Supplementary Material – Supporting the development of evidence-informed policy options: an economic evaluation of hypertension management in Ghana

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Introduction
This appendix describes Version 3.0 of the Ghana Hypertension Model. The model was programmed in Excel by Joanne Lord, initially based on a model developed for the 2006 update of the NICE clinical guideline on hypertension [1], and adapted for Ghana following discussion and agreement of appropriate modelling assumptions and data inputs with the Technical Working Group (see part C) and Kalipso Chalkidou, Francis Ruiz, Martha Gyansa-Lutterodt and Mohamed Gad. The model is available under a Creative Commons Attribution-Non Commercial-Share Alike license (CC BY-NC-SA 4.0).

Section A – The Model
i. The development process
The hypertension model was based on an analysis developed initially for the 2006 update of the UK, National Institute for Health and Care Excellence (NICE) clinical guideline on hypertension [1], updated and adapted for the Ghanaian context and extended to address a wider range of questions. In developing the analysis, a number of workshops and in-country visits were undertaken, supported by teleconferences and email exchanges. In partnership with the UK team, members of the Ghana-based TWG specified the decision problem to be addressed, advised on the adaptation process, the quality and relevance of data sources, the appropriateness and acceptability of assumptions and set out policy makers’ decision needs.

ii. Aims and objectives
The aim of the model is to provide a platform to estimate the cost-effectiveness and budget impact of a range of interventions to prevent cardiovascular disease (CVD) through better control of hypertension in the Ghanaian population.

iii. Population and subgroups
The model estimates outcomes for patients with essential hypertension, excluding those with pre-existing CVD, diabetes and pregnant women. 48 subgroups of prevalent cases are defined by: men and women; by 6 ten-year age groups (from 20-29 to 70+); and 4 levels of blood pressure (normal due to effective control with antihypertensive medication, mild, moderate or severe; see Table 1). In addition, patients with raised blood pressure are further divided according to current treatment status (not aware of raised blood pressure; aware but not treated; treated but not controlled). Thus, in total the model includes 120 subgroups of patients.

| Blood pressure status     | Systolic (mmHg) | Diastolic (mmHg) |
|---------------------------|-----------------|------------------|
| Optimal                   | <120            | <80              |
| Normal                    | 120-129         | or               |
| High normal               | 130-139         | or               |

| Level of hypertension     |                  |                  |
|---------------------------|------------------|------------------|
| Grade 1, mild             | 140-159          | or               |
| Grade 2, moderate         | 160-179          | or               |
| Grade 3, severe           | 180+             | or               |

*Table 1 Classification of hypertension by severity*
iv. **Intervention**
The model can be used to compare expected outcomes assuming no treatment or monotherapy with one of the 5 main classes of antihypertensive medication:

1. Angiotensin Converting Enzyme Inhibitor (ACEi)
2. Angiotensin Receptor Blockers (ARB)
3. Betablockers (BB)
4. Calcium Channel Blockers (CCB)
5. Thiazide like diuretics (TZD)

v. **Policy Scenarios**
The analyses presented in this report include the following types of policy change:

1. Price reductions for listed drugs: e.g. 10% reduction in mean price of ACEi, ARB, BB and CCB, no change in numbers of patients treated by drug class.
2. Reduced use of less effective/more expensive drugs: e.g. switch 10% of patients currently treated with ACEi, ARB and BB to TZD.
3. Increased use of better value drugs: e.g. switch 10% of patients treated with CCB to TZD.
4. Increased treatment of diagnosed patients: e.g. use of TZD for patients aware of hypertension but not currently on treatment.
5. Increased case detection: e.g. 5% of population aged 40 years and over offered screening in community pharmacy [2].

For simplicity, the policy options that were modelled assumed a one-off change, instituted in a single year for a proportion of the current prevalent population with hypertension. The model then estimates consequent health effects and costs over the remaining lifetime for those individuals. The impact of extending the policies to more patients in future years (whether members of the initial prevalent population or to new incident cases) could be estimated in separate modelled scenarios.

Note that the modelled examples do not generally assume 100% uptake of the suggested treatment changes, because it is not likely that such major shifts in practice could be achieved in a single year. In addition, there are individual factors not included in the model that mean that the changes would not be clinically appropriate for all patients. For example, treatment may reasonably differ for patients with co-morbidities: such as use of beta blockers for patients with cardiac arrhythmia or ACEi/ARB for those with heart failure. And some patients may be contra-indicated or intolerant of some antihypertensive medications.

