish child considered to have an immediately life-threatening illness should be transferred without delay to the care of a paediatric specialist by the most appropriate means of transport (usually 999 ambulance).

Health economics

The GDG recognised that in order to improve the NHS's ability to detect serious illness in children, it might be necessary to assess more, both in primary care and secondary care. The GDG also recognised that the number of children with 'amber' features with no focus on infection is a small proportion of face-to-face and remote access healthcare contacts by children with fever, and children with 'red' features make up an even smaller proportion of these children. Data on this is lacking, but the GDG consensus was that a normal GP practice will see an incidence of 1/100 children/year with 'red' symptoms, and a district general hospital may see three patients a week.

Attempts at modelling this were made but the number of possible variables and lack of evidence regarding outcomes impeded these attempts (see Appendix C).

GDG translation

The GDG determined that children with fever receiving non-specialist care should be referred or allowed home according to their risk of serious illness, as defined in the traffic light table. Children with 'red' features are at risk of serious illness and should usually be referred to a paediatric specialist by the most appropriate route. Children with 'amber' features are at intermediate risk and should be provided with a safety net that may also involve referral to a specialist. The decision as to what form the safety net takes will depend on the experience, training and expertise of the non-specialist clinician. It will also depend on the local health service configuration and the family's social situation.

The GDG recognised that adherence to the recommendations in this section may cause changes in referral patterns between primary and secondary care. The health economists attempted to model these patterns but could not find sufficient evidence about current referral patterns and the associated risks. The GDG called for research to be undertaken so that the health economic model could be populated.

Recommendations on management according to risk of serious illness

Children whose symptoms or combination of symptoms and signs suggest an immediately life-threatening illness (see Chapter 4) should be referred immediately for emergency medical care by the most appropriate means of transport (usually 999 ambulance).

Children with any 'red' features but who are not considered to have an immediately life-threatening illness should be referred urgently to the care of a paediatric specialist.

If any 'amber' features are present and no diagnosis has been reached, healthcare professionals should provide parents or carers with a 'safety net' or refer to specialist paediatric care for further assessment. The safety net should be one or more of the following:

- providing the parent or carer with verbal and/or written information on warning symptoms and how further health care can be accessed (see Chapter 9)
- arranging further follow-up at a specified time and place
- liaising with other healthcare professionals, including out-of-hours providers, to ensure direct access for the child if further assessment is required.

Children with 'green' features and none of the 'amber' or 'red' features can be managed at home with appropriate advice for parents and carers, including advice on when to seek further attention from the healthcare services (see Chapter 9).

Research recommendation on management according to risk of serious illness

The GDG recommends that research is carried out on referral patterns between primary and secondary care for children with fever, so the health economic impact of this and future guidelines can be estimated.

6.4 Tests by the non-paediatric practitioner

In children with fever who are not referred to hospital, the use of investigations is determined by both pragmatic factors and clinical value. The delay in obtaining results of blood tests may preclude their use in non-specialist care.

Clinical question

In children presenting to primary care with fever and no obvious focus of infection, what is the predictive value of the following investigations in identifying children with a serious illness?

- urinalysis
- chest X-ray
- pulse oximetry
- capillary glucose.

The use of pulse oximetry and capillary glucose in the evaluation of children with fever was discussed but no evidence was found for or against their use. The GDG was unable to make a recommendation about these two investigations. Evidence was available regarding the use of chest X-rays and urine testing.

6.4.1 Chest X-rays

The GDG considered the question whether clinical acumen plus chest X-ray is better than clinical acumen alone in diagnosing chest infection in children aged 2 months to 59 months.

Narrative evidence

One EL 1+ SR[152] including one RCT[153] investigating the effects of chest radiography for children with acute lower respiratory infections was identified. They found that the odds of recovery by 7 days were 1.03 (95% CI 0.64 to 1.64). The OR for remaining ill at both 4 and 14 days were 0.74 (95% CI 0.45 to 1.23) and 0.82 (95% CI 0.45 to 1.48) for the study and control group, respectively. Thirty-three percent of radiography participants and 32% of control participants made a subsequent hospital visit within 4 weeks (OR 1.02, 95% CI 0.71 to 1.48); 3% of both radiography and control participants were subsequently admitted to hospital within 4 weeks (OR 1.02, 95% CI 0.40 to 2.60).

Evidence summary

There was one systematic review of chest radiographs in children who met the criteria for clinical pneumonia, which included only one randomised controlled trial. This study of 522 children aged 2 months to 5 years demonstrated that children with clinical features of pneumonia based on the World Health Organization (WHO) criteria were less likely to be prescribed antibiotics, more likely to be diagnosed with bronchiolitis and had exactly the same rates of recovery, repeat attendance rates and subsequent admission rates when compared with those children who underwent a chest X-ray.

GDG translation

The GDG felt that in the presence of clinical signs of pneumonia or bronchiolitis, a chest X-ray is of no added diagnostic benefit in ambulatory care.

Recommendation on chest X-rays

Children with symptoms and signs suggesting pneumonia who are not admitted to hospital should not routinely have a chest X-ray.

6.4.2 Urinalysis

In children with fever, urine should be tested for infection as described in *Urinary Tract Infection in Children*.*

Recommendation on urinalysis

Urine should be tested on children with fever as recommended in *Urinary Tract Infection in Children*.*

6.5 Use of antibiotics by the non-paediatric practitioner

There are two situations in which a GP or prescribing professional may want to give antibiotics to a child with fever in the absence of a firm diagnosis of a bacterial infection. These are, firstly, in a

* NICE clinical guideline (publication expected August 2007).

child who is not particularly unwell and where the focus of infection cannot be found or initially established, and, secondly, in a very unwell child where the prescribing professional wants to prevent deterioration before transfer to hospital. This guideline relates to fever in children in both circumstances. Antibiotics have sometimes been prescribed empirically in this situation. The rationale behind this is sometimes put that these antibiotics might treat an unapparent bacterial infection or prevent development of SBI. The temptation for a healthcare professional to recommend antibiotics may be increased by parental expectations and pressure.

However, inappropriate prescribing of antibiotics is a major cause of antibiotic resistance. Antibiotics also have adverse effects, commonly rash and diarrhoea but also severe reactions such as allergy, anaphylaxis and Stevens–Johnson syndrome.

The use of antibiotics in children without a specific bacterial infection is thus not regarded as good clinical practice except when meningococcal disease is suspected, where immediate parenteral benzylpenicillin is currently recommended.[154]

6.5.1 Oral antibiotics

Clinical question

What are the benefits and risks of giving oral antibiotics to febrile children with no known focus of infection and no symptoms or signs of serious illness?

Narrative evidence

Three studies were found that evaluated antibiotics in children with no major focus of infection and who were well appearing. Two were EL 2+ SRs comprising eleven and four papers, respectively.[155,156] They examined the effect of oral and parenteral antibiotics in preventing SBI in well-appearing children with *Streptococcus pneumoniae* occult bacteraemia. Fewer cases of SBIs but not meningitis were observed to develop in those children treated with antibiotics, compared with those who were not ($P = 0.003$). Furthermore, both oral and parenteral antibiotics were found to be equally effective in preventing SBI, which resulted in extremely low rates of complications observed in both groups (pooled OR = 1.48 in each group). Similarly, in another EL 1+ RCT[157] which looked at the effect of antibiotic treatment (amoxicillin) for acute otitis media in children between 6 months and 2 years, there was a reduced risk of 13% in the persistence of symptoms on day 4 in the amoxicillin group compared with the group which did not take amoxicillin (risk difference 13%, 95% CI 1% to 25%). In addition, median duration of fever was 2 days in the amoxicillin group versus 3 days in the placebo group ($P = 0.004$). Analgesic consumption was also higher in the group that went without antibiotics during the first 10 days (4.1 versus 2.3 doses, $P = 0.004$). However, no significant difference was observed in duration of pain or crying. No otoscopic differences were observed at days 4 and 11, and hearing tests findings were similar in both groups at 6 weeks The researchers concluded that, since seven to eight children aged 6–24 months with acute otitis media needed to be treated with antibiotics to improve symptomatic outcome on day 4 in one child, the modest effect does not justify the prescription of antibiotics at first visit.

Decreasing inappropriate antibiotic prescribing for children may also help decrease antibiotic resistance. In Finland, after nationwide reductions in the use of macrolide antibiotics for outpatient therapy, there was a significant decline in the frequency of erythromycin resistance among group A streptococci.[158]

Evidence summary

There is some evidence that oral antibiotics may decrease the risk of developing complications in children with *Streptococcus pneumoniae* occult bactaeremia, but insufficient evidence to conclude that it prevents meningitis.

There was no significant difference between children who were treated with oral or parenteral antibiotics.

However, over 1000 children at risk of occult pneumococcal bacteraemia would need to be treated to possibly reduce one case of meningitis.[159] There is evidence that campaigns to reduce the prescription of oral antibiotics are associated with a reduction in antimicrobial resistance.[158]

Health economics

There are very wide variations at both local and national levels in both rates and costs of antibiotic prescribing, with little evidence of associated variations in morbidity from infections. A decrease in inappropriate prescribing might also reduce antibiotic resistance. A decrease in inappropriate antibiotic prescribing would provide a saving in the overall NHS prescribing costs and delay antibiotic resistence. It is also possible that reduced antibiotic prescribing might increase the need or demand for reassessment and hospital admission of a febrile child either during surgery hours or by out-of-hours service providers, but while it would be possible to undertake research to assess the impact on healthcare demand (and costs and savings) of changes in antibiotic prescribing for children with suspected SBI, the GDG did not identify relevant data on this for the guideline.

GDG translation

The vast majority of well-appearing children (97%) with fever without cause do not have occult bacteraemia, and they will therefore not benefit from empirical oral antibiotics.

Occult pneumococccal bacteraemia is likely to be reduced markedly after conjugate pneumococcal vaccine was introduced in the routine UK immunisation schedule in September 2006.

Even for infections such as otitis media, the modest effect does not justify the prescription of antibiotics at first visit (NNT = 7–8).

The GDG also recognised the risks of the unnecessary prescribing of antibiotics such as adverse side effects and the development of antimicrobial resistance. The GDG also acknowledged the possibility of cost savings.

Recommendation on oral antibiotics

Oral antibiotics should not be prescribed to children with fever without apparent source.

6.5.2 Empirical treatment with parenteral antibiotics

Clinical question

When should children in primary care be treated with empirical parenteral antibiotics in an attempt to decrease mortality or morbidity?

Narrative evidence

Two studies[159,160] that reported on the effect of empirical antibiotics on reducing mortality and morbidity were identified. An EL 2++ SR[159] comprising 14 studies evaluated the effectiveness of such antibiotics in reducing case fatality in meningococcal disease in patients of all ages. Twelve of the papers contained information on parenteral antibiotics given before admission and outcome, of which eight showed that there was a beneficial effect in giving parenteral antibiotics before admission and four reported an adverse effect. Risk ratios for mortality in these studies ranged from 0.16 (95% CI 0.01 to 2.63) to 2.36 (95% CI 0.25 to 22.54). Only one study reported a statistically significant result (risk ratio 0.35, 95% CI 0.16 to 0.80).[161] Since the proportion of cases treated differed among the reported studies (differences ranged from 15% to 59%, chi-squared for heterogeneity was 11.02 ($P = 0.09$), $I^2 = 46\%$ (95% uncertainty interval 0% to 77%)), studies were reported and examined on an individual basis. The reviewers could not conclude whether or not antibiotics given before admission had an effect on case fatality. However, they stated that the data are consistent with benefit when a substantial proportion of cases are treated.

A recent EL 2++[160] case–control study that was not included in the SR was also found. The study looked at the use of parenteral penicillin by GPs who had made the diagnosis of meningococcal disease in 26 children who died from the condition, and 132 survivors. Administration of parenteral penicillin was associated with increased risk of death (OR 7.4, 95% CI 1.5 to 37.7). Children who received penicillin had more severe disease on admission (median Glasgow meningococcal septicaemia prognostic score 6.5 versus 4.0, $P = 0.002$). The association between parenteral penicillin and poor outcome may be because children who were more severely ill were given penicillin before admission.

Evidence summary

In meningococcal disease, the evidence cannot conclude whether or not parenteral antibiotics given before admission have an effect on case fatality. However, the data are consistent with benefit when a substantial proportion of cases are treated.

Health economics

Since the evidence of effectiveness is equivocal, the cost-effectiveness of parenteral antibiotics cannot be established.

GDG translation

The GDG noted that all good-quality evidence referred to meningococcal disease and therefore looked at meningococcal disease in great detail compared with the other SBIs. Meningococcal disease is the leading infectious cause of mortality among children in the UK. No evidence on empirical treatment with parenteral antibiotics was found for other conditions, including meningitis, and therefore these conditions do not appear in the evidence tables. However, the GDG noted that current advice on immediate treatment in primary care refers to meningitis as well as meningococcal disease.

Children with meningococcal disease may benefit from pre-admission parenteral antibiotics, especially if most children with meningococcal disease are treated.

The GDG considers that there is insufficient evidence of effectiveness or cost-effectiveness to change the current UK practice (to give parenteral antibiotics at the earliest opportunity). As with oral antibiotics, the difference in costs (including consumables) should be taken into account when prescribing. Treatment should normally be initiated with the drug with the lowest cost (taking consumables into account).

Recommendation on empirical treatment with parenteral antibiotics

Children with suspected meningococcal disease should be given parenteral antibiotics at the earliest opportunity (either benzylpenicillin or a third-generation cephalosporin).

7 Management by the paediatric specialist

7.1 Introduction

Young children with fever presenting to a paediatric specialist may be assessed initially by a non-paediatric practitioner or they may present directly to specialist care. Those children referred by a healthcare professional after an initial assessment are probably in a higher risk group for having a serious illness than those who are self-referred, although some may be referred simply for the opinion of a specialist because of uncertainty. Children who are reassessed because of parental concerns are probably also in a higher risk group for having a serious illness. For this reason, the recommendations have been separated into the assessment made by the non-paediatric practitioner and by the paediatric specialist. It has been assumed that both the paediatric specialist and non-paediatric practitioner have the skills required to make a clinical assessment of a feverish child. However, it has also been assumed that the paediatric specialist will have the training to perform, and access to, some investigations that may be necessary to complete the assessment of some febrile children. Almost all the tests and initial management considered in this chapter are part of the standard package of routine care for children with suspected SBI referred for specialist paediatric management. The guideline has reviewed the evidence of effectiveness for each intervention individually. In cases where the clinical benefit of a specific test or intervention has not been established, the recommendation is that these tests should not be performed, thus increasing the potential cost-effectiveness of care in this setting.

7.2 Clinical assessment

It is assumed that children with feverish illnesses presenting to paediatric specialist care will be assessed or reassessed using the 'traffic light' features described in Chapter 4. In addition to looking for these features, the clinician will look for a focus of infection or other symptoms and signs that might suggest a particular diagnosis.

Recommendation on clinical assessment by the paediatric specialist

Management by the paediatric specialist should start with a clinical assessment as described in Chapter 4 The healthcare professional should attempt to identify symptoms and signs of serious illness and specific diseases as summarised in Tables 4.1 and 4.4.

7.3 Children less than 3 months old

Although fever in the young infant is relatively uncommon, when it occurs there is a higher risk of SBI than in later life. Hospital Episode Statistics suggest that the incidence of the serious illnesses defined in this guideline are 19 316 per 100 000 for infants less than 3 months old in England, compared with 1400 per 100 000 for all children less than 5 years old. The neonate is at risk of rapidly developing infection because of a relatively poorly developed immune system and of permanent disability, especially from meningitis. Babies born preterm or with low birthweight are particularly vulnerable. The infections may be those acquired from the mother at the time of delivery (e.g. group B streptococcus), or hospital- or community-acquired infections. Rarely, devastating infections such as disseminated herpes simplex may present in the neonatal period. The host response to these infections and those presenting later in early infancy is fairly non-specific. For this reason, the GDG decided to provide separate recommendations for this group.

Narrative evidence

The studies suggested that SBI, particularly meningitis and UTI, are more common in the first 3 months than later in childhood. Among a series of infants in this age group with fever, the incidence of SBI lies in the range 6–10%.[108,162,163]

Three EL 2+ studies[108,162,164] and an EL 2+ meta-analysis[163] were found suggesting that neither clinical examination alone nor any single test is able to identify those with SBI. However, clinical assessment and investigations combined can help to identify those infants more likely to have SBI. These babies appear ill to the clinician and/or have one or more abnormal test results from the following:

- WBC > 15 × 10^9/litre
- urine microscopy > 10 WBC per high power field (hpf)
- cerebrospinal fluid (CSF) with > 8 WBC per hpf or positive gram stain
- if diarrhoea is present more than 5 WBC per hpf in stool.

Another meta-analysis[152] of febrile infants less than 3 months old studied the usefulness of chest X-rays. This showed that chest radiographs were normal in 361 infants without respiratory signs. However, of 256 infants with one or more respiratory sign, 85 (33.2%) had positive chest radiographs for pneumonia. Signs included tachypnoea more than 50 breaths/minute, rales (crackles), rhonchi (wheeze), coryza, grunting, stridor, nasal flaring and cough.

An EL 1+ SR comprising six studies[165] which examined whether procalcitonin (PCT) was a useful marker of SBI in neonates and children was also found. A significant increase in serum PCT concentration during sepsis was found in both term neonates and a heterogeneous group of preterm neonates. However, PCT lacked specificity compared with C-reactive protein (CRP) as an early marker in the diagnosis of SBI. The performance characteristics of CRP as a marker of SBI varied as different cut-off levels were used in the various studies.

GDG translation

Because young infants with fever are at relatively high risk of SBI (especially meningitis) which cannot be predicted by clinical features alone, the GDG concluded that, on the basis of clinical effectiveness and cost-effectiveness, all febrile infants less than 3 months old require basic investigation as well as observation. This is not a change to usual clinical practice for this patient group. Those in the high-risk groups (neonates and those appearing unwell or with WBC < 5 × 10^9/litre or > 15 × 10^9/litre) should also be investigated for meningitis and receive empirical parenteral antibiotics, since they have the highest risk of infection. The GDG was unable to recommend a specific cut-off level for CRP, but expected paediatric specialists to use the CRP result as part of their overall assessment of a child with fever.

Recommendations on management of children less than 3 months old

Infants younger than 3 months with fever should be observed and have the following vital signs measured and recorded:

- temperature
- heart rate
- respiratory rate.

Infants younger than 3 months with fever should have the following investigations performed:

- full blood count
- blood culture
- C-reactive protein
- urine testing for urinary tract infection*
- chest X-ray only if respiratory signs are present
- stool culture, if diarrhoea is present.

* See *Urinary Tract Infection in Children*, NICE clinical guideline (publication expected August 2007).

Lumbar puncture should be performed on the following children (unless contraindicated):

- infants younger than 1 month
- all infants aged 1–3 months who appear unwell
- infants aged 1–3 months with white blood cell count (WBC) less than 5×10^9/litre or greater than 15×10^9/litre.

When indicated, a lumbar puncture should be performed without delay and, whenever possible, before the administration of antibiotics.

Parenteral antibiotics should be given to:

- infants younger than 1 month
- all infants aged 1–3 months who appear unwell
- infants aged 1–3 months with WBC less than 5×10^9/litre or greater than 15×10^9/litre.

When parenteral antibiotics are indicated for infants less than 3 months of age, a third-generation cephalosporin (e.g. cefotaxime or ceftriaxone) should be given plus an antibiotic active against listeria (e.g. ampicillin or amoxicillin).

7.4 Children aged 3 months or older

7.4.1 Investigation by the paediatric specialist

Young children with fever will present to the paediatric specialist in three groups. The first group will appear well, with no symptoms or signs of serious illness, the vast majority of these children having viral or self-limiting illnesses (children with only 'green' symptoms/signs). A few of these children will have bacterial infections but they will not be identifiable by clinical assessment alone. This is particularly true of children less than 3 months of age and for this reason their management by the paediatric specialist is covered in a dedicated section of this chapter (Section 7.3). Information is required regarding which serious illnesses occur in well-appearing children with fever, together with evidence of which investigations may help to identify these children.

A second group of children will arrive appearing very unwell with symptoms and signs of serious illness (mostly 'red' symptoms/signs) and will often be given immediate empirical antibiotic treatment.

The final group comprises those children with fever displaying symptoms and/or signs which may indicate the presence of a serious illness (one or more 'amber' or 'red' symptoms/signs). Few investigations will give results quickly enough to definitively identify serious illness in this group. For example, bacterial cultures will identify those with meningitis or bacteraemia but these results take 24–36 hours to become available. Treatment for these conditions should not be delayed until these results are available. It may be that identification of serious infection comes from a combination of signs and symptoms as well as simple tests such as WBC, etc. Markers of inflammation (e.g. WBC, CRP) may help to identify children with serious illness.

One controversial area is occult bacteraemia. Well-appearing children with fever can have bacteria in their blood, often pneumococcus. Most of these children will clear the bacteria without any antibiotic treatment, whereas a few will go on to develop significant sequelae, such as persistent bacteraemia and meningitis. Most information on this condition is from the USA and Australia, with little if any from the UK. In the USA, meningococcal disease occurs much less frequently than in the UK. A raised WBC has been used in the USA to identify those at increased risk of occult bacteraemia; however, in the UK this might not detect cases of meningococcaemia, as only one-third of cases have a raised WBC on presentation. US data on the prevalence and causes of occult bacteraemia need to be viewed cautiously and UK data sought. The pattern of occult pneumococcal bacteraemia is also likely to change in the UK in 2006–07 following the introduction of conjugate pneumococcal vaccine to the childhood immunisation schedule.

