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Christmas 2013: Research

Were James Bond's drinks shaken because of alcohol induced tremor?

BMJ 2013; 347 doi: <http://dx.doi.org/10.1136/bmj.f7255> (Published 12 December 2013)

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Graham Johnson, *ST5 emergency medicine*¹, Indra Neil Guha, *clinical associate professor of hepatology*², Patrick Davies, *consultant paediatric intensive care*³

Author Affiliations

Correspondence to: P Davies patrick.davies@nuh.nhs.uk

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Abstract

Objective To quantify James Bond's consumption of alcohol as detailed in the series of novels by Ian Fleming.

Design Retrospective literature review.

Setting The study authors' homes, in a comfy chair.

Participants Commander James Bond, 007; Mr Ian Lancaster Fleming.

Main outcome measures Weekly alcohol consumption by Commander Bond.

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Assessment of inflamed joint

Overview	Emergencies	Diagnosis	Resources
Summary Aetiology	Urgent considerations	Step-by-step Differential diagnosis Guidelines	References Images Patient leaflets Contributors Related BMJ content

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Summary

Inflammatory arthritis is a common term for several conditions that manifest as joint pain, swelling, and stiffness, with varying degrees of functional impairment.  These diseases can be broadly categorised as:

- Infectious arthritis
- Immune-mediated arthritis
- Non-infectious and non-immune-mediated inflammatory arthritis
- Paraneoplastic arthritis
- Neoplastic arthritis.

In cases of pain and swelling in a single joint, acute infection is a relatively common cause - one that can result in rapid and irreversible damage. In contrast, the majority of patients with involvement of multiple joints tend to have disorders of chronic duration. The prognosis is good for those who remain unclassifiable, with nearly 50% of such patients undergoing remission requiring no pharmacological therapy on follow-up at 1 year. A multinational collaborative study on undifferentiated peripheral inflammatory arthritis summarised the diagnostic approach to this problem quite succinctly. [1] [2]

Differentiation of joint pain

Joint inflammation is not the only cause of joint pain. In addition to inflammatory joint diseases, pain can also be due to joint damage (e.g., osteoarthritis, or trauma leading to a fracture or internal abnormality), referred pain, or an altered pain threshold (as is seen in central sensitisation syndromes such as fibromyalgia). Pain due to an intra-articular pathology needs to be differentiated from referred pain arising from adjacent soft tissues or extra-articular bone. In the context of referred pain, the range of motion of the joint is usually unaffected, and joint motion does not aggravate pain, whereas palpation over a regional bursa, tendon, or ligament can elicit pain.

Differential diagnosis

Sort by: **common/uncommon** or category

Common

- Septic non-gonococcal arthritis
- Gonococcal arthritis
- Rheumatoid arthritis
- Gout
- Pseudogout

Uncommon

- Indolent infections
- Parvoviral syndrome
- Lyme disease
- Juvenile idiopathic arthritis (pauci-articular type)
- Acute rheumatic fever (ARF)
- Sarcoidosis
- Spondyloarthropathy
- Systemic lupus erythematosus (SLE)
- Adult-onset Still's disease (AOSD)
- Psoriatic arthritis
- Reactive arthritis
- Ankylosing spondylitis (AS)
- Osteoarthritis
- Trauma
- Non-traumatic haemarthrosis
- Hypertrophic osteoarthropathy
- Intra-articular metastatic cancer



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Rheumatoid arthritis

Highlights	Basics	Prevention	Diagnosis	Treatment	Follow Up	Resources
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History & exam

Key factors

- active symmetric arthritis lasting >6 weeks
- age 50 to 55 years
- female sex
- joint pain
- joint swelling
- rheumatoid nodules

Other diagnostic factors

- morning stiffness
- swan neck deformity
- Boutonniere's deformity
- ulnar deviation
- vasculitic lesions
- pleuritic chest pain
- scleritis and/or uveitis

History & exam details

Diagnostic tests

1st tests to order

- rheumatoid factor (RF)
- anti-cyclic citrullinated peptide (anti-CCP) antibody
- radiographs

Tests to consider

- disease activity score(s)

Diagnostic tests details

Treatment details

Acute

mild or moderate disease activity at initial presentation; not pregnant/planning pregnancy

