

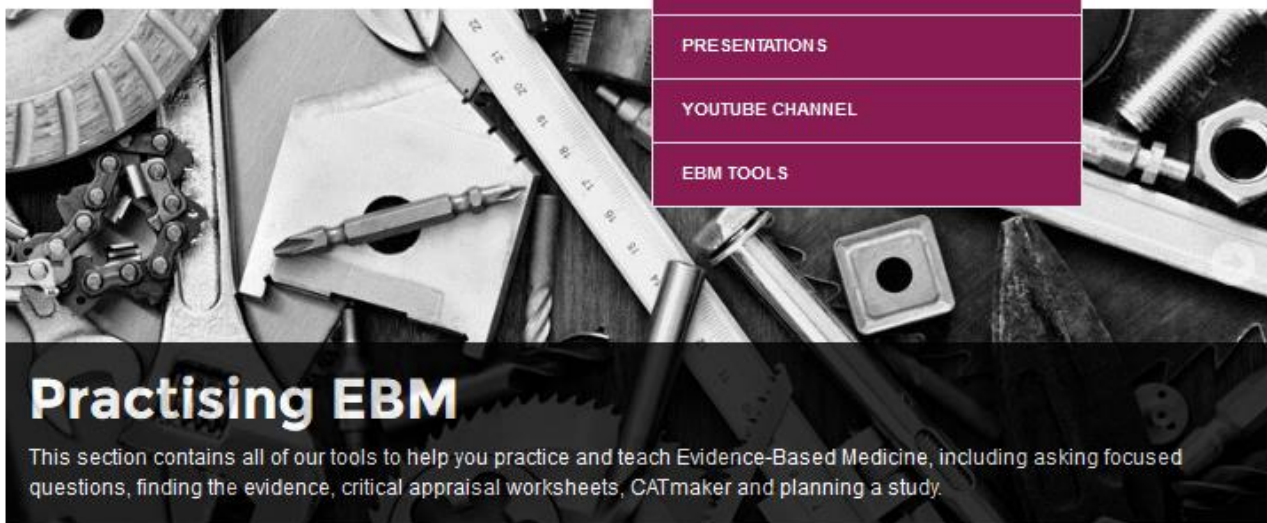


**CEBM**  
www.cebm.net

# Introduction to Evidence-Based Medicine

Prof. Carl Heneghan  
Director CEBM  
University of Oxford





**RECOMMENDED READING**

**PRESENTATIONS**

**YOUTUBE CHANNEL**

**EBM TOOLS**

## Practising EBM

This section contains all of our tools to help you practice and teach Evidence-Based Medicine, including asking focused questions, finding the evidence, critical appraisal worksheets, CATmaker and planning a study.

### EDUCATION AND TRAINING

Confused about confidence intervals? Frantic about forest plots? One of our courses can sort you out, whether it's a one-day refresher or a two-year Masters degree.

### EBM RESOURCES

Practical tools for asking focused questions, searching the literature, critically appraising the evidence, making a decision and evaluating your performance. You can even design your own study. No excuses then! Get cracking!

### CEBM BLOGS

Up to date comment and review of current issues in Evidence-Based Medicine, brought to you by our team of bloggers.



### CEBM PROJECTS

We like to get ourselves involved in projects about developing and implementing EBM. You can find out about them in this section, and get hold of all of our publications.



### RECOMMENDED CONTENT

#### Deadly Devices & Dangerous Drugs



Deadly Devices and Dangerous Drugs  
Improving the evidence that underpins routine clinical care. Saturday 20th September 2014 16:30 – 18:00 Oxford Museum of Natural History - [Read More](#)

### OCEBM Levels of Evidence



The Levels of Evidence help you to target your search at the type of evidence that is most likely to provide a reliable answer.

### TWITTER FEED

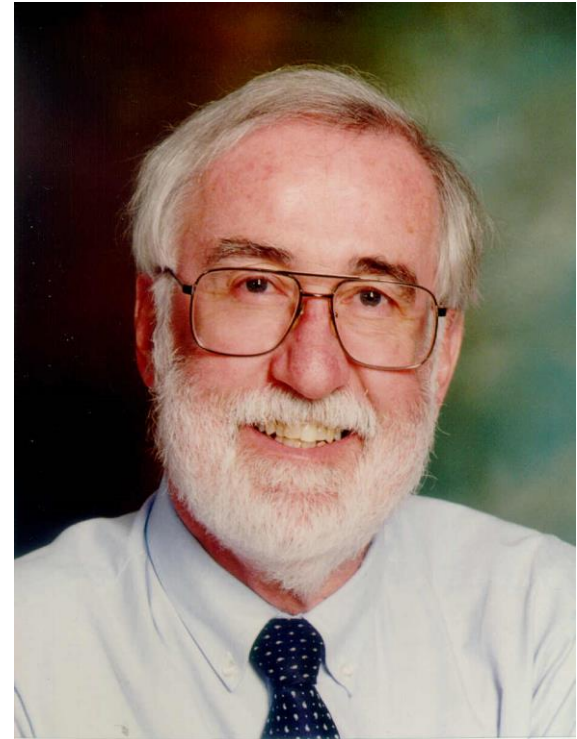


Getting ready for Evidence Live 2015 please refer to <http://t.co/bG50CKE8G9>



# What is Evidence-Based Medicine?

“Evidence-based medicine is the integration of best research evidence with clinical expertise and patient values”





Why do we need EBM?





Do You Know Who Frances Kelsey Is? // Pharmalot - Mozilla Firefox

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http://www.pharmalot.com/2010/09/do-you-know-who-frances-kelsey-is/?utm\_sor

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Ph Do You Know Who Frances Kelsey Is?...

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## Do You Know Who Frances Kelsey Is?

By Ed Silverman // September 16th, 2010 // 12:35 pm [6 Comments](#)



The odds are that you don't, but her actions a half-century ago helped transform the way prescription drugs are tested and approved. Kelsey, you see, was a new FDA employee in 1960, when she was assigned to review Kevadon, which was the brand name for thalidomide. The drug caused severe birth defects in thousands of babies born overseas after being prescribed to help women sleep or manage morning sickness. But babies often had limbless arms, malformed legs or extra appendages.

A physician and pharmacologist, Kelsey questioned its safety. "It just came with so many extravagant claims that I didn't believe," Kelsey, now 96, tells *The Washington Post*. Her decision set in motion a lot of intrigue as the manufacturer, Merrell, pushed back by complaining about her to the FDA. But Kelsey held her ground and after the scandal became known, President John Kennedy gave her the Federal Civilian Service award.

Congress, meanwhile, amended the Food, Drug & Cosmetic Act to require safety and effectiveness testing and informed consent in clinical trials. What did informed consent have to do with it? As the paper notes, Merrell gave the drug to more than 1,000 US docs to distribute to 20,000 patients as part of a so-called investigational trial, but some patients were not informed they were participating in a trial. The upshot - about 40 babies in US were born with deformities.

To honor Kelsey on the 50th anniversary of her groundbreaking effort, FDA commish Margaret Hamburg yesterday gave her the agency's first Kelsey Award which, in the future, will be given to an FDA employee to "celebrate courage and scientific decision-making." Want to know more? Read [this](#) and [this](#).

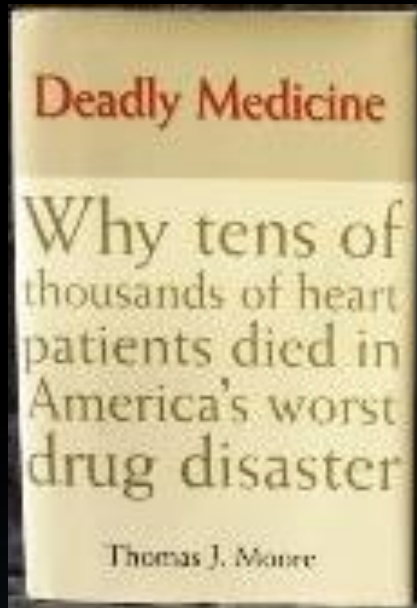
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## Why do we need RANDOMIZED CONTROLLED TRIALS ?



In the early 1980s newly introduced antiarrhythmics were found to be highly successful at suppressing arrhythmias.

Not until a RCT was performed was it realized that, although these drugs suppressed arrhythmias, they actually increased mortality.

The CAST trial revealed Excess mortality of 56/1000.

By the time the results of this trial were published, at least 100,000 such patients had been taking these drugs.

# Bad Pharma™

## Ben Goldacre

Bestselling author of *Bad Science*

How drug companies  
mislead doctors and  
harm patients

364 pages

## INTRO

Medicine is broken. And I genuinely believe that if patients and the public ever fully understand what has been done to them – what doctors, academics and regulators have permitted – they will be angry. On this, only you can judge.