Clinical question

In a febrile child what is the predictive value of the following in detecting serious illness?

- WBC
- absolute neutrophil count (ANC)

- CRP
- PCT
- ESR
- urinalysis
- lumbar puncture
- chest X-ray
- combination of those above.

Narrative evidence

White blood cell count

Nine studies[166–174] evaluating WBC as a diagnostic marker for serious illness were found. The age ranges for these studies were birth to 16 years but in seven studies the upper limit was 36 months (age range mode: 3–36 months). Conditions studied were serious bacterial infection (SBI), meningococcal disease (MCD), bacterial meningitis, occult bacterial infection (OBI) and bacterial pneumonia. The cut-off value for WBC ranged from 15 to 17.1 × 10^9/litre. The ranges of performance of WBC as a marker of the presence of these serious illnesses were reported as sensitivity 20–76%, specificity 58–100% and RR 1.5–5.56.

Although one EL II study[168] did demonstrate a 'perfect' specificity of 100% with a WBC of > 15 × 10^9/litre identifying all children with SBI, the next highest result was 77%. Another EL II study[175] demonstrated an increased prevalence of occult bacteraemia with increasing height of fever and increasing WBC, but this was a US study conducted before the introduction of the conjugate pneumococcal vaccine, recently added to the UK childhood immunisation programme. These data are therefore likely to be less useful now.

One EL II prospective cohort study[176] looked at the combination of WBC > 20 × 10^9/litre combined with fever > 39 °C in identifying 'occult pneumonia' (i.e. those with no clinical evidence of pneumonia) in children less than 5 years old. Between 26% and 30% of children with both these features had pneumonia on chest X-ray.

Absolute neutrophil count

Three EL II studies[169–171] evaluating absolute neutrophil count (ANC) were found. Two looked at children aged 1–36 months[169,171] and one at children aged 3–36 months.[170] The studies evaluated markers to identify SBI and OBI or to differentiate invasive bacterial infection from localised bacterial or viral infection.[170] The cut-off values for ANC were 10.2,[169] 10.6[170] and 9.6 × 10^9/litre.[170] The ranges of performance of ANC in identifying SBI were reported as sensitivity 50–71%, specificity 76–83% and RR 1.5–6.4.

C-reactive protein

A heterogeneous group of 11 EL II prospective cohort studies[166–174,178] evaluating CRP was identified. Age ranges for these studies were birth to 16 years, but only three EL II studies contained data on children older than 36 months.[166,172,174] Conditions studied were SBI, MCD, bacterial meningitis, bacteraemia, OBI and bacterial pneumonia. The cut-off value for CRP varied from 27.5 to 70 mg/litre. Table 7.1 shows sensitivities, specificities and relative risks for CRP values in identifying serious illness or discriminating non-serious from serious illness for each study.

Two other EL II studies[170,171] looked at differences in CRP depending on the timing of the sample from the onset of symptoms. There was no significant difference in sensitivity or specificity between those CRP values collected more than 12 hours after the onset of feverish illness compared with those collected less than 12 hours after onset.[170] Slightly lower sensitivity (61.3% versus 63.5%) and specificity (80% versus 84.2%) was reported for CRP in infants when taken less than 12 hours after the onset of symptoms, but this was at a lower cut-off value of 19 mg/litre.[170] Furthermore, the study which evaluated the differences in CRP performance at greater than and less than 12 months old was examined. At a CRP cut-off value of 40 mg/litre, for children less than 12 months old, sensitivity and specificity were reported to be 94% and 84%, respectively (RR 31.5), whereas for those greater than 12 months old, sensitivity and specificity were reported as 80% and 59%, respectively (RR 4.0).

This study also demonstrated increased post-test probability of SBI with increasing CRP (10% at CRP < 40 mg/litre versus 86% at CRP > 100 mg/litre).

Table 7.1 Summary of sensitivity, specificity and relative risk of included studies evaluating CRP

Study	CRP cut-off (mg/litre)	Sensitivity (%)	Specificity (%)	Relative risk
Galetto-Lacour[178a]	40	79	79	6.1
Galetto-Lacour[178a]	40	89	75	12.75
Carrol[166]	30	81	89	3.79
Thayyil[167]	50	75	68.7	5.23
Kohli[168]	40	95	86	33.5
Pulliam[169]	70	79	91	13
Isaacman[170]	44	63	81	5.0
Fernandez[171]	27.5	63.5	84.2	1.97
Gendrel[172]	20	73	88	5.43
Lembo[173]	10	80	55	2.3
Moulin[174b]	60	69.8	52	1.94
Moulin[174b]	20	88.4	40	2.14

[a] Galetto-Lacour *et al*. produced two papers from the same data set
[b] Moulin *et al*. performed analysis at two CRP cut-off values

Procalcitonin

An EL 1+ SR[165] looking at 46 articles which evaluated the role of PCT as an early marker of infection in neonates and young children was identified. Neonatal studies regarding the investigation of children less than 3 months of age are discussed in Section 7.3 of this chapter. The findings of the SR against each clinical condition are summarised below.

Sepsis and meningitis

In children greater than 3 months old, PCT was found to have a significantly better diagnostic performance than CRP or WBC in identifying sepsis, septic shock and meningitis. PCT is also excellent in discriminating between viral and bacterial, and localised and invasive, bacterial infections. There was variation in the cut-off values used for PCT in the studies, with 2 ng/ml being most commonly reported as the best cut-off for distinguishing these groups. PCT was also found to perform better than CRP in identifying bacterial infection in children who had developed fever less than 12 hours prior to presentation. However, the authors added that since the negative predictive value of PCT is not always 100%, it can not be considered a gold standard and a normal PCT level could conceivably falsely reassure clinicians.[165]

Lower respiratory tract infection

Six of the studies looked at PCT as a marker for bacterial lower respiratory tract infection (LRTI) in children. Of these, three found PCT to be more effective than either CRP or WBC in differentiating bacterial from viral LRTI, whereas the other three studies found PCT to be of little value. This inconsistency may have been due to difficulty and differences in the confirmation of bacterial LRTI and also confounded by the use of antibiotics prior to measurement of PCT. PCT is known to fall rapidly once a bacterial infection is appropriately treated compared with CRP, which will fall more slowly and may even rise initially.[165]

Fever without localising signs

In another EL II study,[178] the authors reported the results of PCT assessed in children with fever without localising signs. Children treated with antibiotics during the preceding 2 days were excluded. PCT was more sensitive (93% versus 79%) but less specific (74% versus 79%) than CRP for predicting SBI (bacteraemia, pyelonephritis, lobar pneumonia and meningitis) in children with fever without apparent source.

In addition to this systematic review,[165] one prospective EL II cohort study[167] studied 72 children 1–36 months old with fever without apparent source. Eight (11.1%) children had SBI (one pneumonia, two meningitis, four septicaemia/occult bacteraemia, two pyelonephritis), In identifying

SBI in this group, PCT at a cut-off value of 2 ng/ml showed a sensitivity of 50% and a specificity of 85.9%. In comparison, at a cut-off of 50 mg/litre, CRP showed a sensitivity and specificity of 75% and 68.7% respectively, while the Yale Observation Score had a sensitivity of 87.5% and specificity of 67.2%.

Chest X-ray

The diagnostic performance of chest X-ray in children with fever without apparent source (FWS) in relation to WBC is described above. In addition, one EL 1b SR[179] and one EL II prospective cohort study[180] were found that examined the diagnostic performance of chest radiography in differentiating bacterial and viral pneumonia in children.

The SR looked at five studies which used credible reference standards for identifying bacterial and viral infection. The authors considered identification of a bacterial pneumonia to be a positive test and of a viral pneumonia to be a negative test. As a result of heterogeneity in the studies, the authors could not report on comparable measures of diagnostic accuracy for each of the five studies. Rather, the researchers calculated likelihood ratios (LRs) for each study, as a measure of clinical usefulness of the chest X-ray. Commenting that LRs between 0.5 and 2.0 are rarely clinically useful, they reported no LRs outside these levels in the studies reviewed. The authors concluded that no clinically useful degree of accuracy had been demonstrated with regard to differentiating bacterial from viral pneumonia using chest radiography.

In an EL II study[180] of children admitted to hospital with community-acquired pneumonia, those with bacterial pneumonia had a significantly higher incidence of alveolar infiltrates compared with those with exclusively viral disease (72% versus 49%, $P = 0.001$). In children with exclusively interstitial infiltrates, half had bacterial infection and half viral.

Evidence summary

In children older than 3 months with fever without apparent source who appear well, 5% will have a bacterial infection, likely to be UTI or pneumonia. Occult bacteraemia is not often seen in the UK and is likely to decrease with the introduction of the universal pneumococcal vaccination. The currently available tests (CRP, PCT and WBC) do not improve the detection of SBI in this group, compared with features from the YOS.

In children who have fever with no focus but who display signs and symptoms that indicate a higher risk of serious illness, investigations looking for markers of bacterial infection may be useful, especially PCT and CRP. However, none will identify all children with serious illness. PCT appears to outperform CRP in identifying sepsis and meningitis in this group, using a cut-off value for PCT of around 2 ng/ml. This difference was not large, however, and after allowing for 95% confidence intervals may conceivably be even smaller. CRP still performs reasonably well at a typical cut-off value of 20 mg/litre. WBC and ANC perform less well than either CRP or PCT in helping to identify the presence of SBI. A combination of temperature > 39 °C and a WBC > 20×10^9/litre does, however, have a high specificity for occult pneumonia. Evidence is conflicting regarding the performance of chest radiography in differentiating bacterial and viral pneumonia in children but, at best, it has limited clinical usefulness.

Few studies were found looking at the usefulness of markers of bacterial infection in the management of children with fever without apparent source presenting to the paediatric specialist who were considered sufficiently unwell that intravenous anti-bacterial treatment should be initiated empirically. The sensitivities and specificities for CRP and PCT were not high enough to be able to definitively rule in or rule out serious illness and thus influence the decision to stop or to continue intravenous antibiotic treatment after it had been started. A raised CRP and/or PCT is not diagnostic of serious illness but can be useful as an aid to ongoing management of this group of patients.

Health economics

An economic evaluation was undertaken to assess the cost-effectiveness of CRP versus PCT to investigate the presence of SBI in children without apparent source (Appendix D). Health economic evaluation was required since PCT is not routinely used. All other diagnostic tests are offered on the NHS and are part of the usual package of tests for children over 3 months where SBI is suspected. The results indicated that under certain assumptions CRP is both less costly

and more effective than PCT in correctly diagnosing and ruling out SBI in children with FWS. However, the results were sensitive to the prevalence of SBI. CRP no longer dominated PCT when the prevalence of SBI was over 27%, keeping all the other baseline assumptions constant. However, given the lack of robust evidence underpinning these baseline assumptions, the analysis cannot support the replacement of CRP with PCT at present. The GDG has recommended more research on the performance characteristics of CRP and PCT in children with feverish illness of uncertain cause.

GDG translation

'Green' group

Because tests such as CRP, PCT and WBC do not improve the detection of SBI in this group, the GDG concluded that routine blood tests on well-appearing children with fever are not justified. This would not change current practice since well-appearing children over 3 months old with fever rarely have blood tests in the UK at present. In contrast, there is a significant risk of UTI in this group and only by testing the urine will this be identified.

'Amber' and 'red' groups

Although PCT is more sensitive than CRP in identifying sepsis and meningitis in young children with fever, the GDG did not feel that this difference was sufficient to recommend PCT over CRP, potentially changing current UK practice. The GDG noted that there was only limited evidence on the use of PCT in children with fever without apparent source, and they decided to call for more research in this area. In children with no symptoms or signs of pneumonia, a combination of temperature > 39 °C and a WBC > 20 × 10^9/litre has a high specificity for bacterial pneumonia and therefore the GDG concluded that a chest X-ray is indicated in this small group of children. In children considered sufficiently unwell to require empiric antibiotics, the GDG acknowledged that the result of a CRP or WBC would not influence immediate management. However, they should be measured as an aid to ongoing management of this group.

Recommendations on investigations by the paediatric specialist (children aged 3 months or older)

'Red' group

Children with fever without apparent source presenting to paediatric specialists with one or more 'red' features should have the following investigations performed:

- full blood count
- blood culture
- C-reactive protein
- urine testing for urinary tract infection.*

The following investigations should also be considered in children with 'red' features, as guided by the clinical assessment:

- lumbar puncture in children of all ages (if not contraindicated)
- chest X-ray irrespective of body temperature and white blood cell count (WBC)
- serum electrolytes and blood gas.

'Amber' group

Children with fever without apparent source presenting to paediatric specialists who have one or more 'amber' features should have the following investigations performed unless deemed unnecessary by an experienced paediatrician:

- urine should be collected and tested for urinary tract infection*
- blood tests: full blood count, C- reactive protein and blood cultures
- lumbar puncture should be considered for children younger than 1 year
- chest X-ray in a child with a fever greater than 39 °C and white blood cell count (WBC) greater than 20 × 10^9/litre.

* See *Urinary Tract Infection in Children*, NICE clinical guideline (publication expected August 2007).

'Green' group

Children who have been referred to a paediatric specialist with fever without apparent source and who have no features of serious illness (that is, the 'green' group) should have urine tested for urinary tract infection* and be assessed for symptoms and signs of pneumonia.

Routine blood tests and chest X-rays should not be performed on children with fever who have no features of serious illness (that is, the 'green' group).

Research recommendation on investigations by the paediatric specialist (children aged 3 months or older)

The GDG recommends that a UK study of the performance characteristics and cost-effectiveness of procalcitonin versus C-reactive protein in identifying serious bacterial infection in children with fever without apparent source be carried out.

7.4.2 Viral co-infection

Only a minority of young children with fever have bacterial infections. The rest are presumed to have viral infections, although these are rarely confirmed and mostly do not need treatment. If it were possible to identify those children with definite viral infections, this might help identify those at low risk of serious illness. However, if bacterial infection co-existed with viral infection then differentiating between serious and non-serious illness would not be helped by identifying those with viral infection.

Clinical question

What is the incidence of co-existing bacterial infection in a child presenting with fever in which a virus (e.g. influenza or RSV) is detected (with a rapid test)?

Narrative evidence

Three EL 3 retrospective studies[181–183] which investigated co-existing bacterial infection in children with respiratory syncytial virus (RSV) infection were found. One retrospective cohort[181] investigated the prevalence of co-existing SBI in 178 children less than 8 weeks old with proven RSV infection and fever. Those children with RSV were over five times more likely to have an increased work of breathing compared with those who were RSV negative (RR 5.1, 95% CI 2.9 to 8.9). The other two retrospective cross-sectional studies investigated children with influenza virus[182] and RSV respiratory tract infection.[183] The odds of any SBI were 72% less in children who tested positive for influenza than in those who did not (OR 0.28, 95% CI 0.16 to 0.48).[182] Febrile RSV-positive infants had a lower rate of bacteraemia compared with febrile RSV-negative infants (1.1% versus 2.3%). Similarly, none of the febrile children with RSV respiratory tract infection tested had positive cerebrospinal cultures, but urinary tract infection was found in 14% of those less than 3 months old and 8.4% of those over 3 months old.[183]

Evidence summary

The incidence of SBI is lower in feverish children with proven RSV or influenza infections compared with those in whom viral investigations are negative. However, SBI, especially UTI and influenza/RSV, infections can co-exist.

GDG translation

Since children with proven viral infection still have a risk of SBI (although this was reduced compared with children without proven viral infection), the GDG felt that they should be assessed for serious illness in the same way as other children. Those with no features of serious illness should have urine tested, while those with features of serious illness should be assessed by a paediatric specialist. Given that rapid detection of viral illness (such as influenza or RSV infection) does not exclude a co-existing SBI, the GDG recognised that the use of these tests is not an efficient use of scarce healthcare resources.

Recommendation on viral co-infection

Febrile children with proven respiratory syncytial virus or influenza infection should be assessed for features of serious illness. Consideration should be given to urine testing for urinary tract infection.*

7.4.3 Observation in hospital

Children with fever are often observed in hospital for a period of time to help differentiate those with serious illness from those with non-serious illness. This observation usually involves the repeated measurement of 'vital signs' such as heart rate, respiratory rate and temperature, as well as repeated assessments of the child to look for the development of any clinical features that would give cause for concern. Investigations, if indicated, can also be done and their results sometimes obtained during a period of observation.

Clinical question

In a child with fever what are the benefits, if any, of a period of observation on an assessment facility?

GDG statement

The GDG found limited research to show the overall benefits of a period of observation in the paediatric assessment unit of the child with fever, in terms of cases of serious illness identified, hospital admission, morbidity, mortality and recovery. Delphi consensus was sought in an attempt to answer the question as to whether or not observation itself can help to differentiate feverish children with non-serious and serious illness. In addition, the Delphi panel were asked to decide how long such a period of observation should be.

Delphi statement 5.1

A period of observation in hospital (with or without investigations) as part of an assessment can help differentiate minor from serious bacterial illness (such as meningitis or pneumonia) in a young child who has a fever without obvious cause.

1 to 3	4 to 6	7 to 9	Don't know	Missing	Total	Median
0	6 (12%)	44 (85%)	2 (4%)		52	8

Delphi statement 5.2

The period of observation in a hospital to help differentiate minor from serious illness in a young child over 3 months of age with fever without obvious cause should be approximately:

2 hours	4 hours	6 hours	12 hours	Don't know	Total	Median
1 (2%)	3 (6%)	26 (50%)	10 (19%)	12 (23%)	52	6

There was 85% agreement (consensus achieved) for Statement 5.1 but no consensus reached for Statement 5.2.

GDG translation

The GDG accepted that Delphi consensus agreeing that a period of observation of young children with fever in hospital was useful in differentiating those with minor illness from those with serious illness. The GDG believes that this period of observation is likely to be cost-effective for the NHS since the cost of observation is outweighed by savings from preventing unnecessary diagnostic tests from being undertaken in children with minor illness. The GDG acknowledged that no evidence was found nor consensus reached to determine the ideal duration of such a period of observation. Since febrile infants less than 3 months of age have an increased risk of SBI which can be missed by observation alone, the guideline does not suggest observation alone in this age group.

* See *Urinary Tract Infection in Children*, NICE clinical guideline (publication expected August 2007).

Recommendation on observation in hospital

In children aged 3 months or older with fever without apparent source, a period of observation in hospital (with or without investigations) should be considered as part of an assessment to help differentiate non-serious from serious illness.

7.4.4 Response to antipyretic medication

It has been suggested that response to antipyretic medication may help differentiate serious from non-serious illness in febrile children. This could occur in two ways:

- a decrease in fever
- improved clinical appearance.

Decrease in fever after antipyretics

Some healthcare professionals think that a decrease in fever with antipyretic therapy indicates a lower likelihood of SBI. It is also assumed that a lack of response to antipyretic therapy makes an SBI more likely. In contrast to this, other healthcare professionals fear that giving antipyretics to reduce fever in febrile children may make the detection of serious illness more difficult as the high fever of bacterial illness is 'masked' by antipyretics. Evidence about fever response to antipyretics in children with both serious and non-serious illness would be useful to help in the assessment of these children.

Improved clinical appearance after antipyretics

Antipyretics may also improve the child's general condition. Many healthcare professionals feel that clinical review of a febrile child 1–2 hours after they have been given antipyretics improves the ability to differentiate between serious and non-serious illness. The antipyretic and analgesic effect of antipyretics may lead to the improvement of features which may suggest serious illness (e.g. irritability, tachycardia, etc). If this improvement in features occurred only in those with non-serious illness, this would help to identify these children. However, if this improvement also occurred in children with serious illness, then these children may not have their illness identified correctly.

Evidence about improved clinical appearance after antipyretics would be useful to help in the assessment of children and would also be relevant to the use of observation in febrile children.

Clinical question

In a child with fever, does a failure to respond to antipyretics increase the likelihood of a serious illness?

Sub-question

Conversely, does a reduction in body temperature in response to antipyretics increase the likelihood of a self-limiting illness?

Narrative evidence

Five EL 2+ prospective cohort studies[162,184–187] and one EL 4 conference abstract,[188] which was judged to be important for inclusion, investigating the relationship between a reduction of body temperature due to antipyretics and the likelihood of serious illness were identified. Four of these[162,184,185, 187,188] were conducted in the USA and one in Japan.[186] All these studies were hospital cohorts with different dosages and type of antipyretics (paracetamol 15 mg/kg[184,185] or 10 mg/kg of paracetamol or aspirin[162,185,186]), different ages of children included (3–24 months,[162,185,186] 8 weeks to 6 years[187] or < 24 months[188]), different definitions of fever and different methods of measuring body temperature. The evidence suggests that a change in temperature 1–2 hours after antipyretics does not help identify children with serious illness. However, assessment with YOS 1 hour after antipyretics seems more specific. The mean repeat YOS was 13.7 in children with serious illness compared with 10.0 in the children without serious illness ($P = 0.004$).[189]

Evidence summary

The results from prospective cohort studies showed that a change in temperature 1–2 hours after antipyretics does not help identify children with serious illness. However, children with serious illness generally appear more ill than those without serious illness after antipyretics.

GDG translation

Some healthcare professionals think that a decrease in temperature after antipyretics makes an SBI less likely. The GDG concluded that this is not supported by evidence. Children with YOS > 10 mostly have 'amber' or 'red' features. The GDG found some evidence that if these children are reassessed after antipyretics, the features may have resolved in those without serious illness. Reassessment after antipyretics may help differentiate those with and without serious illness but the GDG recognised that more research could usefully be undertaken on this subject.

