

The GP's Perspective

With Dr. Malcolm Kendrick

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Dr. Malcolm Kendrick

- An internationally renowned GP.
- Has had a long-term interest in cardiovascular disease.
- A leading light in the formation of the Clinical Trials Unit at Oxford in the International Network of Cholesterol Sceptics (THINCS)
- Runs a very prolific and informative blog (<http://drmalcolmkendrick.org/>).
- Author of two books:
 - ‘*The Great Cholesterol Con*’
 - ‘*Doctoring Data*’.

Reputation

- Previously self-described as a ‘lonely madman tilting at windmills’.
- Now, regularly gives talks and addresses meetings within the general practice profession.
- Now a trend in his direction of thinking, eg
 - The effect of a high-fat, low-carb diet on diabetics.
 - US government shifting its advice on the connection between cholesterol and the diet and cholesterol in your blood and/or heart disease.
- Changing entrenched positions and moving official guidelines is difficult.

Cholesterol

- New cholesterol-lowering agents will lower cholesterol to even lower levels than statins.
- Vast amounts of money behind these things, which has led to renewed pressure to lower cholesterol as far as possible
- Some people have very high cholesterol levels but do not seem to have heart disease. These people get dismissed: “something else must be going on”.
- A Netherlands study proved that familial hypercholesterolemia is not associated with premature heart disease (but was never published). It reversed the normal process by asking subjects if they had a family history of premature heart disease *before* measuring their cholesterol levels – thus removing the bias from the study.

Low-density Lipoprotein

- A little sphere of fluid within the bloodstream.
- To take the LDL into the cell:

- A receptor sticks out of the cell, pulls the LDL in, then closes off the cell membrane behind it.
- The receptor is then normally broken down by PCSK9

PCSK9

- New “evidence” suggests that we need to lower LDLs, particularly with PCSK9 inhibitors.
- Inhibition of PCSK9 means receptor is still present, thus it can continue to absorb lipoproteins into the blood.
- But, by bringing LDLs into the cell, there is also a risk of bringing infection into it.
- Strong evidence that those who use PCSK9 inhibitors are more susceptible to flus and colds etc.
- PCSK9 being launched and used in America and UK. The process:
 - In the US, the Food and Drugs Administration gives a statement of safety and effectiveness.
 - The pharmaceutical companies then rush to sell the product.
 - In the UK and across Europe, the Health Care Evaluation Unit, MHRA or the European equivalent normally follow the FDA.
 - However, the National Institute of Health and Clinical Excellence will question a drugs benefits and cost and will not recommend it, should it not fulfill a certain criteria.
- Difficult to sell a product that NICE has turned down.
- PCSK9 inhibitors (made by Amgen and Sanofi):
 - Injectable twice a week and cost around £8,000 a year per patient.
 - Statins, as a comparison, work out at £30 a year per patient.
- If 7 million people took the inhibitors instead of statins, the cost would reach £56 billion a year, half of the entire NHS budget. Therefore, these will probably only be prescribed to those with familial hypercholesterolemia. Coincidentally(!), the British Heart Foundation has just announced it will screen everyone for this disease.

Role of Funders and Funding

- Organisations like the British Heart Foundation are and believe they are doing good.
- However, they will always be influenced by their funders, eg teaming up with Flora.

Genetic Familial Link of High Cholesterol

- There is a genetic familial link to high cholesterol:
 - If one parent has the gene, it is likely their children will too.
 - If two people with the gene reproduce, they get a ‘double whammy’ of the gene.
- This is homozygous familial hypercholesterolemia.
 - Homozygous is as rare as 1 in a million: up to 50 people in the UK could have it.
 - Sufferers can have cholesterol levels of between 30 and 40 - they die of heart disease at a very young age.
 - It is a storage disease in which their arteries and tissues are full of cholesterol.
- Cholesterol is the problem only due to its extremity - storing six or seven times the normal level of anything in your blood leads to death.