- DMARD
- corticosteroids
- NSAID

high disease activity at initial presentation; not pregnant/planning pregnancy

- methotrexate
- biological agent or tofacitinib
- corticosteroids
- NSAID

planning pregnancy or pregnant

- corticosteroids, sulfasalazine, or hydroxychloroquine

Ongoing

failure to reach low disease activity after 3 months of therapy; not pregnant/planning pregnancy

▼ **Septic non-gonococcal arthritis**[see our comprehensive coverage of Septic arthritis](#)**History**

acute onset, severe pain, fever, malaise; patients at risk include intravenous drug users, those with recent bacteraemia, immunocompromised patients (e.g., those with HIV disease or on chemotherapy or other immunosuppressive drugs), patients with sickle cell disease or other haemoglobinopathies, or those with prosthetic joints

Exam

joint is warm and swollen, with limited range of motion

1st test

- **needle joint aspiration:** identification and recovery of pyogenic bacteria on microscopic examination (Gram stain) of synovial fluid and culture; WBC count in synovial fluid is often $>100 \times 10^9/L$ ($>100,000/mm^3$) (polymorphonuclear leukocytes $>75\%$) [More](#)

Other tests

- **blood cultures :** growth of causative organism [More](#)
- **CT-guided joint aspiration:** WBC count in synovial fluid is often $>100 \times 10^9/L$ ($>100,000/mm^3$) (polymorphonuclear leukocytes $>75\%$)
- **ultrasound-guided joint aspiration:** WBC count in synovial fluid is often $>100 \times 10^9/L$ ($>100,000/mm^3$) (polymorphonuclear leukocytes $>75\%$)

▼ **Gonococcal arthritis**[see our comprehensive coverage of Gonorrhoea infection](#)**History**


fever, chills, malaise, involvement of predominantly lower-extremity joints (knees, ankles), urethritis

Exam

mono- or oligoarthritis, tenosynovitis (wrists, fingers, ankles, toes), pustular or vesiculo-pustular skin lesions

1st test

- **needle joint aspiration:** identification and recovery of *Neisseria gonorrhoeae* from synovial fluid microscopic examination and culture [More](#)
- **blood cultures :** recovery of *N. gonorrhoeae* [More](#)

Other tests**needle joint aspiration**Close 

Synovial fluid culture on Thayer-Martin medium.

- **urethral discharge Gram stain:** gram-negative diplococci

► **Rheumatoid arthritis**► **Gout**► **Pseudogout**Uncommon [show all](#)▼ **Indolent infections****History**

chronic infection, joint pain

Exam

joint swelling and tenderness, usually monoarthropathy

1st test

- **joint aspiration:** may show acid-fast bacillus with special prep and stains, fungal elements [More](#)
- **blood culture:** growth of causative organism

Other tests


- **synovial biopsy:** identification of organism

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Treatment Options

Consult your local pharmaceutical database for comprehensive drug information including contraindications, drug interactions, and alternative dosing.

Ongoing

Patient group	Treatment line	Treatment show all 
confluent scalp lesions	1st	► cryosurgery
	1st	<div><div>▼ topical therapy</div><div><div>→ Topical fluorouracil interferes with DNA and RNA synthesis, influencing fast-growing cells, such as dysplastic cells, more than normal cells, and causing their death. Among patients who tolerate the treatment, the efficacy has been reported to be >90%. [2] Low treatment compliance due to its adverse effects is associated with 60% failure rates. [28] It is available in a 0.5% microsphere delivery system formulation that needs to be used only once daily, rather than twice daily as with regular formulations.</div><div>→ Imiquimod up-regulates the cell-mediated immune response in the skin, which ultimately leads to the death of tumour cells. [88] It can only be used in immunocompetent patients. Advantages include the induction of immune memory, thus minimising the recurrence of AKs, and the ability to also treat sub-clinical, unapparent lesions. [2] Expect exacerbation of erythema during initial weeks. Periods of no treatment suggested for strong local adverse effects and low tolerability.</div><div>→ Ingenol mebutate, a topical treatment extracted from the plant <i>Euphorbia peplus</i>, is recommended for the treatment of AKs. It initially induces disruption of the plasma membrane and rapid loss of the mitochondrial membrane potential in dyskeratotic keratinocytes by chemoablation, followed by cellular death by necrosis. Secondly, it induces tumour-specific antibodies, pro-inflammatory cytokines, and neutrophil infiltration, resulting in the elimination of residual cells by an antibody-dependent cellular cytotoxicity. It is a well-tolerated treatment with transient local skin reactions, such as erythema, flaking/scaling, and crusting, usually spontaneously resolved within 2 to 4 weeks after treatment. Multiple clinical trials have demonstrated significant efficacy when compared with placebo. [108] [109] [110] Evidence C</div><div>Evidence B</div><div>→ Topical diclofenac is less effective than the other three modalities, Evidence C but has the advantage of causing less inflammation due to its anti-inflammatory properties. Evidence C</div><div>→ Additionally, patients are advised to wear broad-spectrum sunscreen.</div></div></div>