Recommendation on response to antipyretic medication

When a child has been given antipyretics:

- healthcare professionals should not rely on a decrease or lack of decrease in temperature after 1–2 hours to differentiate between serious and non-serious illness
- children in hospital with 'amber' or 'red' features should be reassessed after 1–2 hours.

Research recommendation on response to antipyretic medication

The GDG recommends that studies are conducted in primary care and secondary care to determine whether examination or re-examination after a dose of antipyretic medication is of benefit in differentiating children with serious illness from those with other conditions.

7.5 Immediate treatment by the paediatric specialist

Some children with fever have life-threatening serious illness which requires immediate treatment to improve their chances of survival. These treatments will be:

- directed against the causative organism (antibiotics, aciclovir)
- directed against the consequences of the infection, such as shock or respiratory failure (intravenous fluids, oxygen)
- directed against the inflammation caused by the infection (corticosteroids).

Many of these immediate treatments are endorsed in paediatric advanced life support courses and are therefore commonly used in the UK. Specific guidance for the immediate treatment of suspected meningococcal disease was also considered.

Clinical question

For children with symptoms and signs of a serious illness what immediate treatments improve their outcome?

Evidence of the effect of the following interventions in the treatment of serious illness was looked for:

- intravenous fluids
- steroids
- antibiotics
- aciclovir
- oxygen.

7.5.1 Intravenous fluids

Narrative evidence

Two SRs and three RCTs which looked at the use of intravenous fluids as immediate treatments were identified.

The first EL 1++ SR[190] evaluated three RCTs investigating the effect of maintenance fluid volumes in meningitis. Maintenance fluid was calculated as 100 ml/kg per day given for the first 10 kg body weight of the child, 50 ml/kg for the second 10 kg, and 20 ml/kg for over 20 kg. This was given intravenously for the first 48 hours for all three studies. The maintenance fluid volumes were compared with restricted fluid volumes 60% of the initial maintenance fluids. All three studies investigated both children and adults with acute bacterial meningitis. Pooling of

the results of all three trials showed no significant difference between deaths in the maintenance and restricted fluid groups (RR 0.82, 95% CI 0.53 to 1.27). However, the risk of long-term neurological sequelae (spasticity, hemiparesis/hemiplegia, visual impairment and response to sound) was found to be significantly lower in the maintenance fluid group compared with the restricted fluid group (RR 0.42, 95% CI 0.20 to 0.89).

The second EL 1+ SR[191] involving 30 RCTs quantified the effect on mortality of administering either human albumin or plasma protein fraction during the management of 1419 critically ill patients. All patients were reported to have been critically ill as a result of hypovolaemia (state of decrease in the volume of blood plasma, which is characteristic of shock) due to trauma, surgery, burns or hypoalbuminaemia. The risk of death was 1.68 times more in the albumin group compared with the plasma protein group when the results of all the trials were summarised and pooled together (RR 1.68, 95% CI 1.26 to 2.23).

Three studies of which one was an EL 1++[192] study and two EL 1+ studies[50,193] were also found. The first RCT[192] EL 1++ compared the effect of fluid resuscitation with albumin or saline on mortality in both children and adults in the intensive care unit (n = 6997). There was no significant difference in the risk of death in the albumin group compared with the saline group (P = 0.87). At 28 days, there was still no difference in either group in the number of participants that remained in the ICU or hospital (P = 0.09 and 0.10, respectively). These researchers concluded that there was no appreciable difference in the survival times of either group.

The second RCT[50] evaluated the efficacy of normal saline and colloid (polymer from degraded gelatine in saline (Haemaccel)) intravenous fluid in restoration of circulating volume in children aged 0–12 years with septic shock. The median volume of fluid needed for initial resuscitation was significantly higher in the saline group compared with the gelatine group: 50 ml/kg (range 20–108) versus 30 ml (range 20–70) (P = 0.018). However, there was no difference in the time taken for resuscitation between the groups (P = 0.41).

The third RCT[193] determined whether moderate oral fluid restriction (nasogastric tube at 60% of normal maintenance volumes) or intravenous fluid (half-normal saline + 5% dextrose at 100% of normal maintenance volumes at full maintenance volumes) would result in a better outcome, for 346 children with bacterial meningitis, for the first 48 hours of treatment. There was no appreciable reduction in the risk of death or neurological sequelae in either group (P = 0.11).[193]

A fourth EL 2+ case–control study[11] investigated 143 children under 17 years who died from meningococcal diseases matched by age with 355 survivors from the same region of the country. The aim of the study was to determine whether suboptimal management in hospital contributed to poor outcome in children admitted with meningococcal disease. Inadequacies in fluid therapy in terms of too little versus adequate fluid therapy (OR 2.5, 95% CI 1.4 to 4.7, P< 0.004) and inadequate inotropes (OR 5.8, 95% CI 2.3 to14, P< 0.001) were significantly associated with death.

A further retrospective cohort study of children who presented to local hospitals with septic shock reviewed shock reversal (defined by return of normal systolic blood pressure and capillary refill time) and outcome. Shock reversal was successfully achieved in 24 (26%) children, which was associated with 96% survival and a nine-fold increased odds of survival (OR 9.49, 95% CI 1.07 to 3.89). Shock reversal was achieved by both fluid boluses and the early use of inotropes.[194]

Evidence summary

Many of the papers in the evidence table referred to maintenance intravenous therapy for bacterial meningitis, a subject that is outside the scope of this guideline. The GDG decided to address only studies that dealt with intravenous fluids for immediate resuscitation. Resuscitation with intravenous fluids in children with fever and signs of circulatory insufficiency is associated with lower mortality. Failure to administer sufficient intravenous fluids in children with meningococcal disease and septic shock is associated with higher risk of mortality. There is insufficient evidence to recommend colloid over crystalloid fluid and vice versa.

Health economics

The GDG recognises that there is a substantial cost difference, with crystalloids being considerably cheaper than colloids.

GDG translation

The GDG concluded that children with fever and signs of circulatory insufficiency have reduced mortality when given intravenous fluid resuscitation. Current practice would be to give a bolus of 20 ml/kg. The GDG recognises that there is unresolved debate about the relative merits of crystalloid and colloid fluids for this purpose. There remain concerns about the risks of infection from blood products, such as albumin. From a health economics perspective the GDG would favour the use of crystalloids. The GDG was aware that there is particular debate about the relative merits of albumin and crystalloid in the initial treatment of meningococcal disease, but making a recommendation on this issue was considered beyond the scope of this guideline.

Recommendation on intravenous fluids

Children with fever and shock presenting to specialist paediatric care or an emergency department should be:

- given an immediate intravenous fluid bolus of 20 ml/kg; the initial fluid should normally be 0.9% sodium chloride
- actively monitored and given further fluid boluses as necessary.

7.5.2 Steroids

Narrative evidence

One EL 1+ SR[195] which looked at 18 RCTs investigating the effect of adjuvant corticosteroids on mortality, severe hearing loss and neurological sequelae, in the treatment of children and adults with acute bacterial meningitis was found. Overall, the number of participants who died was significantly smaller in the corticosteroid group compared with the placebo group: 8.5% versus 11.6% (RR 0.76, 95% CI 0.59 to 0.97). However, this effect on mortality was not seen in the subgroup of children (RR 0.95, 95% CI 0.65 to 1.37).

The administration of corticosteroids before or with the first dose of antibiotics was associated with a decreased risk of hearing loss. This was also evident for children with *Haemophilus influenzae* type b meningitis (RR 0.31, 95% CI 0.15 to 0.62) and for those with pathogens other than *Haemophilus influenzae* (RR 0.42, 95% CI 0.20 to 0.89).

Evidence summary

For children with bacterial meningitis the early use of steroids may decrease hearing loss. However, this was most evident for children with *Haemophilus influenzae* type b and possibly pneumococcal meningitis.

GDG translation

The GDG found no evidence to support the use of steroids other than in the early treatment of bacterial meningitis, which falls outside the scope of this guideline. The GDG noted the effect of steroids reported in the systematic review, but was unsure about the applicability in the UK, especially in the era of *Haemophilus influenzae* type b and pneumococcal vaccines. The GDG was unable to make a recommendation.

7.5.3 Antibiotics

Narrative evidence

One EL 2– cohort study[196] which evaluated the effect of empirical antibiotics on the outcome of SBI was found.

The prospective cohort study of critically ill adults[196] studied the relationship between inadequate antimicrobial treatment of infections (community-acquired and hospital-acquired) and hospital mortality for patients requiring ICU admission. The mortality rate of infected patients receiving inadequate antimicrobial treatment (52%) was significantly greater than the hospital mortality rate of patients without this risk factor (12%) (RR 4.26, 95% CI 3.52 to 5.15, $P < 0.001$).

Evidence summary

Critically ill children with SBI who are given no or ineffective antibiotics have an increased risk of mortality.

GDG translation

A diagnosis of SBI (especially bacteraemia) may not be confirmed until 12–36 hours from time of culture, since it takes this period of time to grow bacteria. Antibiotic treatment should not be delayed in a critically ill child until bacterial illness is confirmed, since the child may die during this period. Empirical antibiotic treatment should be given to critically ill children, at the earliest opportunity once SBI is suspected.

Recommendations on antibiotics

Children with fever presenting to specialist paediatric care or an emergency department should be given immediate parenteral antibiotics if they are:

- shocked
- unrousable
- showing signs of meningococcal disease.

Immediate parenteral antibiotics should be considered for children with fever and reduced levels of consciousness. In these cases symptoms and signs of meningitis and herpes simplex encephalitis should be sought (see Table 4.4).

When parenteral antibiotics are indicated, a third-generation cephalosporin (for example, cefotaxime or ceftriaxone) should be given, until culture results are available. For children younger than 3 months, an antibiotic active against listeria (for example ampicillin or amoxicillin) should also be given.

7.5.4 Aciclovir

Narrative evidence

Three EL 1– RCTs[197–199] looking at the treatment of serious illness with aciclovir were identified. Two of the RCTs[197,198] compared vidarabine and aciclovir as treatment in adults and children with herpes simplex encephalitis. The study which examined 208 adults reported more deaths (54% versus 28%, $P = 0.008$) and increased mortality (38% versus 14%, $P = 0.021$) in the vidarabine recipients than in the aciclovir recipients.[197] The study which looked at 210 infants less than 1 month old found no difference between vidarabine and aciclovir in either morbidity ($P = 0.83$) or mortality ($P = 0.27$).[198]

The third open-label RCT[199] estimated the treatment efficiency of high-dose aciclovir (HD, 60 mg/kg per day), intermediate dose (ID, 45 mg/kg per day) and standard dose (SD, 30 mg/kg per day) with regard to mortality and morbidity in 88 infants less than 28 days old. The survival rate for neonatal herpex simplex virus infection was found to be 3.3 times higher in those children treated with HD (OR 3.3, 95% CI 1.5 to 7.3). In addition, the children treated with HD aciclovir were 6.6 times more likely to be developmentally normal at 12 months of age, compared with children treated with standard dose therapy.

A large EL 3 retrospective multicentre study[200] studied prognostic factors for herpes simplex encephalitis in adult patients. A delay of greater than 2 days between admission to the hospital and initiation of aciclovir therapy was strongly associated with a poor outcome (OR 3.1, 95% CI 1.1 to 9.1, $P = 0.037$). However, there was still a favourable outcome for 55 of the patients (65%).

Evidence summary

Treatment with aciclovir decreases morbidity and mortality in adults and children with herpes simplex encephalitis. Treatment with aciclovir within 48 hours of admission improves the outcome in herpes simplex encephalitis.

GDG translation

The GDG recognised the difficulty in the early identification and treatment of children with herpes simplex encephalitis as the early features may be non-specific. The diagnosis of herpes

simplex encephalitis may not be confirmed for a number of days after admission as initial investigations can be normal. Early treatment with aciclovir improves outcome in herpes simplex encephalitis.

Recommendation on aciclovir

Children with fever and symptoms and signs suggestive of herpes simplex encephalitis should be given intravenous aciclovir.

7.5.5 Oxygen

Evidence summary

There was a lack of evidence meeting the inclusion criteria examining the effect upon outcome of administering oxygen to the child with symptoms and signs of serious illness.

GDG translation

Recommendations regarding treatment with oxygen were made based on GDG consensus.

Recommendations on oxygen

Oxygen should be given to children with fever who have signs of shock or oxygen saturation (SpO_2) of less than 92% when breathing air.

Treatment with oxygen should also be considered for children with an SpO_2 of greater than 92%, as clinically indicated.

7.6 Causes and incidence of serious bacterial infection

Antimicrobial therapy has significantly improved the outcome for children with SBI. The appropriate antibiotic treatment for SBI will often not be determined for 24–36 hours, since it takes this period of time to grow bacteria and determine their antibiotic sensitivities. However, antibiotic treatment should not be withheld until the causative organism and its antibiotic sensitivities are confirmed, since the child may die or suffer harm in the meantime. Empirical antibiotic treatment is therefore given to children likely to have serious illness. Knowledge of the common organisms causing SBI in children will help decide which antibiotics should be used as empirical treatment for children likely to have SBI.

Clinical questions

What are the most common organisms causing serious illness in young children with fever?

What is the incidence of serious illness in young children with fever?

Narrative evidence

A search for UK-based cohort studies after 1992 found four EL 2+ retrospective studies.[121,201–203] The studies varied in baseline characteristics. For example, one study[121] recruited children aged 8 days to 16 years and another had children of 2 weeks to 4.8 years.[202] Moreover, some studies[201] recruited based on the presenting features of infectious disease or meningococcal disease[121] while others recruited children with a diagnosis of pneumonia[202] or bacterial meningitis.[203]

Hospital Episode Statistics (HES) was also reviewed as a proxy of incidence of serious illness in England and Wales. The data suggested that UTI (217.2/100 000), pneumonia (111.9/100 000), bacteraemia (105.3/100 000) and meningitis (23.8/100 000) were the most likely infections in children aged 7 days to 5 years admitted to hospital in England and Wales.[204]

Moreover, the likely organisms to cause these infections are *Neisseria meningitidis*, *Streptococcus pneumoniae*, *Escherichia coli*, *Staphylococcus aureus* and *Haemophilus influenzae* type b. In children less than 3 months of age, group B streptococcus and listeria may also cause SBI.[203]

Evidence summary

Serious bacterial infection in a child presenting to hospital with fever but without an identified focus is likely to be bacteraemia, meningitis, UTI or pneumonia. The likely organisms to

cause these infections are *Neisseria meningitidis*, *Streptococcus pneumoniae*, *Escherichia coli*, *Staphylococcus aureus* and *Haemophilus influenzae* type b (rare in immunised children). In children less than 3 months of age, group B streptococcus and listeria may also cause SBI.

GDG translation

The GDG noted the causes of SBI and the likely organisms at various ages. The GDG believes that this information could be used to decide which antibiotics could be used when it is decided to treat a suspected SBI without apparent source and in the absence of the results of microbiological cultures. A third-generation cephalosporin (e.g. cefotaxime or ceftriaxone) might not be the treatment of choice for all these organisms but was felt to be adequate initial treatment. This empirical antibiotic treatment could be altered once culture results became available or the focus of infection became apparent.

Recommendations on causes and incidence of serious bacterial infection

In a child presenting to hospital with a fever and suspected serious bacterial infection, requiring immediate treatment, antibiotics should be directed against *Neisseria meningitidis, Streptococcus pneumoniae, Escherichia coli, Staphylococcus aureus* and *Haemophilus influenzae* type b. A third-generation cephalosporin (for example cefotaxime or ceftriaxone) is appropriate, until culture results are available. For infants younger than 3 months, an antibiotic active against listeria (for example ampicillin or amoxicillin) should be added.

Healthcare professionals should refer to local treatment guidelines when rates of bacterial antibiotic resistance are significant.

7.7 Admission to and discharge from hospital

Admission to hospital is frightening for many young children and disruptive for their families. A child with fever should only be admitted to hospital when absolutely necessary. Some conditions require frequent monitoring and treatment adjustments, which can only be done in hospital. Other conditions may be managed at home, sometimes with community healthcare support, such as 'Hospital at Home' schemes. The ability to manage a child at home will vary according to local facilities. The conditions that need admission to hospital will therefore vary.

Factors other than the child's clinical condition can also influence the decision to admit a child with fever to hospital. These will include particular risk factors,. such as travel to an area where malaria occurs, the family's previous experience of illness and the ability of the family to return if their child's condition worsens.

Clinical question

What factors other than the child's clinical condition should be considered when deciding to admit a child with fever to hospital?

Evidence summary

No evidence was found about when to admit children with fever to hospital.

GDG statement

The GDG agreed that the decision to admit or discharge a child with feverish illness should be made on the basis of clinical acumen after the child has been assessed (or reassessed) for the features of serious illness (i.e. 'red' or 'amber') and taking into account the results of investigations. The GDG also recognised that personal and social factors should also be taken into account when deciding whether or not to admit a child with fever to hospital. In the absence of evidence as to what these factors should be, the GDG decided it was appropriate to use the Delphi technique to inform the recommendation on admission to hospital.

When a child has a fever and no features of serious illness it is not usually necessary or appropriate for them to be cared for in hospital. However, there are circumstances where healthcare professionals should consider things apart from the child's clinical condition when deciding whether or not a child needs to be admitted to hospital, especially if alternative support systems,

such as children's community nurses, are not available. No evidence was available for this topic. The GDG therefore used the Delphi panel to help produce broadly applicable recommendations in this area.

Delphi statement 6

Healthcare professionals should consider the following factors, as well as the child's clinical condition, when deciding whether to admit a child with fever to hospital.

6.a Social and family circumstances

First round

1 to 3	4 to 6	7 to 9	Don't know	Missing	Total	Median
7 (13%)	20 (38%)	25 (47%)	1 (2%)		53	6

Second round

1 to 3	4 to 6	7 to 9	Don't know	Missing	Total	Median
2 (4%)	17 (33%)	33 (64%)			52	7

6.b Other illnesses suffered by the child or other family members

First round

1 to 3	4 to 6	7 to 9	Don't know	Missing	Total	Median
2 (4%)	17 (32%)	32 (60%)	2 (4%)		53	7

Second round

1 to 3	4 to 6	7 to 9	Don't know	Missing	Total	Median
1 (2%)	10 (19%)	41 (79%)			52	7.5

6.c Parental anxiety and instinct (based on their knowledge of their child)

First round

1 to 3	4 to 6	7 to 9	Don't know	Missing	Total	Median
1 (2%)	14 (26%)	37 (70%)	1 (2%)		53	8

Second round

1 to 3	4 to 6	7 to 9	Don't know	Missing	Total	Median
2 (4%)	7 (13%)	43 (83%)			52	8

6.g Contacts with other people who have serious infectious diseases

First round

1 to 3	4 to 6	7 to 9	Don't know	Missing	Total	Median
4 (8%)	17 (32%)	28 (53%)	4 (8%)		53	7

Second round

1 to 3	4 to 6	7 to 9	Don't know	Missing	Total	Median
1 (2%)	8 (15%)	42 (81%)	1 (2%)		52	8

6.h Recent travel abroad to tropical/subtropical areas, or areas with a high risk of endemic infectious disease

First round

1 to 3	4 to 6	7 to 9	Don't know	Missing	Total	Median
7 (13%)	12 (23%)	32 (60%)	2 (4%)		53	7

Second round

1 to 3	4 to 6	7 to 9	Don't know	Missing	Total	Median
1 (2%)	2 (4%)	48 (92%)			51	8

6.i When the parent or carer's concern for their child's current illness has caused them to seek support or advice repeatedly

First round

1 to 3	4 to 6	7 to 9	Don't know	Missing	Total	Median
7 (13%)	15 (28%)	30 (57%)	1 (2%)		53	7

Second round

1 to 3	4 to 6	7 to 9	Don't know	Missing	Total	Median
2 (11%)	11 (22%)	38 (75%)			51	8

6.j Where the family has experienced a previous illness or death due to feverish illness which has increased their anxiety levels

First round

1 to 3	4 to 6	7 to 9	Don't know	Missing	Total	Median
2 (4%)	13 (25%)	37 (70%)	1 (2%)		53	8

Second round

1 to 3	4 to 6	7 to 9	Don't know	Missing	Total	Median
1 (2%)	9 (17%)	42 (81%)			52	8

6.k When a feverish illness has no obvious cause, but the child remains ill longer than expected for a self-limiting illness

First round

1 to 3	4 to 6	7 to 9	Don't know	Missing	Total	Median
2 (4%)	13 (25%)	36 (70%)	1 (2%)	1	52	7

Second round

1 to 3	4 to 6	7 to 9	Don't know	Missing	Total	Median
2 (4%)	9 (17%)	41 (79%)			52	8

GDG translation

Seven statements achieved agreement by the Delphi panel and were therefore used as recommendations.

An eighth factor (6.a Social and family circumstances) did not achieve the required level of agreement (64% scored 7–9; Median score 7). However, the GDG was aware of the associations between social deprivation and infection, hospital admission and death. The GDG decided this was an important factor to consider and unanimously agreed to include this as a recommendation.

Recommendations on admission to and discharge from hospital

In addition to the child's clinical condition, healthcare professionals should consider the following factors when deciding whether to admit a child with fever to hospital:

- social and family circumstances
- other illnesses that affect the child or other family members
- parental anxiety and instinct (based on their knowledge of their child)
- contacts with other people who have serious infectious diseases
- recent travel abroad to tropical/subtropical areas, or areas with a high risk of endemic infectious disease
- when the parent or carer's concern for their child's current illness has caused them to seek healthcare advice repeatedly
- where the family has experienced a previous serious illness or death due to feverish illness which has increased their anxiety levels
- when a feverish illness has no obvious cause, but the child remains ill longer than expected for a self-limiting illness.