We like to imagine that medicine is based on evidence, and the results of fair tests. In reality, those tests are often profoundly flawed. We like to imagine that doctors are familiar with the research literature, when in reality much of it is hidden from them by drug companies. We like to imagine that doctors are well-educated, when in reality much of their education is funded by industry. We like to imagine that regulators only let effective drugs onto the market, when in reality they approve hopeless drugs, with data on side effects casually withheld from doctors and patients.

# EBM and management of Common Cardiovascular conditions

## Myocardial infarction with ST-segment elevation (STEMI):

### Immediate management

- i) Ambulance Arrange 'blue light' emergency ambulance if acute myocardial infarction suspected.
- ii) Aspirin In the absence of contraindications given 300mg of aspirin
- iii) Analgesia USE IV opiates (e.g., 5 to 10mg of morphine). Avoid IM injections because of risk of bleeding after thrombolysis

### Hospital management – acute management

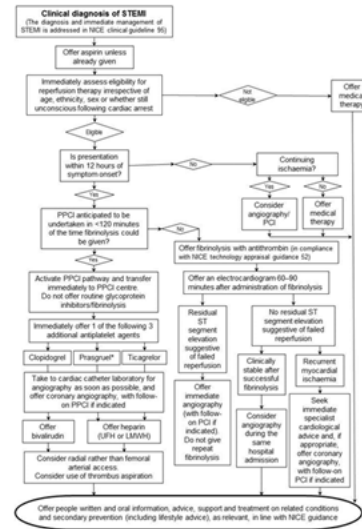
- i) Aspirin In the absence of contraindications given 300mg of aspirin
- ii) Reperfusion therapy See NICE guideline CG167. Immediately assess eligibility (irrespective of age, ethnicity or sex) for coronary reperfusion therapy (either primary PCI or fibrinolysis in people with acute STEMI).
- iii) Additional antiplatelet agents Offer 1 of three additional agents
- iv) Drug therapy See NICE Guidance CG172. Offer all people who have had an acute MI treatment with the following drugs: ACE inhibitor, dual antiplatelet therapy (aspirin plus a 2<sup>nd</sup> antiplatelet agent), beta-blocker, statin.

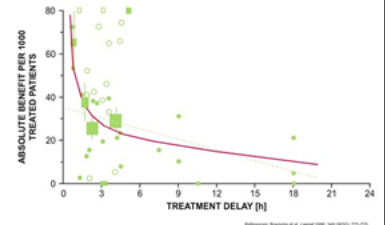
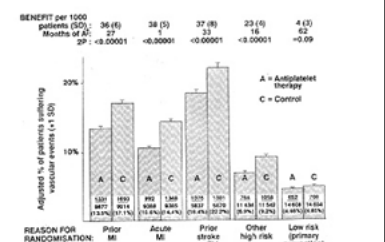
### Diabetes only

Insulin-glucose infusion. Consider insulin glucose infusion followed by intensive subcutaneous insulin in diabetics

### Post discharge

- i) Smoking Advise all who smoke to stop and offer a smoking cessation service.
- ii) Aspirin Offer aspirin to all people after an MI and continue it indefinitely, unless they are aspirin intolerant or have an indication for anticoagulation.
- iii) Beta-blocker Offer beta-blocker as soon as possible after an MI, when the person is haemodynamically stable. Continue for at least 12 months after in people without LVSD or heart failure.
- iv) ACE inhibitor Offer people who present acutely with an MI an ACE inhibitor as soon as they are haemodynamically stable. Continue the ACE inhibitor indefinitely.
- v) Lipids Statin therapy is recommended for adults with clinical evidence of cardiovascular disease
- vi) Additional antiplatelet Offer clopidogrel as a treatment option for up to 12 months to: people who have had an NSTEMI, regardless of treatment or to people who have had a STEMI and received a bare-metal or drug-eluting stent.
- vii) Hypertension Treat hypertension.
- viii) Exercise and Advise people to undertake regular physical activity sufficient to increase exercise capacity and



Intervention	Evidence	Summary of benefits/risks	Key references
Call ambulance ASAP	Systematic reviews show benefit of early intervention	Mortality benefits of fibrinolytic therapy reduced by about 2 lives/100 infarct/hour delay 	Lancet. 1994 Feb 5;343(8893):311-22. Indications for fibrinolytic therapy in suspected acute myocardial infarction: collaborative overview of early mortality and major morbidity results from all randomised trials of more than 1000 patients. Fibrinolytic Therapy Trialists' (FTT) Collaborative Group.  Early thrombolytic treatment in acute myocardial infarction: reappraisal of the golden hour. Boersma E, Maas AC, Deckers JW, Simoons-SL. Lancet. 1996 Sep 21;348(9030):771-5.
Aspirin (300 mg orally) if aspirin is given before arrival at hospital, a note saying that it has been given should be sent with the patient.	Systematic overview of 145 RCTs show aspirin offers worthwhile protection against myocardial infarction	Allocation to antiplatelet therapy produced a highly significant reduction (P<0.00001) of 38 per 1000 in the risk of suffering a subsequent vascular event 	Collaborative overview of randomised trials of antiplatelet therapy. Prevention of death, myocardial infarction, and stroke by prolonged antiplatelet therapy in various categories of patients. BMJ 1994;308:81



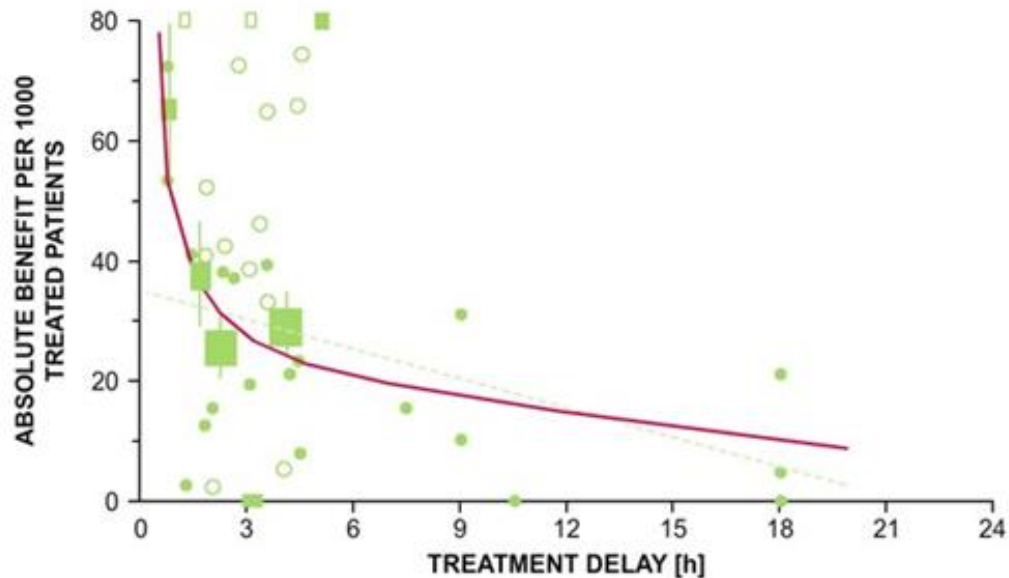
Articles

## Early thrombolytic treatment in acute myocardial infarction: reappraisal of the golden hour

Eric Boersma, MSc<sup>a</sup>, Arthur CP Maas, MD<sup>a</sup>, Prof Jaap W Deckers, MD<sup>a</sup>, Prof Maarten L Simoons, PhD<sup>a</sup>



Show more



References: Boersma et al. *Lancet* 1996; 348 (9030): 771-775.

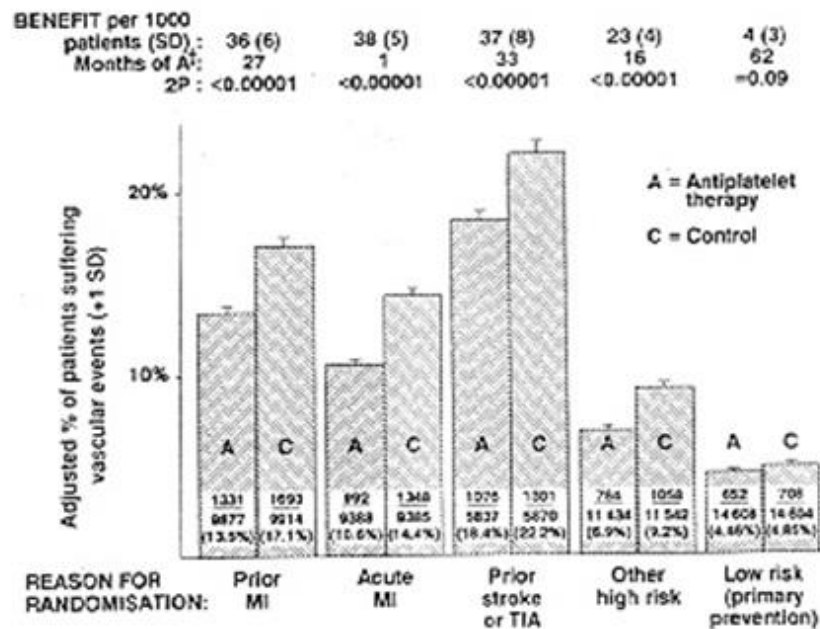
- For every 1000 patients treated 65 more will be alive at 1 month if treatment is administered in the first hour – the ‘golden hour’ – after symptom onset, compared with not giving thrombolysis;
  - 37 lives are saved for every 1000 patients treated in the 1–2 hour interval after symptom onset;
  - 26 lives are saved for every 1000 patients treated in the 2–3 hour interval after symptom onset;
  - 29 lives are saved for every 1000 patients treated in the 3–6 hour interval after symptom onset;
  - 20 lives are saved for every 1000 patients treated in the 7–12 hour interval after symptom onset.