It should also be noted that the estimated numbers of people in the modelled subgroups include people with secondary hypertension (attributable to a specific secondary cause) and also some people with pre-existing diabetes and/or cardiovascular disease. The model estimates of baseline risk and treatment effectiveness will not be accurate for these groups.
vi. Outcomes
The effects of antihypertensive treatment were estimated from high quality meta-analyses of international trial data. There is a good evidence that the effects of the main classes of antihypertensive drugs vary by ethnicity and by relative effects on clinical end points [3] [4] [5]. The model therefore estimates effectiveness of medication by a three-step process. First the mean reduction in Systolic Blood Pressure by drug class is estimated using results from the Brewster et al meta-analysis [6], the incidences of the major events included in the model are then estimated using relative risks per 10 mm Hg reduction in SBP, stratified by baseline blood pressure, from the Ettehad et al 2016 meta-analysis (CHD, stroke, heart failure and all-cause mortality) and Elliott and Meyer 2007 meta-analysis (for onset of type 2 diabetes) [4, 5].

In addition, Disability Adjusted Life Years (DALYs) and healthcare costs associated with interventions and incident adverse events are estimated.

vii. Parameters and sources of data

Population
The number of people in the Ghanaian population by sex and included age groups (age 20 years and older) was estimated from the 2010 census (See Table 2) [7]. People under the age of 20 were not included in the model, as we assumed that the prevalence of essential hypertension in children and teenagers would be negligible.

The population in Ghana has grown since 2010, but for simplicity in this version of the model, the numbers have not been inflated to reflect this. we also present result for the whole nation, but it would be possible to estimate costs and effects by subgroup.

Prevalence of hypertension
The 2014 Ghana DHS included measurement of blood pressure for a representative sample of the population: including 9,396 women between the ages of 15 and 49 and 4,388 men aged 15 to 59 [8]. These individuals were also asked if they were aware of having high blood pressure and if they were receiving treatment for high blood pressure.

The proportions of men and women in each age group with controlled, mild, moderate, and severe hypertension are shown in Figure 1. A greater proportion of women with hypertension were aware of this condition than were men with hypertension. As might be expected, a greater proportion of older people had hypertension than did young people (with a steeper percentage increase per year in women).
The numbers of people in the 120-modelled subgroups were estimated from the data in Table 3. The prevalence of hypertension in men over the age of 60 and women over the age of 50 were estimated by simple linear extrapolation from the observed prevalence in younger age groups: 0.79% (standard error (SE): 0.05%) increase per year for men and 1.14% per year for women (SE 0.15%). The numbers of people in each subgroup were sampled probabilistically for the PSA: using beta distributions to sample the prevalence of hypertension and Dirichlet distributions to sample the split of those with controlled, mild, moderate and severe hypertension for each age/sex group.

Results are presented for the approximately 340,000 people estimated to be covered by the NHIS (based on 42% NHI coverage rates) and receiving treatment for hypertension, including those with adequately controlled blood pressure and those with mild, moderate and severely raised blood pressure despite treatment (see Table 4). About 35% of those on treatment do not have good blood pressure control, and over 17,000 have severe disease despite treatment.
Baseline risks of adverse events

Annual mortality rates for individuals without CVD, diabetes or heart failure were taken from the World Health Organization life table for Ghana, published in 2016 (See Table 5) [9].

The annual probabilities of first incidence of CHD, stroke, heart failure and diabetes for each subgroup in the absence of treatment were estimated from international data. It would have been preferable to use estimates of incidence from Ghana, or other West African countries with a similar population and healthcare profile, but we have not been able to identify good quality cohort studies with longitudinal follow up of a population sample from these contexts.

Baseline estimates of the incidence of CVD (CHD and stroke) were taken from a multivariate analysis of primary care data for black African patients living in the UK (the QRisk2 algorithm) [10]. The derivation cohort included 6,917 individuals of Black African ethnicity, with 33 incidence CVD cases observed in 12,869-person years of follow up. The resulting estimates of incidence over ten years for men and women by age group in the absence of other risk factors are shown in Table 6. For the PSA, incidences by age/sex subgroup were sampled from beta distributions. Additional uncertainty was assumed around these
probabilistic estimates due to the extrapolation of UK data (by assuming an effective sample size of 200 per subgroup).

| Age | MEN  | WOMEN |
|-----|------|-------|
| 25  | 0.4% | 0.9%  |
| 35  | 1.9% | 1.7%  |
| 45  | 4.9% | 3.2%  |
| 55  | 9.2% | 6.0%  |
| 65  | 15.4%| 11.1% |
| 75  | 24.9%| 20.1% |
| N   | 3,316| 3,655 |

Table 6 Ten-year Incidence of CVD in black African patients with no other risk factors (QRisk2)

The relative incidences of CHD, stroke and heart failure were estimated from a meta-analysis of trials of antihypertensive medications [4]. This reported 3,928, 2,220 and 1,844 incident cases of CHD, stroke and heart failure over a total 205,828-person years of follow up: proportions of coronary events and heart failure per case of CVD were 36.8% and 38.3% respectively. These proportions were sampled for the PSA using beta distributions.