If it is decided that a child does not need to be admitted to hospital, but no diagnosis has been reached, a safety net should be provided for parents and carers if any 'red' or 'amber' features are present. The safety net should be one or more of the following:

- providing the parent or carer with verbal and/or written information on warning symptoms and how further health care can be accessed (see Chapter 9)
- arranging further follow-up at a specified time and place
- liaising with other healthcare professionals, including out-of-hours providers, to ensure direct access for the child if further assessment is required.

Children with 'green' features and none of the 'amber' or 'red' features can be managed at home with appropriate advice for parents and carers, including advice on when to seek further attention from the healthcare services (see Chapter 9).

7.8 Referral to paediatric intensive care

Children with life-threatening infections may require paediatric intensive care. This is most likely to be beneficial if intensivists are involved in the child's management at an early stage.

GDG translation

The GDG agreed that children with the features of life-threatening illness that require immediate antibiotic treatment are also those likely to require paediatric intensive care. These children should be assessed and discussed with an intensivist at an early stage of their management.

Recommendation on referral to paediatric intensive care

Children with fever who are shocked, unrousable or showing signs of meningococcal disease should be urgently reviewed by an experienced paediatrician and consideration given to referral to paediatric intensive care.

7.9 Suspected meningococcal disease

The management of individual serious illnesses is strictly beyond the scope of this guideline. However, the GDG did come across evidence from the literature searches that they felt should be included in the guidance. The use of fluids for resuscitation in meningococcal disease is discussed in Section 7.5.1 above.

Narrative evidence

Evidence for the use of immediate parenteral antibiotics is presented in Sections 6.5 and 7.5.3. An EL 2+[11] case–control study on the provision of health care for survivors and those who subsequently died from meningococcal disease was discussed earlier. In this study,[11] the failure to recognise disease complications, particularly in the absence of specific paediatric care, was associated with an 8.7-fold increase in the risk of death ($P = 0.002$). Not being under the care of a paediatrician was associated with a 66-fold increase ($P = 0.005$), failure of supervision a 19.5-fold increase ($P = 0.015$) and failure to administer inotropes a 23.7-fold increase ($P = 0.005$) in the risk of death. Not being under paediatric care was also highly correlated with a failure to recognise complications ($P = 0.002$; Fisher's exact test).

Evidence summary

In meningococcal disease, the evidence cannot conclude whether or not parenteral antibiotics given before admission have an effect on case fatality. However, the data are consistent with benefit when a substantial proportion of cases are treated. Failure to recognise complications of the disease increases the risk of death, as does not being under the care of a paediatric specialist.

GDG translation

The GDG noted that meningococcal disease is the leading cause of mortality among infectious diseases in childhood. Children with meningococcal disease may benefit from immediate parenteral antibiotics, especially if most children with meningococcal disease are treated. The GDG considers that there is insufficient evidence of effectiveness or cost-effectiveness to change the current UK practice, which is to give parenteral antibiotics at the earliest opportunity. The GDG also recognises the importance of children with meningococcal disease being under the care of an experienced paediatric specialist. The GDG noted the need to anticipate complications.

Recommendations on suspected meningococcal disease

Children with suspected meningococcal disease should be given parenteral antibiotics at the earliest opportunity (either benzylpenicillin or a third-generation cephalosporin).

Children admitted to hospital with meningococcal disease should be under paediatric care, supervised by a consultant and have their need for inotropes assessed.

8 Antipyretic interventions

8.1 Introduction

Fever is an increase in temperature that occurs as the result of the action of substances known as pyrogens upon the hypothalamus, the part of the brain that controls body temperature. These pyrogens have the effect of increasing the temperature set-point of the hypothalamus, which causes it to increase the temperature of the body.[205] The hypothalamus is sometimes likened to a thermostat, instigating heat promotion or loss procedures to achieve the desired set-point temperature. It is important to differentiate fever, which is regulated by the body, from hyperthermia, which is caused by external factors and is not regulated by the hypothalamus.

Fever is a normal physiological response to infection and a number of other conditions. Although it is a normal response, some people, including many doctors, nurses and parents, believe that fever should be treated to reduce temperature. This is usually either because of concerns about the damaging effect of fever or because it is thought to be a distressing symptom.[205,206] However, opinions differ about this, with others believing that fever should be allowed to run its course.[207]

If it is thought necessary to reduce fever, there are a number of interventions that are or have been used, either alone or in combination. Pharmacological treatments differ fundamentally from physical treatments, as they aim to lower the hypothalamic set-point rather than simply cool the body. If it is thought necessary to reduce fever, the safest, most clinically and cost-effective treatments and those most acceptable to the child should be used. The first question that the GDG considered was what, if any, antipyretic interventions should be used. A variety of interventions were considered, specifically drugs, such as paracetamol and ibuprofen, and physical methods such as tepid sponging.

8.2. Physical and drug interventions

Clinical question
What if any, antipyretic interventions are effective in reducing body temperature in children with fever?

There are a number of interventions that can be undertaken to reduce temperature, both pharmacological and physical; however, it is not clear whether these treatments are either beneficial or necessary, or what the indications for the treatment of fever should be. Consequently, there is wide variation in practice, both with the use of interventions, and the outcomes that are aimed for. Some healthcare professionals aim to reduce temperature to what they consider to be normal, while others aim simply to reduce temperature. Although the circumstances under which interventions are used will vary, it is important that the possible benefits and harms of treating fever are understood. This includes any adverse effects from the interventions.

Elevations in body temperature result from rising levels of substances such as prostaglandins in the hypothalamus. This has the effect of resetting the hypothalamic temperature set-point and increasing temperature. Paracetamol and nonsteroidal anti-inflammatory agents such as ibuprofen inhibit the action of the cyclooxygenase enzyme involved in the production of this prostaglandin and others and this is the basis of their antipyretic activity, although inflammatory mediators other than prostaglandins may also be potential drug targets. Peripherally, the production of pyrogenic cytokines is also suppressed and the production of endogenous anti-inflammatory compounds is promoted.

Physical treatments such as tepid sponging cool the part of the body being sponged but do not reduce the levels of prostaglandins and so the temperature of the whole body is not reduced.

Furthermore, because the hypothalamus is still set at a higher temperature level, physical treatments may cause shivering and other adverse effects as the body aims to meet the hypothalamic set-point temperature, which continues to be raised. Shivering with a high temperature is sometimes referred to as a rigor.

8.2.1 Physical interventions

There are a number of physical interventions that can be used to reduce body temperature, including undressing, fanning and sponging with cool or cold water. These take advantage of heat loss through convection and evaporation but do not treat the underlying causes of the fever; either the disease or the alteration in hypothalamic set-point.

Narrative evidence

Two reviews[208,209] with EL 1+ and EL 2+ ratings, respectively, due to the nature of the included studies, were found. These compared tepid sponging with antipyretic drugs. One SR[210] which evaluated the benefits and harms of sponging techniques was also found. One further study compared undressing with paracetamol and tepid sponging.[211] There is a lack of evidence regarding opening windows or fanning as methods of reducing temperature. Tepid sponging offers no significant benefit over antipyretic agents alone.[209] In studies looking at combinations of sponging techniques and drugs, sponging seemed to have no or only short-lived additive effects on the reduction in temperature. Adverse effects in some children included crying and shivering in those treated with sponging. Undressing alone had little effect on temperature. A small study in adult volunteers with artificially induced fever showed that, during active external cooling, shivering was common, and both heat production and blood pressure were raised.[212] Discomfort was also significant, a finding that is supported by some studies of tepid sponging in children.[213]

GDG translation

Physical methods of temperature reduction do not treat the cause of fever, which is circulating pyrogens occurring as the result of the underlying condition. Tepid sponging is time consuming, may cause distress, and has minimal medium- to long-term effects on temperature. Undressing appears to have little, if any, effect on temperature. There was no evidence regarding other physical methods of temperature control, for example fanning, although this shares the above limitation. Physical methods may also cause shivering if the cooling is too much or too quick.[213] This may cause vasoconstriction and an increase in temperature and metabolism.

Because there is limited evidence regarding clothing of the feverish child, the GDG agreed by consensus that children with fever should be clothed appropriately for their surroundings, with the aim of preventing overheating or shivering. The major consideration should be the comfort of the child, and the prevention of over-rapid cooling that may cause shivering which may be distressing for child and parents. Care also needs to be taken not to overdress febrile children. It is not possible to be prescriptive about this because of varying environmental and other conditions, and the provision of information about appropriate clothing is an important role for healthcare professionals. In view of the lack of evidence from clinical studies for or against the use of physical cooling methods, the GDG concluded that research in this area may be beneficial.

Recommendations on physical interventions for reducing temperature

Tepid sponging is not recommended for the treatment of fever.

Children with fever should not be underdressed or over-wrapped.

Research recommendation on physical interventions for reducing temperature

The GDG recommends that studies are conducted on the effectiveness of physical methods of attempting to reduce fever, for example lowering ambient temperature, fanning and cold oral fluids.

8.2.2 Drug interventions

The primary method of temperature control is the use of antipyretic drugs such as paracetamol and ibuprofen. Unlike the physical methods previously discussed, these do treat the proximal cause of fever, the increased hypothalamic set-point, although neither physical nor pharmacological methods treat the ultimate cause, for example an underlying infection. The GDG sought to identify the most appropriate pharmacological treatment for fever (as distinct from the cause of the fever), considering not only antipyretic efficacy but also safety and cost.

Narrative evidence

Two EL 1+ reviews[210,214] and four EL 1+ RCTs[215–218] comparing paracetamol and ibuprofen were found. Paracetamol and ibuprofen were both shown to be effective at reducing fever in children.[210,214,215,217,218] Both reviews[210,214] demonstrated that ibuprofen had a more pronounced and/or longer lasting effect on fever compared with paracetamol. However, in many of those studies paracetamol was used in doses below those currently recommended in the UK.

Adverse effects of antipyretic drugs

One EL 1+ meta-analysis[210] which compared patients receiving single doses of paracetamol or ibuprofen was found. Despite the widespread use of ibuprofen and paracetamol, adverse events were rare. No evidence was found to suggest a difference in the risk of either minor or major harm between the two drugs. However, there have been reports of serious suspected adverse reactions even at therapeutic doses for both drugs.[4,219] There is greater experience with the use of paracetamol but ibuprofen use is increasing and different adverse effect profiles may emerge.

Delphi consensus

There is a lack of evidence regarding indications for when children should be given antipyretic drugs. The GDG therefore decided to use the Delphi survey to provide information for these questions. After two rounds of Delphi the results below were obtained.

Delphi statement 8.1

Antipyretic drugs should be given to all children with fever.

1 to 3	4 to 6	7 to 9	Don't know	Missing	Total	Median
10 (19%)	11 (21%)	29 (56%)	2 (4%)		52	7

After two rounds of Delphi this question failed to reach consensus and this statement was not therefore included in the draft version of the guideline. The second question to answer was Statement 8.2 of the Delphi consensus.

Delphi statement 8.2

Antipyretic drugs should be offered to children who are miserable with fever because they may make them feel better.

1 to 3	4 to 6	7 to 9	Don't know	Missing	Total	Median
3 (6%)	5 (10%)	43 (83%)	1 (2%)		52	8

This reached agreement by consensus of 83% of respondents after round 2 and is therefore included as a recommendation in the guideline.

Evidence summary

Paracetamol and ibuprofen are both effective antipyretics. Physical methods of temperature reduction offer little additional benefit and cause crying and shivering in some children. There is no evidence of a significant difference in the incidence of adverse events between the two drugs. On current evidence both drugs are equally effective but paracetamol has a longer established safety record.

There is no evidence for any specific indications for the administration of antipyretics. Care should, however, be taken with all drugs, including antipyretics if given in combination with

other drugs, or if the child is suffering other complications or conditions such as dehydration. Delphi consensus provided strong agreement that antipyretic drugs should be offered to children who are miserable with fever because they may make them feel better, but not that they should be given to all children with fever.

Health economics

Since no evidence of difference in the effectiveness of paracetamol and ibuprofen was identified, decisions on which should be used in the NHS should be based on individual prices available to trusts at the time of purchase.

GDG translation

Ibuprofen and paracetamol are widely used as antipyretic drugs. Although adverse effects and toxicities are possible with their use, paediatric formulations are safe in most children. Healthcare professionals and others involved in the supply of these drugs should ensure that parents understand how to administer them safely.

Despite their common use, there is no evidence regarding the indications for the administration of antipyretic drugs. Consequently, the GDG included questions on this in the Delphi survey. The results of this partly confirmed the lack of evidence, with no consensus on the statement that antipyretic drugs should be given to all children with fever. However, there was strong support for the statement that antipyretics should be offered to children who are miserable with fever because they may make them feel better. In response to stakeholder comments that antipyretics should not be given just because a child has a fever, the GDG decided to revisit the question as to whether all children with fever should be given antipyretics. The GDG achieved consensus among themselves that children with fever do not necessarily need to be given antipyretic agents, especially in light of the following recommendation that children who are miserable with fever may benefit from treatment. Because of the uncertainties about the benefits of antipyretic agents and their indications, the GDG recommended that more research should be conducted on the topic.

Because both drugs are safe and effective, no recommendation can be made about which should be used. The health economic analysis suggests that decisions on which should be used in the NHS should be based upon individual prices available to trusts at the time of purchase.

Recommendations on drug interventions for reducing temperature

The use of antipyretic agents should be considered in children with fever who appear distressed or unwell. Antipyretic agents should not routinely be used with the sole aim of reducing body temperature in children with fever who are otherwise well. The views and wishes of parents and carers should be taken into consideration.

Either paracetamol or ibuprofen can be used to reduce temperature in children with fever.

Research recommendation on drug interventions for reducing temperature

Efficacy and cost-effectiveness studies are required which measure symptom relief associated with fever relief.

8.2.3 Combining pharmacological treatments

Paracetamol and ibuprofen, the drugs most commonly used to treat fever, are often used together by healthcare professionals, parents and patients, either in combination or alternately.[220]

Narrative evidence

Two EL 1– RCTs[221,222] investigating the combination of antipyretic drug therapies and one EL 1+ RCT[223] and one EL 1– RCT[222] investigating the alternation of antipyretic drug therapies were found.

Combination treatment

One EL 1– RCT[221] from the UK examined the administration of paracetamol, ibuprofen or both. It has to be noted that this study had no blinding and small numbers (n = 37, 35, 36) in each arm. A statistically significant difference between the combination and paracetamol groups was found, but this was only 0.35 °C and was not considered to be clinically significant. Follow-up of the majority of patients was only for 1 hour and therefore failed to detect any delayed differences. A second EL 1– RCT[222] from India with small patient numbers (n = 80) showed that ibuprofen combined with paracetamol and nimesulide and paracetamol had almost identical antipyretic effects. No marked adverse effects were detected. Statistical data were not reported.

Neither study was of sufficient methodological quality to provide reliable evidence on the combined use of paracetamol and ibuprofen, which is therefore not recommended.

Alternating treatment

Two RCTs[222,223] were found which examined the use of alternating regimens of antipyretic agents.

One EL 1+ RCT[223] from Israel assigned children to receive either paracetamol or ibuprofen or to receive alternating paracetamol and ibuprofen for 3 days. The group given the alternating regimen was characterised by a lower mean temperature, more rapid reduction of fever, receiving less antipyretic medication, less stress, and less absenteeism from day care as compared with the other groups; all of the differences were statistically significant ($P < 0.05$). However, the study involved the use of a double dose loading dose, used low paracetamol maintenance doses and relied on parental temperature measurement and documentation at home. The second EL 1– RCT[224] from Lebanon randomly allocated patients into one of two treatment groups: an intervention group where a single oral dose of ibuprofen was administered at baseline followed by a single oral dose of paracetamol 4 hours later; and a control group where a similar dose of ibuprofen was administered initially, followed by placebo 4 hours later. Those in the intervention group were significantly more likely than those in the control group to become afebrile at 6, 7 and 8 hours ($P < 0.05$). The two groups had similar maximum decline in temperature. No serious adverse reactions were observed. Although these results suggest the superiority of the combined alternating regimen, the findings need to be confirmed in larger trials, since the study had small numbers in each arm and failed to achieve its calculated sample size.

Evidence summary

Current limited evidence from a small number of RCTs suggests that combination treatment offers no advantage over single drug therapy and would not lead to clinically significant further reduction of body temperature. There is also inadequate evidence to demonstrate the safety of combination treatment. An individual case report has highlighted potential interactions between these drugs.[225] More methodologically sound studies are therefore required to investigate the use of antipyretic combination treatment before recommendations can be made.

There is some limited evidence to suggest that alternating ibuprofen and paracetamol treatment is superior to monotherapy, although the safety of this treatment has not been studied.

GDG translation

The GDG recognises that combinations of paracetamol and ibuprofen, or regimens alternating the two drugs, are in common use by healthcare professionals and families. There is insufficient evidence to support or refute these practices. The potential for adverse drug reactions of the two used together is not known. Theoretical interactions are recognised and reliable safety data do not exist. Furthermore, each drug is known to be effective as a single agent and the potential for confusion and drug administration errors is increased by using more than one drug.

The studies examining administering paracetamol and ibuprofen at the same time have demonstrated no benefit above giving either agent alone, but these had low patient numbers. The two studies which have claimed benefit from an alternating regimen of ibuprofen and paracetamol do not provide sufficient evidence to support such a recommendation. The GDG is aware that an HTA study is currently examining the use of combined regimens of paracetamol and ibuprofen and will report in 2009.

The GDG noted that, from the evidence, antipyretic agents do not appear to be effective in the prevention of febrile convulsions. There is very limited evidence regarding the effect of paracetamol on activity and other areas contained within the clinical question, which showed inconsistent effects.

Recommendations on combining pharmacological treatment to reduce temperature

Paracetamol and ibuprofen should not be administered at the same time to children with fever.

Paracetamol and ibuprofen should not routinely be given alternately to children with fever. However, use of the alternative drug may be considered if the child does not respond to the first agent.

Research recommendation on combining pharmacological treatment to reduce temperature

The GDG recommends that a study is conducted on the effectiveness and safety of alternating doses of paracetamol and ibuprofen in reducing fever in children who remain febrile after the first antipyretic.

8.3 Effects of body temperature reduction

In addition to the underlying illness, fever may be accompanied by a number of unpleasant symptoms including pain, reduced eating and drinking, and reduced activity. In some cases, for example pain, this is likely to be the result of the illness causing the fever. However, in other cases it is not always clear whether these are the direct result of the fever, or of the underlying illness, or a combination of the two. The GDG therefore considered the use of antipyretic interventions in the treatment of these symptoms.

Because fever is a normal response to infection, some studies have been undertaken to look at the effect of the treatment of fever on specific conditions, including malaria,[226] chickenpox[227] and various viral infections.[228] These showed that antipyresis does appear to slow recovery, and makes little difference to some aspects of wellbeing, although the clinical significance of these findings is marginal. As these studies were undertaken on patients who had a diagnosis, these fell outside of the scope of this guideline, and are not discussed further.

A particular concern of many parents about fever in children is that it may cause fits, or febrile convulsions.[206] These are common in young children, and are very rarely associated with epilepsy or other problems in later life.[230] Because antipyretics reduce temperature, there is a theoretical rationale for their use in the prevention of febrile convulsions.

Clinical question

Does the use of antipyretic interventions in children with fever serve a benefit or harm in terms of any of the following:

- time to recovery
- wellbeing
- activity
- eating and drinking
- prevention of febrile convulsions?

We did not find any evidence against other interventions.

Narrative evidence

Although there are some studies looking at the effect of pharmacological antipyresis on recovery from specific conditions such as chickenpox and malaria, and viral conditions, these fell outside of the scope of this guideline.

Research regarding the use of antipyretics in the prevention and treatment of febrile convulsions is limited. One EL 1+ review[231] that was judged to be adequate for inclusion owing to its clinical relevance, after obtaining methodological details from the author, and one EL 1+ SR[232] examining the use of antipyretic drugs as prophylaxis against febrile convulsions were found.

The first[231] investigated the hypothesis that paracetamol and ibuprofen, used prophylactically, will reduce the incidence of febrile convulsions across a wide variety of conditions. It found no evidence that the prophylactic use of antipyretics has any effect in reducing the incidence of febrile convulsions. The second review[232] assessed 12 studies of the effects of paracetamol for treating children in relation to fever clearance time, febrile convulsions and resolution of associated symptoms. It also found no evidence that the use of prophylactic paracetamol influenced the risk of febrile convulsions.

An EL 1+ double-blind RCT[228] analysing 225 datasets was also identified, which found that there was no significant difference in mean duration of fever (34.7 hours versus 36.1 hours, *P* not given) or of other symptoms (72.9 hours versus 71.7 hours). Children treated with paracetamol were more likely to be rated as having at least a 1-category improvement in activity ($P = 0.005$) and alertness ($P = 0.036$).

Evidence summary

Limited evidence was found regarding the use of antipyretic medications in the promotion of well-being, activity, eating and drinking, and no evidence of cost-effectiveness. One study suggested that parents could identify some improvement in activity and alertness after the administration of paracetamol, but not in mood, comfort, appetite or fluid intake. There is no evidence that the use of antipyretic agents reduces the incidence of febrile convulsions. (EL 1)

GDG translation

The GDG noted that, from the evidence, antipyretic agents do not appear to be effective in the prevention of febrile convulsions. There is very limited evidence regarding the effect of paracetamol on activity or other areas contained within the clinical question, which showed inconsistent effects.