## Papers

### Collaborative overview of randomised trials of antiplatelet therapy Prevention of death, myocardial infarction, and stroke by prolonged antiplatelet therapy in various categories of patients

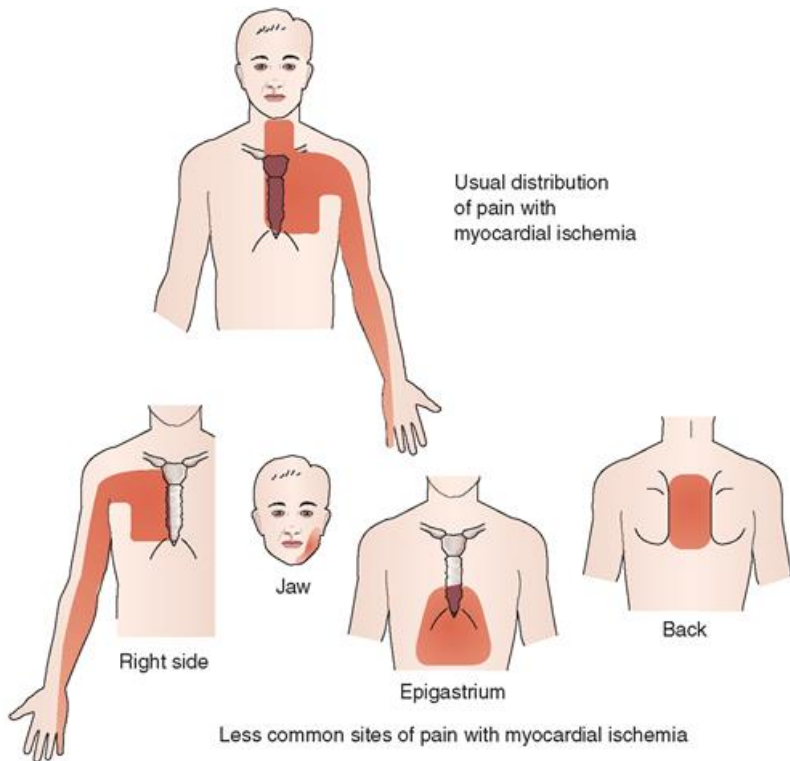
*BMJ* 1994 ; 308 doi: <http://dx.doi.org/10.1136/bmj.308.6921.81> (Published 08 January 1994)

Cite this as: *BMJ* 1994;308:81



- Allocation to antiplatelet therapy produced a highly significant reduction ( $P < 0.00001$ ) of 38 per 1000 in the risk of suffering a subsequent vascular event

# Pain relief



# Beware of text books


**Immediate** treatment of **Myocardial Infarction (MI)**:

**MOAN**

- Morphine
- Oxygen
- Aspirin
- Nitroglycerine



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## OXYGEN THERAPY IN ACUTE MYOCARDIAL INFARCTION – GOOD OR BAD?

**By:** Pascal Meier, Shah Ebrahim, Catherine Otto & Juan Pablo Casas

**On:** August 21, 2013, 13:00

[Read comments on this editorial](#)



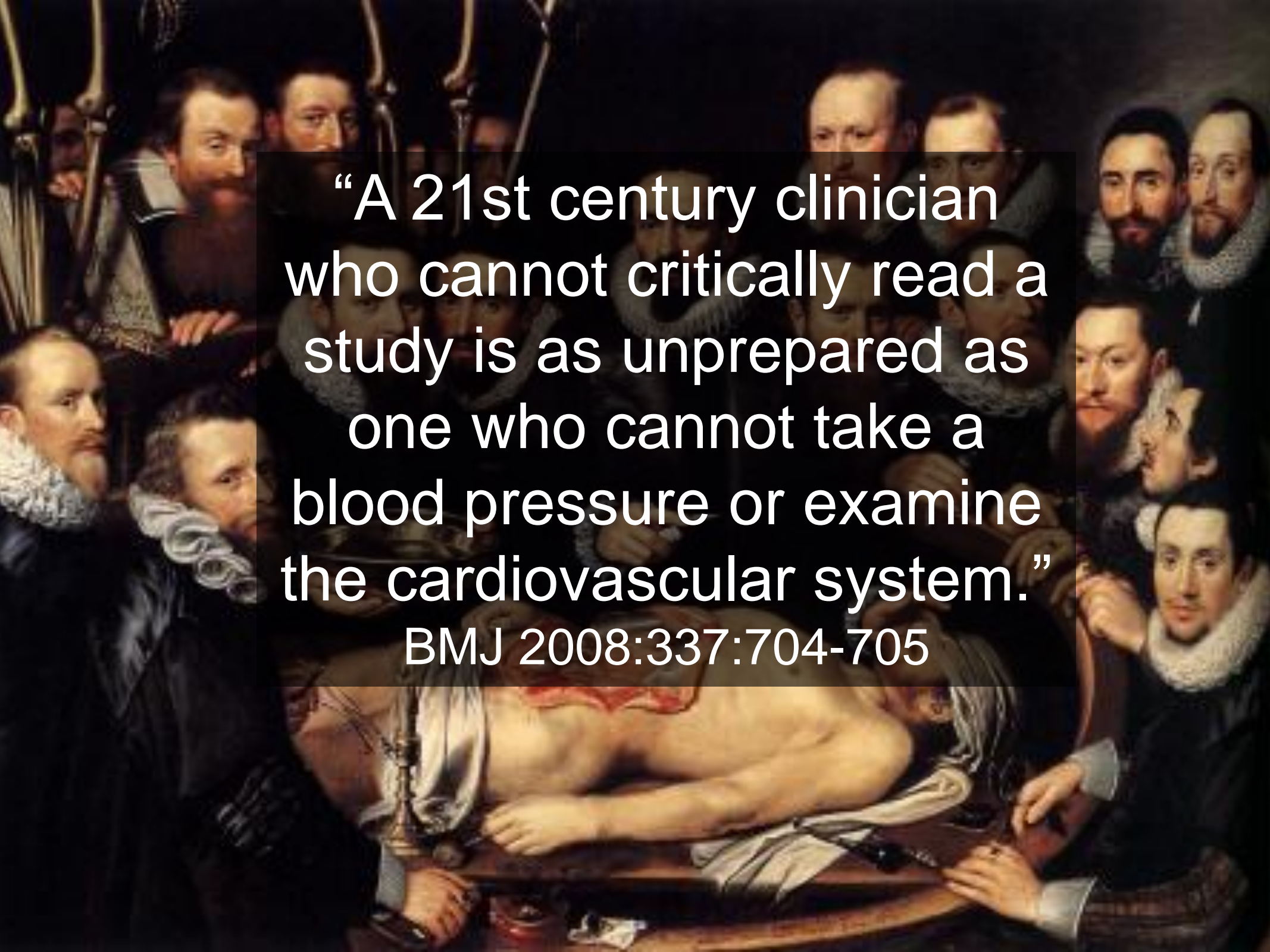
Most patients with acute coronary syndromes (ACS) receive oxygen therapy as part of their emergency treatment, initiated by paramedics during transfer and before their first contact with a physician. A survey among physicians involved with acute myocardial infarction cases found that 96% of their patients with ACS received oxygen therapy.<sup>[1]</sup> About 50% of all responders believed that oxygen decreases mortality, 25% thought it helps to relieve pain and 25% thought it has no effect.<sup>[1]</sup> Many therapies and interventions are not based on proven benefit, but on anecdotal evidence, expert opinion and tradition. This is especially true for oxygen therapy, which is usually not questioned and has been used for over 100 years. We could argue that as long as it does no harm, it does not really matter whether we continue to provide oxygen in these situations. However, is it really harmless?