The QRisk2 estimates of incidence cited in Table 6 are for people with normal blood pressure (SBP of 135) and no other risk factors. We adjusted the estimated risks of CHD, stroke and heart failure for people with mild, moderate and severe hypertension using relative risks per 10mm Hg increase in SBP from a pooled analysis of large cohort studies (see Table 7)[11]. These relative risks were sampled probabilistically from a log-normal distribution, with standard error based on the reported 95% confidence intervals.

Incidence of type 2 diabetes in people with hypertension was estimated from the QDiabetes algorithm, based on a multivariate analysis of 17,057 black African patients living in the UK: see Table 8 [12]. These estimates were used for the hypertensive population in our model, irrespective of the level of blood pressure (controlled, mild, moderate or severe). The risks of diabetes in each age/sex subgroup were sampled probabilistically, assuming an effective
sample size of 500 per subgroup (less than the actual number of observed person years to increase uncertainty due to extrapolation from the UK context).

### Table 8 Incidence of type 2 diabetes in black African patients with hypertension (QDiabetes)[12]

| Age | MEN | WOMEN |
|-----|-----|-------|
| 25  | 0.9%| 0.9%  |
| 35  | 4.6%| 3.5%  |
| 45  | 12.2%| 8.8% |
| 55  | 21.1%| 15.5%|
| 65  | 25.1%| 19.4%|
| 75  | 22.3%| 18.3%|
| N   | 7,695| 9,362|

**Treatment effects**

The effects of antihypertensive treatment were estimated from high quality meta-analyses of international trial data. There is good evidence that the effects of the main classes of antihypertensive drugs vary by ethnicity [3]. Brewster et al reported estimates of the mean reduction in systolic blood pressure in black patients, pooled from 26 RCTs: see Table 8 [6]. This shows that in this population, CCBs and TZD medications are more effective at reducing blood pressure.

### Table 9 Mean reduction in SBP for black patients (Brewster et al 2004) [6]

| Reduction (mmHg) | Mean | 95% CI |
|------------------|------|--------|
| ACEi             | 6.96 | 4.27   | 9.64 |
| ARB              | 3.63 | 1.78   | 5.47 |
| BB               | 3.53 | -0.45  | 7.51 |
| CCB              | 12.46| 10.08  | 14.85|
| TZD              | 11.81| 9.55   | 14.07|

**Ettehad et al (2016) reported summary estimates of the effects of blood pressure lowering on the incidence of different endpoints: CHD, stroke, heart failure and all-cause mortality: see Table 10 [4]. Effects on the incidence of new onset of diabetes was reported by Elliot and Meyer (2007) [5].

### Table 10 Relative risk of adverse events with blood pressure lowering

| RELATIVE RISK PER 10MM HG REDUCTION | SOURCE |
|------------------------------------|--------|
| CHD 0.83 0.78 0.88 | Ettehad et al 2016 [4] |
| STROKE 0.73 0.68 0.77 | Ettehad et al 2016 [4] |
| HF 0.72 0.67 0.78 | Ettehad et al 2016 [4] |
| DEATH 0.87 0.84 0.91 | Ettehad et al 2016 [4] |
| DIABETES 0.87 0.75 1.01 | Elliot et al 2007 [5] |

There is also evidence that different classes of antihypertensive vary in their relative effects on these endpoints: see Table 11.
The model combines the above estimates of the effect of antihypertensive class on blood pressure lowering in black patients, the overall effect of blood pressure lowering on the incidence of adverse outcomes, and the relative effect of different antihypertensive class on these outcomes. These estimates are shown in the right-hand column of Table 11.

Probabilistic estimates of these relative risks are sampled, based on the reported confidence intervals from the underlying meta-analysis estimates: assuming a normal distribution for the reduction in mean SBP (Table 11) and log-normal for the relative risks with blood pressure lowering (Table 10) and per antihypertensive class (Table 11).

