RISK EQUIVALENTS IN HYPERLIPIDAEMIA

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Background

- Hypercholesterolaemia is one of several major risk factor for death from ischaemic heart disease and stroke that is modifiable by lifestyle changes or drugs.
- Individuals make their own risk-benefit assessments of interventions, which ultimately affect adherence.
- Decision-support tools that help individuals gain perspective on the risk-benefits of particular interventions could help to maximise their risk reduction while minimising cost in personal.
- We attempted to translate the risk reduction from a unitary fall in the total cholesterol to high density lipoprotein ratio (TC:HDL) to equivalent interventions: reductions in number of cigarette consumed per day (CPD); systolic blood pressure (SBP); or body mass index (BMI).
- Individuals with familial hypercholesterolaemia (FH) can use the comparative measures to better understand the impact of the different choices they have to reduce risk.

Methods

- We built a deterministic Markov model of mortality using risk factors to modify population mortality rates for individual causes of death by comparing risk factor values to mean population values. The relationship between risk factor values and mortality rates by cause were assumed to have a linear relationship. Hazard ratios were determined using published evidence, with a preference for multivariate risk ratios. The causes of death specifically modelled were cardiovascular disease, lung cancer, other cancers, chronic obstructive pulmonary disease, and other respiratory disease.
- The risk factors used were TC:HDL, SBP, CPD, BMI, age and gender. All the subjects in this analysis were free from existing CVD or diabetes and were assumed to have no other occult disease. All calculations used hazards and hazard ratios before conversion to probabilities (initial mortality rates 'q_x') for each individual year of life (x) through to a limiting age of 120 years. The q values were then used to generate a probability density curve for the risk of death by age for each subject and an estimate of the mean age of death.
- We used the model to estimate the likely increase in lifespan associated with a reduction in TC:HDL of 1.0. Eight scenarios were selected, 4 of which reflected a hypercholesterolaemic profile and 4 with average values for all risk factors for the given age and gender. The risk factor profiles for each scenario are shown in table 1.
- For each scenario the improvement in life expectancy with a unitary fall in the TC:HDL ratio was calculated using the model, and the equivalent change in the SBP or BMI was found. For equivalent changes in CPD, three scenarios were compared: a reduction in cigarette consumption to 0, 10 or 20 CPD.