From a physiological perspective, treating ACS patients with oxygen may seem reasonable. In ACS there is a lack of myocardial perfusion and consequently a lack of oxygenation of the myocardium. Therefore, it seems logical to increase the oxygenation of the blood reaching the jeopardised myocardium by administering oxygen therapy. However, another theory argues that oxygen may increase microvascular resistance, leading to reduced coronary blood flow thus reducing cardiac output and increasing radical oxygen species, which can have multiple negative effects including increased risk for arrhythmias and cell damage leading to heart failure.<sup>[2,3]</sup>

Randomised trial data on oxygen delivery in acute myocardial infarction (AMI) are also conflicting. A systematic review is therefore very useful. In the August 2013 issue of the Cochrane Database of Systematic Reviews Cabello et al report a systematic review including a total of 4 randomised trials and 430 patients.<sup>[4]</sup> These trials randomised patients to inhaled oxygen at 4 to 6 L/min (given by mask [3 studies] or by nasal cannula [1

In conclusion, we do not know whether routine oxygen administration in patients with an acute MI has any impact on outcome. Nonetheless, this systematic review challenges the status quo predicated by international guidelines on the treatment of acute coronary syndromes and highlights the need for large-scale trials.

Pascal Meier<sup>1</sup>, Shah Ebrahim<sup>2</sup>, Catherine M Otto<sup>3</sup>, Juan P Casas<sup>4</sup>

A historical painting depicting a medical dissection of a human body, surrounded by a group of men in 17th-century attire. The scene is set in a dark, dimly lit room, likely a lecture hall or a classroom. The central figure is a man lying on a table, with his torso open, revealing internal organs. Several men are gathered around the table, some pointing at the dissection, others looking on with interest. The men are dressed in dark, heavy clothing with white ruffled collars, characteristic of the 17th century. The overall atmosphere is one of serious study and observation.

“A 21st century clinician who cannot critically read a study is as unprepared as one who cannot take a blood pressure or examine the cardiovascular system.”

BMJ 2008;337:704-705




# EBM as a medical student?

The cover features silhouettes of several people in various poses against a blue background. Overlaid on the silhouettes are the following terms: Support, Advice, Standards, Communication, Professionalism, and Health. A vertical orange bar on the right side contains the word 'Education'.

**Medical students:  
professional values  
and fitness to practise**

Guidance from the GMC and the MSC

 Medical  
Schools  
Council

General  
Medical  
Council

Regulating doctors  
Ensuring good medical practice

### Good clinical care

- 15 Being able to provide good clinical care is fundamental to becoming a doctor. This objective should guide a student's behaviour in both their clinical and academic work. Medical students should reflect on how they can support and promote good clinical care as part of their medical education.
- 16 In order to demonstrate that they are fit to practise, students should:
- (a) recognise and work within the limits of their competence and ask for help when necessary
  - (b) accurately represent their position or abilities
  - (c) make sure they are supervised appropriately for any clinical task they perform
  - (d) respect the decisions and rights of patients
  - (e) be aware that treatment should be based on clinical need and the effectiveness of treatment options, and that decisions should be arrived at through assessment and discussion with the patient
  - (f) not unfairly discriminate against patients by allowing their personal views to affect adversely their professional relationship or the treatment they provide or arrange (this includes their views about a patient's age, colour, culture, disability, ethnic or national origin, gender, lifestyle, marital or parental status, race, religion or beliefs, sex, sexual orientation, and social or economic status)
  - (g) behave with courtesy
  - (h) report any concerns they have about patient safety to the appropriate person.<sup>3</sup>

Be aware that treatment options should be based on clinical need and the effectiveness of treatment options, and that decisions should be arrived at through assessment and discussion with the patient

### Maintaining good medical practice

- 17 Students must be aware of their responsibility to maintain their knowledge and skills throughout their careers.
- 18 Students are expected to keep up to date and to apply knowledge necessary for good clinical care. They should understand that as doctors they will have to participate in audit, assessments and performance reviews throughout their careers as part of revalidation and licensing.
- 19 In order to demonstrate that they are fit to practise, students should:
  - (a) reflect regularly on standards of medical practice in accordance with *Good medical practice* and *Tomorrow's Doctors*
  - (b) attend compulsory teaching sessions or make other arrangements with the medical school
  - (c) complete and submit course work on time
  - (d) be responsible for their own learning
  - (e) reflect on feedback about their performance and achievements and respond constructively
  - (f) be familiar with guidance from the GMC and other organisations, such as medical schools, hospitals, trusts and health boards
  - (g) respect the knowledge and skills of those involved in their education
  - (h) make sure they can be contacted and always respond to messages in relation to care of patients or their own education.

Must be aware of their responsibility to maintain their knowledge and skills throughout their careers.

Students are expected to keep up to date and to apply knowledge necessary for good clinical care.

# what skills will you need to keep up to date with the best evidence?

Must be aware of their responsibility to maintain their knowledge and skills throughout their careers.

Students are expected to keep up to date and to apply knowledge necessary for good clinical care.

- to find the evidence more efficiently
- to appraise the quality of the evidence more effectively
- to use good quality evidence more systematically

about 1/2 of 'valid'  
evidence today is out of  
date in 5 years

about 1/2 of valid  
evidence is not  
implemented



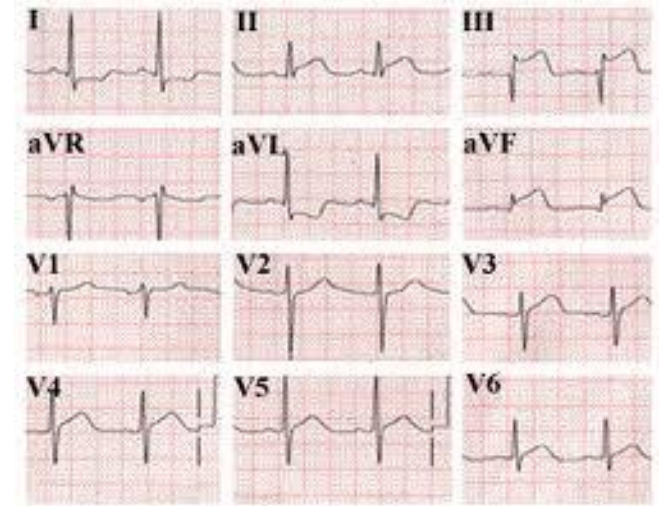
"...and, as you go out into the world, I predict  
that you will, gradually and imperceptibly,  
forget all you ever learned at this university."

# the steps of practicing EBM

1. **Ask a focused question.**
2. Track down the evidence
3. Critically appraise evidence for its validity, effect size, precision
4. Apply the evidence in practice:
  - a. *amalgamate* the valid evidence with other relevant information (values & preferences, clinical/health issues, & system issues)
  - b. implement the decision in practice

# 1. Ask a focused question.

Patient presenting with MI



# ‘Background’ Questions

---

About the disorder, test, treatment, etc.

a. Root\* + Verb: “What causes ...”

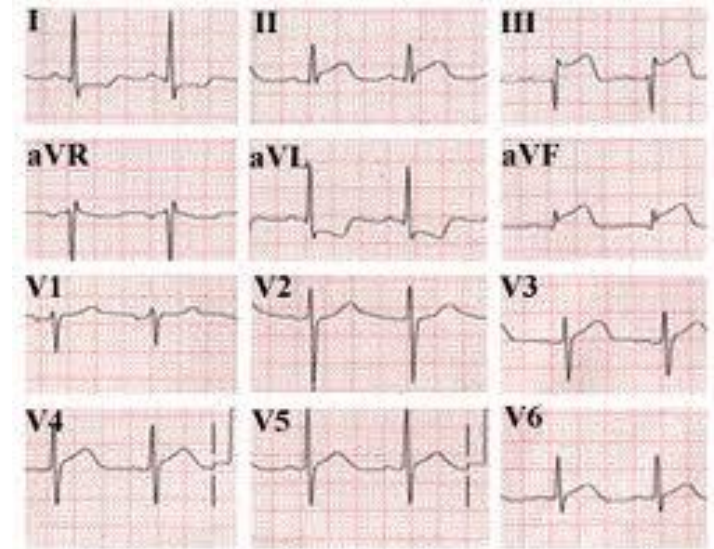
b. Condition: “HIV?”

\* Who, What, Where, When, Why



# Patient presenting with MI

1. What are the symptoms and signs of someone presenting with MI?
2. What are the diagnostic tests for MI?
3. What are the causes of MI?
4. What are the treatments of MI?