**Medication costs**

The costs of antihypertensive medications are based on the NHIS price for drugs on the essential medicines list, and assuming a daily dose as recommended in the Ghana Standard Treatment Guidelines (median of range) [22, 25, 37]. Some data were available on the level of prescribing by drug, but not by brand or formulation. Based on the NHIS price, and estimated use within class, the mean cost per year ranged from GH₵ 26 per year for diuretics to GH₵ 399 per year for CCBs (see Table 12). In sensitivity analysis, we also tested the impact of using the least and most expensive drug and formulation within each class.

|        | RR vs pooled comparators* | RR of outcome in black population (vs. control) |
|--------|---------------------------|-----------------------------------------------|
|        | Mean | 95% CI |                                        |
| ACEi   |      |       |                                        |
| CHD    | 0.95 | 0.90  | 1.01                                  |
| Stroke | 1.08 | 1.01  | 1.16                                  |
| HF     | 0.98 | 0.92  | 1.05                                  |
| Diabetes | 0.87 | 0.75  | 1.01                                 |
| Death  | 1.01 | 0.97  | 1.05                                  |
| ARB    |      |       |                                        |
| CHD    | 1.06 | 0.98  | 1.15                                  |
| Stroke | 0.92 | 0.85  | 0.99                                  |
| HF     | 0.96 | 0.89  | 1.04                                  |
| Diabetes | 0.75 | 0.61  | 0.91                                 |
| Death  | 0.99 | 0.94  | 1.04                                  |
| BB     |      |       |                                        |
| CHD    | 1.03 | 0.96  | 1.10                                  |
| Stroke | 1.24 | 1.14  | 1.35                                  |
| HF     | 1.04 | 0.93  | 1.16                                  |
| Diabetes | 1.17 | 0.98  | 1.40                                 |
| Death  | 1.06 | 1.01  | 1.12                                  |
| CCB    |      |       |                                        |
| CHD    | 0.98 | 0.94  | 1.03                                  |
| Stroke | 0.90 | 0.85  | 0.95                                  |
| HF     | 1.17 | 1.11  | 1.24                                  |
| Diabetes | 0.97 | 0.82  | 1.15                                 |
| Death  | 0.97 | 0.94  | 1.00                                  |
| TZD    |      |       |                                        |
| CHD    | 1.02 | 0.97  | 1.09                                  |
| Stroke | 0.97 | 0.90  | 1.05                                  |
| HF     | 0.81 | 0.75  | 0.88                                  |
| Diabetes | 1.30 | 1.07  | 1.58                                 |
| Death  | 1.02 | 0.97  | 1.06                                  |

*Table 11 Relative risk of adverse events by antihypertensive class*
Table 12 Antihypertensive prices

|                      | Cost per year |          |          |        |        |
|----------------------|---------------|----------|----------|--------|--------|
|                      | Daily dose    | NHIS     | Lowest generic | Highest branded | % use in class NHIS |
| **ACEI**             |               |          |          |        |        |
| Lisinopril 2.5mg Tablet | 22.5          | 690      | 690      | 690    | 25%    |
| Lisinopril 5mg Tablet  | 22.5          | 345      | 181      | 2957   | 25%    |
| Lisinopril 10mg Tablet | 22.5          | 246      | 205      | 2751   | 25%    |
| Lisinopril 20mg Tablet | 22.5          | 177      | 90       | 1992   | 25%    |
| Ramipril 2.5mg Tablet  | 6.3           | 274      | 256      | 420    | 0%     |
| Ramipril 5mg Tablet    | 6.3           | 228      | 160      | 228    | 0%     |
| **ARB**              |               |          |          |        | 364    |
| Losartan 25mg Tablet   | 62.5          | 365      | 237      | 365    | 33%    |
| Losartan 50mg Tablet   | 62.5          | 228      | 125      | 282    | 33%    |
| Losartan 100mg Tablet  | 62.5          | 183      | 91       | 237    | 33%    |
| **BETA BLOCKERS**     |               |          |          |        | 259    |
| Atenolol 25 mg Tablet  | 75            | 142      | 126      | 142    | 33%    |
| Atenolol 50 mg Tablet  | 75            | 110      | 77       | 110    | 33%    |
| Atenolol 100 mg Tablet | 75            | 55       | 49       | 55     | 33%    |
| **CCB**              |               |          |          |        | 102    |
| Amlodipine 5mg Tablet  | 7.5           | 110      | 93       | 2738   | 8%     |
| Amlodipine 10mg Tablet | 7.5           | 82       | 52       | 2190   | 8%     |
| Nifedipine 10mg Capsules | 50         | 894      | 894      | 1898   | 21%    |
| Nifedipine 10mg (slow release) | 50  | 456      | 456      | 548    | 21%    |
| Nifedipine 30mg (GITS)  | 50            | 335      | 335      | 1570   | 21%    |
| Nifedipine 20mg (slow release) | 50  | 155      | 155      | 456    | 21%    |
| **DIURETICS**         |               |          |          |        | 399    |
| Bendrofluazide 2.5 mg Tablet | 2.5          | 26       | 26       | 51     | 100%   |
| Bendrofluazide 5 mg Tablet | 2.5          | 18       | 18       | 26     | 26     |