Scientific Studies and Trials

- The study in the Netherlands over 15 years ago regarding familial hypercholesterolemia was not published.
- In theory, studies should be declared and the outcome measures specified in advance: it is always possible to find something positive in a trial with a sufficiently small sample and a large enough range of measurable variables:

- A science journalist published a study “proving” that ‘eating chocolate causes weight loss’¹. This was reported around the world in quality papers and was published in at least one serious, supposedly peer-reviewed medical journal. The journal published the report verbatim, within weeks of receiving its fee...
- The peer review process merely maintains the status quo.
 - The reviewers are often other experts in the same field.
 - Usually, the reviewer knows the author, meaning the paper is quickly approved.
 - Kendrick twice failed to get a paper on statins published by the British Medical Journal. The study looked at outcome measure from a different perspective: instead of looking at reductions to health risks, it asked will this make me live longer? Eventually, the answer was calculated as 15 days. The BMJ had previously printed a paper by Malhotra and Abramson from Harvard in which the high rate of adverse effects of taking statins was rounded the up to 18-20%. This provoked an angry reaction from Professor Rory Collins of Oxford University’s Clinical Trials Unit, who claimed that people would stop taking statins and become seriously ill. He demanded that the paper be withdrawn (a very serious step), but the figure was corrected to 17.6%. This spat may have influenced the BMJ’s decision.
- The life-extension outcome measure is often used when considering cancer treatment but less so much when looking at cardiovascular medicine. The outcome measure in this field depends on the paper: The most important outcome measure would be alive or dead, but it’s easier to measure in cancer treatments as people die quicker.
- When gathering outcomes, there are further problems with statistical evidence.
 - It can be reported that something reduces strokes by 50% etc, but if you do not know the actual numerical risk, the figure is meaningless and the differences made could actually be unnoticeable.
 - It is no longer possible to do a placebo-controlled trial of statins – they are considered the best possible treatment for heart disease, and it would therefore be unethical not to prescribe them.
 - The PCSK9 inhibitors were only trialled alongside statins.
 - No one has ever used statins versus no statins in familial hypercholesterolemia, therefore nobody knows if they work at all.

Bias

- Clinical Trial Service Unit at Oxford University (run by Prof Rory Collins) has received £220 million from one company alone that produces statins. Therefore, it can be suggested that institutional bias influences their support of statins.
- Professor Collins is not paid directly by funders, but the CTSU receives the money that in turn pays the individual, so this may also influence him personally. One professor at Oxford is paid ~£650k pa. (the name of the individual has not been disclosed...), so the sums involved could be large.
- Influences can also be affected by responsibilities for the well-being and livelihoods of staff.
- Biased findings may not just be motivated by money but by power: status, authority, respect and being appointed to committees are all important. Individuals involved in high-level research give talks at conferences, go to guidelines committees, and are invited to NICE and become a very important, powerful person.

Conflicts of Interest

- Conflict of interest statements are ridiculous:
 - Either you accept that a group will not be biased, meaning there is little point in the statement

¹ <http://tinyurl.com/jjejdcl> (it’s a good read!)

OR

- Their findings are biased, meaning they should not be publishing the paper at all.
- In the USA, the “Sunshine Act” means that money received from within the industry must be cleared, but the actual amount of money is not disclosed.

Pre-diabetes and Cholesterol Levels

- “Pre-Diabetes” is term coined, probably by the pharmaceutical companies, in an attempt to expand the size of the market.
- A cholesterol level of 5 is considered high in the UK - this would suggest that 80% of people are ill and need treatment.
- According to a risk factor calculator in the US which measures age, gender and other medical factors, if you have more than a 7.5% chance of suffering a cardiovascular event in the next 10 years, you should be taking statins. By this measure, even without any risk factors, every man over the age of 63 would have to take statins for the rest of their life.
- The risk level in the UK has been reduced to 10% (despite unanimous disagreement by GPs in a vote), but that still means virtually everyone at that age.
- The cost of this is in the region of a billion pounds: 14 million GP appointments for 7 million statin users, plus the blood tests and dealing with side effects.