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## Signs and symptoms [[edit source](#) | [edit beta](#)]

The onset of symptoms in myocardial infarction (MI) is usually gradual, over several minutes, and rarely instantaneous.<sup>[17]</sup> **Chest pain** is the most common symptom of acute myocardial infarction and is often described as a sensation of tightness, pressure, or squeezing. Chest pain due to **ischemia** (a lack of blood and hence oxygen supply) of the heart muscle is termed **angina pectoris**. Pain radiates most often to the left **arm**, but may also radiate to the lower **jaw**, **neck**, right arm, **back**, and **epigastrium**,<sup>[7][18]</sup> where it may mimic **heartburn**. **Levine's sign**, in which the patient localizes the chest pain by clenching their fist over the **sternum**, has classically been thought to be predictive of cardiac chest pain, although a prospective observational study showed that it had a poor positive predictive value.<sup>[19]</sup>

Shortness of breath (**dyspnea**) occurs when the damage to the heart limits the **output** of the **left ventricle**, causing **left ventricular failure** and consequent **pulmonary edema**. Other symptoms include **diaphoresis** (an excessive form of **sweating**),<sup>[1]</sup> weakness, **light-headedness**, **nausea**, **vomiting**, and **palpitations**. These symptoms are likely induced by a massive surge of **catecholamines** from the **sympathetic nervous system**<sup>[20]</sup> which occurs in response to pain and the hemodynamic abnormalities that result from cardiac dysfunction. **Loss of consciousness** (due to inadequate cerebral perfusion and cardiogenic shock) and **sudden death** (frequently due to the development of ventricular fibrillation) can occur in myocardial infarctions.<sup>[7]</sup>

Female, elderly, and diabetic patients report atypical symptoms more frequently than their male and younger counterparts.<sup>[21][22]</sup> Women also report more numerous symptoms compared with men (2.6 on average vs 1.8 symptoms in men).<sup>[21]</sup> The most common symptoms of MI in women include **dyspnea** (shortness of breath), weakness, and **fatigue**. Fatigue, sleep disturbances, and dyspnea have been reported as frequently occurring symptoms that may manifest as long as one month before the actual clinically manifested ischemic event. In women, **chest pain** may be less predictive of coronary **ischemia** than in men.<sup>[23]</sup>

At least one-fourth of all myocardial infarctions are silent, without chest pain or other symptoms.<sup>[3][24]</sup> These cases can be discovered later on electrocardiograms, using blood enzyme tests or at autopsy without a prior history of related complaints. Estimates of the prevalence of silent myocardial infarctions vary between 22 and 64%.<sup>[3]</sup> A silent course is more common in the **elderly**,<sup>[3]</sup> in patients with **diabetes mellitus**<sup>[25]</sup> and after **heart transplantation**, probably because the **donor** heart is not fully innervated by the nervous system of the recipient.<sup>[26]</sup> In people with diabetes, differences in **pain threshold**, **autonomic neuropathy**, and **psychological** factors have been cited as possible explanations for the lack of symptoms.<sup>[25]</sup>

Any group of symptoms compatible with a sudden interruption of the blood flow to the heart are called an **acute coronary syndrome**.<sup>[27]</sup>

The **differential diagnosis** includes other catastrophic causes of chest pain, such as **pulmonary embolism**, **aortic dissection**, **pericardial effusion** causing **cardiac tamponade**, **tension pneumothorax**, and **esophageal rupture**. Other non-catastrophic differentials include **gastroesophageal reflux** and **Tietze's syndrome**.<sup>[28]</sup>

## Causes [[edit source](#) | [edit beta](#)]

Home ► [Health Information](#) ► Myocardial Infarction (Heart Attack)

# Myocardial Infarction (Heart Attack)

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## On this page

<a href="#">Understanding the heart and coronary arteries</a>	<a href="#">How is a myocardial infarction diagnosed and assessed?</a>
<a href="#">What happens to your heart with a myocardial infarction?</a>	<a href="#">What is the treatment for a myocardial infarction?</a>
<a href="#">What causes a myocardial infarction?</a>	<a href="#">Treatment after you have had a myocardial infarction</a>
<a href="#">Who is at risk of having a myocardial infarction / heart attack?</a>	<a href="#">How serious is a myocardial infarction?</a>
<a href="#">What are the symptoms of a myocardial infarction?</a>	<a href="#">After having a myocardial infarction</a>
<a href="#">What should I do if I think I am having a myocardial infarction?</a>	<a href="#">Further sources of information and help</a>
	<a href="#">References</a>

A heart attack (myocardial infarction) is usually caused by a blood clot, which stops the blood flowing to a part of your heart muscle. You should call for an

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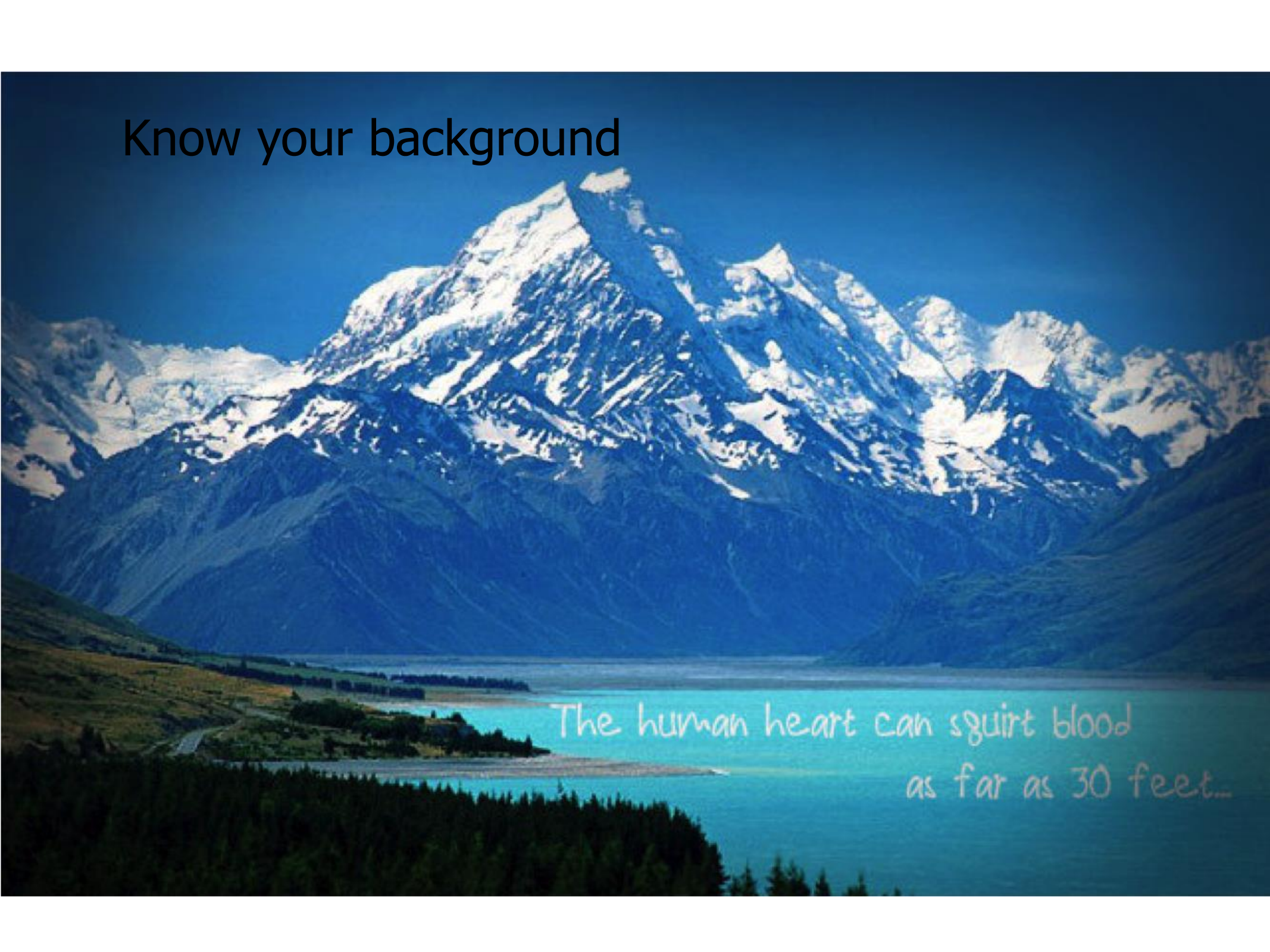
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35	36	37	38	39	40	41	42	43	44
45	46	47	48	49	50	51	52	53	54
55	56	57	58	59	60	61	62	63	64+

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Know your background



The human heart can squirt blood  
as far as 30 feet...