Primary Options

fluorouracil topical : (0.5%) apply to the affected area(s) once daily for 2-4 weeks; (1-5%) apply to the affected area(s) twice daily for 2-4 weeks

OR

imiquimod topical : (3.75%) apply to the affected area(s) once daily for 2 weeks initially, followed by 2 weeks of no treatment, followed by a further 2

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Actinic keratosis

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Step-by-step diagnostic approach



Characteristic history and examination findings are often sufficient to diagnose the condition.

History

AK presents typically in a man with light-coloured skin, >40 years old, who has spent a lot of time outdoors since childhood without sun protection.

AKs are more prevalent in people living at lower latitudes, and in people with genetic conditions such as albinism and melanin deficiency (e.g., autosomal recessive albinism, and xeroderma pigmentosum). [15] [16] [17] [18]

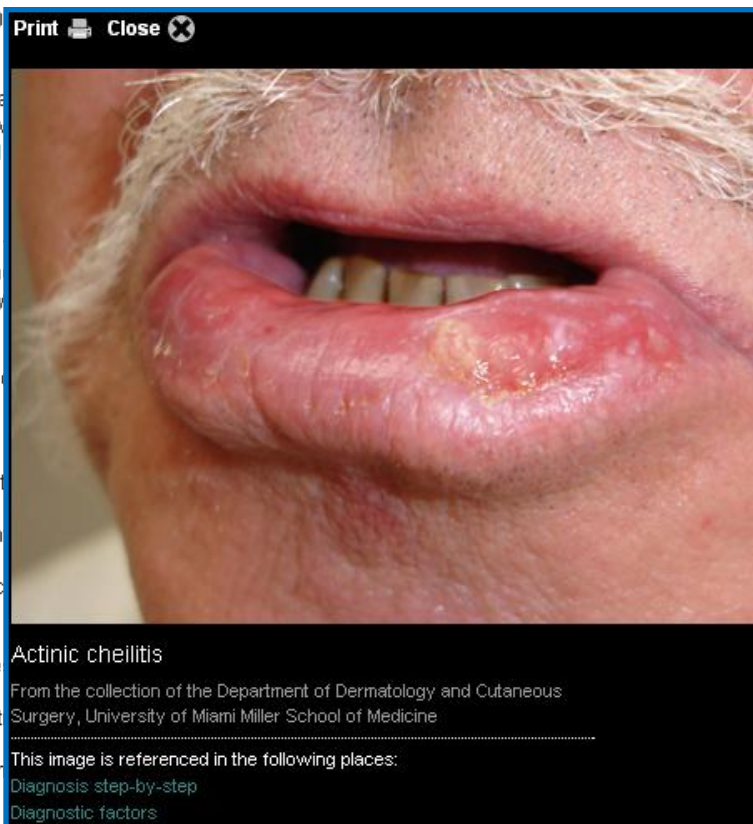
Physical examination

Single or multiple lesions in sun-exposed areas including the face, ears, lower lip, and dorsum of the hands and forearms. The lesions are typically well-defined, scaly, brown, yellowish, or erythematous, ill-defined, irregularly shaped, and may be accompanied by scaly macules or plaques.  

There may be mild pruritus, irritation, or bleeding if the lesion is scratched or rubbed.