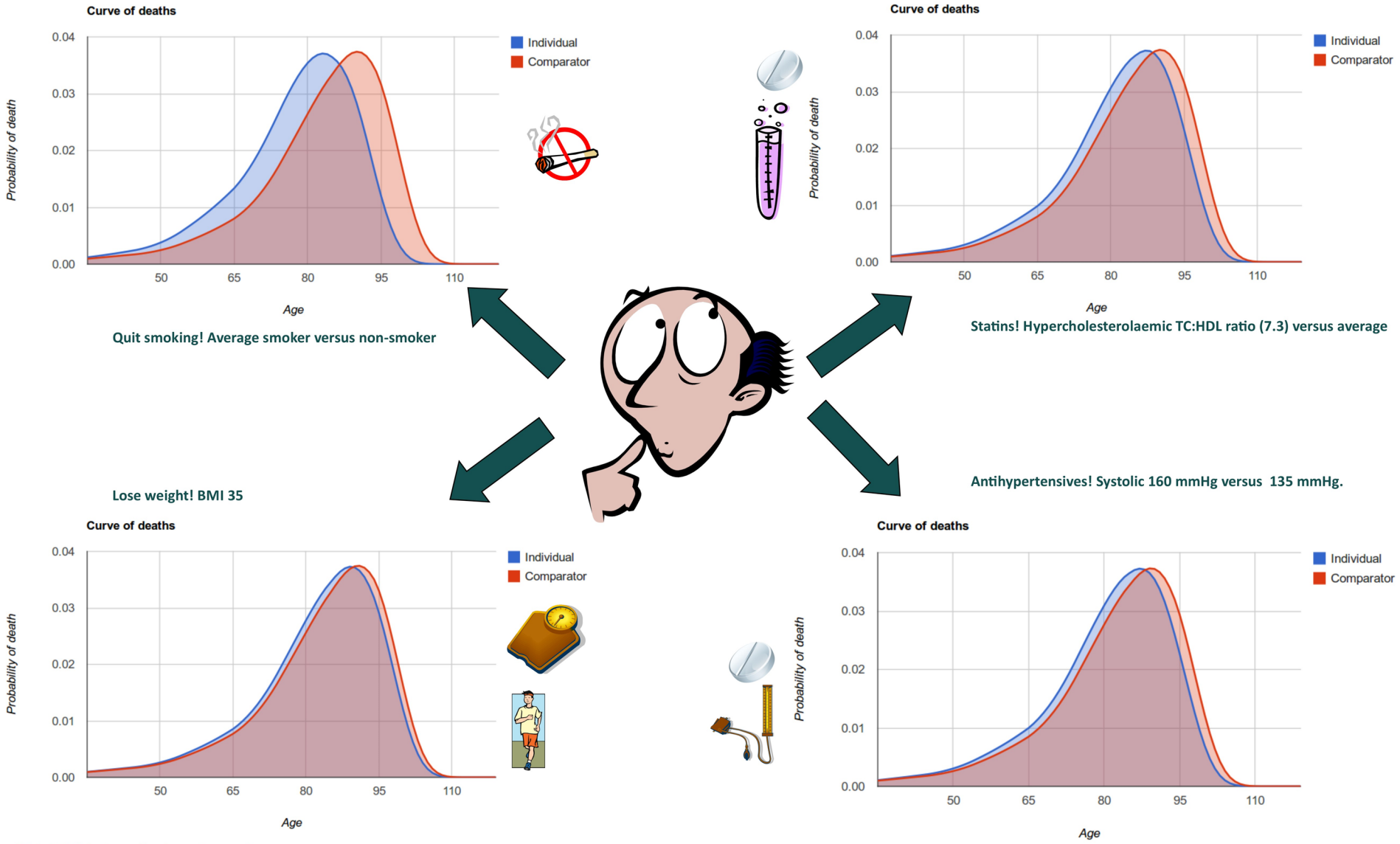

Table 1 Risk factor profiles for each scenario.

	Gender	Age	TC (mmol/l)	HDL (mmol/l)	TC/HDL	BMI	SBP (mmHg)
FH 1	M	35	8	1.1	7.3	27.4	127
Mean 1	M	35	5.5	1.3	4.2	27.4	127
FH 2	M	65	8	1.1	7.3	29.1	138
Mean 2	M	65	5.3	1.4	3.8	29.1	138
FH 3	F	35	8	1.1	7.3	26.7	114
Mean 3	F	35	4.9	1.5	3.3	26.7	114
FH 4	F	65	8	1.1	7.3	28.5	134
Mean 4	F	65	6	1.7	3.5	28.5	134

Table 2 Risk equivalents for each comparison factor for each scenario. (*Disregards end BMI value)

Baseline lipid profile	Increased survival with drop in TC:HDL of 1.0	Equivalent change in mortality: number of cigarettes vs non-smoker	Equivalent change in mortality: number of cigarettes vs 10/ day	Equivalent change in mortality: number of cigarettes vs 20/ day	Equivalent change in mortality: drop in SBP (mmHg)	Equivalent change in mortality: drop in BMI
FH 1	0.7	1.3	2.5	3	5	3.6
Mean 1	0.9	2.3	3	4	10	7.1*
FH 2	0.5	1	2	3	7	3.4
Mean 2	0.6	2	3	4	15	7.4*
FH 3	0.6	1	2	3	3	3.0
Mean 3	0.9	3	4	5	8	8.3*
FH 4	0.4	1	2	3	6	3.5
Mean 4	0.6	2	3	5	16	8.6*

Results

- Having a TC:HDL ratio typical of FH (7.3) brings forward the mean age of death, compared with 2008 UK population means, by 1.7 to 2.3 years, depending on age and gender.
- The mean increase in age of death associated with a 1.0 reduction in TC:HDL from baseline ranged from 0.4 years for a 65 year-old woman with FH to 0.9 years for a 35 year-old man with a population mean TC:HDL ratio of 4.2. This absolute difference in survival was equivalent to a change in smoking rates of 1–5 CPD; a decrease in SBP of 5–16 mmHg; and a decrease in BMI of 3.0–8.6 kg/m^2, depending on age, gender and baseline lipid levels.
- The absolute impact on mortality of smoking, SBP and BMI was higher in people with FH-level lipids than in those with mean lipid levels, regardless of gender or age.
- The scenario risk factor profiles are shown in Table 1 and the risk equivalents for the 1.0 change in the TC:HDL ratio are shown in Table 2.

Conclusion

- The model allows a comparison of the impact of cardiovascular risk factors on mortality using a TC:HDL difference of 1.0 as a standard unit of risk, and reinforces the importance of lipid lowering and smoking cessation.
- More research is needed to evaluate the potential impact of this type of decision-support tool on risk communication and individual choices.

Discussion

- The equivalent change to a 1.0 drop in the TC:HDL ratio is dependent on other factor values, particularly for smoking: the equivalent decrease in cigarette consumption ranges from 1 CPD in elderly males with FH who are light smokers, to 5 CPD in heavy smoking women without FH. The CPD equivalent of a 1.0 drop in TC:HDL is lower in those with FH than those without, since this reduction is proportionally smaller when the TC:HDL ratio is larger, and the risk from smoking is magnified by a raised cholesterol.
- The complexity of the interaction between risk factors and the equivalent risks makes it more difficult for individuals to put different intervention options into perspective. It is unclear how information from decision support tools based on these risk intervention equivalents would alter lifestyle and treatment choices.
- The realistic choices an individual faces are the use of statin drugs to reduce cholesterol, with typical reductions of 25% in the TC and an 8% rise in the HDL (4S study), or whether to quit smoking or not. Figure 2 shows the difference in the curve of deaths for a 35 year old male, average smoker (~15 CPD) versus a non-smoker.
- Figures 3 and 4 show equivalent graphs for the use of antihypertensive drugs (for a 35 year old male hypertensive with SBP of 160 mmHg reduced to 135 mmHg), and for a reduction in BMI (for a 35 year old obese male with a BMI of 32 reduced to 24).
- The intervention with the greatest impact is cessation of smoking, which affects the risk of cancer and respiratory disease as well as CVD. A correction of a typical FH lipid profile to the average for age and gender has the second largest impact on life expectancy.

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