* Ettehad et al (2016) [4] for CHD, stroke, heart failure and all cause mortality.
* Elliot and Meyer (2007) [5] for incident type 2 diabetes

**Adverse event costs**

The unit costs of services were based on a weighted average of NHIS tariffs for public hospitals, private hospitals and tertiary hospitals (Table 13) [13-15]. For the base case analysis we assumed a distribution of 40%, 40% and 20% for public, private and tertiary hospitals respectively, with uncertainty over this distribution included in the PSA (Dirichlet distribution, with assumed sample size of 100 to reflect high uncertainty over this assumption).
Estimates of the cost to the NHIS of diagnosis, treatment and care associated with adverse events are shown in Table 14 (year 1) and Table 15 (subsequent years). The percentage of patients assumed to access a package of covered services was 80% in the base case, varying between 60% and 100% (uniform distribution) in PSA. The package of services for stroke was based on recommended outpatient follow up every 2 weeks for 4 times after discharge, then every month for 3 times, then every six months for at least 3 years. We assumed similar follow up after acute admission for CHD and heart failure.

Table 13 Unit costs of services: Ghana NHIS Tariffs [13-15]

Table 14 Cost of adverse events: first year
Years of life lost by age, and the disability loss per year lived with CHD, stroke, heart failure and type 2 diabetes were calculated. Years of life lost by age are based on standard life expectancy as set by WHO Global Health Estimates [16], discounted at 3% per year. Please see Table 16 for WHO Standard Life Table for Years of Life Lost (YLL).

Disability weights for CHD, stroke, heart failure and type 2 diabetes were 0.124, 0.266, 0.201 and 0.015 respectively, from the 2003 WHO estimates [17]. We could not use more recent estimates of disability weights, because these have not been presented as averages for these broad conditions, but by a more detailed breakdown of level of disability and type of complication [18]. In the base case, the model uses the default constant of 0.1658. In accordance with the WHO adopted simplified DALYs calculations there was no discounting for age-weight in our DALY calculations [16]. These parameters can be changed for sensitivity analysis.
Table 16 WHO Standard Life Table for Years of Life Lost (YLL) [16]

| Age | SEYLL* | Age | SEYLL  | Age | SEYLL  | Age | SEYLL  |
|-----|--------|-----|--------|-----|--------|-----|--------|
| 0   | 91.94  | 35  | 57.15  | 70  | 23.15  |
| 1   | 91.00  | 36  | 66.16  | 71  | 22.23  |
| 2   | 90.01  | 37  | 55.17  | 72  | 21.31  |
| 3   | 89.01  | 38  | 54.18  | 73  | 20.40  |
| 4   | 88.02  | 39  | 53.19  | 74  | 19.51  |
| 5   | 87.02  | 40  | 52.20  | 75  | 18.62  |
| 6   | 86.02  | 41  | 51.21  | 76  | 17.75  |
| 7   | 85.02  | 42  | 50.22  | 77  | 16.89  |
| 8   | 84.02  | 43  | 49.24  | 78  | 16.05  |
| 9   | 83.03  | 44  | 48.25  | 79  | 15.22  |
| 10  | 82.03  | 45  | 47.27  | 80  | 14.41  |
| 11  | 81.03  | 46  | 46.28  | 81  | 13.63  |
| 12  | 80.03  | 47  | 45.30  | 82  | 12.86  |
| 13  | 79.03  | 48  | 44.32  | 83  | 12.11  |
| 14  | 78.04  | 49  | 43.34  | 84  | 11.39  |
| 15  | 77.04  | 50  | 42.36  | 85  | 10.70  |
| 16  | 76.04  | 51  | 41.38  | 86  | 10.03  |
| 17  | 75.04  | 52  | 40.41  | 87  | 9.38   |
| 18  | 74.05  | 53  | 39.43  | 88  | 8.76   |
| 19  | 73.05  | 54  | 38.46  | 89  | 8.16   |
| 20  | 72.06  | 55  | 37.49  | 90  | 7.60   |
| 21  | 71.06  | 56  | 36.52  | 91  | 7.06   |
| 22  | 70.07  | 57  | 35.55  | 92  | 6.55   |
| 23  | 69.07  | 58  | 34.58  | 93  | 6.07   |
| 24  | 68.08  | 59  | 33.62  | 94  | 5.60   |
| 25  | 67.08  | 60  | 32.65  | 95  | 5.13   |
| 26  | 66.09  | 61  | 31.69  | 96  | 4.65   |
| 27  | 65.09  | 62  | 30.73  | 97  | 4.18   |
| 28  | 64.10  | 63  | 29.77  | 98  | 3.70   |
| 29  | 63.11  | 64  | 28.82  | 99  | 3.24   |
| 30  | 62.11  | 65  | 27.86  | 100 | 2.79   |
| 31  | 61.12  | 66  | 26.91  | 101 | 2.36   |
| 32  | 60.13  | 67  | 25.96  | 102 | 1.94   |
| 33  | 59.13  | 68  | 25.02  | 103 | 1.59   |
| 34  | 58.14  | 69  | 24.08  | 104 | 1.28   |
|     |        |     |        |     |        | 105 | 1.02   |

