Projected impact of polypill use among US adults: medication use, cardiovascular risk reduction and side effects

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Abstract

**Background**—Polypills which include multiple medications for reducing cardiovascular disease (CVD) risk in a single pill have been proposed for population-wide use. The number of US adults eligible for polypills and potential benefits are unknown.

**Methods**—The National Health and Nutrition Examination Survey 2003-2004 and 2007-2008 were analyzed to estimate treatment rates for medications proposed for inclusion in polypills (aspirin, statin, an ACE-inhibitor, and a thiazide-type diuretic for those without, a beta-blocker for those with, a history of myocardial infarction) among US adults. The number of coronary heart disease (CHD) and stroke events potentially prevented through polypill use was projected by published meta-analyses and three large population-based cohort studies. Two polypill eligibility criteria were analyzed (1) US adults ≥ 55 years and (2) US adults with a history of CVD.

**Results**—There are 67.6 million US adults ≥ 55 years and 15.4 million US adults with a history of CVD and, thus, eligible for polypills using the two outlined criteria. In 2007-2008, 37.3% of US adults ≥ 55 years and 57.0% of those with a history of CVD were taking statins. Use of other polypill medications was also low. Polypill use by US adults age ≥ 55 years is projected to potentially prevent 3.2 million CHD events and 1.7 million strokes over 10 years. Amongst those with a history of CVD, the potential to prevent of 0.9 million CHD events and 0.5 million strokes is projected.

**Conclusions**—Polypills have the potential to lower CVD incidence substantially among US adults.
risk by attacking several biological processes simultaneously(2). Rather than limiting the polypill to secondary prevention, it has been proposed as a public health intervention for use by all adults ≥ 55 years of age regardless of, and with little to no monitoring of, risk factor levels. Using such a population-based approach, polypills have been projected to result in reductions in coronary heart disease (CHD) and stroke incidence as high as 88% and 80%, respectively(2). Multiple different polypill formulations have been developed over the past 5 years, with randomized controlled trials of their benefit currently underway(3-5).

The purpose of the current analysis was to determine the number of US adults eligible for polypills aimed at reducing CVD risk. As the criteria for polypill eligibility are not fixed, we investigated the number of eligible US adults using two approaches: (1) a population-based approach as recommended by Wald and Law in which all US adults age ≥ 55 years would be recommended polypills, and (2) a high risk approach wherein those with a history of CVD would be recommended a polypill. Additionally, we calculated the proportion of each of these populations currently taking cardio-protective medications including aspirin, antihypertensive medications, and statins and projected the number of CHD and stroke events that could be prevented through the administration of polypills in these populations.

Methods

Study Population

The National Health and Nutrition Examination Survey (NHANES) is conducted in two year cycles with each cycle including representative samples of the non-institutionalized civilian population of the US(6). The main analyses included 2,554 participants, 20 years and older, who completed an in-home interview and a medical evaluation as part of NHANES 2007-2008. Analyses including LDL-cholesterol and fasting plasma glucose values were based on 977 participants whose medical evaluation was conducted after an overnight fast of 9 or more hours. While NHANES 2007-2008 included a pill bottle review to capture prescription medication use, daily aspirin use was not collected in this survey cycle. Thus, daily aspirin use was obtained from NHANES 2003-2004 (n=2,112).

Data Collection

Questionnaires were used to record demographics, cigarette smoking, personal and family history of CHD, and history of diabetes. Diabetes was defined as a self-report of a previous diagnosis while not pregnant and/or current antidiabetes medication use and/or fasting plasma glucose ≥ 126 mg/dL. Blood pressure was measured three times and averaged(7). Hypertension was defined as a systolic blood pressure ≥ 140 mmHg and/or diastolic blood pressure ≥ 90 mmHg and/or current antihypertensive medication use. Current use of antihypertensive medication classes and statins was determined through pill bottle review by trained study staff. Aspirin use was ascertained via standardized questions and flash cards listing different types of analgesic medications. Participants with LDL-cholesterol exceeding cut-points defined in the National Cholesterol Education Panel Adult Treatment Panel III guidelines (≥ 160 mg/dL for adults without CHD and 0-1 CHD risk factors, ≥ 130 mg/dL for adults without CHD and ≥ 2 CHD risk factors, and ≥ 70 mg/dL for adults with CHD or a CHD risk equivalent) or taking statins were considered to have high LDL-cholesterol(8).

