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SUPPLEMENTAL MATERIAL

Appendix 1

Search strategy: Cochrane databases (searched 20 March 2015 14:00:51,676 for the period 2000 to 2015)

NHS EED (economic evaluations)

| ID | Searches - CRD (NHS-EED) |
|----|--------------------------|
| #1 | MeSH blood pressure EXPLODE PERMUTE |
| #2 | MeSH hypertension EXPLODE PERMUTE |
| #3 | cost utility analys* |
| #4 | mathematical model |
| #5 | decision analys* |
| #6 | Markov chain* or Markov process* or decision tree |
| #7 | Economics |
| #8 | cost effective* or cost effective* analys* |
| #9 | #3 OR #4 OR #5 OR #6 OR #7 OR #8 |
| #10 | #1 OR #2 |
| #11 | #9 AND #10 |
| #12 | MeSH primary prevention EXPLODE PERMUTE |
| #13 | #11 AND #12 |

*NHS EED* National Health Service Economic Evaluation Database, */S* wildcard characters
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Appendix 2

EMBASE and MEDLINE databases (searched 20 March 2015 16:59) via OVID MEDLINE(R)

| ID | Searches (via OVID)                                                                                     |
|----|--------------------------------------------------------------------------------------------------------|
| #1 | (lowering blood pressure or lowering-blood-pressure or blood pressure lowering).mp. [mp=ti, ab, sh, hw, tn, ot, dm, mf, dv, kw, nm, kf, px, rx, an, ui] |
| #2 | (hypertensi$ or antihypertensi$ or anti-hypertensi$).mp. [mp=ti, ab, sh, hw, tn, ot, dm, mf, dv, kw, nm, kf, px, rx, an, ui] |
| #3 | 1 OR 2                                                                                                 |
| #4 | (cost effective$ OR cost-effective$ OR mathematical model OR decision-analys$s OR decision analys$s OR Markov OR decision tree OR economic evaluation OR cost utility).mp. [mp=ti, ab, sh, hw, tn, ot, dm, mf, dv, kw, nm, kf, px, rx, an, ui] |
| #5 | 3 AND 4                                                                                                 |
| #6 | limit 5 to English language                                                                            |
| #7 | limit 6 to yr="2000 -Current"                                                                          |
| #8 | limit 7 to humans                                                                                       |
| #9 | Exclude conference abstracts, methodological papers, commentaries, editorials, notes                    |
| #10| remove duplicates from 9                                                                                 |
Appendix 3 Framework to assess adherence to good practice guidelines in Decision-Analytic Modelling (DAM)

Source: Peñaloza et al. A Systematic Review of Research Guidelines in Decision-Analytic Modeling. Value in Health 18 (2015), Table 5, p. 524-527.

| Components of good practice | Questions for review | Yes, No, or NA | Attributes |
|-----------------------------|----------------------|----------------|------------|
| Decision problem            | Is there a written statement of the decision problem and scope of the study? | Yes, No, or NA | A clear statement of the decision problem and scope would determine the interventions and health outcomes to be measured |
|                             | Are the objective(s) of the study and model structure consistent with the stated decision problem and scope? | Yes, No, or NA | They are expected to be consistent |
| Analytical perspective      | Has the perspective of the model been stated? | Yes, No, or NA | Most common perspectives are: patient, health system (insurer) and society |
| Target population           | Has the target population been identified? | Yes, No, or NA | Target population should be defined in terms of features relevant to the decision (geography, patient characteristics, including comorbid conditions, disease prevalence and stage) |
| Health outcomes             | Are the outcomes of the model stated and consistent with the perspective, scope and overall objective(s) of the model? | Yes, No, or NA | Health outcomes may be events, cases of disease, deaths, life-years gained, quality-adjusted life-years, disability-adjusted life-years or other measures important to stakeholders and should be directly relevant to the question being asked |
|                             | Has any adverse effect of the intervention(s) been captured? | Yes, No, or NA | Interventions may cause negative health consequences that need to be modelled and discussed as part of the study’s results. The impact of assumptions regarding adverse effects of interventions should be assessed as part of the structural uncertainty analysis |
| Comparators                 | Is there a clear definition of the alternative interventions under evaluation? | Yes, No, or NA | Usually the choice of comparators is governed by the scope of the model. Impact of assumptions adopted when deciding upon comparators should be assessed as part of the structural uncertainty analysis |
|                             | Is there a discussion around feasible options or justification for the exclusion of feasible options? | Yes, No, or NA | The choice of comparators affects results and should be determined by the decision problem, not by data availability. All feasible and practical strategies as determined by the scope of the model should be considered. Constraining the range of strategies should be justified |
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| Time horizon | Is the time horizon of the model justified and sufficient to reflect all important differences between options? | Time horizon of the model should be long enough to capture relevant differences in outcomes across strategies (lifetime). Time horizon is dictated by the problem scope |
|--------------|----------------------------------------------------------------------------------------------------------|----------------------------------------------------------------------------------------------------------------------------------|