*SEYLL: Standard expected years of life lost. Based on projected frontier period life expectancy and life table for year 2050 (UN Population Division 2013).

viii. Cost effectiveness acceptability curve

Figure 2 below shows the cost-effectiveness acceptability curves for the most cost-effective options. Below a willingness to pay threshold of GH₵ 200 per DALY avoided, the probability that any antihypertensive treatment is cost effective is negligible. Between a threshold of
about GH₵ 400 and 8,600 per DALY avoided, it appears almost certain that diuretics are the most cost-effective option. Above GH₵ 8,600 cedi per DALY avoided (about twice Gross National Income (GNI) per capita) the probability that CCB are cost-effective begins to rise, reaching 100% of simulations at GH₵ 15,100 cedi per DALY avoided.

Figure 2 Cost-effectiveness acceptability curve (CEAC)

Section B – Discussion

i. Comparing this Study’s ICER value with other studies in the Ghanaian context

The estimates presented here for the most cost-effective hypertension treatment options are in line with results of other analyses undertaken within a Ghanaian context, looking at different technologies in other disease areas. In the Zelle et al (2012) study for example, which looked at the cost effectiveness of various breast cancer control options, it would seem that thiazides and CCBs are at least as cost-effective as screening by clinical breast examination or undertaking an awareness raising campaign using mass media, and substantially more cost-effective than mammography screening of women of aged 40–69 years.

After adjusting for inflation from year 2009 to 2017, the ICER values from Zelle et al study for breast cancer control interventions shows that the most cost-effective intervention (CBE and treatment of all stages breast cancer) as highlighted by the study, has an ICER value pf $3,340/DALY averted comparable to $2,456/ DALY averted for CCBs use in management of hypertension. Both studies used modelling and adaptation techniques undertaken by identifying data sources for the collection of country-specific data, and their analyses were based on local demographic, epidemiological and economic data, to the extent these data were available within the Ghanaian context. See Table 8.
Inflation adjustment
Consumer Price Index of 2017 (Ghana) 232.256
Consumer Price Index of 2009 (Ghana) 90.328

| Study details | Referenced value | Adjustments |
|---------------|------------------|-------------|
|               |                  |             |
| Study         | Referenced year  | Intervention | ICER (GH₵ per DALY averted) | ICER value ($ per DALY averted) | Inflation factor | Adjusted ICER Value (2017) |
| Ghana Hypertension Study | 2017 | Thaizides | 276 | 61 | - | 61 |
|                  |                  | Calcium Channel Blockers (CCBs) | 11,061 | 2,456 | - | 2,456 |
| Zelle et al. 2012 | 2009 | Biennial screening by clinical breast examination (CBE) of women aged 40-69 years, in combination with treatment of all stages | 1,853 | 1,299 | 2.57 | 3,340 |
|                  | Mass media awareness raising | 1,946 | 1,364 | 2.57 | 3,505 |
|                  | Mammography screening of women of aged 40–69 years | 18,414 | 12,908 | 2.57 | 33,174 |