Eligible populations—Two populations were evaluated for potential polypill use. The first population, included all US adults ≥ 55 years of age. The second population included individuals with a history of CVD defined as a self-report of a prior diagnosis of myocardial infarction, CHD, or stroke by a healthcare professional.
**Treatment recommendations**—Current treatment recommendations for aspirin, antihypertensive medications and statins were based on published guidelines. Aspirin therapy is recommended for adults with a history of CVD or a 10-year risk of CHD ≥ 10%(9). Antihypertensive medications and statins are recommended for adults with hypertension and high LDL-cholesterol, respectively. Beta-blockers are recommended for adults with a history of myocardial infarction(10).

**Polypill ingredients**—Two polypill formulations which are currently being evaluated in randomized controlled trials were investigated for the current analysis(11). Polypill one was assumed to contain aspirin, an ACE-inhibitor, a thiazide-type diuretic, and a statin, and was deemed applicable for the general population without a history of myocardial infarction. Polypill two was assumed to contain aspirin, an ACE-inhibitor, a beta-blocker, and a statin, and was deemed applicable for those with a history of myocardial infarction.

**Projected CVD risk reduction with polypill use**—The expected reduction in CHD and stroke incidence due to medication use was obtained from published meta-analyses. For aspirin, the risk reduction benefits (95% CI) for individuals without and with a history of CVD were 18% (10%, 25%) and 20% (12%, 27%), respectively, for CHD and 5% (-17%, +10%) and 19% (4%, 32%), respectively, for stroke. The CHD and stroke risk reduction benefits were 26% (23%, 29%) and 16% (95 CI: 9%, 21%) for statins, 20% (12%, 27%) and 28% (19%, 36%) for ACE-inhibitors, 21% (8%, 31%) and 29% (19%, 37%) for low-dose diuretics, and 7% (0%, 19%) and 20% (4%, 34%) for beta-blockers(12-18). As such, assuming independent multiplicative effects, in a population not receiving treatment, polypill one (aspirin, ACE-inhibitor, thiazide-type diuretic, and at statin for primary prevention) is projected to reduce the incidence of CHD and stroke by 62% and 59%, respectively, and polypill two (aspirin, ACE-inhibitor, beta-blocker, and a statin for secondary prevention) is projected to reduce the incidence of CHD and stroke by 61% and 59%, respectively.

**Projected side effects with polypill use**—The rates (95% CI) of side effects from aspirin, thiazide-type diuretics, ACE-inhibitors, beta-blockers and statins have been reported to be 3.9% (2.2%, 5.6%), 9.9% (6.6%, 13.2%), 3.9% (-0.5%, 8.3%), 7.5% (4.0%, 10.9%), and 0.1% (-1%, 1%), respectively(2;19;20). Assuming independent additive effects, polypill one and two are estimated to result in side-effects in 17.8% and 15.4% of its users, respectively.

Individuals already taking components of the poly pills (e.g., statins) were projected to experience only the risk reduction benefit and side effect disadvantage from the polypill ingredients that they were not already taking.

**Incidence rates of coronary heart disease**—CHD and stroke incidence rates for all adults ≥ 55 years of age and individuals with a history of CVD, separately, were determined by pooling individual-level data from limited-access databases for three prospective population-based cohort studies: the Framingham Offspring Study, the Atherosclerosis Risk in Communities Study (ARIC), and the Cardiovascular Health Study (CHS)(21-23). In the pooled data set used for analysis, there were 14,568 adults ≥ 55 years of age and 3,104 adults with a history of CVD. Event data in the public-access datasets are limited to 9 years of follow-up. Ten-year event rates were calculated by multiplying the 9 year event rates by 10 and dividing this product by 9. Protocols were approved by the relevant institutional review boards and informed consent was obtained from all study participants.
Statistical Analysis

Two parallel analyses were performed, one for each set of polypill eligibility criteria (i.e., [1] the general population approach of US adults ≥ 55 years of age and [2] restricted to individuals with a history of CVD). Using NHANES 2007-2008, the number and characteristics of US adults eligible for polypills was calculated. The percentages of polypill-eligible US adults recommended aspirin, antihypertensive medications and statins under current treatment guidelines were calculated. Additionally, the percentage of those recommended each therapy who was actually taking it was calculated.

