Response from the Faculty of Public Health to the Department of Health's *Technical Consultation on Economic Modeling of a Policy of Vascular Checks*

The UK Faculty of Public Health

The Faculty of Public Health (FPH) is the leading professional body for public health specialists in the UK. It aims to advance the health of the population through three key areas of work: health promotion, health protection and healthcare improvement. In addition to maintaining professional and educational standards for specialists in public health, FPH advocates on key public health issues and provides practical information and guidance for public health professionals.

Response to consultation

FPH welcomes the Department of Health's (DH) increased emphasis on the primary prevention of cardiovascular disease in the Putting Prevention First (PPF) initiative. An annual cardiovascular death rate of 100,000 and a total annual cost exceeding £30bn means that every legal step must be taken to reduce this massive burden of disease.

We therefore congratulate DH for the thoroughness of this analysis which has taken a comprehensive look at a complex set of interventions. The investment of an additional £250m per year on this objective sends strong prevention messages to the National Health Service and beyond.

FPH also welcomes the openness and enthusiasm for inviting referee comments in order to develop and improve the current model. We therefore offer a few suggestions and comments, very much in a spirit of constructive feedback.

VRA model architecture and steps in the model building

These appear very sensible. We note that this screening programme focuses on individuals aged up to 75 years, and specifically excludes patients with diagnosed cardiovascular disease and those already on statins or antihypertensives. We agree that it is important to keep separate these two groups (conventionally labelled as 'CVD Primary Prevention' and 'CVD Secondary Prevention').

Data Sources

All models require data. The decision to use the QRESEARCH database appears reasonable and pragmatic. The strengths and limitations of this database are increasingly well understood. Future plans to use the 'Framingham Equation' would be welcome, especially with the recalibration proposed by Brindell *et al* in 2006. However, 72% of QRESEARCH individuals having a missing cholesterol reading and 24% are without a blood pressure reading. This is clearly an issue, raising concerns about selection bias and the problems of confidently generalising to the entire UK population.

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Assumptions
The next major issue for any model is the assumptions made. A number of key assumptions are helpfully summarised in the 'Parameters within SIMUL8 model' (Table 2, page 13). Such assumptions can be tested in a sensitivity analysis and the selection of the highest and lowest plausible values for every parameter is crucial.

For instance, the assumption that attendance for vascular screening will be as good as for breast screening (70% always attend with a further 15% having a one-third chance of attending) appears optimistic for women, and probably even more so for men.

The 15% quit rate in smokers presumably reflects the four week figure. This requires amendment to a one year figure closer to 2% (recognising that about 85% relapse). The 68% completion rate for a weight loss programme is a process measure. The key issue is sustained weight loss at one or two years and beyond; RCTs suggest that this may be disappointingly small.

The assumption of 40% hypertensives going on to receive medication appears reasonable. However, the assumption that 87% of diagnosed hypertensives will then comply with medication conflicts with the extensive literature; 50% is more realistic. Likewise for individuals for high cholesterol; the probability of taking up statins is set at 85% - again, this appears a little high. The key issue is longterm sustainability, with the literature suggesting an adherence of 50% or less and not the 70% assumed here. The values for compliance with blood testing also appear a little optimistic. The values for compliance with blood glucose testing are left blank in this table.

The model seems to assume that a blood pressure of 139 mmHg is acceptable, whereas this carries much the same risk as a systolic blood pressure of 140 mmHg. This highlights the limitation of any model which uses categorical variables, rather than continuous variables with log-linear risks described by beta coefficients (in comparison, relative risk represents a rather simplistic approach).

Efficacy measures require an RCT
The published evidence is not encouraging. Although not identical, the OXCHECK RCT had much in common with the interventions included in PPF. Effects were modest, and costs were substantial.

Although the evidence for a particular intervention being efficacious in motivated people (and in some cases, in random samples of the general population people) is NICE-based, it does not necessarily mean that it is effective as part of a population-based screening programme. This needs to be evaluated as an RCT (possibly clustered) just like any other screening programme. Perhaps one could randomise encouraging opportunistic screening in a third arm (vs usual care) eg. advising people to stop smoking (and referring them for support) is more effective when they come with a smoking-related problem than as a random statement.