Recommendation on the role of antipyretics in the prevention of febrile convulsions

Antipyretic agents do not prevent febrile convulsions and should not be used specifically for this purpose.

9 Advice for home care

9.1 Introduction

Feverish illness in children is a normal and common event although it can cause significant anxiety for some parents and carers. Parents may seek support from healthcare services but in most cases the parents can be reassured that the child is best cared for at home. They may need support and advice to do this confidently. The overwhelming majority of children will recover quickly and without problems. However, in a few cases the child's condition may worsen or fail to improve. Parents need information on when and how to seek further advice.

The GDG has found evidence to show that administering antipyretics can make a child look better and feel better and therefore make it easier to differentiate those with serious illness from those with non-serious illness. However, there is no evidence to show that it is desirable to administer antipyretics to reduce fever. The desirability of reducing fever is controversial.

Where no evidence was found to answer the questions, the Delphi survey was used. Full details of the survey are available in Appendix A.

9.2 Care at home

The GDG considered subjects that could usefully be included in written or verbal advice for parents and carers following an encounter with the health services regarding a febrile child.

Clinical question
What advice should be given to parents for further management of a febrile child?

Need to consider:

- hydration
- feeding
- frequency of temperature monitoring
- methods of cooling
- when to attend nursery or school
- appearance of non-blanching rash.

9.2.1 Methods of cooling

Antipyretic interventions are discussed in Chapter 8, and they should be included in advice for parents or carers.

9.2.2 Fluids

One SR[233] reporting that there were no RCTs assessing the effect of increasing fluid intake in acute respiratory infections was found. No further studies were found meeting the inclusion criteria about giving oral fluids and thus the Delphi survey was used.

Delphi statement 1.1
Parents/carers looking after a feverish child at home should be advised to offer the child regular fluids (where a baby or child is breastfed the most appropriate fluid is breast milk).

In round 1 of the survey the rating categories were:

1 to 3	4 to 6	7 to 9	Don't know	Missing	Total	Median
0	1 (2%)	48 (96%)	1 (2%)	3	50	9

The statement achieved 96% agreement and thus consensus.

9.2.3 Dehydration

A lack of evidence was found about whether to advise the parents/carers to look for signs of dehydration. This then was included in the Delphi survey.

Delphi statement 1.2
Parents/carers looking after a feverish child at home should be advised how to detect signs of dehydration.

In round 1 of the survey the rating categories were:-

1 to 3	4 to 6	7 to 9	Don't know	Missing	Total	Median
0	6 (12%)	42 (84%)	2 (4%)	3	50	8.5

The statement achieved 84% agreement and thus consensus.

There was some evidence about which features parents and carers should look for. Refer to Section 4.5.4 for symptoms and signs of dehydration for this purpose. The GDG decided that parents or carers should be advised to look for the most sensitive symptoms and signs of dehydration so that cases are not missed, and if signs of dehydration are detected the parents/carers should encourage their child to drink more fluids and consider seeking further advice. The relevant features are:

- sunken fontanelle
- dry mouth
- sunken eyes
- absence of tears
- poor overall appearance.

9.2.4 Checking temperature

A lack of relevant evidence was found about advising parents/carers to regularly measure their child's temperature if the condition is stable. Therefore this was included in the Delphi survey.

Delphi statement 1.3
Parents/carers looking after a feverish child at home should be advised that regular measurement of the child's temperature is not necessary if the child's condition is stable.

In round 1 of the Delphi survey the rating categories were:

1 to 3	4 to 6	7 to 9	Don't know	Missing	Total	Median
8 (16%)	17 (33%)	24 (47%)	2 (4%)	2	51	7

Consensus was therefore not reached in round 1.

In round 2 the rating categories were:

1 to 3	4 to 6	7 to 9	Don't know	Missing	Total	Median
9 (18%)	10 (20%)	32 (63%)		1	51	7

As sufficient level of consensus was not achieved, no recommendation could be made about this statement.

There was a lack of evidence to show whether parents/carers looking after a feverish child should check their child during the night. This therefore was included in the Delphi survey.

Delphi statement 1.4
Parents/carers looking after a feverish child at home should be advised to check their child during the night.

In round 1 the rating categories were:

1 to 3	4 to 6	7 to 9	Don't know	Missing	Total	Median
2 (4%)	11 (22%)	35 (70%)	2 (4%)	3	50	8

Sufficient consensus was not achieved in round 1.

In round 2 the rating categories were:

1 to 3	4 to 6	7 to 9	Don't know	Missing	Total	Median
1 (2%)	5 (10%)	45 (88%)		1	51	8

Therefore sufficient consensus was achieved. As there is no evidence to show how often the parents/carers should check the child during the night, the healthcare professional assessing the child may want to advise on this.

9.2.5 School attendance

The Department for Education and Skills (DfES) has strict policies that emphasise the importance of good school attendance, and that parents should notify their school on the first day of absence through illness, for health and safety reasons. Nevertheless, although there is a document readily available in schools that shows how long a child should be absent if the child has a known infectious disease, there is no evidence that shows how long a child with a fever of unknown origin should be absent from school or nursery and, this was sent to the Delphi panel.

Delphi statement 1.5
Parents/carers looking after a feverish child at home should be advised to keep their child away from nursery or school while the child's fever persists but to notify the school or nursery of the illness.

In round 1 the ratings categories were:

1 to 3	4 to 6	7 to 9	Don't know	Missing	Total	Median
1 (2%)	5 (10%)	43 (86%)	1 (2%)	3	50	8.5

Consensus was therefore achieved for this statement.

9.2.6 Appearance of non-blanching rash

At the suggestion of a stakeholder, the GDG decided that parents/carers should be told how to identify a non-blanching rash. A non-blanching rash is a feature of meningococcal disease (see Section 4.6.2) and many parents and carers are aware of its significance. Advice centres around the 'tumbler test' in which the rash is found to maintain its colour when glass is pressed on to the skin.

Health economics
The GDG did not identify any health economics issues for the NHS in this section of the guideline.

GDG translation
The GDG accepted that all Delphi statements that achieved consensus should be used to make recommendations about advice for care at home following an encounter with the health services. For clarity, information about the relevant features to look for was added to the recommendation on dehydration.

Recommendations on care at home

Parents or carers should be advised to manage their child's temperature as described in Chapter 8.

Parents or carers looking after a feverish child at home should be advised:

- to offer the child regular fluids (where a baby or child is breastfed the most appropriate fluid is breast milk)
- how to detect signs of dehydration by looking for the following features:
  - sunken fontanelle
  - dry mouth
  - sunken eyes
  - absence of tears
  - poor overall appearance
- to encourage their child to drink more fluids and consider seeking further advice if they detect signs of dehydration
- how to identify a non-blanching rash
- to check their child during the night
- to keep their child away from nursery or school while the child's fever persists but to notify the school or nursery of the illness.

9.3 When to seek further help

In addition to advice about how to care for their febrile child at home, parents and carers also need advice about when they should seek further attention from the health services. This should allow them to take appropriate action if their child deteriorates or does not recover as expected.

Clinical question
In children with fever at home following a clinical encounter, what indications should direct the parents or carers to seek further advice?

A lack of evidence was found about when parents should seek further advice following a contact with a healthcare professional. Therefore the following statements were included in the Delphi survey.

9.3.1 Fits

Delphi statement 3.1a
Following contact with a healthcare professional, parents/carers who are looking after their feverish child at home should seek further advice if the child suffers a fit.

The first round consensus rating categories were:

1 to 3	4 to 6	7 to 9	Don't know	Missing	Total	Median
0	0	52 (98%)	1 (2%)		53	9

Consensus was therefore achieved for this statement.

9.3.2 Less well

Delphi statement 3.1b
Following contact with a healthcare professional, parents/carers who are looking after their feverish child at home should seek further advice if the parent/carer feels that child is less well than when they previously sought advice.

The first round ratings categories for this statement were:

1 to 3	4 to 6	7 to 9	Don't know	Missing	Total	Median
0	2 (4%)	50 (94%)	1 (2%)		53	8

Consensus was therefore achieved for this statement.

9.3.3 Increased parental concern

Delphi statement 3.1c
Following contact with a healthcare professional, parents/carers who are looking after their feverish child at home should seek further advice if they are more worried than when they previously sought advice.

The first round consensus rating categories were:

1 to 3	4 to 6	7 to 9	Don't know	Missing	Total	Median
0	9 (17%)	43 (81%)	1 (2%)		53	8

Consensus was therefore achieved for this statement.

9.3.4 Length of fever

Delphi statement 3.1d
Following contact with a healthcare professional, parents/carers who are looking after their feverish child at home should seek further advice if the fever lasts longer than 48 hours.

The first round survey ratings categories were:

1 to 3	4 to 6	7 to 9	Don't know	Missing	Total	Median
4 (8%)	14 (27%)	33 (63%)	1 (2%)	1	52	7

As no consensus was achieved, it went to round 2 where the ratings categories were**:**

1 to 3	4 to 6	7 to 9	Don't know	Missing	Total	Median
2 (4%)	9 (17%)	40 (77%)	1 (2%)		52	7

Consensus was therefore achieved for this statement.

Delphi statement 3.1e
Following contact with a healthcare professional, parents/carers who are looking after their feverish child at home should seek further advice if the fever lasts longer than 5 days.

The first round ratings categories were:

1 to 3	4 to 6	7 to 9	Don't know	Missing	Total	Median
1 (2%)	0	50 (96%)	1 (2%)	1	52	9

Consensus was therefore achieved for this statement.

9.3.5 Parental distress and unable to cope

Delphi statement 3.1f
Following contact with a healthcare professional, parents/carers who are looking after their feverish child at home should seek further advice if the parent/carer is very distressed or unable to cope with their child's illness.

The first round ratings categories were:

1 to 3	4 to 6	7 to 9	Don't know	Missing	Total	Median
1 (2%)	5 (9%)	46 (87%)	1 (2%)		53	9

Consensus was therefore achieved for this statement.

9.3.6 Non-blanching rash

After suggestions from stakeholders, the GDG also decided that parents and carers should seek further advice if the child develops a non-blanching rash.

Health economics

The GDG did not identify any issues that required cost-effectiveness analysis for this question.

GDG translation

The GDG decided to include all but one of the Delphi statements that had achieved consensus as recommendations in the guideline. The exception was the statement about seeking further advice if the fever lasts for more than 48 hours. The GDG unanimously decided not to include this statement because they had found evidence on the predictive value of duration of fever after the statement had been put to the Delphi panel. This evidence, which is detailed in Section 4.5.3.2, suggests that a duration of fever of around 1–2 days is not predictive of serious illness. The GDG considered that it would therefore be contradictory to advise carers to seek medical attention if the fever lasts longer than 48 hours. The statement on seeking advice if the fever lasted longer than 5 days was retained because the GDG considered this situation to be unusual and because a fever of 5 days duration could be a marker of Kawasaki disease or other serious illnesses such as pneumonia or UTI.

Recommendation on when parents or carers should seek further help

Following contact with a healthcare professional, parents and carers who are looking after their feverish child at home should seek further advice if:

- the child has a fit
- the child develops a non-blanching rash
- the parent or carer feels that the child is less well than when they previously sought advice
- the parent or carer is more worried than when they previously sought advice
- the fever lasts longer then 5 days
- the parent or carer is distressed, or concerned that they are unable to look after their child.

Appendix A

The formal consensus survey

A.1 Background

NICE clinical guidelines are typically based on a review of evidence from published literature, ideally from large, well-conducted studies. The methods used to develop these guidelines are explicit and transparent. They include literature search, assessment and synthesis of evidence and the final judgements made by the Guideline Development Group (GDG) to reach final decisions. While the use of formal consensus methods in NICE guideline is not customary, there are circumstances when they may be warranted, in the absence of robust evidence.[234] This process is separate from the stakeholder consultation of the draft guideline.

A core objective of this guideline on feverish illness in children was to provide practical recommendations for the clinical assessment of children (aged 0–5 years) presenting with a feverish illness, including risk stratification. An extensive review of the literature revealed major deficiencies with the evidence to answer some of the key clinical questions. The main problems were the poor quality of the studies retrieved (small, poorly conducted studies, or incomplete reporting) and generalisability (studies were often conducted in very different settings from the NHS). Moreover, there was recognition that opinions diverged considerably in these areas among clinicians and parents.

Against this background, the GDG decided to use a formal consensus approach with a larger external group of consultees on selected questions. Formal consensus methods are used increasingly in combination with the best available evidence to develop clinical practice guidelines.[235–237] The purpose of the consensus was to obtain the opinions of an external multidisciplinary group to assist the GDG in making reliable recommendations in areas where evidence was deficient.

A.2 Methods

A.2.1 Choosing the consensus method

The GDG chose a modified Delphi method.[238] Delphi is one of the most widely used formal consensus techniques for obtaining opinions from groups of experts and stakeholders.[239] It involves sending participants questionnaires and asking them for their views. The responses are collated and sent back to participants in a summary form allowing them to revise their original opinion in light of the group feedback.[240,241] This process is repeated several times, with the aim of obtaining consensus. The GDG used a two-round postal/e-mail survey.

A.2.2 Defining the project plan

A plan protocol was designed initially that incorporated all stages and details of the work, including the consensus method to be used, recruitment of participants, data collection and analysis. Importantly, the GDG agreed the ground rules they would use for analysing the results and for formulating the recommendations based on the results from the survey. These are presented in Box A.1.

A timetable was drawn up early in the process to ensure the work could be carried out during the timeline of the guideline development. The Royal College of Paediatrics and Child Health and the Patient and Public Involvement Programme (PPIP) unit at NICE confirmed that the consensus work did not require ethical approval.

- The results of the group ratings will be presented to the GDG, together with comments.
- Whenever appropriate the GDG will aim to formulate a recommendation for each statement. The statements will be worded in a way that can be directly translated into recommendations.
- The GDG will explicitly state the basis for its decision using the 'translation' template currently used with other recommendations for which there is evidence.
- Statements for which 75% or more of the ratings fall in the 7 to 9 range will be classified as agreement and the GDG will use the statement as a basis for making a recommendation.
- Statements for which 75% or more of the ratings fall in the 1 to 3 range will be classified as disagreement. The GDG will usually make a negative recommendation (e.g. does not recommend). In certain circumstances the GDG may decide to make a research recommendation or discard the statement. The decision not to make a negative recommendation will need to be agreed unanimously by the GDG and it will need to be justified.
- In all other cases, the GDG will discard the statement. Exceptionally, it may decide to make a recommendation, depending on the degree of variation in the ratings for that statement. Again, this decision will need to be justified and agreed unanimously by the GDG.
- In cases where there is agreement in the rating group but the GDG considers there are grounds to discard the results, the GDG reserves the right to use its own opinion in making the recommendation. This will need to be agreed unanimously by the GDG. In such cases, the GDG will explain in detail the reasons why it rejected the results.

Box A.1 Ground rules agreed by the GDG for making recommendations from survey results

A.2.3 Selecting clinical questions for formal consensus

A systematic search for the evidence was conducted on all clinical questions and relevant published studies were assessed. On examining the evidence the GDG identified a number of questions/issues for which they did not think they could competently make recommendations based on the published studies, or on their collective experience. These questions are listed in Box A.2.

The following criteria were used for selecting the questions:

- there was no appropriate published evidence to answer the question
- there was some evidence but the GDG failed to reach consensus among themselves as to what the recommendation should be.
- the GDG did not think the question could be answered by standard quantitative studies
- the GDG was concerned that the evidence found was not applicable or acceptable to practice in England and Wales.

A.2.4 Developing the statements

The statements focused on issues that were commonly seen in practice and were clinically important both for health professionals and for parents/carers. They were generated for each selected question based on the literature review using the following steps:

- a member of the topic group with the help of the systematic reviewer drafted a background summary describing what was known about the issue, based on available evidence and known current practice as agreed by the GDG
- the summary was presented to the GDG, together with a draft statement for discussion
- the GDG finalised the statement.

The statements were worded as recommendations to ensure that the final guideline recommendations reflected the results from the consensus.

A.2.5 Piloting the statements

The draft statements, background and instructions were piloted for clarity and readability with ten people, including members from another GDG, parents and colleagues at the National Collaborating Centre for Women's and Children's Health. They were asked to read through all the documentation and to provide any feedback on potential improvements. Seven responses were received. On the whole, respondents felt the statements and background were clear. There were comments relating to presentation and ratings for some statements. Based on these suggestions

some of the sections were re-ordered, the wording was clarified when relevant and the rating scale for two sets of statements was modified. A member of the Patient and Public Involvement Programme (PPIP) unit at NICE checked the final wording to ensure it was understandable for parents and carers.

Question 2

How accurate are the different types of thermometer in the measurement of body temperature in young children and how do they compare in their ability to detect fever?

Question 3

How accurate are the readings of temperature from different sites of the body in young children and how do these sites compare in the ability to detect fever?

Question 12

In a child with fever what are the benefits, if any, of a period of observation on an assessment facility?

Question 21

Does the use of antipyretic interventions in children with fever serve a benefit or harm in terms of any of the following:

- time to recovery
- wellbeing
- activity
- eating and drinking
- prevention of febrile convulsions?

Question 22

In children with fever at home following a clinical encounter, what indications should direct the parents or carers to seek further advice?

Need to consider:

- *height of temperature*
- *length of temperature*
- *colour*
- *drowsiness*
- *rash*
- *poor feeding*
- *fluid intake*
- *reduction in urine output*
- *altered consciousness*
- *rigors*
- *parental anxiety/instinct*
- *inconsolable crying*
- *irritability.*

Question 23

What advice should be given to parents for further management of a febrile child?

Need to consider:

- *hydration*
- *feeding*
- *frequency of temperature monitoring*
- *methods of cooling*
- *when to attend nursery or school.*

Question 24

What factors other than the child's clinical condition should be considered when deciding to admit a child with fever to hospital?

Need to consider:

- *social*
- *comorbidity*
- *parental wishes and instinct*
- *distance from home*
- *time of day*
- *contacts with other serious illness*
- *recent travel abroad.*

Box A.2 Clinical questions selected for formal consensus

A.2.6 Selecting participants

Number of participants

There is little evidence about the effect the number of participants has on the reliability or validity of consensus. This depends on the purpose of the study and the diversity of the targeted population.[235] It was aimed to obtain at least 50 ratings for each statement with a response rate of at 80%. This was based on the assumption that if 75 people were invited to take part at least 65 would agree.

Inviting and recruiting participants

The purpose of the consensus was to seek the opinions of an external multidisciplinary group including the health professionals and patients/carers /parents who are directly involved with or are affected by the issue covered. Three key groups were identified: professionals from primary care including NHS Direct, professionals from secondary care, and parents/carers. It was aimed to obtain 25 nominations in each of the three groups.

Key professional and patient organisations registered as stakeholders were asked to nominate potential participants. Sure Start was approached separately to identify parents from disadvantaged backgrounds. In addition, a message was posted on the NICE website inviting parents to participate.

A letter of invitation was sent to each nominee, together with a document explaining the background to the survey, its aim, and the task involved, including timing and deadlines. An example of a background summary and statement was provided as illustration. Nominees were asked to respond within 2 weeks. They were requested to sign a letter of confidentiality before participating. Table A.1 shows the number of nominations received and the numbers who responded.

A.2.7 Rating

The GDG generated 35 statements for consensus. A pack containing a covering letter, the statements/background and response document, an instruction sheet and background notes was sent to each of the 61 people who had agreed to take part. Respondents were asked to indicate their agreement with each statement using a scale of 1–9 (1 being strongly disagree, 9 being strongly

Table A.1 Nominations to and acceptance of participation in the Delphi survey

Group/profession	Organisation	Number of nominations received	Number who accepted
Paediatrician Paediatrician (A&E) Paediatrician (infectious diseases)	Royal College of Paediatrics and Child Health	6	6
A&E consultant	College of Emergency Medicine	2	2
Paediatric nurse A&E nurse	Royal College of Nursing	20	18
Hospital pharmacist	NPPG	2	2
Parent/carer	Stakeholder and NICE website (through PPIP) Sure Start	33 (25 selected)	15
General practitioner	Royal College of General Practitioners	6	5
Practice nurse	Primary care trusts	9	6
Out-of-hours provider	Primary care trusts	2	1
Community pharmacist	Royal Pharmaceutical Society	1	1
NHS Direct	NHS Direct	6	5
Total		**79**	**61**

agree). For statements 2.1 and 5.2, participants were asked to indicate which optimum time they preferred. A 'Don't know' box and space for comments were provided. The ratings were done independently. Box A.3 shows an example of a statement sent for the first round. For the full list see Annex A.1 on the accompanying CD-ROM.

For each round, participants were given 2 weeks to return their ratings. Most documents were sent by e-mail. A self-addressed labelled envelope was included for postal respondents. The participants were contacted after a week to remind them about the deadline.

Data analysis and presentation to the GDG

Results were analysed using Stata (version 8). In addition to the agreed ground rules (e.g. 75% or more of ratings 7 to 9 = *agreement*, 75% or more 1 to 3 = *disagreement*), the median score was calculated for each statement as a measure of central tendency classified as agreement (7 to 9), disagreement (1 to 3), or uncertainty (4 to 6). For statements 2.1 and 5.2 there was agreement if 75% of the ratings were in one of the response categories.

The results were presented to the GDG. For each statement, the results included the median, distribution of ratings for each of the three categories and the comments. All the information was anonymised. Statements for which there was no agreement (according to the ground rules) were discussed. When appropriate, the GDG reworded the background and/or statement, using the participants' comments as a guide.

The statements were sent for a second round of rating. The results from the first round described above were included without the comments but participants were able to obtain them on request. The participants were asked to consult their first round ratings and to compare them with their second rating.