The 10-year incidence rates of CHD and stroke was calculated for adults ≥ 55 years of age and individuals with a history of CVD using data from the pooled Framingham Offspring Study, ARIC Study, and CHS cohort databases. The number of CHD and stroke events expected to occur over the next 10 years among US adults was calculated as the product of these incidence rates and the number of US adults ≥ 55 years and the number of US adults with a history of CVD, according to NHANES 2007-2008. The percent and number of CHD and stroke events potentially saved, over 10 years, simulating polypill use, was projected by applying the risk reduction rates from meta-analyses to the expected number of CHD and stroke events among the population eligible for polypill use. An identical approach was taken to estimate the number of side effects caused by polypill use. Sensitivity analyses were conducted by calculating the risk reduction and side effects projections of the two polypills using the lower (worst case) and upper bounds (best case) of the confidence intervals from the meta-analyses. Also, as individuals not currently taking antihypertensive medications or statins may not take a polypill, a separate sensitivity analysis was conducted to assess the reduction in CHD and stroke incidence and side effects, assuming that only individuals already taking at least one of these medications would take a polypill. Finally, as the benefit of polypill medications may not be multiplicative when combined, we also projected the benefits of polypills using a sub-multiplicative model wherein each medication was assumed to have 80% of its effects estimated from the meta-analyses. Under these assumptions, in a population naïve to all polypill medications, polypill one is projected to potentially reduce the incidence of CHD and stroke by 55% and 50%, respectively, and polypill two is projected to potentially reduce the incidence of CHD and stroke by 50% and 51%, respectively.

SUDAAN (version 9.1, Research Triangle Park, NC) was used for all NHANES analyses to account for its complex sampling design. SAS (version 9.2, Cary, NC) was used for the analysis of the pooled cohort data.

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Results

Polypill-eligible population

Using the criteria of all US adults ≥ 55 years of age and those with a history of CVD, there are 67.6 and 15.4 million US adults eligible for a polypill, respectively. Table 1 presents the demographic characteristics and levels and prevalence of CVD risk factors for these two populations.

Current medication use

Under current guidelines, 84.2% of US adults ≥ 55 years of age and all individuals with a history of CVD are recommended aspirin (Table 2). Due to the presence of hypertension and
high cholesterol, a majority of these two populations are recommended antihypertensive 
medications and statins. However, among US adults ≥ 55 years of age who are 
recommended each treatment, only 37.5%, 79.5%, and 58.6% were taking aspirin, 
antihypertensive medications and statins, respectively. Among those with a history of CVD, 
uptake rates of aspirin, antihypertensive medications and statins were 44.5%, 87.8%, and 
64.6%, respectively. Additionally, among US adults with a history of myocardial infarction, 
54.1% were taking beta-blockers.

**CHD risk reduction**

The 10 year incidence of CHD and stroke events in the pooled Framingham Offspring 
Study, ARIC study, CHS cohorts were 10.7% and 6.7%, respectively, for adults ≥ 55 years 
of age and 18.3% and 10.6%, respectively, for participants with a history of CVD (Figure 1, 
top panels). After accounting for current medication use, it is projected that polypill use 
among all US adults ≥ 55 years of age would potentially reduce the 10 year incidence of 
CHD and stroke by 44% and 37%, respectively. The equivalent potential CHD and stroke 
risk reductions for those with a history of CVD would be 32% and 30%, respectively. Over 
10 years of follow-up, polypill use is projected to potentially result in 3.2 and 1.7 million 
fewer CHD and stroke events, respectively, among US adults ≥ 55 years of age, and 0.9 and 
0.5 million fewer CHD and stroke events, respectively, for US adults with a history of CVD 
(Figure 1, bottom panels).

**Side Effects**

If polypills were taken by all US adults ≥ 55 years of age, adverse side effects are projected 
to occur in 9.9% of users. The corresponding percentage for polypill use by US adults with a 
history of CVD is 6.7%.

**Sensitivity Analyses**

Modeling the lower bound of risk benefits (i.e., the lower end of the expected risk reductions 
from the meta-analyses), polypill use is projected to result in 18% and 23% reductions in 
CHD and stroke, respectively, among US adults ≥ 55 years of age and 20% and 14% risk 
reductions, respectively, for those with a history of CVD (Table 3). Modeling the upper 
limits of benefits resulted in projected 58% and 48% reductions in CHD and stroke, 
respectively, among US adults ≥ 55 years of age and 38% and 42% risk reductions, 
respectively, for US adults with a history of CVD. Using the lower bound, side effects are 
projected to occur in 5.0% and 2.8% of US adults ≥ 55 years of age and with a history of 
CVD, respectively. Modeling the upper bounds, side effects are projected for 15.7% and 
11.0% of these groups, respectively.

If only individuals currently taking an antihypertensive medication or a statin were to take a 
polypill, the 10 year incidence of CHD and stroke would be reduced by 27% and 22%, 
respectively, among US adults ≥ 55 years of age and by 25% and 24%, respectively, among 
US adults with a history of CVD (Table 4). Use of polypills by individuals currently taking 
at least one medication contained in the polypill is projected to potentially prevent 2.4 and 
1.1 million CHD and stroke events, respectively, among US adults ≥ 55 years of age and 1.4 
and 0.7 million CHD and stroke events, respectively, among US adults with a history of 
CVD.