Other presentations include:

- Scaly lesions with a hyperkeratotic surface (hyperkeratotic AKs)
- Well-defined, scaly, brown lesions resembling solar lentigines
- Lesions resembling seborrhoeic keratosis, melanocytic nevi, or melanoma (spreading pigmented AKs) [5]
- Skin-coloured, papillomatous, elevated wart-like papules
- Plaques with very mild scale over very thin shiny skin (atrophic AKs)
- Violaceous well-defined papules with fine white lines or dots (lichenoid AKs)
- Hypertrophic conical-shaped protuberances growing from the surface of the skin (cutaneous horn)
- Scaly red roughness with induration, fissuring, and ulceration of the lower lip to the



Von Willebrand disease

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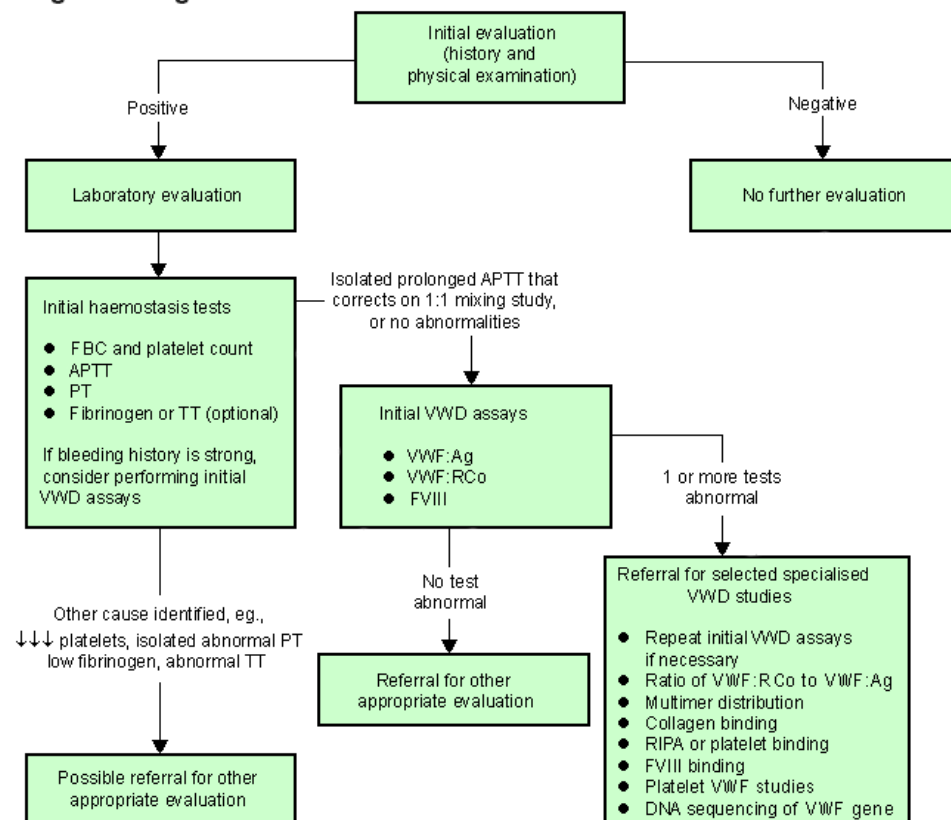
Notes



Tools

Step-by-step diagnostic approach

Diagnostic algorithm



Diagnostic algorithm for von Willebrand disease. APTT: activated partial thromboplastin time; FVIII: factor VIII; PT: prothrombin time; RIPA: ristocetin-induced platelet agglutination; TT: thrombin time; VWD: von Willebrand disease; VWF:Ag: von Willebrand factor antigen; VWF:RCo: VWF activity by ristocetin cofactor

ST-elevation myocardial infarction

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Treatment Options

Consult your local pharmaceutical database for comprehensive drug information including contraindications, drug interactions, and alternative dosing.