An approach for manual therapists dealing with patients on statins

- Tiredness, aching joints and pain in the muscles can all be adverse effects of statins (“statins can make you feel 15 years older”).
- Irritability is a common sign, often overlooked.
- If statins are suspected to be the cause, suggest that a number of individuals feel similar, and they are on statins.
- Propose that the patient asks their GP to try a break from the drugs for a few months.

GP’s Perspective

- There’s a increasing concern about overmedication. A BMA campaign “Too Much Medicine” aims to reduce the burden on patients who are prescribed a large numbers of meds.
- The Quality Outcome Framework means that GPs get paid a considerable amount of their income for things such as:
 - Trying to help people to stop smoking.
 - Checking cholesterol levels.
 - Checking blood pressure and sugar levels
 - Checking medication usage etc
 - GPs also get paid for prescribing certain groups of drugs.
- Difficult to deny medication to a patient after (e.g.) a cardiovascular event when NICE believes they should be continually prescribed.
- Nobody would be struck off but should a patient complain, life can become very uncomfortable.

Blood Pressure

- A study (“SPRINT”) has suggested that lowering blood pressure from 140 to 120 would be beneficial, although the findings are difficult to interpret.
- Companies making blood pressure-lowering medications are making great efforts to prove this.
- If true, the findings suggest you’d have to treat 197 people for three years to get minimal benefit.
- With side-effect rates of 5%, 1/20 people would be suffering side-effects for very little gain.

- American figures, suggest that anything above or below a systolic blood pressure of 90mm Hg is considered a risk - highly beneficial for the companies who can give treatment and claim benefit.

Blood thinners

- New blood thinners (Apixaban) are not safer than Warfarin, but are more convenient:
 - There is an antidote to Warfarin (Vitamin K), however none for Apixaban.
 - But there is no need to monitor the patient – so fewer GP appointments needed.
 - Warfarin is very cheap, but the new drugs cost around £2,000 a year.

Statins and Hypothyroidism

- Cholesterol can be a marker for thyroid disease, but mechanism not clear.
- Always good to check thyroid when cholesterol levels are high.
- No coincidence that the Swiss, who have a high level of hypo-thyroidism (cretinism), have the highest level of cholesterol.
- T4 is a pro-hormone which is converted into its natural form in the cell; it helps cells work and creates energy.
- T4:T3 produced in a ratio of 5:1 in the thyroid gland.
- When T4 is low, synthetic T4 (UK: Levothyroxine/US: Synthroid) is given to reduce TSH level to correct level.
- To monitor the levels TSH is measured (often T4 is not). The test for TSH is wildly inaccurate, and T4 is itself inactive.
- So it is possible for T4 and TSH to appear normal, but still be hypothyroid.
- One alternative treatment is Armour Thyroid (desiccated pig's thyroid), which includes T1, T2, T3 and calcitonin has been seen to be effective clinically, but is not recommended in UK as there have been no trials to support it, it costs considerably more and the (flawed) tests indicate that simply supplementing T4 works.

Thyroid Concerns

- Symptoms can include but are not limited to:
 - Tiredness
 - Low temperature
 - Low energy
 - Dry skin
- There are so many symptoms that could be linked with thyroid issues – it's both easy and impossible to diagnose.
- A lack of measurements and trials means that we probably don't know what the normal levels for TSH etc. actually are.

Non-drug Approaches

- Not appropriate if thyroid has been removed.
- High sugar/carbohydrate consumption can affect the secretion of cortisol and function of the thyroid.

WHO Advice on Health Effects of Eating Processed Meat

- Reviewing such evidence is complex, as statements are based on multitudes of previous statements.
- The WHO will collate all available research and attempt to look for associations between X and Y.
- There has been no change to Malcolm's diet in light of this advice!