Potential effects on inequalities.
The PPF individual high risk approach will tend to favour affluent and educated individuals, thus potentially increasing social inequalities in health. A large body of literature demonstrates that disadvantage can occur at every stage in the process, from the person's health beliefs and

health behaviour, through presentation, negotiation, and participation to long term adherence with medication. The potential effects on increasing inequalities should therefore be urgently quantified.

In other words, no distributional effects have been examined as yet (this will have to be done for a full Policy Impact Assessment). If the current situation is that deprived populations are less likely to have these interventions, then a population-based programme should be implemented to reduce inequalities.

Detailed comments

Page 16 - Cholesterol

This currently assumes no change in individual cholesterol scores over time. UK cholesterol levels rise with age. Perhaps the Health Survey for England (HSE) could be used to construct synthetic cohorts. This may be important because cholesterol is such a powerful risk factor (whether measured as total or as a sub-fraction or a ratio).

Part of the apparent fall in cholesterol since 1994 reported by HSE may actually reflect a transition to a different laboratory method of measurement. This could perhaps be considered in a sensitivity analysis, along with an analysis of subgroups (larger falls in people with CHD or stroke, smaller falls in people with diabetes or hypertension, and virtually no change in disease free individuals).

Page 17 – Changes in risk with interventions

The combination of relative risks using a multiplicative approach appears sensible and has been previously recommended by Mant & Hicks 1997, Yusuf 2002 and Ford 2007.

Page 18 – Lifetime costs, QALYS and time horizons

The horizon of 20-40 years has been chosen. In the absence of RCT data, this makes assumptions necessary. It is frustrating that there is no evidence to support the assumption that individuals will continue to take therapy for that long, nor that benefits will continue.

At a time horizon of 2-4 decades, the choice of discount rate (1.5%, 3.5% or even 6%) also becomes a very important issue and merits a sensitivity analysis.

Costs and GP workload

The model assumes that over 95% of the health service activity will be undertaken by practice nurses and healthcare assistants. What exactly are healthcare assistants? Will they ever be legally permitted to prescribe?

The model assumes that very little GP time will be committed to the PPF programme. However, this appears unrealistic and has already been questioned by GP colleagues more familiar with the realities. Substantial GP time investment may actually be required. Practical challenges include negotiating a medication regime for statins or anti-hypertensives, then monitoring and amending it over months and years. For instance, anti-hypertensive therapies often need to be changed; a proportion of patients will not respond to mono-therapy and thus require drug combinations. Only medical practitioners have prescribing rights and expertise to undertake this potentially hazardous clinical activity. (These drugs can produce side-effects, serious disease and even occasionally, death.)

Furthermore, many patients initially managed by practice nurses may then demand appointments with their GPs to discuss the issues.

The practice nurse and health care assistants will also need training initially and over the longer term. This will have cost implications.

Referrals to weight management clinics run by physicians will probably require a GP letter (or something similar).

There needs therefore to be a cost estimation of the total GP and administrative time required, not just the provision of the intervention.

Page 21 – Statins
The model assumes that net costs of primary prevention equal those of secondary prevention. This is questionable, and probably requires further justification.

The model also assumes that 80% of new statins prescriptions are for simvastatin and only 20% for more expensive alternatives. Does current prescribing data provide supporting evidence?

Page 22 – Smoking cessation
This needs to include Varenicline. The model appears to assume that 14% of cessation clinic attendees will stop smoking. In fact, recent HTA funded research from York has demonstrated 85% of these four-week quitters relapse by 12 months. This gives a longterm quit rate of about 2%, dramatically lower than the current model assumption.

Page 22 – Exercise intervention
The model assumes that 50% of participants maintain increased levels of physical activity long-term. However, even an assumption of 25% appears optimistic, given the published evidence of no significant effect at 12 months (recent NICE reviews in 2007).

Page 22 - Weight loss intervention
The assumption of a 0.01 QALY as benefit, appears very reasonable. Sustained weight loss represents a very tough clinical challenge at the present time.