Presumptive

Patient group

Treatment line

Treatment [show all](#)

suspected MI

1st

▼ aspirin plus oxygen

- Patient should be admitted to a unit with continuous cardiac monitoring and started on strict bed rest for the first 12 to 24 hours.
- Oxygen saturation should be maintained over 90% with supplemental oxygen. [\[7\]](#) [\[17\]](#) International guidelines diverge concerning routine oxygen administration. US guidelines recommend that oxygen may be administered routinely to all patients with STEMI in the first 6 hours. [\[7\]](#) Other guidelines recommend that oxygen not be routinely administered in non-hypoxic people. [\[17\]](#)
- Aspirin is given immediately. **Evidence A**

Primary Options

aspirin: 300 mg orally immediately, followed by 75 mg once daily

aspirin

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and

oxygen: consider oxygen to maintain oxygen saturation >90%

■ ongoing chest pain

plus







▶ **morphine**

adjunct

▶ **glyceryl trinitrate**

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ST-elevation myocardial infarction

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Treatment approach

The main goals of treatment are to limit myocardial damage by restoring myocardial blood flow as quickly as possible and to decrease subsequent remodelling, which can have deleterious effects on ventricular function and prognosis. [14]

Immediate
90 minutes
or decrease
complication

Reference

14. Verma VK, Hollenberg SM. Update on acute coronary syndromes and ST-elevation myocardial infarction. Curr Opin Crit Care. 2005;11:401-405.

Initial management

Patient should
bed rest for
supplement
with arterial

administration. US guidelines recommend that oxygen may be administered routinely to all patients with STEMI in the first 6 hours. [7] Other guidelines recommend that oxygen not be routinely administered in non-hypoxic people. [17] Aspirin is given immediately. Evidence A

Adequate analgesia with morphine is essential to relieve pain and its related sympathetic activity, which can further increase myocardial oxygen demand.

Glyceryl trinitrate should also be given immediately, if the patient is not hypotensive, as it reduces myocardial oxygen demand and lessens ischaemia, and may rarely abort MI if there is coronary spasm. However, it should not be given in doses that interfere with analgesic therapy. Sublingual dosing should be given first to all patients, while intravenous therapy is reserved for patients with hypertension or heart failure.

Non-ST-elevation myocardial infarction

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Myocardial infarction (ST-elevation)

- Which treatments improve outcomes in people with myocardial infarction (ST-elevation)?
- Which treatments improve outcomes in people with cardiogenic shock after acute MI?

View this review's [GRADE table](#), the basis of our judgements about evidence quality.

[Read more](#)

Non ST-elevation acute coronary syndrome

- What are the effects of antiplatelet treatments in people with non ST-elevation acute coronary syndrome?
- What are the effects of antithrombin treatments in people with non ST-elevation acute coronary syndrome?
- What are the effects of anti-ischaemic treatments in people with non ST-elevation acute coronary syndrome?
- What are the effects of lipid-lowering treatments in people with non ST-elevation acute coronary syndrome?
- What are the effects of invasive treatments in people with non ST-elevation acute coronary syndrome?

View this review's [GRADE table](#), the basis of our judgements about evidence quality.

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Evidence Scores

Evidence A Prevention of MI: there is good-quality evidence that ticlopidine plus conventional treatment reduces vascular deaths and MI at 6 months compared with conventional treatment alone in people with unstable angina. Ticlopidine has been associated with reversible neutropenia.

Online resources

1. TIMI risk score calculator



2. GRACE risk score calculator



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Use of drug eluting stents in ST segment elevation myocardial infarction (STEMI) ☐

Pre-hospital diagnosis, triage and treatment in patients with ST elevation myocardial infarction ☐