Table 8 Comparison of different ICER values across various interventions in Ghanaian Context

ii. Pricing and procurement
The cost-effectiveness results were highly sensitive to assumptions about the price of drug formulations. For example, if the lowest price CCB is used (generic amlodipine 10mg tablet, 52 GH₵ per year), rather than the NHIS median (399 GH₵ per year), the incremental cost effectiveness ratio (ICER) for CCB vs. diuretic falls to GH₵ 806 per DALY avoided. Conversely, the most expensive CCB covered by the NHIS (branded amlodipine 5mg, at 2,738 GH₵ per year) has an ICER of over GH₵ 80,231 per DALY avoided. Similar estimates have been calculated for thiazides (See Table 9 below). This highlights the importance of implementing more effective mechanisms aimed at pricing and procurement. The analysis suggests there are significant potential savings by switching to lower priced formulations or negotiating lower prices for medicines. This generates potential savings in budget impact represented by 83% drop in budget impact value for CCBs and 35% for thiazides.
| Class               | Scenario | Drug formulation | Cost (GH₵ per patient per year) | ICER compared to no intervention (GH₵ per DALY avoided) | % change from default ICER value | 5-year Budget Impact (GH₵ million) | % change from default Budget Impact value |
|---------------------|----------|------------------|---------------------------------|---------------------------------------------------------|---------------------------------|-----------------------------------|----------------------------------------|
| Calcium Channel Blockers | Default | Weighted average based on current NHIS formulations use across brands | 399                             | 11,061                                                  | n/a                             | 510                               | n/a                                    |
|                     | Highest price formulation | Branded Amlodipine 5 mg | 2,738                           | 80,231                                                   | 625%                            | 3,525                             | 591%                                   |
|                     | Lowest price formulation | Generic Amlodipine 10 mg | 52                              | 806                                                      | -93%                            | 87                                | -83%                                   |
| Thiazides           | Default | Weighted average based on current NHIS formulation use across brands | 25.6                            | 276                                                      | n/a                             | 26                                | n/a                                    |
|                     | Highest price formulation | Bendrofluazide 2.5 mg Tablet | 51                              | 606                                                      | 120%                            | 59                                | 127%                                   |
|                     | Lowest price formulation | Bendrofluazide 5 mg Tablet | 18                              | 183                                                      | -34%                            | 17                                | -35%                                   |

*Table 9 Effect of drug prices on ICER and budget impact*
### Section C - iDSI reference case assessment of Ghana hypertension model

| Statement of principle | Reference Case Methods Specifications | Ghana Hypertension Model Specifications | Comments |
|------------------------|---------------------------------------|----------------------------------------|----------|
| 1                      | • The decision problem must be fully and accurately described and the economic evaluation characterised | [✓] |          |
| 2                      | • Limitations of the economic evaluation in informing policy should be characterised | [✓] |          |
| 2                      | • Declarations of interest should be made | [✓] |          |

1. **An economic evaluation should be communicated clearly and transparently to allow the decision maker(s) to interpret the methods and results**

2. **The comparators against which costs and effects are measured should accurately reflect the decision problem.**

   • At a minimum, the following comparative analysis should be undertaken:
     - The intervention(s) that is(are) currently offered to the population as defined in the decision problem as the base case comparator
     - A “do nothing” analysis representing best supportive (non-interventional care) for the population as additional analysis

   |                  | Ghana Hypertension Model Specifications | Comments |
|-------------------|----------------------------------------|----------|
| 2                 | [✓]                                   |          |
### An economic evaluation should consider all available evidence relevant to the decision problem

- A systematic and transparent approach should be taken to obtain evidence and make judgements about evidence exclusion

- Estimates of clinical effect of intervention and comparator(s) should be informed by a systematic review of the literature

- Single-study or trial-based analyses should outline how the single study or trial is a sufficient source of evidence and should ensure that the stated decision problem is specific to particular context and time of the study or trial

- Budget and time allocated to perform an economic evaluation should not determine selection of evidence

### The measure of health outcome should be appropriate to the decision problem, should capture positive and negative effects on length of life and quality of life, and should be generalizable across disease states

- Disability-Adjusted Life Years (DALYs) averted should be used [stated methodological specification]