Patient presenting with MI

Foreground' Questions

About actual patient care decisions and actions

For treatment

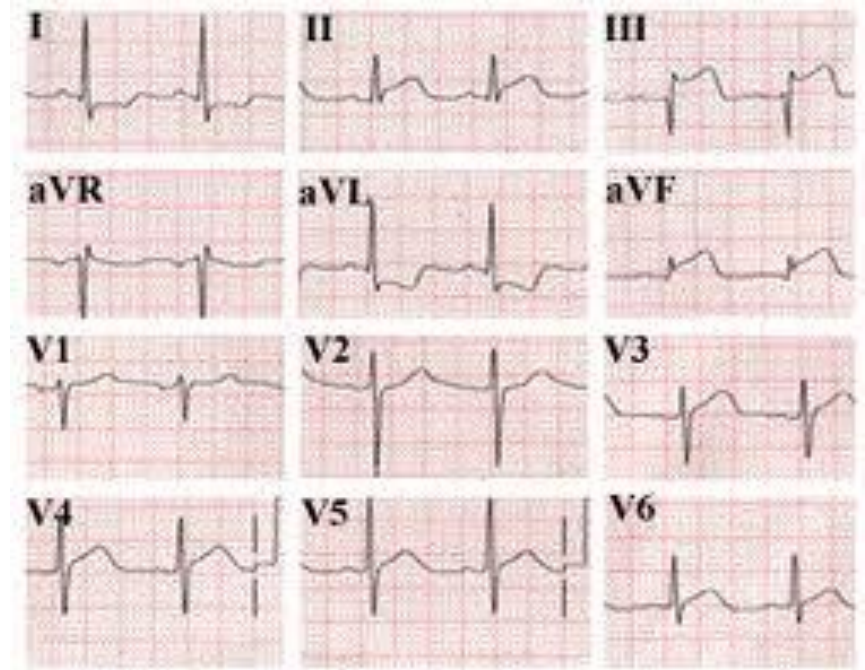
4 (or 3) components:

In **P**atients with a MI

Does (**I**) cholesterol lowering therapy

**C**ompared to placebo

reduce mortality (**O**)

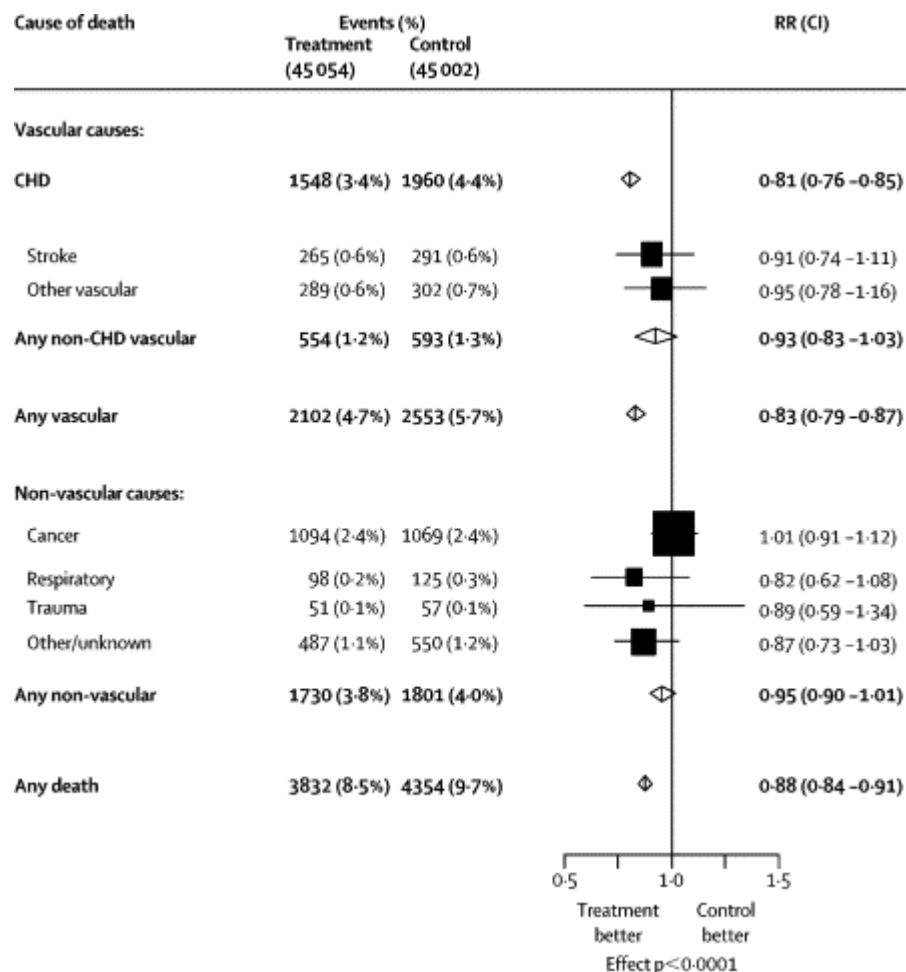




Fast track — Articles

## Efficacy and safety of cholesterol-lowering treatment: prospective meta-analysis of data from 90 056 participants in 14 randomised trials of statins

Cholesterol Treatment Trialists' (CTT) Collaborators <sup>\*\*\*†</sup>

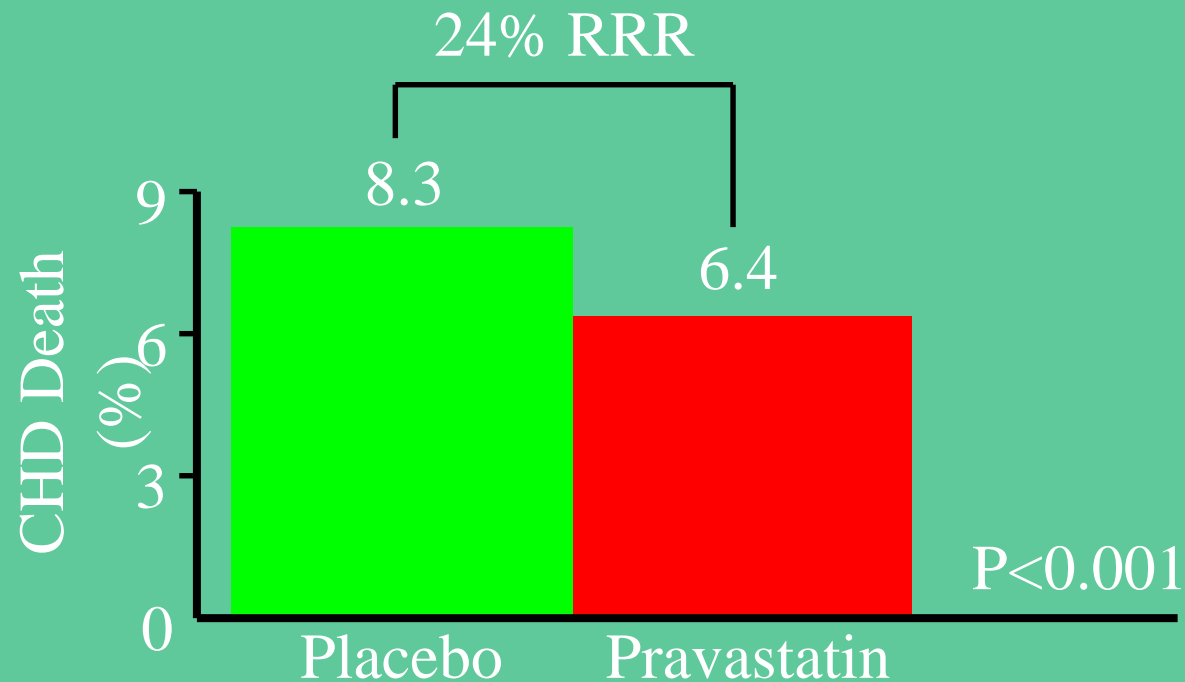


During the scheduled treatment period, there were 3832 (8·5%) deaths among the 45 054 participants allocated a statin compared with 4354 (9·7%) among the 45 002 controls. This difference represents a 12% proportional reduction in all-cause mortality per mmol/L LDL cholesterol reduction (RR 0·88, 95% CI 0·84–0·91;  $p < 0.0001$ ; figure 1).