A.3 Results

A.3.1 Round 1

Fifty-seven participants (93%) completed their ratings but only 53 returns were used in the analysis as four were received too late. There were 32 missing responses (2%) out of a total of 1855 and 79 (4%) 'Don't know'. Table A.2 shows the distribution of ratings. The ratings for each statement are shown in Annex A.1 on the accompanying CD-ROM together with the comments. There was *agreement* with 12 out of the 35 statements and *disagreement* with three (on rectal thermometers). For statement 2.1, 43 (83%) of the ratings fell into the 2 hours category. This was accepted as agreement. For the remaining 20 statements there was a range of response across the three categories. Statement 8.1 had agreement (75% in the 7 to 9 category). However, the GDG decided to reword the first two statements in Section 8 in the light of comments made by the participants and also because they realised that the original statements could not be used to make unambiguous recommendations. Therefore Statement 8.1 was included in the second round, taking the number of statements for re-rating up to 21. In general, the comments indicated that several statements/background needed clarifying or to be made more specific.

Background

Most of the care of feverish children takes place at home and is provided by parents or other carers. Some parents/carers will seek initial advice from healthcare professionals. Most of these children will recover without problems. In some cases, however, their condition may change or fail to improve. Parents need to know when to seek further help and may require further advice about the best way to care for their child.

Statement 3.1

Following contact with a healthcare professional, parents/carers who are looking after their feverish child at home should seek further advice if:

a) the child suffers a fit

Box A.3 Example of a statement sent for first round consensus

Table A.2 Distribution of ratings and median for all statements after round 1

Statement	Rating category				Responses		
	1 to 3	**4 to 6**	**7 to 9**	**Don't know**	**Missing**	**Total**	**Median**
1.1	0	1 (2%)	48 (96%)	1 (2%)	3	50	9
1.2	0	6 (12%)	42 (84%)	2 (4%)	3	50	8.5
1.3	8 (16%)	17 (33%)	24 (47%)	2 (4%)	2	51	7
1.4	2 (4%)	11 (22%)	35 (70%)	2(4%)	3	50	8
1.5	1 (2%)	5 (10%)	43 (81%)	1 (2%)	3	50	8.5
3.1a	0	0	52 (98%)	1 (2%)		53	9
3.1b	0	2(4%)	50 (94%)	1 (2%)		53	8
3.1c	0	9 (17%)	43 (81%)	1 (2%)		53	8
3.1d	4 (8%)	14 (27%)	33 (63%)	1 (2%)	1	52	7
3.1e	1 (2%)	0	50 (96%)	1 (2%)	1	52	9
3.1f	1 (2%)	5 (9%)	46 (87%)	1 (2%)		53	9
4.1	2 (4%)	8 (15%)	39 (75%)	3 (6%)	1	52	9
4.2	7 (14%)	14 (28%)	21 (42%)	8 (16%)	3	50	7
5.1	4 (8%)	10 (19%)	36 (69%)	2 (4%)	1	52	8
6.a	7 (13%)	20 (38%)	25 (47%)	1 (2%)		53	6
6.b	2 (4%)	17 (32%)	32 (60%)	2 (4%)		53	7
6.c	1 (2%)	14 (26%)	37 (70%)	1 (2%)		52	8
6.d	6 (12%)	23 (44%)	22 (42%)	1 (2%)	1	53	6
6.e	13 (25%)	22 (42%)	17 (32%)	1 (2%)		53	6
6.f	12 (23%)	20 (38%)	20 (38%)	1 (2%)		53	6
6.g	4 (8%)	17 (32%)	28 (53%)	4 (8%)		53	7
6.h	7 (13%)	12 (23%)	32 (60%)	2 (4%)		53	7
6.i	7 (13%)	15 (28%)	30 (57%)	1 (2%)		53	7
6.j	2 (4%)	13 (25%)	37 (70%)	1 (2%)		53	8
6.k	2 (4%)	13 (25%)	36 (70%)	1 (2%)	1	52	7
7.1	8 (15%)	6 (12%)	29 (56%)	9 (17%)	1	52	8
7.2	2 (4%)	4 (8%)	44 (85%)	2 (4%)	1	52	9
7.3	45 (87%)	3 (6%)	3 (6%)	1 (2%)	1	52	1
7.4	46 (88%)	4 (8%)	1 (2%)	1 (2%)	1	52	1
7.5	47 (92%)	3 (6%)	0	1 (2%)	1	51	1
8.1	3 (6%)	10 (20%)	39 (75%)	0	1	52	8
8.2	12 (23%)	18 (35%)	20 (38%)	2 (4%)	1	52	5.5
8.3	2 (4%)	18 (35%)	28 (55%)	3 (6%)	2	51	7

	2 hours	**6 hours**	**12 hours**	**24 hours**	**Don't know**	**Total**	**Median**
2.1	43 (83%)	5 (10%)	1 (2%)	0	3 (6%)	52	2

	2 hours	**4 hours**	**6 hours**	**12 hours**	**Don't know**	**Total**	**Median**
5.2	2 (4%)	7 (13%)	19 (37%)	10 (19%)	14 (27%)	52	6

Statement for which there was no agreement

Statement for which there was disagreement

A.3.2 Round 2

Fifty-three (93%) of the 57 participants completed the task. There were three missing responses out of 1325. There were 26 'Don't know' responses, 12 of which were for statement 5.2, about the period of observation in hospital. Table A.3 shows the distribution of ratings. The ratings for each statement are shown in Annex A.2 on the accompanying CD-ROM together with the comments. There remained 10 statements for which agreement could not be reached.

A.4 Formulating the recommendations

The GDG discussed all the statements again after the two consensus rounds. They removed nine of the ten statements with no agreement. In addition,, statement 5.2 was discarded because there was a high degree of uncertainty about the optimum time around the period of observation for assessment in hospital to help differentiate minor from serious illness. This was illustrated in the comments (see Annex A.1 on the accompanying CD-ROM). Box A.4 shows the 25 statements that were retained as recommendations. In most cases, the statement was reproduced exactly as a recommendation. While there was consensus agreement for statement 3.1d, the GDG unanimously decided to remove it because evidence was found after the consensus survey that duration of fever at 48 hours is not a sufficiently important sign to prompt review. However, the recommendation on seeking advice at 5 days, statement 3.1e, was retained because fever

Table A.3 Distribution of ratings and median for statements after round 2

Statement	Rating category				Responses		
	1 to 3	4 to 6	7 to 9	Don't know	Missing	Total	Median
1.3	9 (18%)	10 (20%)	32 (63%)		1	51	7
1.4	1 (2%)	5 (10%)	45 (88%)		1	51	8
3.1d	2(4%)	9 (17%)	40 (77%)	1 (2%)		52	7
4.2	2 (4%)	15 (30%)	33 (65%)	1 (2%)	1	51	7
5.1	0	6 (12%)	44 (85%)	2 (4%)		52	8
6.a	2 (4%)	17 (33%)	33 (64%)			52	7
6.b	1 (2%)	10 (19%)	41 (79%)			52	7.5
6.c	2 (4%)	7 (13%)	43 (83%)			52	8
6.d	7 (13%)	22 (42%)	23 (44%)			52	6
6.e	12 (23%)	24 (46%)	16 (31%)			52	6
6.f	14 (27%)	16 (31%)	22 (42%)			52	8
6.g	1 (2%)	8 (15%)	42 (81%)	1 (2%)		52	8
6.h	1 (2%)	2 (4%)	48 (92%)			51	8
6.i	2 (11%)	11 (22%)	38 (75%)			51	8
6.j	1 (2%)	9 (17%)	42 (81%)			52	8
6.k	2 (4%)	9 (17%)	41 (79%)			52	8
7.1	11 (21%)	8 (15%)	28 (54%)	5 (10%)		52	7
8.1	10 (19%)	11 (21%)	29 (56%)	2 (4%)		52	7
8.2	3 (6%)	5 (10%)	43 (83%)	1 (2%)		52	8
8.3	2 (4%)	15 (29%)	34 (65%)	1 (2%)		52	7

	2 hours	4 hours	6 hours	12 hours	Don't know	Total	Median
5.2	1 (2%)	3 (6%)	26 (50%)	10 (19%)	12 (23%)	52	6

Statement with no agreement

of this duration is unusual and Kawasaki disease and other serious causes of prolonged fever should be considered at this stage. An explanatory text was added to statement 4.1 (in italics) after comments suggested the statement needed qualifying ('Healthcare professionals examining children with fever must measure and record heart rate as part of their routine assessment *because a raised heart rate can be a sign of serious illness particularly septic shock.')*. Statement

1. Care at home

Parents/carers looking after a feverish child at home should be advised:

- to offer the child regular fluids (where a baby or child is breastfed the most appropriate fluid is breast milk)
- how to detect signs of dehydration
- to check their child during the night
- to keep their child away from nursery or school while the child's fever persists and to notify the school or the nursery of the illness.

2. Assessment by telephone

An urgent face-to-face assessment means that the child should be seen within 2 hours.

3. When to seek medical help

Following contact with a healthcare professional, parents/carers who are looking after their feverish child at home should seek further advice if:

- the child suffers a fit
- the parent/carer feels that child is less well than when they previously sought advice
- the parent/carer is more worried than when they previously sought advice
- the fever has not settled after 5 days
- the parent/carer is very distressed or unable to cope with their child's illness.

4. Face-to-face assessment

Healthcare professionals examining children with fever must measure and record heart rate as part of their routine assessment because a raised heart rate can be a sign of serious illness, particularly septic shock.

5. Observation in hospital

A period of observation in hospital (with or without investigations) as part of an assessment can help differentiate minor from serious bacterial illness (such as meningitis or pneumonia) in a young child who has a fever without obvious cause.

6. Other factors for admitting a feverish child to hospital

Healthcare professionals should consider the following factors, as well as the child's clinical condition, when deciding whether to admit a child with fever to hospital:

- social and family circumstances
- other illnesses suffered by the child or other family members
- parental anxiety and instinct (based on their knowledge of their child)
- contacts with other people who have serious infectious diseases
- recent travel abroad to tropical/subtropical areas, or areas with a high risk of endemic infectious disease
- when the parent or carer's concern for their child's current illness has caused them to seek help repeatedly
- where the family has experienced a previous serious illness or death due to feverish illness which has increased their anxiety levels
- when a feverish illness has no obvious cause, but the child remains ill longer than expected for a self-limiting illness.

7. Thermometers

Healthcare professionals should not routinely use the oral route to measure body temperature in children under the age of 5 years.

Healthcare professionals should not routinely use electronic thermometers by the rectal route to measure body temperature in children aged 0–3 months.

Healthcare professionals should not routinely use electronic thermometers by the rectal route to measure body temperature in children aged 3 months to 2 years.

Healthcare professionals should not routinely use electronic thermometers by the rectal route to measure body temperature in children aged 2–5 years.

8. Cooling methods

Antipyretic drugs should be offered to children who are miserable with fever because they may make them feel better.

Box A.4 Statements retained for recommendations after two rounds of Delphi consensus

6.a, for which there was no agreement, was retained by unanimous consensus in the GDG. The GDG slightly modified the wording of statement 8.2 as comments indicated the message should be more specific. The three statements on rectal thermometers (7.3, 7.4 and 7.5) for which there was *disagreement* were retained because the GDG considered there was a sufficiently important need for guidance on their use. To reflect the strength of disagreement from the consensus they reworded the statements negatively.

The final 25 statements were incorporated as recommendations in the guideline.

A.5 Acknowledgements

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Appendix B

Cost analysis of thermometers for use in children and infants with fever

B.1 Introduction

A cost analysis of the various types of thermometers available in the UK was undertaken in order to demonstrate the range of costs associated with thermometers. The prices for each type of thermometer were obtained from a review of clinical thermometers in the UK market published by the Medicines and Healthcare products Regulatory Agency (MHRA).[27] This review provided an overview of the clinical and procurement issues for each reported thermometer.

The report showed that the price of 'stand-alone' thermometers is highly variable. Prices range from 7p each for disposable chemical thermometers to £400 for some models of electronic contact thermometers. Given this variation, it is important to take into account a range of issues before determining which device is the best choice and achieves best practice.

Apart from the cost of purchasing it is necessary to consider the cost associated with the use of them. For instance, the manufacturers of some thermometers recommend the use of specific disposable covers to help to reduce the risk of cross-infection for those devices that can not be adequately cleaned. Also, in some cases it may be necessary to take into account the cost of training for the clinical staff. The clinical risk from incorrect readings may be reduced by the staff undertaking competency-based training programmes. Some electronic thermometers are battery powered so the cost of battery replacement should be included in a detailed costing analysis of thermometers. Also, the cost of recalibration and the cost of maintenance are important elements of cost for some specific types of thermometer.

B.2 Description of the costing analysis

In general, thermometry can be categorised by the type of the instrument used and by the site at which the temperature is read. Mercury in glass, electronic and chemical dot thermometers can be used sublingually (orally), in the axilla (under arm) or rectally. Temperature assessment accuracy is critically important. False high readings may lead to expensive and unnecessary painful diagnostic tests and medical interventions. False low readings may lead to greater morbidity and mortality.

Accuracy of body temperature measurement depends not only on the type of thermometer but also on the site of measurement. Given that the site of measurement is a clinically important decision, the classification of the thermometers for this cost analysis was based on the site of measurement. Some types of thermometers cannot provide readings from all the sites of measurements. For instance, chemical thermometers cannot give rectal measurements.

B.3 Methods

The structure of the cost analysis and the assumptions in it are based on that devised by Crawford *et al*.[27] The analysis includes three types of thermometer: chemical, electronic and infrared sensing, and classified according to two different sites of measurements: axilla and tympanic.

The thermometers were subdivided into subcategories of electronic and chemical thermometers since there are cost differences between them. The category of electronic thermometers was split into contact/electronic and contact/compact electronic thermometers.

A robust cost comparison between different technologies should ideally encompass all the contributory costs over a prescribed period: in this case, a 10 year time horizon was used, discounted at 3.5%. The analysis calculated both the most expensive and the least costly model of each category of thermometer in order to demonstrate the range of costs for each type and how the costs might overlap depending on which model is chosen.

This economic assessment only includes the direct costs of purchase price and, where applicable, the costs of consumables (e.g. disposable covers, sterilised alcohol-impregnated wipes and replacement batteries). Cleaning, maintenance, repair, and calibration costs, although important, were not included here owing to time constraints in collecting the data for the guideline. However, they are not considered to have an important influence on the relative costs of each model compared with its alternatives.

Device-specific costs were obtained from the MHRA.[27] The same assumptions were used as a basis for the calculation of the costs as were used by Crawford *et al*.[85] Table B.1 summarises the assumptions used in the costing model.

Axilla measurements can be provided by electronic and chemical thermometers. Tympanic measurements are by specialised infrared sensing thermometers only. Chemical thermometers supplied by different companies use different chemicals. Some change permanently when the temperature is raised (e.g. 3M Tempadot) and others change colour for only a short while when placed in contact with a hot object and then return to the original colour (e.g. Insight Nextemp). Both may be labelled single use, but the second type can be used again on the same patient (providing that it is kept clean with alcohol wipes), and is considered to be a reusable model in this analysis.

The cost of staff time required to measure temperature using each type of thermometer was included in the analysis. Each thermometer has an average time to reading, which gives a total number of hours required to read the thermometer per year, which was then calculated up to the 10 year time horizon used in the cost analysis. This average time to reading is based on best guesses and not on empirical data. These times are indicative only since they exclude any time to locate the device, clean the device or fit and remove probe covers. Also, it does not take into account that nurses may be undertaking other tasks while waiting for a reading for thermometers where this may take more than a few seconds. For some adhesive chemical thermometers (e.g. Insight Traxit), the time to reading changed depending on whether it was a first measurement or subsequent measurement since the thermometer was already in position and at the correct temperature. Therefore the average time per patient episode was calculated to be 180 seconds plus 85 seconds (17 × 5) for the 18 measurements, giving a total of 265 seconds.

Table B.1 Assumptions used in the costing model

	Contact/chemical	**Electronic contact**	**Compact contact electronic**	**Infrared sensing (tympanic)**
Number purchased	One per measurement (1 550 000)	One per unit (450)	One per hospital bed (2205)	One per unit (450)
Consumables	Alcohol wipes may be required if single-patient-use devices are used	Probe covers	Alcohol wipes	Probe covers
Battery replacement	No	Yes	Yes	Yes
Replacement	Each patient or each measurement, depending on the model	0%	10% per annum	0%
Approximate readings per inpatient episode	18	18	18	18
Inpatient episodes per year	86 000	86 000	86 000	86 000

The nursing cost per hour (£22) was the hourly cost for a staff nurse on a 24 hour ward published in the *Unit Costs of Health and Social Care* for 2006,[242] which was based on the Agenda for Change salaries for the April 2005 scale at the midpoint for Band 5 (with qualifications).

It should be noted that the analysis did not take into account the additional staff time to change batteries and undertake basic performance checks, although it was recognised that for some models the manufacturers recommend (at least annual) performance and accuracy checks using specialised equipment that can be arranged when a battery needs replacement.

The costs of calibration (a specialised accuracy check) and warranty are not included in the analysis, which is a limitation of the model.

The cost of cleaning (alcohol wipes) is included where these are required after each measurement. For the contact/chemical thermometers used on a single patient, alcohol wipes are not required. For the contact/compact electronic thermometers (axilla using disposable covers), alcohol cleaning of the thermometer body is only required 'when needed' and this is unlikely to be after every measurement. Therefore it was assumed that an alcohol wipe was used after every 50 measurements.

An approximation of 18 readings per inpatient episode was estimated by dividing the estimated number of measurements per year by the number of inpatient episodes per year, and rounding up to the nearest whole number.

Using the above assumptions, the overall cost for each type of thermometer was calculated for those which can provide axilla and ear measurements. The total cost for each type of thermometer for 10 years was calculated using for each site of measurement the minimum and maximum price of the thermometers.

The clinical accuracy of the thermometers is assumed to be the same for all models of thermometer and in all measurement sites in this analysis. This is due to the lack of data on comparative accuracy or ability to detect fever by different models of thermometer, and the lack of data on the impact of temperature accuracy on time to correct diagnosis and initiation of clinical management in children with suspected serious bacterial infection. The assumption is that, used correctly, all the thermometers considered in this analysis can detect a clinically important rise in temperature.

B.4 Results

B.4.1 Axilla measurements

Tables B.2 and B.3 show the results of the cost analysis for axilla measurement showing the comparative costs over 10 years using maximum and minimum prices for each type of thermometer.

Table B.2 indicates that, in an acute care setting, using the least cost models available on axilla sites and including the cost of staff, the compact contact electronic thermometer is the best value for money, followed by the reusable contact/chemical thermometer, although this is four times more expensive. The cheapest electronic contact and the single-use chemical thermometers are more than 12 times more expensive than the cheapest contact/electronic thermometer. The large difference in staff time required to take a temperature (5 seconds versus 3 minutes) account for much of the large difference in cost between these types of thermometer.

Table B.3 shows that using the most expensive models of reusable chemical thermometers in terms of initial purchase price can be less costly over 10 years than the cheaper models. The total cost of the high-priced model including staff time was more than 12 times less than the total cost using the cheapest priced reusable chemical thermometer because the expensive model took only 5 seconds to read after the first initial 3 minute reading. Overall, the results suggest that, in an acute care setting, the best option for a top of the range thermometer was the reusable chemical model, followed by the compact contact electronic model. The worst option was the single-use chemical thermometer which cost over £20 million over 10 years (£14 million when discounted by 3.5%), which was over 14 times more expensive than the next most expensive, which was the electronic contact model (undiscounted).