Note: NA= Not Apply
## DIMENSION 2: MODEL CONCEPT

| Components of good practice | Questions for review                                                                 | Attributes                                                                                                                                                        |
|-----------------------------|--------------------------------------------------------------------------------------|------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| Choice of model type        | Has the unit of representation been given?                                            | Usually stated in terms of groups or individuals. If groups are being modelled most frequently decision trees, Markov processes or infectious disease models are the correct choice; if individuals are being modelled then the choice is between DES, dynamic transmission models or agent-based models |
|                             | Is there a need to model the interaction between individuals in this model? Has this been discussed? | If interactions between individuals is required (when the disease or treatment includes interactions between individuals) then DES, dynamic-transmission, or agent-based models may be the correct choice |
|                             | Does the decision problem require a short time horizon?                              | For simple models or problems (short time horizon, few outcomes) a decision tree may be appropriate; time horizon should be large enough to capture all health effects and costs directed related to the decision problem |
|                             | Is it necessary to model time in discrete cycles?                                     | Continuously for Individual STM or in discrete cycles for Markov STM; if the assumption that transition probabilities do not depend on history is not required, then individual state-transition models are an alternative; If disease or treatment process need to be represented as health states, state transition models are appropriate (Markov type) |
|                             | Is there a need to model competition for resources or the development of waiting lists or queues? | If the problem requires the ability of a model to incorporate interactions between individuals and other model parts for example to answer questions on resource allocation i.e., organ allocation for transplantation, distribution of antiretroviral medications in resource-poor environments, then a DES may be appropriate |
|                             | Has a type of model been chosen and discussed?                                        | It is expected that studies report on the reasons for choosing a type of model                                                                                     |
| Model structure             | Has the starting cohort been defined by demographic and clinical characteristics affecting the transition probabilities or state values? | If results may vary by subgroups (age, sex, risk factors) is advisable to report results for different cohorts                                                     |
|                             | Has health states and transitions reflecting the biological/theoretical understanding of the disease or condition been modelled? | States should adequately capture the type of intervention (prevention, screening, diagnostics, and treatment) as well as the intervention’s benefits and harms. States need to be homogeneous with respect to both observed and unobserved characteristics that affect transition probabilities |

Note: NA = Not Apply
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| Components of good practice | Questions for review                                                                 | Yes, No, or NA | Attributes                                                                                                                                                                                                 |
|-----------------------------|--------------------------------------------------------------------------------------|----------------|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| Data sources                | Has transition probabilities and intervention effects been derived from representative data sources for the decision problem? |                | Most common sources of data include population-based epidemiological studies, control arms of trials or literature                                                                                       |
|                             | Has (all) methods and assumptions used to derive transition probabilities and intervention effects been described/justified?      |                | Attention should be given to the use of transition probabilities and rates; conversion of transition probabilities from one time unit to another should be done through rates and never presented as percentages |
|                             | Has parameters relating to the effectiveness of interventions derived from observational studies been controlled for confounding? |                | If results of meta-analyses were used as data sources then consider how potential confounders are addressed; consider the likelihood of increased heterogeneity resulting from residual confounding and from other biases across studies. Efficacy derived from RCT may have to be adjusted for compliance to reflect real-world effectiveness. Effectiveness derived from observational studies must be adjusted for confounding (e.g., using multivariate regression techniques or propensity scoring). Adjustment for time-varying confounding (confounders that simultaneously act as intermediate steps in the pathway between intervention and outcome) require special methods such as marginal structural analysis or g-estimation. When results from observational studies are used in the model, causal graphs can be used to explicitly state causal assumptions |
|                             | Has the quality of the data been assessed appropriately?                              |                | Sources of data and data limitations are expected to be discussed                                                                                                                                       |
|                             | Has expert opinion been used, are the methods described and justified?                 |                | An expectation that strengths and limitations of assumptions adopted should be included                                                                                                                     |
| Utilities                   | Are the utilities incorporated into the model appropriate?                             |                | methods used to obtain utility weights and methodology used to transform health estate estimates into quality of life scores                                                                            |
|                             | Is the source for the utility weights referenced?                                     |                | Sources of data and data limitations are expected to be discussed                                                                                                                                       |
| Cycle length and half cycle correction | Has the choice of cycle length been justified?                                         |                | It should be based on the clinical problem and remaining life expectancy                                                                                                                                   |
|                             | Has the use of a half cycle correction been stated?                                   |                | Any assumption adopted is expected to be disclosed                                                                                                                                                      |
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| Resources/ costs | Are the costs incorporated into the model justified and sources described? | Sources of data and data limitations are expected to be discussed |
|------------------|------------------------------------------------------------------------|---------------------------------------------------------------|
|                  | Has discount rates been reported and justified given the target decision-maker? |                                                                      |
| Patient heterogeneity | Has patient heterogeneity been considered? | For example, in a cohort model states need to be homogeneous to observed or unobserved characteristics affecting transition probabilities |
| Parameter precision | Has mean values and distributions around the mean and the source and rationale for the supporting evidence been clearly described for each parameter included in the model? | Sources of data and data limitations are expected to be discussed |