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Heart attack ☐

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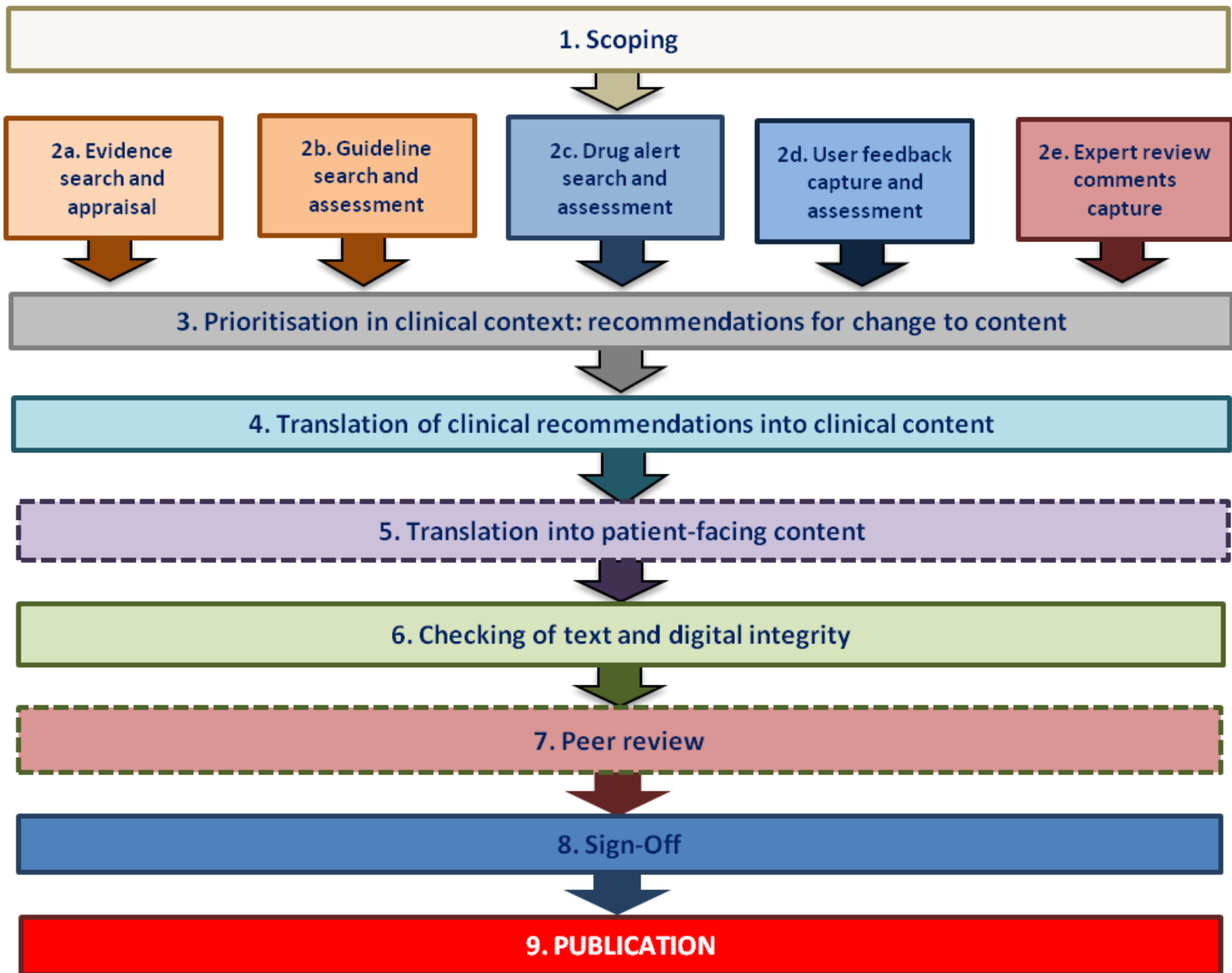
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pricing/content	10%	Pricing was important, but not more important than the overall quality and functionality of the products. NEHL reserved the right to consider how content was reflected in the price
access levels	4%	NEHL have two access levels; full national access and limited access. Full national access means that all Norwegian Internet Protocol address (IPs) have access. Limited access means that users must come from a known institutional IP address
authentication	4%	
Helsebiblioteket.no branding	6%	
enterprise search	6%	
technical requirements	3%	
linking and integration	6%	
HHC support	2%	
rights to reference and re-use	4%	
agreements	4%	
full version	2%	
accessibility and availability	2%	
language	2%	
search features	2%	
user interface	6%	
administrative tools	3%	
scope and purpose	2%	
coverage and comprehensiveness	8%	
stakeholder involvement	2%	
rigour of development	6%	
clarity and presentation	2%	
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metadata	2%	
training provision	2%	Training programs provided by the vendor
operational services	2%	Documentation on performance, disruptions and security systems
helpdesk services	2%	Availability of support staff when needed

Serials – 24(1), March 2011

Kjell Tjensvoll National licensing for the NEHL

Selecting the winners

All deliveries were checked for any significant reservations. Then copies were distributed to the reference group for analysis. NEHL staff assessed the input from the reference group and used the information to score the quotes.

The highest score was for BMJ Best Practice from BMJ and the second highest score was for UpToDate from UpToDate Inc. NEHL chose to make agreements with both vendors for national access to their products.