- Other generic measures that capture length and quality of life (e.g. the QALY) can be used in separate analysis where information is available
| 5 | **All differences between the intervention and the comparator in expected resource use and costs of delivery to the target population(s) should be incorporated into the evaluation** |
|---|---|
| Estimates should reflect the resource use and unit costs/prices that are expected if the intervention were to be rolled out to the population defined in the decision problem | ✓ |
| Costs not included in study settings used to inform the analysis but would be incurred if the intervention was rolled out should be included in the base case analysis | ✓ |
| All resource implications relevant to the decision problem should be costed, including donated inputs and out of pocket inputs from individuals | ✗ |
| Analysis should include estimation of changes in costs estimates due to scalability | ✓ |

This version of the model only includes costs to the NHIS. It was agreed that further extensions of this model can explore out of pocket inputs.

| 6 | **The time horizon used in an economic evaluation should** |
|---|---|
| Lifetime time horizon should be used in first instance | ✓ |
| be of sufficient length to capture all costs and effects relevant to the decision problem; an appropriate discount rate should be used to discount cost and effects to present value |
|---|---|---|
| • Shorter time horizon can be used where shown that all costs and effects that are relevant to the decision problem have been captured | ✓ | |
| • A 3% annual discount rate for costs and effects should be used in base case analysis [stated methodological specification]. Additional analysis exploring differing discount rates appropriate to the decision problem should be used | ✓ | |
| • Additional analysis should explore an annual discount rate that reflects the rate at which the government can borrow funds on the international market | ✗ | It is straightforward to conduct sensitivity analysis on the discount rates, but advice is needed on government borrowing rates. |
| • Where time horizon used is greater than 30 years, the impact of lower discount rates should be explored in sensitivity analysis | n/a | |

| 7 Non-health effects and costs associated with gaining or providing access to health interventions that don't | | |
| --- | --- | --- |
| • Base case analysis should reflect direct health costs and health outcomes; however the analysis | ✓ | |
| **accrue to the health budget**<br>should be identified where relevant to the decision problem. All costs and effects should be disaggregated, either by sector of the economy or to whom they accrue | should adopt a disaggregated societal perspective | • Non-health effects and costs that fall outside the health budget should be included in additional analysis; the mechanism of inclusion will differ depending on the decision problem and context | It was agreed to potentially consider this in future extensions of the model. |
| --- | --- | --- | --- |
| • Where external funding or individual OOP payments substitute for costs that would otherwise fall on a health budget, these costs should be included in the base case analysis, however the impact of excluding these payments must be explored in sensitivity analysis | This version of the model only includes costs to the NHIS. It was agreed that further extensions of this model can explore out of pocket inputs |  |
| 8 | The cost and effects of the intervention on sub-populations within the decision problem should be explored and the implications appropriately characterised | • Heterogeneity should be explored in subgroups of the population identified in the decision problem, where subgroup formation should be informed by: <br> o Relevant effect of the intervention differs in different populations <br> o Characteristics of different populations that may influence the absolute health effects <br> o Characteristics that influence direct costs of provision or other associated costs such |  |
|   |   | as geographical location across the constituency |
|---|---|------------------------------------------------|
| • Subgroup analysis should always be determined by: |   | ✓   |
| o The evidence base regarding differences in relative effect, baseline risk or other characteristics |   | ✓   |
| o Whether the differences are likely to have an important influence on costs and effects |

| 9 | The uncertainty associated with an economic evaluation should be appropriately characterised |
|---|--------------------------------------------------|
| • The economic evaluation should explore: |   |
| o Uncertainty in the structure of the analysis | ✓ |
| o Uncertainty due to source of parameters | ✓ |
| o Uncertainty due to precision of parameters |

| 10 | The impact of implementing the intervention on the health budget and on other constraints should be identified clearly and separately |
|---|------------------------------------------------------------------------------------------------------------------|
| • Budget impact analysis should be performed that provides an estimate of the implications of implementing the intervention on various budgets | ✓ |
| • Budget impact analysis should reflect the decision problem and the constituency in which the intervention will be implemented | ✓ |
|   | An economic evaluation should explore the equity implications of implementing the intervention |
|---|-----------------------------------------------------------------------------------------------|
|   | • There are various mechanisms available for how the equity implications of an intervention should be assessed. The method chosen should be appropriate to the decision problem and justifiable to the decision-maker |
|   | • Equity implications should be considered at all stages of the economic evaluation, including design, analysis and reporting |
|   | There was discussion of whether to disaggregate results for sections of the population (e.g. urban vs. rural). However, policy makers wanted to focus initially on national average results. |
|   | As above. |
### Section D – Acknowledgements

Below is the full list of the HTA Technical Working group members:

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