Table B.2 Comparative cost of thermometers that can provide axilla measurements in a large teaching hospital for 10 years – minimum prices

	Type of thermometer			
	Single-measurement contact/chemical (phase change)	**Reusable contact/ chemical (phase change)**	**Electronic contact**	**Compact contact electronic**
Model used	3M Tempadot	EzeTemp	Sure Temp. Plus	Microlife MT 1671
Supply of thermometers	One per measurement	One per patient episode	One per ward	One per bed
Purchase cost	£0.07	£0.14	£150.00	£3.36
Price of consumables items and ongoing costs (per item)				
Covers			£0.0275	
Battery life (readings)			5 000	3 000
Cost of batteries			£0.75	£0.2200
Cost of cleaning (alcohol wipes)		£0.008	£0.008	£0.008
Annual cost of consumables and ongoing costs calculated using the assumptions stated in Table B.1				
Initial purchase cost	£108,500	£12,040	£67,500	£7,409
Replacement cost per year (10%)				£741
Number of batteries/year			310	517
Cost of batteries /year			£233	£114
Cost of alcohol wipes/year		£12,400	£248	£12,400
Cost of covers/year			£42,625	
Total cost consumables		£12,400	£43,416	£13,771
Time to reading (seconds)	180	180	6	60
Seconds on reading/year	279 000 000	279 000 000	9 300 000	93 000 000
Hours on reading/year	77 500	77 500	2 583	25 833
Annual staff costs	£1,705,000	£1,705,000	£56,833	£568,333
Recurring costs per year (consumables, replacement, staff)	£1,813,500	£1,729,440	£100,249	£582,845
Recurring costs per year (consumables and replacement)	£108,500	£24,440	£110,916	£14,512
Total undiscounted 10 year cost (with staff costs)	£18,135,000	£17,294,400	£1,069,988	£5,835,863
Discounted at 3.5%	*£12,856,243*	*£12,260,326*	*£758,535*	*£4,137,153*
Total undiscounted 10 year cost (without staff costs)	£1,085,000	£244,400	£1,176,655	£152,530
Discounted at 3.5%	*£769,177*	*£173,260*	*£834,153*	*£108,131*

Table B.3 Comparative cost of thermometers that can provide axilla measurements in a large teaching hospital for 10 years – maximum prices

	Type of thermometer			
	Single-measurement contact/chemical (phase change)	**Reusable contact/ chemical (phase change)**	**Electronic contact**	**Contact/compact electronic**
Model used	Insight NexTemp	Insight Traxit	Ivac Temp. Plus II	Proact ST 714
Supply of thermometers	One per measurement	One per patient episode	One per ward	One per bed
Initial purchase cost	0.24	£0.61	£400.00	£13.95
Price of consumables items and ongoing costs (per item)				
Covers			£0.047	£0.045
Battery life (readings)			2 000	1 800
Cost of batteries			£0.95	£0.5900
Cost of cleaning/alcohol wipes			£0.008	
Annual cost of consumables and ongoing costs calculated using the assumptions stated in Table B.1				
Initial purchase cost	£372,000	£52,460	£180,000	£30,760
Replacement cost per year (10%)				£3,076
Number of batteries/year			775	861
Cost of batteries/year			£736	£508
Cost of alcohol wipes/year			£12,400	
Cost of covers/year			£72,850	£69,750
Total cost consumables			£85,986	£70,258
Time to first reading (seconds)	180	180	4	5
Time to subsequent readings, if different (seconds)		5		
Seconds on reading/year	279 000 000	7 310 180	6 200 000	7 750 000
Hours on reading/year	77 500	2 031	1 722	2 153
Annual staff costs	£1,705,000	£44,673	£37,889	£47,361
Recurring costs per year (consumables, replacement, staff)	£2,077,000	£97,133	£123,875	£120,695
Recurring costs per year (consumables and replacement)	£372,000	£52,460	£85,986	£73,334
Total undiscounted 10 year cost (with staff costs)	£20,770,000	£971,333	£1,418,751	£1,237,711
Discounted at 3.5%	*£14,724,244*	*£688,596*	*£1,005,780*	*£877,437*
Total undiscounted 10 year cost (without staff costs)	£3,720,000	£524,600	£1,039,863	£764,100
Discounted at 3.5%	*£2,637,178*	*£371,899*	*£737,178*	*£541,685*

B.4.2 Tympanic measurements

Tympanic measurements can be provided by infrared sensing thermometers only, so there is no comparative analysis by different types of thermometer, only by the least and most expensive type of infrared sensing model. The total cost of using exclusively the least costly model and the most expensive model of infrared sensing thermometer was calculated (Table B.4).

Table B.4 shows that the lowest purchase price model (the infrared sensing thermometer) has a higher overall cost that the highest priced thermometer because of the increased cost of consumables (nearly double the price) which contribute to the total cost. The cost of covers is lower in the most expensive model. The recurring costs per year (consumables and staff) are more than £50,000 more per year for the cheaper model, which outweighs the higher initial purchase price of the most expensive model. The results also indicate that time to reading is not an important cost driver for tympanic measurement since the assumption is that it takes only 2 seconds to make a temperature reading. The (discounted) cost over 10 years including staff costs is in the range £732,000 to £1,064,000, which is the same order of magnitude of costs as the thermometers used for axilla measurement, except that of the single-use chemical thermometer.

Table B.4 Ten-year costs for infrared sensing thermometers, discounted at 3.5%: summary results for tympanic measurements – minimum and maximum prices

	Model of infrared sensing thermometer (tympanic)	
	TB-100 (thermo Buddy)	**First Temp. Genius**
Purchase cost	£18.32	£249.49
Supply of thermometers	One per ward	One per ward
Price of consumable items and ongoing costs (per item)		
Probe covers	£0.0760	£0.047
Battery life)readings)	6000	5000
Cost of batteries	£0.68	£0.950
Cost of cleaning (alcohol wipes)	£0.008	
Annual cost of consumables and ongoing costs calculated using the assumptions stated in Table B.1		
Initial purchase cost	£8,244	£112,271
Number of batteries/year	258	310
Cost of batteries/year	£176	£295
Cost of alcohol wipes/year	£12,400	
Cost of covers/year	£117,800	£72,850
Total cost consumables	£130,376	£73,145
Time to reading (seconds)	2	2
Hours on reading/year	861	861
Annual staff costs	£18,944	£18,944
Recurring costs per year (consumables, replacement, staff)	£149,320	£92,089
Recurring costs per year (consumables and replacement)	£130,376	£73,145
Total undiscounted 10-year cost (with staff costs)	£1,501,445	£1,033,160
Discounted at 3.5%	*£1,064,403*	*£732,427*
Total undiscounted 10-year cost (without staff costs)	£1,312,001	£843,716
Discounted at 3.5%	*£930,102*	*£598,126*

B.4.3 Comparison of costs of axilla and tympanic measurement

Table B.5 shows the combined results for all types of thermometer used in axilla and tympanic measurement. It indicates that the relative cost of each type of thermometer changes depending on whether an expensive or a cheap model is used and whether staff time is included in the cost, as the time required to read the temperature is an important driver of total cost.

B.5 Conclusions

The cost analysis undertaken here is based on the use of thermometers on a ward of an acute hospital. The study[85] on which this analysis is based suggests that staff time is an important driver in determining which thermometer should be used. The analysis presented here supports this hypothesis. The 10 year cost of a (high- and low-priced) thermometer including staff time includes ranges between approximately £600,000 and £1,000,000 for all types of thermometers, except for the single-use chemical thermometer which is far more expensive. The analysis incorporates a number of assumptions about time to reading for accurate measurements, but it suggests that the initial purchase price of thermometers can be misleading as the total cost of using a specific model of thermometer depends on the number of uses, the cost of consumables and the staff time needed to make an accurate reading. Clearly different clinical settings will give different results and may change the relative cost between thermometers, making it more cost-effective to choose one type of thermometer in a low-volume clinical setting and another in a high-volume setting. This analysis shows that those in charge of purchasing thermometers need to consider staff costs and consumables as well as initial purchase price when considering bulk purchases.

Table B.5 10 year costs by thermometer, with and without staff costs, discounted at 3.5%: summary results for both axilla and tympanic measurements

	10 year cost by type of thermometer				
	Chemical (single use)	**Chemical (reusable)**	**Electronic contact**	**Compact contact electronic**	**Infrared sensing (tympanic)**
Minimum priced model (with staff costs)	£12,856,243	£12,260,326	£758,535	£4,137,153	£1,064,403
Maximum priced model (with staff costs)	£14,724,244	£688,596[a]	£1,005,780	£877,437[a]	£732,427[a]
Minimum priced model (without staff costs)	£769,177	£173,260	£834,153	£108,131	£930,102
Maximum priced model (without staff costs)	£2,637,178	£371,899	£737,178	£541,865	£598,126

[a] Indicates a lower total discounted 10 year cost than the least expensive version of the model due either to higher cost of staff time or consumables.

Appendix C

Economics of referral to a specialist paediatric team of a child with fever without source

C.1 Background

One of the key areas where the guideline has important resource-use implications is in its impact on changes in referral patterns. Some recommendations in the guideline may lead to a change in current referral practice from general 'first-line' medical care to specialist paediatric services (that is, from primary care, or an emergency department, or following a telephone call to NHS Direct to either hospital-based or community-based paediatricians).

The recommendations in the guideline that may change referral patterns are for a child considered to have an immediately life-threatening illness to be transferred without delay to the care of a paediatric specialist. All children with 'red' features will need to be referred to specialist care, and all children with 'red' or 'amber' features need to be seen within 2 hours if referred from remote assessment.

It was envisaged that the clinical guideline would include an economic analysis of the impact of changing referral patterns. Time was set aside in GDG meetings to develop a decision tree to analyse the costs and outcomes of such a change.

The decision tree is presented in Figure C.1. The aim was to undertake a threshold analysis to evaluate the additional costs (or savings) associated with one additional case of serious bacterial illness (SBI) detected.

C.2 Structure of the decision model

An outline of the pathways of the decision tree is presented in Figure C.1. The model starts with a population (say, of an average GP practice) of which a proportion of children per year present to 'first-line' services with signs or symptoms of undifferentiated fever.

The first decision (the first split in the pathway) in the model is whether or not to refer the child to specialist paediatric services. If a child is referred, there is a chance that the child has an SBI or they do not. There is a chance that the child may have SBI confirmed through diagnostic tests and subsequently be treated for SBI, and there is a chance that no SBI is confirmed and the child is sent home.

If a child is sent home following referral to a specialist paediatric team, they will improve without treatment if they have no SBI. If they have an untreated SBI, their condition will worsen at home. They will consequently either be sent to hospital (usually as an emergency) or not be sent to hospital. Of those children not sent to hospital, a proportion will improve and be well at home, a proportion will deteriorate but remain unwell, and a proportion will die at home.

If a child is not referred to a specialist paediatric service, there is a chance that they do not have an SBI and would improve without treatment, and a chance that they have an SBI. If they have an SBI, they will either be referred again to a specialist paediatric team for a second time, or not. The structure of the pathway of children referred for a second time to a specialist paediatric team was the same as for children referred the first time, except that it was assumed that a child would not be sent home after a second referral. All children referred to hospital a second time with the same episode of fever without source would be diagnosed and treated for SBI in hospital. This is an assumption and not based on any clinical evidence that could be identified.

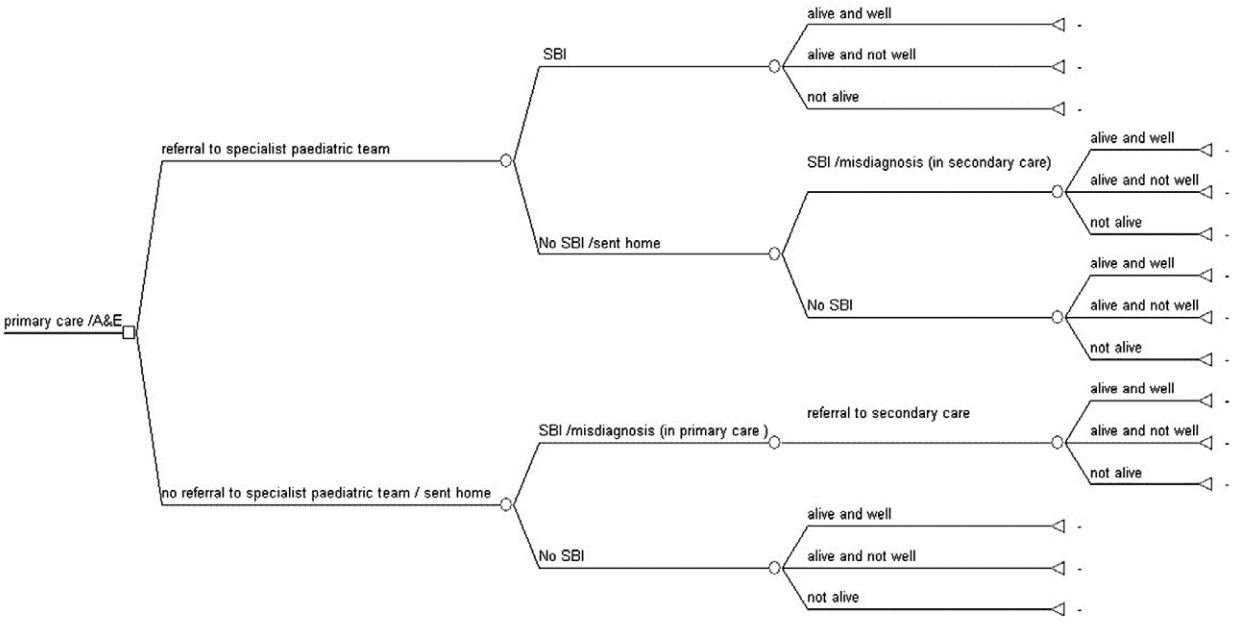

Figure C.1 Decision tree for analysing the impact of changing referral patterns for a child with fever without source

C.3 Data required for the model

In order to make this analysis viable, the decision tree required specific data which the GDG thought might be available in some form, through either the published literature or in unpublished data such as national (or even local) audit data. A table with all the key model parameters was circulated among the GDG members to try to locate this data. At the same time, the GDG members were asked whether they could arrive at some consensus about the values required for the model from their collective expert opinion.

As the discussion progressed, it was agreed that the meaningful comparison of referral patterns required other data that would be very hard to obtain either from published sources or from GDG consensus.

A number of key assumptions in the model could not be agreed upon. The first was that the outcomes of care would be worse if treatment was delayed by sending a child home, either from primary care or from secondary care with undiagnosed SBI. Nor was it clear that the costs of care would be substantially different if there were a delay in treatment. It was not possible to estimate the impact that such a delay would have on final outcomes (the death rate) or costs because of the uncertainty around the natural history of specific serious bacterial diseases such as meningitis. Also, it was not possible to agree upon the proportion of children with fever that are currently referred for primary care.

It became apparent after two GDG meetings that it was not possible to reach a consensus on the data required to populate the model, especially because the model considers all forms of SBI and no one specific diagnosis, such as meningitis or pneumonia. Also, since the guideline focused on diagnosis and initial management of SBI only, it would be difficult to obtain reliable data on the number of children alive and well or not alive following detection and initial management of SBI, without looking at treatment and longer term outcomes.

A further problem was the lack of baseline data on the underlying prevalence of SBI in the population. The most uncertain data of all was the estimate of the proportion of cases of SBI that might be missed by sending children home without further tests, in both primary or specialist care settings.

Some data were available from two published studies, one American[243] and one from the UK.[121] Table C.1 below indicates the data that could be used in the model (part I) and the gaps where no data could be found (part II).

Table C.1 Data required to complete the economic model for referral of children to specialist paediatric services of children with fever without source

Parameter	Data
Part I: Values where some data were identified	
Primary care	
Proportion of children under 5 referred to a specialist paediatric team (secondary or community care setting) from first-line services (primary care and A&E)	96% secondary care referrals, 4% tertiary referrals[121]
Specialist paediatric care	
In specialist paediatric setting, the proportion of children presenting with undifferentiated fever who screen positive for SBI	62% (460/747 infants)[244]
In specialist paediatric setting, the proportion of children with undifferentiated fever who screened negative for SBI	38%[244]
OR	
In specialist paediatric setting, the proportion of children tested positive for suspected SBI and treated	29% (41/141 infants)[121]
In specialist paediatric setting, the proportion of children screened positive for SBI with a confirmed diagnosis	14% (64/460 infants), 8.7% of all infants admitted (64/747)[244]
In specialist paediatric setting, the proportion of children with no suspected SBI who are admitted for review and go on to develop confirmed SBI	0.68% (1 patient)[244]
In specialist paediatric setting, the proportion of children with no suspected SBI who are sent home (managed as outpatients or under observation at home, with review), who subsequently are admitted to hospital with confirmed SBI	0%[244]
Part II: Values where no data were identified	
Number of children (per year) presenting in primary care with undifferentiated fever (e.g. by region/PCT/GP practice)	
Proportion of children in primary care not referred to specialist paediatric care (no signs/symptoms) who are sent home and subsequently develop SBI	
Proportion of children referred to specialist paediatric care who are sent home and subsequently develop SBI	
Additional healthcare resource use of children sent home from primary care who go on to develop SBI	
Additional healthcare resource use of children sent home from specialist paediatric care who go on to develop SBI	
Outcomes (although outside the scope of the guideline)	
Prognosis/outcome for children who are referred immediately from primary to a specialist paediatric team for suspected SBI: • with confirmed SBI treated in hospital • sent home with no confirmed SBI which subsequently develops into SBI • no subsequently confirmed SBI	Differentiate between: • alive and well • alive and not well • not alive
Prognosis/outcome for children who are NOT referred immediately to a specialist paediatric team for suspected SBI: • who go on to develop SBI • with no SBI	Differentiate between: • alive and well • alive and not well • not alive

Appendix D

Economic evaluation of C-reactive protein versus procalcitonin

Fever without localising signs in young children remains a diagnostic problem. There is evidence that procalcitonin (PCT) may be more effective in terms of sensitivity than commonly used C-reactive protein (CRP). However, the evidence on diagnostic accuracy is not robust. An economic evaluation approach was adopted to assess the cost-effectiveness of using different estimates of specificity and sensitivity of these tests from the published data.

A simple decision-analytic model was constructed which incorporated both the sensitivity and specificity of each test. Additional correct diagnosis was the outcome used. The model is based on limited information on PCT in children with fever without apparent source (FWS) and in other situations PCT may perform better than CRP.

Figure D.1 is a schematic representation of the decision tree used in the analysis. Before investigations, febrile children were assumed to have one of two health states: either with no serious bacterial illness (SBI) or with SBI. After the investigations, febrile children were assigned a true positive or negative diagnosis, or a false positive or negative diagnosis. The model covers only the initial diagnosis and not the cost of treatment of SBI. The term SBI for this guideline includes seven potential types of serious infection. Each type of infection would require a different pathway. The description of this pathway and its potential outcomes was beyond the scope of this guideline.

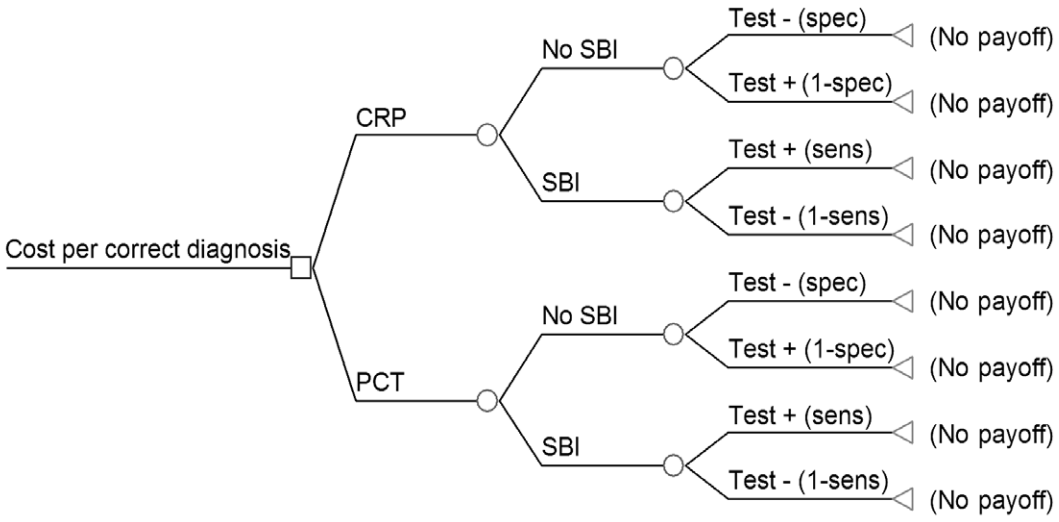

Figure D.1 Cost-effectiveness of PCT versus CRP decision tree

Methods

Clinical effectiveness

'Correct diagnosis' was identified as the outcome of the analysis. This can take into account both sensitivity and specificity in order to derive the precise levels of correctly diagnosed cases for each type of investigation.

Correct diagnosis = true positive + true negative diagnosis

Data used in the model

Diagnostic accuracy

Estimates of the diagnostic accuracy are taken from the systematic review of the clinical evidence presented in this guideline. Specifically, there are two studies which provide clinical effectiveness for the model. Table D.1 summarises the data on diagnostic accuracy of PCT and CRP presented in these studies of children with FWS. The levels of specificity and sensitivity from the most recent study are used as baseline parameters for the model.

Table D.1 Source of effectiveness data from the existing published studies

	CRP	PCT	Source
Sensitivity	0.79	0.93	Galetto-Lacour *et al.* (2003)[178]
Specificity	0.79	0.74	
Sensitivity	0.89	0.93	Lacour *et al.* (2001)[245]
Specificity	0.75	0.78	

Prevalence of SBI for children with fever without localising signs is a key parameter of the model. However, no accurate prevalence data for the UK could be identified. Therefore, an estimate of 5% was used in the first instance based on GDG expert opinion, which is a strong assumption of the analysis. Table D.2 summarises all the clinical data used as baseline parameters in the model.

Table D.2 Baseline parameters for the effectiveness data

	CRP	PCT	Source
Prevalence	0.05	0.05	GDG expert opinion
Sensitivity	0.79	0.93	Galetto-Lacour *et al.* (2003)[178]
Specificity	0.79	0.74	

Costs

The perspective adopted by the economic analysis was that of the NHS, and prices are for 2006. The cost of the test included the cost per investigation only. It was assumed that the price of the investigation reflects the cost of reagents and the cost of labour as well. The cost of CRP could be identified by the GDG members from their local services. However, the cost of PCT was more difficult to estimate since a published price, including all associated costs, could not be identified from the sources available. One GDG member provided the price for a PCT assay. Table D.3 shows the cost of each type of investigation and the source of the cost data. The potential cost of SBI treatment is not included in the analysis.

Table D.3 Baseline parameters for the cost data

	CRP	PCT	Source
Cost per investigation	£1.50	£9.00	GDG

Results

A cohort of 1000 febrile children without localising signs for each type of investigation was assumed. The results of the economic analysis are presented as cost per correct diagnosis. Using baseline data, CRP appears to be a significantly less costly and possibly more accurate diagnostic test than PCT in terms of correctly diagnosed cases (Table D.4). Taking into account only the levels of sensitivity, PCT is a better diagnostic test than CRP as it manages to capture more SBI (more

true positives). However, PCT may have a lower level of specificity than CRP which means that PCT identifies fewer true negative results than CRP. Also, the decrease in the correctly diagnosed cases having no SBI is higher than the increase in the correctly diagnosed cases having SBI and for this reason the final number of correctly diagnosed cases is lower for PCT than CRP.