Note: NA= Not Apply
### DIMENSION 4: ANALYSIS OF MODEL UNCERTAINTY

| Components of good practice | Questions for review | Yes, No, or NA | Attributes |
|----------------------------|----------------------|----------------|------------|
| **Uncertainty**            | Has analyses of uncertainty pertaining to the decision problem been included and reported? If not, has the reasons been explained for its omission? |               | Analysis of uncertainty is expected to be include as part of the DAM |
|                            | Has one-way DSA or two-way sensitivity analysis been performed? |               | Tornado diagrams, threshold plots or simple statements of threshold parameter values, are all appropriate. Uncertainty of parameters may be represented by several discrete values, instead of a continuous range, called ‘scenario analyses’. It is a good practice to include the specification of parameter’s point estimate and a 95% CI range. |
|                            | Has a Probabilistic Sensitivity Analysis (PSA) been included? |               | The specific distribution (e.g. Beta, normal, lognormal) as well as its parameters should be disclosed. When PSA is performed without an accompanying EVPI, options for presenting results include CEAC and distributions of net monetary benefit or net health benefit. When more than two comparators are involved, curves for each comparator should be plotted on the same graph. |
|                            | Has correlation among parameters been assessed? |               | Lack of evidence on correlation among parameters should not lead to an assumption of independence among parameters |
| If model calibration was used to derive parameters, has the uncertainty around calibrated values been tested using DSA or PSA? |               | Calibration is commonly used to estimate parameters or adjust estimated values such as overall and disease specific mortality and event incidence rates |
| **Structural uncertainty** | Has a discussion about the inclusion/exclusion of assumptions affecting the structure of the model been included? (refers to potentially relevant comparators, health states and recurrent events or any other assumption affecting the structure of the model) |               | For example: i) health states and the strategies adopted following the recurrence of events; ii) length of treatment effects; iii) types of adverse effects included; iv) duration of treatment effects; v) time dependency of probabilities (in a time dependent utility, the cost of delaying treatment as a function of the time a patient has remained in an untreated acute pathological state); vi) prognostic implications of surrogate end points; vii) clinical events; viii) comparators. Although these structural assumptions are not typically quantified, it is uncertain whether they express reality accurately and for that reason they should be assessed as part of structural uncertainty analysis |
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Other reporting of uncertainty analyses

| Questions for review | Yes, No, or NA | Attributes |
|----------------------|---------------|------------|
| Has the EVPI being measured /discussed? | If the purpose of a PSA is to guide decisions about acquisition of information to reduce uncertainty in the results, EVPI should be presented in terms of expected value of information. EVPI is commonly reported in monetary terms using net monetary benefit or net health benefits; EVPI should be reported for specified ICER thresholds. |

Note: NA= Not Apply

DIMENSION 5: MODEL TRANSPARENCY AND VALIDATION

| Components of good practice | Questions for review | Attributes |
|-----------------------------|----------------------|------------|
| **Transparency**            | Has a graphical description of the model been provided? | |
|                             | Has all sources of funding and their role been identified? | |
|                             | Has all methods used been customised to specific application(s) and settings? | |
|                             | Has the report used nontechnical language and clear figures and tables to enhance the understanding of the model? | |
|                             | Has limitations and strengths been acknowledged/discussed? | |
|                             | Is there any reference as to whether technical documentation would be made available at request? | Can occur in several ways: the group that develop the model can appeal to members of the modelling group, people in the same organisation who did not build the model, or external consultants. Any reader can perform his/her own evaluation. Peer review (previous to publication) |
| **Validation**              | Is there any evidence of model’s face validity? | Verification or technical validity; models should be subject to rigorous verification and the methods used should be described and results made available on request |
|                             | Has internal validity been assessed? | or external consistency (involves examining different models that address the same problem and comparing their results) its meaningfulness depends on the degree to which methods and data are independent. Modellers should search for modelling analyses of the same or similar problems and discuss insights gained from similarities and differences in results |
|                             | Has cross-validation been assessed? | |


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| Has external validity been assessed? | This compares the model's results with actual event data; a formal process needs to be developed including identifying suitable sources of data; results of external validation should be made available |
|------------------------------------|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| Has the model’s predictive validity been assessed? | If feasible given the decision problem and future's sources availability |

Note: NA= Not Apply