Page 24
The 10 minutes of GP time per year for monitoring appears optimistic as discussed earlier.
The assumption that diabetes screening would detect disease seven years earlier also appears optimistic, reflecting the optimal conditions in a randomised control trial. Likewise, the detection of kidney disease 10 years earlier also appears rather optimistic.

Furthermore, evidence from HSE and the English Longitudinal Study of Ageing suggests that relatively few cases of diabetes are now undiagnosed (around one in six [paper about to be submitted]), so screening will not be as cost-effective as when one in two or one in three cases were undiagnosed.

The DH website specifies anticipated health benefits of 2,000 fewer deaths and 10,000 fewer cardiovascular events per annum. It is crucial that the methodology underlying this estimate is exposed to peer review. At present, these estimates are not mentioned in this technical

consultation. This will be essential to increase confidence in the soundness of the QALY estimates.

Page 25 Diabetes
Diabetes care needs costing to recognise involvement of a wide team, including dieticians and podiatrists (and not just practice nurses) as well as regular eye checks as a minimum. Patients will also require a blood for U&E annually, not just in year one. Diabetes is assumed to be managed in primary care with just 30 minutes of GP time. This appears slightly idealistic.

Likewise the 10 minutes GP time assumed for hypertension management. As discussed above, this looks unrealistic, even if all is going smoothly.

Page 26 – Scenario modeling and Monte Carlo simulation
High and low costs were tested by increasing and decreasing values by 5-15% compared to the base case. It is not clear if this was done as a one-way sensitivity analysis or a multi-way sensitivity analysis. Some other published models have used a multi-way analysis and a more robust approach of +20% and-20% values. This limitation is demonstrated very clearly in graph one on page 32 which shows remarkably narrow 10th and 90th percentile error bars.

Page 34 – Workforce impact
As discussed above, the additional time for GPs, less than one hour per week per practice, appears optimistic. The additional work for hospitals has not been quantified or costed.

Appendix B – Assumptions on uptake, compliance, attribution and relative risk reduction (RRR)
We strongly welcome publication of these key variables. This transparency is commendable.

Compliance at one year might usefully be extended, with estimates for 10 years or 40 years, given the time horizon for the model. A number of the relative risk reductions for therapies have been taken from single studies of questionable relevance to the UK population. Meta-analyses would be a more reliable measure of efficacy. For instance, anti-hypertensive effect was assumed to be 0.24 (whereas 0.15 is more realistic). Likewise, reduction of events by statins assumed to be 0.31 (0.25 more realistic).

The weight management relative risk reduction of 0.36 appears excessive, particularly given that most of the benefit of weight loss apparently operates through reductions in ‘downstream factors’: blood pressure and cholesterol and decreased diabetes prevalence, which have already been considered.

Issues around the assumed 14% smoking quit rate at one year have already been highlighted. The 0.14 RRR for exercise is apparently based on the InterHeart study. In that study, the value for men aged under 55 years was in fact reported as 1·02 (0·83-1·25) in Table 5. The relative risk reduction for the PPF diabetes prevention programme comes from a randomised control trial in Finland. The relevance to ordinary clinical practice in the UK merits some discussion.

The RRR for statins merits a sensitivity analysis to include Abramson 2007, who suggested a much smaller effect, particularly in women.

We therefore commend using a peer-reviewed technical appendix like that published with Ford's NEJM article in 2007, (this addressed these issues in some detail and provided efficacy values and sources for all the key meta-analyses of interventions).

Appendix D – Sensitivity analysis
Most of the sensitivity analysis work was based on high and low estimates of cost. This is a good start. However, it will be important for further work to look at high and low plausible values of intervention effectiveness, uptake and long-term sustainability/adherence.

Conclusions
We strongly welcome the Department of Health Vascular Team's increased emphasis on the primary prevention of cardiovascular disease.

The Putting Prevention First screening initiative represents an ambitious and potentially useful exercise. The Simul8 Model Version 1 represents a useful first step to quantify health gains. However, the current calculations of benefit appear to be substantially over-estimated, particularly given the issues we have highlighted above. The rapid production of a second version will therefore be extremely valuable.

We hope our constructive comments and suggestions will be helpful in this development.