

Evidence Based Medicine

(NICE if it works)

DR MALCOLM KENDRICK





John Locke – ‘A letter concerning Toleration’

*‘No man can be forced to be healthful, whether he will or not.
In a free society, individuals must judge for themselves what
information they choose to heed and what they ignore.’*



A bit about me

- Graduated from Aberdeen University in Scotland – many years ago
- Work as a GP in Cheshire
- Wrote The Great Cholesterol Con
- Wrote Doctoring Data
- Wrote A Statin Nation [Books on sale]
- Set up the NICE website
- Set up ESC educational website
- Write a blog drmalcolmkendrick.org



A bit about me



Not yet referred to the General Medical Council



NICE – a brief history

From DECs to INTERDEC

Then the National Institute for Cost Effectiveness

Then the National Institute for Clinical Effectiveness

Then the National Institute for Clinical Excellence [Double plus good]

Then the National Institute for Health and Care Excellence [Double plus extra good]

The power of NICE

Guidelines are based on NICE evaluations

Clinical practice is based on guidelines

QoF is based on them

Medic-legal cases are won and lost on them

Their guidelines rule the world

They, in turn, are based on EVIDENCE



Based on
evidence

NICE evaluations



£20,000 per QALY
(Quality adjusted
life year)



Maybe £30,000
depending on
circumstances



What
circumstances?



Difficult to say



Did you say maybe
more than
£30,000...



Sometimes we need
no evidence at all –
Cancer Drugs Fund

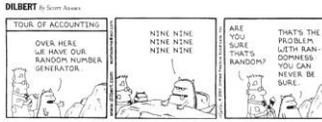


Total value of a
human life £30K x
80 = £2,400,000



National Take a Wild Guess Day April 15
www.NationalDayCalendar.com

What figure will we use for cost per QALY?



NICE experts – statin guidelines

'We continue to be concerned about the 'independence' of this guideline group in particular where 8 of 12 members had direct financial ties to the companies that manufacture statins.

We thus think it would be helpful if NICE were to be investigated by an independent parliamentary body. We therefore recommend that the Health Select Committee consider addressing this matter.

We respectfully feel that NICE has failed in its very purpose to act in accordance with independence.'

NICE experts – statin guidelines

Letter sent to Sarah Wollaston – chair of Health Select Committee:

Some of those who signed

Professor Klim McPherson, Chair UK Health Forum,

Dr Kallash Chand OBE, Deputy Chair BMA Council

Lord Ian Mccoll of Dulwich, CBE

Dr Clare Gerada, GP, Past Chair, RCGP

Professor David Haslam, Chair, National Obesity Forum

NICE -
evaluations



The NEW ENGLAND
JOURNAL of MEDICINE



Editor in Chief
Dr. Marcia
Angell

A crises with the evidence?

'It is simply no longer possible to believe much of the clinical research that is published, or to rely on the judgement of trusted physicians or authoritative medical guidelines.'
Marcia Angell

A crisis with the evidence

'The case against science is straightforward: much of the scientific literature, perhaps half, may simply be untrue. Afflicted by studies with small sample sizes, tiny effects, invalid exploratory analyses, and flagrant conflicts of interest, together with an obsession for pursuing fashionable trends of dubious importance, science has taken a turn towards darkness.' Richard Horton



A crisis with the evidence

"The poor quality of medical research is widely acknowledged, yet disturbingly the leaders of the medical profession seen only minimally concerned about the problems and make no apparent efforts to find a solution."
Richard Smith



A crisis with the evidence

"Moreover, for many current scientific fields, claimed research findings may often be simply accurate measures of the prevailing bias."
"It is more likely for a research claim to be false than true."

J Ioannidis: 'Why most published research findings are false'.





Money

Why is there a crisis- Money

Dr Robert Califf (Obama's nominee for the head of the FDA)

Senator Lamar Alexander of Tennessee, the Republican who chairs the committee, said Califf had been through an exhaustive vetting process to make sure he had no conflicts of interest.

"My staff tells me they haven't found anything that would call into doubt your ability to lead the FDA fairly and impartially," he said.



Money

Conflict of interest statement

Dr Califf currently holds the post of Deputy Commissioner for Medical Products and Tobacco, US Food and Drug Administration. Prior to holding this post, Dr Califf received grant funding from the Patient-Centered Outcomes Research Institute, the National Institutes of Health, the US Food and Drug Administration, Merck, Roche, Aterovax, Bayer, Janssen Pharmaceuticals, Eli Lilly & Company, and Schering-Plough; grants and personal fees from Novartis, Amylin, Scios, and Bristol-Myers Squibb/Bristol-Myers Squibb Foundation; and personal fees from WebMD, Kowa Research Institute, Nile, Parkview, Oxeigen, Pozen, Servier International, Bayer Healthcare, Bayer Pharma AG, CV Slight, Daiichi Sankyo/Lilly, Gambro, Gilead, Heart.org-Bayer, Medscape, Pfizer, Regeneron, TMC, GlaxoSmithKline, Genentech, Heart.org-Daiichi Sankyo, and Amgen.

Dr Califf also reported holding equity in Nitrox/N30 and Portola.