# Secondary Prevention

## Long-term Intervention with Pravastatin in Ischemic Disease (LIPID) Study

9,014 patients with a history of MI or hospitalization for unstable angina randomized to pravastatin (40 mg) or placebo for 6.1 years



**Statins provide significant benefit across a broad range of cholesterol levels**

CHD=Coronary heart disease, MI=Myocardial infarction,  
RRR=Relative risk reduction

LIPID Study Group. *NEJM* 1998;339:1349–1357

# Patient presenting with MI

1. How common is the problem
2. Is early detection worthwhile
3. Is the diagnostic test accurate
4. What will happen if we do nothing
5. Does this intervention help
6. What are the common harms of an intervention
7. What are the rare harms of an intervention

Prevalence

Screening

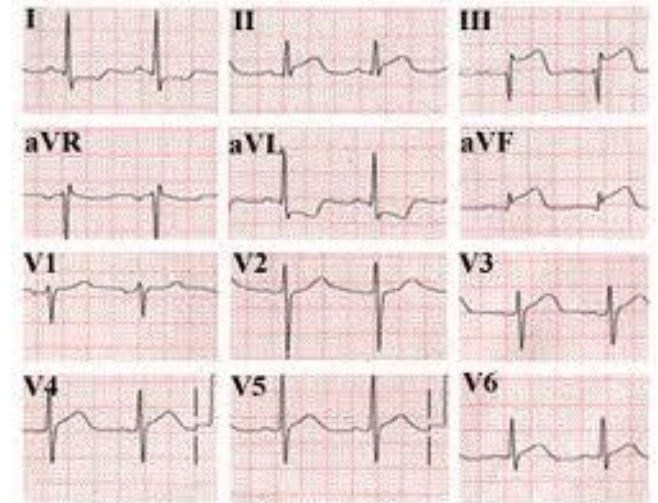
Diagnosis

Prognosis

Treatment

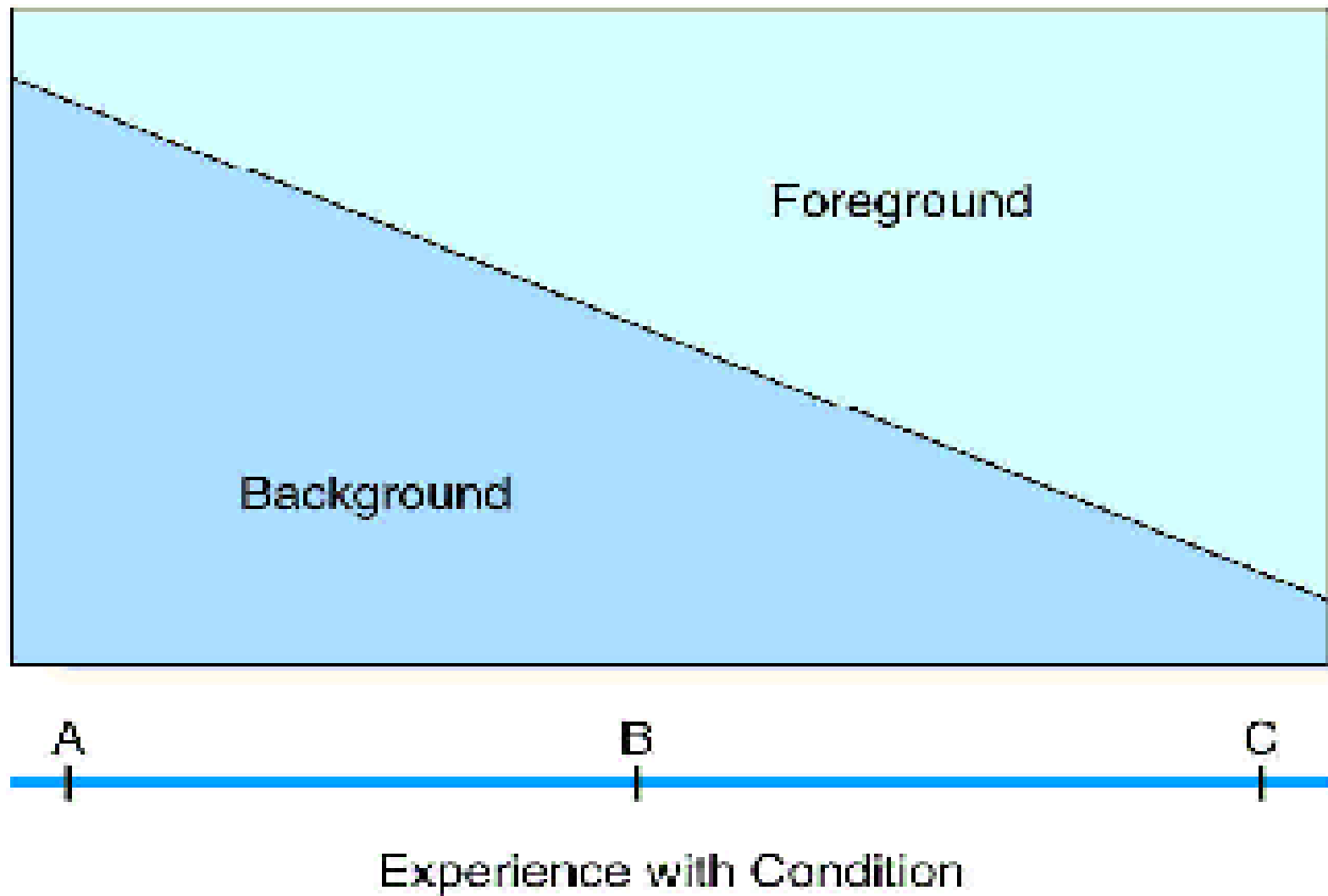
Treatment

Treatment





**Figure 1.1** Background and foreground questions.



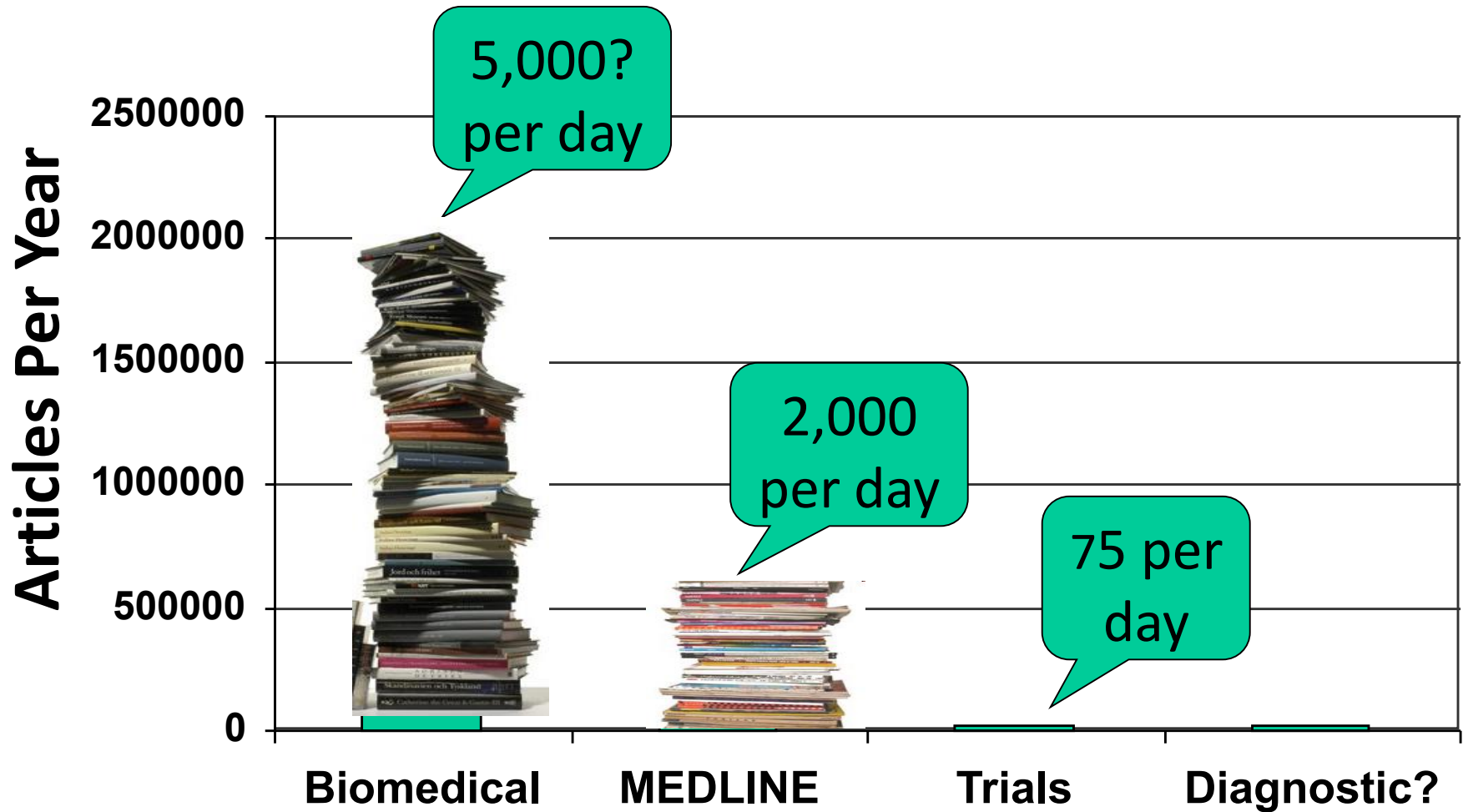
# Size of Medical Knowledge

- NLM MetaThesaurus
  - 875,255 concepts
  - 2.14 million concept names
- Diagnosis Pro
  - 11,000 diseases
  - 30,000 abnormalities (symptoms, signs, lab, X-ray,)
  - 3,200 drugs (cf FDAs 18,283 products)