Product	Vendor	Final score
BMJ Best Practice	BMJ Group	0,9604
UpToDate	UpToDate	0,7092
Product 3	Vendor 3	0,6584
Product 4	Vendor 4	0,5990
Product 5	Vendor 5	0,4994
Product 6	Vendor 6	0,4594
Product 7	Vendor 7	0,3964
Product 8	Vendor 8	0,2476

Table 2. Scoring table

often less precise and cannot be answered with yes or no.

Example: Search features? The competing products have big variations in how they approach search and the presentation of search results. They all more or less comply with the requirements, but Best Practice got the best score from the users.

- Nice-to-have criteria are less important, but can still be critical to win a competition. These criteria can range from yes or no to more vague questions.

Example 1: Support for SNOMED ontology? Yes or no.

Example 2: NEHL welcomes creative solutions that can enhance the user experience or the overall value of the product.

Today, NEHL have agreements with most publishers and vendors where national access and support for enterprise search are included. A significant number of agreements are also invoiced in Norwegian Kroner. None of these issues has

Table 1. Table of decision criteria produced by NEHL to aid the tender process

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Related systematic reviews: Questions

Intervention Table

Evidence

Treatments in MI (ST-elevation)

Aspirin

In this section:

[Summary statement](#) | [Benefits](#) | [Harms](#) | [Comment](#)

Summary statement

Top

Mortality

Compared with placebo Aspirin is more effective at reducing all-cause and vascular mortality for up to 4 years in people with acute MI (high-quality evidence).

Cardiovascular events

Compared with placebo Aspirin is more effective at reducing recurrent infarction and non-fatal stroke at 1 month in people with acute MI (high-quality evidence).

For GRADE evaluation of interventions for acute MI, see [table](#).

Benefits

Top

Aspirin versus placebo:

We found one systematic review (search date 1990, 9 RCTs, 18,773 people) comparing antiplatelet agents begun soon after the onset of acute MI and for at least 1 month afterwards versus placebo. [11] Almost all (over 95%) of the people in these studies were randomised to either aspirin or placebo. The review found that aspirin significantly reduced mortality, reinfarction, and stroke at 1 month compared with control. The absolute and relative benefits found in the systematic review are shown in [figure 2](#). In the systematic review, the most widely tested aspirin regimens were 75 to 325 mg daily. [11] Doses throughout this range seemed similarly effective, with no evidence that higher doses (aspirin 500–1500 mg: AR 1243/9223 [13%] with aspirin v 1514/9248 [16%] with placebo; OR 0.79, 95% CI presented graphically) were more effective than "medium" doses (aspirin 160–325 mg: AR 1303/11,906 [11%] with aspirin v 1740/11,862 [15%] with placebo; OR 0.72, 95% CI presented graphically) or "lower" doses (aspirin 75–160 mg: AR 129/1440 [9%] with aspirin v 168/1438 [12%] with placebo; OR 0.74, 95% CI presented graphically). The review found insufficient evidence for efficacy of doses below 75 mg daily. One RCT identified by the review found that a loading dose of 160 to 325 mg daily achieved a prompt antiplatelet effect. [12] The largest of the RCTs identified by the review (17,187 people with suspected acute MI) compared aspirin 162.6 mg versus placebo chewed and swallowed on the day of acute MI and continued daily for 1 month. [13] There was a 2.4% absolute reduction in vascular death at 35 days. The survival benefit was maintained for up to 4 years. [14]

Harms

The largest RCT identified by the review found no significant difference between aspirin and placebo in rates of cerebral haemorrhage or bleeds requiring transfusion (AR: 0.4% with aspirin and placebo). [13] It also found a small absolute excess of "minor" bleeding (ARI 0.6%, CI not reported; P <0.01).

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Treatment Options

Consult your local pharmaceutical database for comprehensive drug information including contraindications, drug interactions, and alternative dosing.

Presumptive

Patient group	Treatment line	Treatment	show all
suspected MI	1st	aspirin plus oxygen <ul style="list-style-type: none">→ Patient should be admitted to a unit with continuous monitoring and started on strict bed rest for the first 12 to 24 hours.→ Oxygen saturation should be maintained over 90% [7] [17] International guidelines diverge concerning administration. US guidelines recommend that oxygen be given routinely to all patients with STEMI in the first 6 hours. Other guidelines recommend that oxygen not be routinely administered [17]→ Aspirin is given immediately. Evidence A	

Evidence Score

Mortality: there is good-quality evidence that aspirin reduces mortality, re-infarction, and stroke at 1 month compared with placebo in people with acute MI.