"My staff tells me they haven't found anything that would call into doubt your ability to lead the FDA fairly and impartially"



There is a crisis with the evidence

There is a crisis with evidence

'Substantial numbers of clinical trials are never reported in print, and among those that are, many are not reported in sufficient detail to enable judgments to be made about the validity of their results. Failure to publish an adequate account of a well-designed clinical trial is a form of scientific misconduct that can lead those caring for patients to make inappropriate treatment decisions.' JAMA 1990

<http://www.ncbi.nlm.nih.gov/pubmed/2041226>

There is a crisis with medical evidence

'...research that is completed is not made fully accessible. Half of studies are never published at all, and there is a bias in what is published, meaning that treatments may seem to be more effective and safer than they actually are. Then not all outcome measures are reported, again with a bias towards those are positive.' BMJ 2004

<http://www.bmj.com/content/329/7474/1000>

There is a crisis with medical evidence

'Failure to report the results of clinical trials threatens the public's trust in research and the integrity of the medical literature, and should be considered academic misconduct at the individual and institutional levels.' Annals of Internal Medicine May 2019

https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6680000/pdf/annals.2019.05.001.pdf

Hiding data

Participants 9423 women and men aged 20-97; measured cholesterol for 2355 participants
Interventions Cholesterol lowering diet. Saturated fat was replaced with linoleic acid (unsaturated fat from corn oil and corn oil polyunsaturated margarine).
Control diet was high in saturated fat from animal fats, common margarines, and shortenings.

Hiding data

The low saturated fat group had a significant reduction in serum cholesterol compared with controls.
For every 0.78mmol/l reduction in serum cholesterol, there was a 22% higher risk of death [This is about a 20% reduction in cholesterol level]
There was no evidence of benefit in the intervention group for coronary atherosclerosis or myocardial infarcts

Hiding data

"Whatever the explanation for key MCE data not being published, there is growing recognition that incomplete publication of negative or inconclusive results can contribute to skewed research priorities and public health initiatives. Recovery of unpublished data can alter the balance of evidence and, in some instances, can lead to reversal of established policy or clinical practice positions."

<http://www.bmj.com/content/353/bmj.g244>

Newer antidepressants – Hiding Data

- 38 out of 74 trials were considered positive, with benefits for the antidepressant
- 37 of these 'positive' trials were published
- 3 negative studies were published, as negative
- 11 negative trials published, where the results were presented in such a way as to make them seem positive
- 22 negative trials were 'silenced' and never appeared in the literature

<http://www.ncbi.nlm.nih.gov/pmc/articles/PMC411388/>

Newer antidepressants

"These data suggest that antidepressants may be less effective than their wide marketing suggests. Short-term benefits are small and long-term balance of benefits and harms is understudied."

<http://www.ncbi.nlm.nih.gov/pmc/articles/PMC411388/>

Gabapentin - whistle-blower

Dr Franklin's suit detailed how the company suppressed study results, planted people in medical audiences to ask questions intended to put gabapentin in a good light, lavished perks on doctors

They used ghostwriters, gave generous "consultation fees" to "thought leaders," and used psychological profiling of doctors in its successful bid to move gabapentin to so called blockbuster status (annual sales in excess of \$1bn)

Dr Franklin said that off-label uses accounted for more than 90% of the drug's \$2.7bn sales worldwide last year.



Gabapentin

More than half the clinical trials that we included in our analysis (11 of 20) were not published as full-length research articles.

For 7 of the 9 trials that were published as full-length research articles, a statistically significant primary outcome was reported

For more than half these trials, the outcome specified in the published report differed from the outcome originally described in the protocol.



The end result(s)

Beyond Confusion and Controversy, Can We Evaluate the Real Efficacy and Safety of Cholesterol-Lowering with Statins?

A careful examination of the most recent statin RCTs clearly shows that contrary to what has been claimed for decades, statins do not have a significant effect in primary and secondary prevention of cardiovascular disease.

The obvious final conclusion for physicians is that the present claims about the efficacy and safety of statins are not evidence-based.



Where does this leave us?

'Heart disease deaths in under 75's going up for the first time in 50 years.'

'Health experts typically expect longevity to increase as the economy grows and more health advancements are made, so the fact that life expectancy has been flat or trending downward for years now is concerning.'

This data point, says Christopher Murray, the director of the Institute for Health Metrics and Evaluation at the University of Washington, "confirms that there's a profound change in the trajectory of mortality. This should really be getting everyone's attention in a major way.'



Where does this leave us?

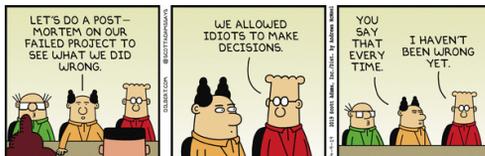
Life expectancy of adults in England and Wales has fallen by around six months, show new figures from the Institute and Faculty of Actuaries.

The institute, which calculates life expectancy on behalf of the UK pensions and insurance industries, expects men who are now aged 65 to die at 86.9 years on average. This is down from last year's estimate of 87.4 years. The average age of death of women who are now 65 is 89.2 years, down from 89.7 years.

Compared with 2015, projections of life expectancy are down by 13 months for men and 14 months for women.



How did it happen?



Armageddon



THE END