1 disease per day  
for 30 years

*To cover the vast field of medicine in four years is an impossible task.  
- William Osler*

# why do we need to use evidence efficiently?

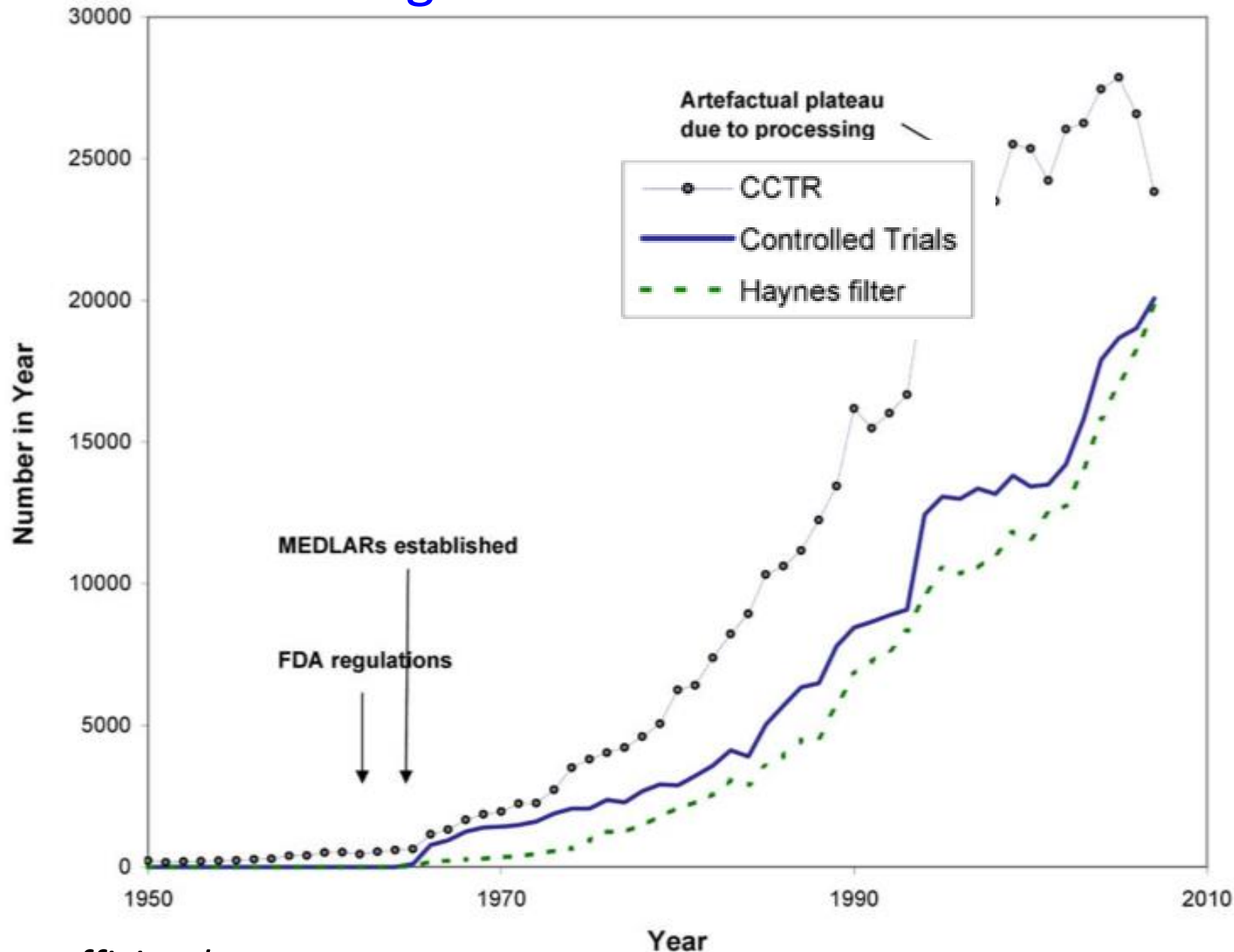


# Median minutes/week spent reading about my patients

## Self-reports at 17 Grand Rounds:

- Medical Students: 90 minutes
- House Officers (PGY1): 0 (up to 70%=none)
- SHOs (PGY2-4): 20 (up to 15%=none)
- Registrars: 45 (up to 40%=none)
- Sr. Registrars 30 (up to 15%=none)
- **Consultants:**
  - Grad. Post 1975: 45 (up to 30%=none)
  - Grad. Pre 1975: 30 (up to 40%=none)

clinical evidence increasing so rapidly we need better skills  
to keep up-to-date **more** efficiently than previous  
generations of clinicians



*more efficiently*

# the steps of practicing EBM

1. ask a focused question.
2. Track down the evidence
3. Critically appraise evidence for its validity, effect size, precision
4. apply the evidence in practice:
  - a. *amalgamate* the valid evidence with other relevant information (values & preferences, clinical/health issues, & system issues) and make an evidence-based decision; and
  - b. implement the decision in practice

# Effect of rosiglitazone on the frequency of diabetes in patients with impaired glucose tolerance or impaired fasting glucose: a randomised controlled trial

*The DREAM (Diabetes REduction Assessment with ramipril and rosiglitazone Medication) Trial Investigators\**

## Summary

**Background** Rosiglitazone is a thiazolidinedione that reduces insulin resistance and might preserve insulin secretion. The aim of this study was to assess prospectively the drug's ability to prevent type 2 diabetes in individuals at high risk of developing the condition.

**Methods** 5269 adults aged 30 years or more with impaired fasting glucose or impaired glucose tolerance, or both, and no previous cardiovascular disease were recruited from 191 sites in 21 countries and randomly assigned to receive rosiglitazone (8 mg daily; n=2365) or placebo (2634) and followed for a median of 3 years. The primary outcome was a composite of incident diabetes or death. Analyses were done by intention to treat. This trial is registered at ClinicalTrials.gov, number NCT00095654.

**Findings** At the end of study, 59 individuals had dropped out from the rosiglitazone group and 46 from the placebo group. 306 (11.6%) individuals given rosiglitazone and 686 (26.0%) given placebo developed the composite primary outcome (hazard ratio 0.40, 95% CI 0.35–0.46;  $p < 0.0001$ ); 1330 (50.5%) individuals in the rosiglitazone group and 798 (30.3%) in the placebo group became normoglycaemic (1.71, 1.57–1.87;  $p < 0.0001$ ). Cardiovascular event rates were much the same in both groups, although 14 (0.5%) participants in the rosiglitazone group and two (0.1%) in the placebo group developed heart failure ( $p = 0.01$ ).

**Interpretation** Rosiglitazone at 8 mg daily for 3 years substantially reduces incident type 2 diabetes and increases the likelihood of regression to normoglycaemia in adults with impaired fasting glucose or impaired glucose tolerance, or both.

# Prevention of diabetes

*Drug trials show promising results, but have limitations*

**D**iabetes affects one in 20 adults worldwide and 333 million cases are projected worldwide by 2025.<sup>1</sup> Treatment can prevent some of the

confidence interval 0.35 to 0.46,  $P < 0.0001$ ). Ramipril did not reduce the risk of diabetes.

These results are promising but they should be

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## Editorial

### Prevention of diabetes

Carl Heneghan (carl.heneghan@dphpc.ox.ac.uk), deputy director, M Thompson, clinical lecturer, R Perera, senior statistician

Author Affiliations

*Drug trials show promising results, but have limitations*

Diabetes affects one in 20 adults worldwide and 333 million cases are projected worldwide by 2025.<sup>1</sup> Treatment can prevent some of the microvascular and



## DRUG REGULATION



# ROSIGLITAZONE WHAT WENT WRONG

Over 10 years after the diabetes drug rosiglitazone was approved by regulators, and despite studies on tens of thousands of people, questions remain about its cardiovascular safety.

An investigation by **Deborah Cohen** looks at why this happened.



# the steps of practicing EBM

1. Ask a focused question.

2. Track down the evidence

3. Critically appraise evidence for its validity, effect size, precision

(NEXT month)

4. Apply the evidence in practice:

- a. *amalgamate* the valid evidence with other relevant information (values & preferences, clinical/health issues, & system issues)
- b. implement the decision in practice

# In the next 4 weeks



- **Try to ask for one patient you have seen:**
  1. What causes the disease?
  2. How was the disease diagnosed?
  3. How was the patient treated?
  4. What is the natural history of the disease?
  5. Consider formulating a PICO

**And try to find some evidence**