Table D.4 Additional cost per additional correct diagnosis detected of PCT over CRP

Investigation	Cost	Effectiveness (correct diagnoses)	Incremental cost (additional cost of PCT over CRP)	Incremental effectiveness (additional correct diagnosis)	Additional cost per additional correct diagnosis
CRP	£1,500	790			
PCT	£9,000	750	£17,500	–41	Dominated (more costly, less effective)

Sensitivity analysis

Both one-way and two-way sensitivity analyses were undertaken. One-way sensitivity analysis involves altering the value of a single parameter while holding all the others constant, to determine how robust the conclusion is to the values used in the model. Two-way sensitivity analysis means that two parameters are changed simultaneously.

1. Varying the prevalence of SBI in the population

Given that there is lack of published evidence with regard to the prevalence of SBI for the febrile children, sensitivity analysis was conducted by varying the levels of prevalence in order to assess the extent to which the final results are dependent on change in this parameter. CRP dominated PCT until the prevalence reached 27% in the population. However, the additional cost per additional correct diagnosis was £5,769.

2. Diagnostic accuracy of CRP and PCT

Sensitivity analysis was conducted by using various estimates of the diagnostic accuracy of the tests. Data from an older study conducted by the same authors[245] was inputted into the cost analysis. Table D.5 shows that, using different data for diagnostic accuracy, the additional cost per additional correct diagnosis by switching from using CRP to PCT to detect SBI may be up to £246 per test.

Table D.5 Results of sensitivity analysis using levels of diagnostic accuracy from the second study[245]

Investigation	Cost	Effectiveness (correct diagnoses)	Incremental cost (additional cost of PCT over CRP)	Incremental effectiveness (additional correct diagnosis)	Additional cost per additional correct diagnosis
CRP	£1,500	757			
PCT	£9,000	788	£7,500	31	£246

3. Sensitivity of the diagnostic tests

One-way sensitivity analysis was conducted to test the robustness of the final results by varying the levels of sensitivity of the tests only. CRP still dominated PCT when the level of sensitivity for PCT was increased to 1.00 (maximum). Also, CRP still dominated PCT even after decreasing significantly the level for CRP. This means that the CRP was still more cost-effective than PCT even when changing only the levels of sensitivity of PCT and CRP.

4. Specificity of the diagnostic tests

Sensitivity analysis was undertaken to check the robustness of the results with regard to the levels of specificity. The final results were sensitive to the level of specificity of the tests. By increasing the level of specificity from 0.74 to 0.79, the PCT became more effective than CRP. However, the additional cost per additional correct diagnosis was £1,071 per test.

Limitations

The economic analysis of PCT versus CRP was based on the best available evidence, which was completely absent for prevalence of SBI. Also, the sensitivity and specificity data were from a very limited number of studies of children with FWS. Generally, PCT performs better than CRP in other situations, so FWS data may not be reliable.

Therefore, great care is needed when interpreting and deriving the final results of this analysis, as there are some limitations. Sensitivity analysis shows that the final results are sensitive to the prevalence of SBI and to the levels of diagnostic accuracy at a cost per test of £1.50 and £9.00 for CRP and PCT, respectively (cost data was from GDG members and not published data). This indicates that the validity of the results depends considerably on the quality of the data which are used in order to derive the levels of correct diagnosis.

Another caveat of the model is the choice of outcome measure. The preferred methodology according to the NICE technical manual is to present outcomes in terms of the quality-adjusted life year (QALY). Given the range of SBIs under consideration, and the associated range of treatment pathways, it was impossible to estimate the cost per QALY for these diagnostic tests. This may have some influence over the results, as some children may undergo unnecessary treatment, while others will not be given required treatment, based on false results following diagnosis. By measuring the results in cost per correct diagnosis, the model may not reflect the true long-term costs and outcomes associated with each diagnostic method.

Conclusions

Using the strong baseline assumptions, CRP appears to be both less costly and to provide more correct diagnoses than PCT. However, this result was highly sensitive to test accuracies, which were different in the two studies that reported data for diagnosing SBI in children with fever without localising signs. PCT became more effective than CRP even with small changes in specificity but this increase in effectiveness is associated with higher cost per correct diagnosis.

Without conversion to QALYs, it is not possible to assess whether this additional cost is 'worth' the additional benefits of PCT.

Given current published evidence, this economic analysis does not support the replacement of CRP with PCT in routine practice.

Appendix E

2 hour time limit for an urgent face-to-face consultation following remote assessment: GDG reasoning and justification in the absence of data to inform a formal economic analysis

E.1 Background

The GDG was asked to produce a guideline to aid healthcare professionals in identifying children with serious bacterial illness (SBI) in an attempt to reduce mortality and morbidity in young children. During the guideline development process, the GDG identified evidence-based symptoms and signs that indicate whether a child has a high risk of having SBI. It also identified symptoms and signs that indicate that a child is at very low risk of SBI and can be looked after at home. Current practice is not evidence based and is variable. It is likely that referral patterns from some healthcare providers will change when the guideline is implemented. It is anticipated that some children who would previously not always have been recognised as needing specialist attention (a very small proportion of children who present with fever) will in the future be referred for consultation with a specialist. Furthermore, a number of children for whom referral is not indicated (the far larger proportion) and who would previously have been referred for consultation or unnecessary investigations, will now not be referred unnecessarily under this new guidance. The focus of the guideline is that the right children should be getting the right treatment at the right time and adverse health outcomes (including death) will therefore be avoided. The GDG noted the evidence that problem-based guidelines with care pathways for children with medical problems reduce invasive investigations, and lead to more appropriate treatment and reduced time spent in accident and emergency (A&E) services.[246]

E.2 GDG justification of the 2 hour waiting time for an urgent referral

An important feature of this clinical guideline on children with feverish illness is the introduction of a 'traffic light' system to identify children with varying degrees of risk of serious illness. The guideline makes clear recommendations on which children are unlikely to require medical attention beyond information and reassurance (children with 'green' features) and who can thus be confidently managed at home. The guideline identifies children who require an urgent face-to-face consultation with a healthcare professional ('red') and those who may require a face-to-face consultation or require a healthcare 'safety net' to be put in place ('amber').

Because of the limited information that can be obtained from a remote assessment, the GDG originally recommended that all children with 'red' or 'amber' features should be referred for urgent face-to-face assessment. The GDG felt it was necessary to make a recommendation on the maximum time a child should have to wait to be first assessed by a healthcare professional if they were classified as requiring an urgent consultation during a remote assessment. The aim of this was to recommend a time frame within which action taken will make a difference to the outcome for the child.

Despite an extensive search of the published and grey literature, no clinical data could be identified to define this limit. The GDG debated the issue among themselves and decided that it was such an important question that wider consensus was required. Accordingly, the question went out as part of the Delphi consultation exercise as agreed in the guideline methods protocol. A high level of agreement was reached for a maximum wait of 2 hours following referral for urgent face-to-face assessment (83% agreement). 2 hours was chosen as one of the time periods for the

Delphi exercise because it is an existing Department of Health standard for urgent referrals for out-of-hours health care.[247]

It was recognised by the GDG that children with one or more 'amber' signs included children who may not require an urgent referral. It was agreed to make a recommendation on specific waiting times only for children with 'red' features, and to recommend that a child with one or more 'amber' features is seen face-to-face by a healthcare professional, but that the timing of the consultation for these children could be carried out within a longer time frame which could be based on the clinical judgement of the person carrying out the initial remote assessment.

The GDG believes that a 2 hour maximum wait for an urgent consultation does not represent an uplift in care and is a cost-effective use of NHS resources. The reasons for this conclusion are outlined here. First, there is audit data to suggest that this is already accepted routine practice for children at a high risk of SBI. Second, the GDG strongly believes that a wait longer than 2 hours could potentially increase mortality and morbidity. Finally, the GDG believes that by using a traffic light system to classify children according to their risk of having a serious illness, healthcare professionals will have a clearer indication as to which children do genuinely require an assessment by a healthcare professional within 2 hours. By excluding the children with 'green' features and most of the children with 'amber' features from this urgent referral group, the GDG believes the number of children who are referred for a face-to-face assessment by a healthcare professional within 2 hours will be reduced.

Evidence was presented to the GDG to show that the Department of Health has already set a national standard for response to urgent calls as part of the *National Quality Requirements in the Delivery of Out-of-Hours Services*.[247] This specifies a maximum 2 hour wait for a face-to face urgent consultation for out-of-hours care: 'Face-to-face consultations (whether in a centre or in the patient's place of residence) must be started within the following timescales, after the definitive clinical assessment has been completed:

- Emergency: Within 1 hour.
- Urgent: Within 2 hours.
- Less urgent: Within 6 hours'.

Further evidence was presented from NHS Direct that, in line with the out-of-hours Quality Requirements, currently recommends a time frame of less than 2 hours for a child requiring an urgent face-to-face assessment. Audit data from NHS Direct was presented to the GDG to show that, of those who contact NHS Direct via the 0845 telephone number, 31.8% of children under 5 years with a primary diagnosis of fever were referred on for an urgent face-to-face clinical assessment within 2 hours, following detailed nurse assessment (Figure E.1). Also, 47% of out-of-hours calls for the same patient group were referred for a face-to-face clinical assessment within 2 hours. (It is important to note that during the course of these assessments a focus for the fever may be identified which in itself justified the referral within this time period.)

One stakeholder comment suggested that a 2 hour time limit for an urgent referral would be very difficult to implement in an A&E care setting where the 4 hour waiting time directive is the current target for the NHS. The guideline is clear that primary care should continue to be the first point of contact for a child with fever (as validated by the NHS Direct data presented here showing that children with fever are referred to the GP within 2 hours, 6 hours or for a routine appointment). The GDG clarified that the new recommendation means that a child with 'red' features should be offered an *initial* assessment (for example, by an A&E triage nurse) within 2 hours, and that the current target of 4 hours for A&E is the time limit for initial assessment, treatment and discharge. The promise to patients derived from the NHS Plan in 2000 set out in *Your Guide to the NHS* stated that, on arrival in A&E, 'you should be assessed by a nurse or doctor, depending on how urgent your case is, within 15 minutes of arrival …'.[248]

These two waiting time targets are therefore compatible and in keeping with the Department of Health NHS Plan and Quality Requirements. Other stakeholders who commented on the 2 hour time frame felt that it was too long a wait for children requiring an urgent referral.

The GDG believes that, if the traffic light system is adhered to, the recommendation for a 2 hour urgent referral will apply to a smaller but more relevant proportion of children with fever than are currently referred for an urgent assessment. A GDG member who is a GP presented evidence

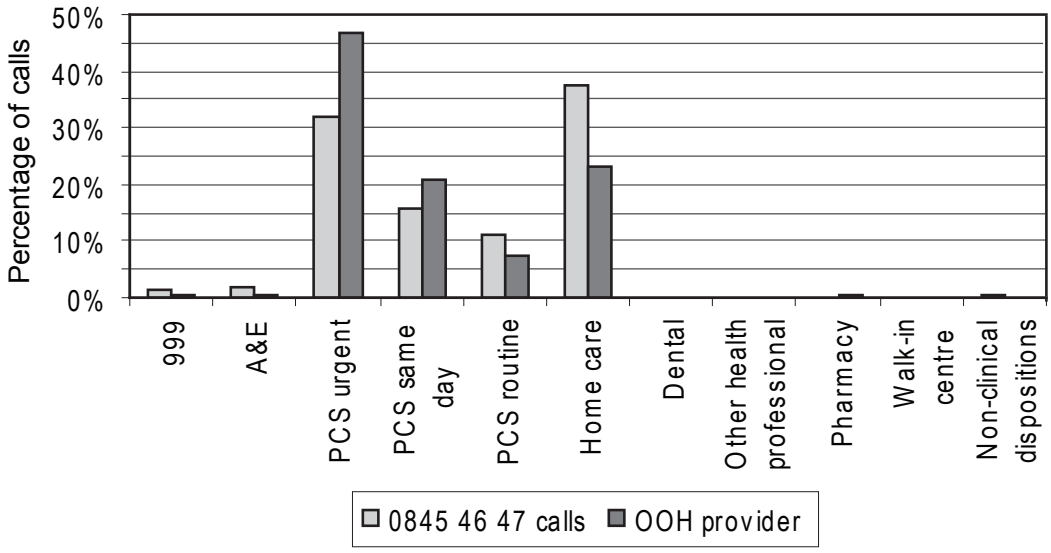

Figure E.1 NHS Direct audit data covering the period 1 January 2006 to 31 December 2006; this data equates to a coverage of the whole of the population of England for the 0845 46 47 calls and a population coverage of 708,500 for the out-of-hours calls

to the GDG from a survey of children presenting with fever as their predominant symptom and the prevalence of 'amber' features in this patient group. The practice has 9518 patients, with 633 children aged 5 years and under.

There were 157 consultations in this age group, involving 77 children with 83 episodes of acute fever with no other symptoms that worried the parent. Fifty-three episodes were telephone triage, and in 24 of these cases a face-to-face consultation was advised (45.2%). In thirteen of these cases, an 'amber' symptom was noted. The rest (104) were all face-to-face consultations without telephone triage, and in 18 consultations, 'amber' symptoms were recorded, with a diagnosis made in nine cases. Six of these children were referred for a paediatric assessment unit for specialist advice, which represents 3.8% of children presenting with fever as their primary symptom. During the period of the survey, there were no children who would have been classified as 'red' under the traffic light system.

Only 13 of those assessed remotely and 18 of those assessed face-to-face showed 'amber' features, and thus potentially none of these children fell into the urgent referral group. The absence of either 'red' or 'amber' features would have allowed at least some of these children to be confidently managed at home, and those with 'amber' features only could have been referred within a longer time frame of safety netting, which could have been put into place following face-to-face assessment. The data suggests that the proportion of children who require an urgent face-to-face referral following remote assessment would potentially be reduced and is very small compared with the far greater number of children who have either 'amber' symptoms and require assessment within a longer time frame by a healthcare professional or have self-limiting illness (who can be confidently managed at home).

Having reviewed the data and based on their own experience, the GDG consensus was that an individual GP in a group practice such as the one surveyed would be unlikely to see more than one or two cases of SBI a year, and for some of the more rare conditions would be unlikely to see one case in their professional career. During the period of the survey there were no children who would have been classified as 'red' under the traffic light system. This is because urgent referrals would only be needed for children with 'red' features and a proportion of children with 'amber' features. This assertion is supported by the data in the GP survey referred to above where no children were classified as 'red' and 19% were 'amber'.

Further evidence of the number of children likely to present to secondary care with 'red' symptoms was considered. An American study of 6611 febrile children presenting to an emergency department found that 3.3% of children had a Yale Observation Score greater than 10.[101] A YOS score of 10 means the child has symptoms that are 'red' signs and symptoms on the proposed traffic light system. It is important to note that the 3.3% is a small fraction of the total number of children with fever but it still may be an overestimate because the data do not indicate how many of the 3.3% of children with a YOS score over 10 have other symptoms which are 'red' features in the traffic light system. Also, the study was done in a hospital setting and it is based on the American healthcare system. Furthermore, the GDG's recommendation would only apply to children referred from remote assessment in this context and not all children with 'red' symptoms, many of whom will present for a face-to-face clinical assessment as their first point of healthcare contact.

E.3 Cost-effectiveness of a 2 hour referral for face-to-face assessment

The GDG did not identify any data on the likely cost or cost savings from recommending a 2 hour time limit for an urgent face-to-face assessment or the likelihood of this leading to an increase in referrals to specialist care. The issue was discussed in detail during a number of GDG meetings. The main point that was agreed was that the GDG believes that the guideline's recommendations will support the identification of those children requiring urgent assessment, referral and initiation of management which in some cases will be life-saving and certainly prevent unnecessary long-term morbidity. There is a cost-effectiveness threshold under which any intervention that saves lives or prevents serious morbidity is generally seen to be cost-effective. If we assume that a life-saving intervention that prevents one death in a very young child is worth around 25 QALYs (75 years discounted at 3.5%), then an intervention that costs £500,000 (25 × £20,000) and saves one life is within the threshold for cost-effectiveness.

The GDG found it impossible to guess how many children with 'red' symptoms who were seen face-to-face urgently from a remote assessment (within 2 hours) would be saved from death or serious morbidity. The argument for cost-effectiveness is that £500,000 (to save one child's life) could be spent on additional face-to-face assessments for it to be cost-effective if it saved one life. The cost of additional face-to-face assessment is hard to estimate if it is within surgery hours, but it costs around £35–40 for an out-of-hours consultation*[249] or £70 for a home visit.[250] Therefore if an additional 7,100 (£500,000/£70) patients could be seen for face-to-face assessment, this would be cost-effective if it saved one additional child's life.

This does not take into account the potential savings from preventing the health and social care costs of serious morbidity in children which would make the intervention more cost-effective. Nor does it take into account that the carers of children with 'red' symptoms will contact health services somehow, and the guideline emphasises the fact that this should almost always be primary care in the first instance. This is a less expensive option than A&E services which cost £77–105 per visit for 2005/06, depending on the cost of investigations.[250]

This very brief analysis of cost-effectiveness assumes that at least three children's deaths are prevented every year in the district general hospital by putting in place a 2 hour assessment in a population of 250,000, and there are children are currently at risk of death and serious morbidity who are not currently being urgently assessed and referred for specialist advice. It also assumes that all children at risk of death from SBI are seen eventually by a healthcare professional, and do not die at home without any health service contact. It is assumed that deaths can be prevented by more timely referral to specialist services for those children who urgently need it, and that the cost of investigations and initial management once reaching a specialist care unit would be the same at whatever stage they were referred (that is, a standard package of investigations and management of a child with suspected SBI would be initiated).

Clearly there are costs around diagnosis and initial management of a child with suspected SBI once they reach specialist services, but the GDG was not clear that these would be any different (whether higher costs if a child is referred urgently or higher if referred after a delay of more than

* Annual cost or provision of out-of-hours care in England was £316 million in 2004–05, and the number of people using the service in England was 9 million.

2 hours). Without empirical data, these assumptions cannot be verified, but the GDG members believe that these are conservative assumptions that reflect the real world closely enough to make the assertion that the 2 hour face-to-face referral is very likely to be cost-effective.

E.4 Conclusion

The aim of this guideline is to improve the identification of those children who are genuinely at a high risk of serious illness and require urgent assessment and treatment to prevent death and serious morbidity. Using the traffic light system, those children in the 'red' category have been identified as being at a high risk of serious illness and the GDG believes that it is already established best clinical and cost-effective practice for this small group to be seen urgently within 2 hours and this guidance will reinforce that practice. The guideline will also reduce unnecessary assessment (urgent and routine) and diagnostic testing of children who are at low risk of serious illness.

Appendix F

Declaration of interests

GDG member	Description (industry/organisation)				
	Personal		Non-personal		Non-current interests
	Specific	Non-specific	Specific	Non-specific	
Andrew Riordan	Received sponsorship from an immunoglobulin manufacturer to attend a scientific meeting in Hungary		Member of North West Advisory Board on Human Papilloma Virus Vaccine (GlaxoSmithKline UK)	Funding for Rotavirus epidemiology study (GSK vaccines)	
Peter Rudd	Commentary on paper in *Arch Dis Childhood* on neonatal infection, publication date 2007 (BMJ Publications); chapter on fever in children for Forfar and O'Neill *Textbook of Paediatrics*, publication date 2007 (Churchill Livingstone)				
Richard Bowker	Systematic review study on the use of fluid for resuscitation of children with circulation shock				
James Cave				Director of Downland Services Ltd, a company that runs a dispensing NHS pharmacy. Company holds agreements with pharmaceutical companies on the purchasing of drugs. Partner in The Downland Practice which dispenses medicines to a number of its patients and holds agreements with pharmaceutical companies on the purchasing of drugs.	

GDG member	Description (industry/organisation)				
	Personal		Non-personal		Non-current interests
	Specific	Non-specific	Specific	Non-specific	
Martin Richardson	Writing an article on childhood infections for *Independent Nurse*				
Sharon Conroy	Member of the executive committee of the Neonatal and Paediatric Pharmacists group. This body has a number of corporate partners who are pharmaceutical manufacturers. Their financial support is used by the group to subsidise conferences, support research projects and other professional activities of the group for the educational benefit of its members and ultimately paediatric patients and their families.				
Edward Pursell	Received thermoscan thermometers and covers for use in research costing £200 (Braun Healthcare)				
Monica Lakhanpaul			Funding by the RCPCH for a project on children presenting acutely to hospital, funding to Leicester University (Well Child)	£80,000 grant from PCT and University for Research Fellow to develop a multimedia package for implementation of EBM to undergraduates, funding to Leicester University	Research Fellow for a study of pimecrolimus effects on children, funding to Leicester University (Novartis); £201,000 grant for a randomised placebo-controlled trial of oral steroids versus placebo for treatment of pre-school wheeze, funding to Leicester University (Asthma UK); part of a project paid by Well Child for the development of clinical guidelines for paediatric emergency care, £350,000 paid to Nottingham University; co-applicant of grant for 'RCT for treatment of community-acquired pneumonia: intravenous versus oral treatment', £96,000; co-applicant for guideline on children with altered consciousness (Peyes Foundation)

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Notes
Abbreviations used are listed on page ix.
All entries refer to feverish illness, particularly in children, unless otherwise noted.
Page numbers in **bold** refer to major discussions.
vs denotes comparisons.

Other NICE guidelines produced by the National Collaborating Centre for Women's and Children's Health include:

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