Evidence level A

Systematic reviews (SRs) or randomized controlled trials (RCTs) of >200 participants.

[More info from BMJ Clinical Evidence](#)

Acute

Patient group	Treatment line	Treatment	show all
haemodynamically unstable	1st	emergency revascularisation	
	adjunct	inotrope support or intra-aortic balloon pump (IABP)	

Infective endocarditis

Highlights	Basics	Prevention	Diagnosis	Treatment	Follow Up	Resources
Summary Overview	Definition Epidemiology Aetiology Pathophysiology Classification	Primary Secondary	History & examination Tests Differential Step-by-step Criteria Guidelines Case history	Details Step-by-step Emerging Guidelines	Recommendations Complications Prognosis	References Images Online resources Patient leaflets Contributors Related BMJ content

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Treatment guidelines

Europe [show all](#)

[Guidelines on the prevention, diagnosis, and treatment of infective endocarditis \(new version 2009\)](#)

Published by: European Society of Cardiology; European Society of Clinical Microbiology and Infectious Diseases; International Society of Chemotherapy for Infection and Cancer

Last published: 2009

[► Summary](#)

[Antimicrobial prophylaxis against infective endocarditis](#)

Published by: National Institute for Health and Care Excellence
Last published: 2008

[► Summary](#)

North America [show all](#)

[Clinical practice guidelines by the Infectious Diseases Society of America for the treatment of methicillin-resistant Staphylococcus aureus infections in adults and children](#)

Published by: Infectious Diseases Society of America
Last published: 2011

[► Summary](#)

[Infective endocarditis: diagnosis, antimicrobial therapy, and management of complications](#)

Published by: American Heart Association
Last published: 2005

[► Summary](#)

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Secondary prevention

Patients with a previous history of IE are at high risk of a further episode of endocarditis. Therefore, the American Heart Association recommends that these patients receive antibiotic prophylaxis for the following procedures: [\[5\]](#) [\[14\]](#) [\[15\]](#)

- Dental procedures that involve manipulation of gingival tissues or periapical region of the tooth or perforation of the oral mucosa
- Invasive procedures of the respiratory tract that involve incision or biopsy of the respiratory mucosa, such as tonsillectomy and adenoidectomy. Instrumentation of the respiratory tract to treat a septic focus (e.g., drainage of an empyema or an abscess)
- Invasive treatment for infected skin, skin structures, or musculoskeletal tissues.

In the UK, the National Institute of Health and Care Excellence (NICE) has recommended that at-risk patients undergoing interventional procedures should no longer be given antibiotic prophylaxis against IE. However, it emphasised that antibiotic therapy is still necessary to treat active or potential infections. [\[16\]](#) The recommendations from the American Heart Association and from NICE may not be universally accepted in other countries.

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Sialadenitis

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Contributors

Authors

Chris Avery, BDS, MB BChir, FDSRCS, FRCS, FRCS (OMFS)

*Consultant Oral and Maxillofacial Surgeon/Honorary Senior Lecturer
University Hospitals of Leicester NHS Trust - Leicester Royal Infirmary
Leicester
UK*

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Peer Reviewers

Issac van der Waal, DDS, PhD

*Professor of Oral Pathology
Head of the Department of Oral and Maxillofacial Surgery and Oral Pathology
VU University Medical Centre and Academic Centre for Dentistry
Amsterdam
The Netherlands*

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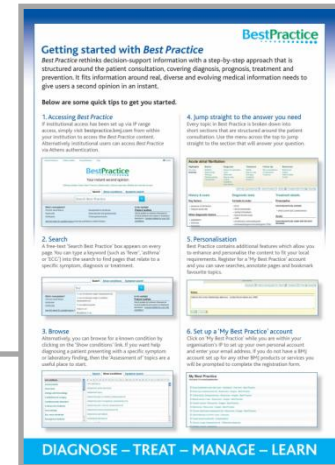
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