In a final sensitivity analysis, the potential CHD and stroke prevention benefits were 
calculated assuming each polypill medication had a sub-multiplicative effect of 80% 
efficacy. Under this assumption, the use of polypills may potentially prevent 2.6 and 1.4 
million CHD and stroke events, respectively, among US adults ≥ 55 years of age and 0.7
and 0.4 million CHD and stroke events, respectively, among US adults with a history of CVD.

**Discussion**

The current study suggests that cardiovascular risk reduction medications are under-utilized among US adults. Even among the 15.4 million US adults with a history of CVD, fewer than 60% are taking aspirin and beta-blockers. We project that the population-wide use of polypills containing aspirin, a thiazide-type diuretic, an ACE-inhibitor and a statin among all US adults ≥ 55 years of age has the potential to prevent millions of CHD and stroke events over the next 10 years. The potential for substantial risk reduction was also present when polypills were considered only for US adults with a history of CVD.

Results from a recent randomized controlled trial indicated a polypill containing aspirin, simvastatin, atenolol, ramipril and a thiazide diuretic improved individuals’ cardiovascular risk profile(24;25). In this trial, the polypill provided a similar degree of lowering blood pressure and heart rate lowering effects when compared to its individual antihypertensive components. Additionally, the polypill resulted in a significant lowering of LDL-cholesterol and urinary 11-dehydrothromboxane B2, compared to placebo. However, the effect in those randomized to the polypill was less than their counterparts randomized to simvastatin (27 versus 32 mg/dL) and aspirin (283.1 versus 350.0 ng/mmol creatinine). Thus, the authors concluded that the polypill being tested may not provide the benefits expected based on the multiplicative effects of its individual components. Despite this caveat, based on the reductions experienced for individuals randomized to receive this polypill (7.4 mmHg reduction in systolic blood pressure, 27 mg/dL reduction in LDL-cholesterol and 283.1 reduction in ng/mmol creatinine 11-dehydrothromboxane B2), a substantial reduction in CVD risk could be expected. In fact, in a sensitivity analysis assuming 20% lesser reductions in events than expected from use of individual polypill medications, we project that millions of CHD and stroke events may still be prevented over a 10 year period.

Prior epidemiological analyses have investigated the potential benefits of polypills. For example, a study by Gaziano and colleagues reported a multi-drug primary prevention strategy of treating patients from low and middle income countries with a 10-year absolute risk of cardiovascular disease of more than 5% may result in reductions of 42% to 57% in lifetime risk of death from cardiovascular disease(26). Additionally, a report “Assessing Cost-Effectiveness in Prevention” from Australia detailed a potential for 230,000 disability-adjusted life years gained through population-wide polypill use(27). The polypill was also found to result in cost-savings.

While the projected potential benefits of polypills as estimated in the current study are compelling, Lonn and colleagues recently described several reservations regarding the polypill that need to be addressed prior to fully advocating their broad adoption (11). Importantly, data are still needed from randomized controlled trials on the benefits of polypills in preventing CHD and strokes. Additional items cited include determining the ideal pharmaceutical formulation of polypills, polypill adherence issues, the abandonment of healthy lifestyles by patients taking polypills, and the acceptability of taking additional medications by the population at large. Caution is warranted until data become available to address these uncertainties.

The expected benefits of wide-spread polypill use must be balanced by the projected occurrence of new adverse side effects in up to 17% of its users. However, these will not tend to be severe (e.g., cough, dizziness, nausea, and abdominal discomfort). While more severe side effects (e.g., bleeding, angioedema) do occur with the use of the polypill drugs,
these are unlikely to occur frequently. However, such side effects may also limit the beneficial effects of polypill use.

Cardio-protective medications are under-utilized among US adults. The reasons why patients do not take these medications are varied and include their beliefs about pharmacologic medications, side effects, and lack of access to healthcare(28). Incorporating aspirin, antihypertensive medications and statins into a single pill is widely predicted to improve medication use and adherence(29). Several studies suggest that complex medication taking regimens are an important barrier to achieving high medication adherence among patients with hypertension and high cholesterol. The use of polypills has the potential to make medication-taking regimens simpler, likely resulting in improved medication adherence and possibly reduced CVD incidence.

The current study has potential limitations. For example, we relied on projections to estimate the CHD and stroke risk reduction associated with polypill use. Additionally, while risk reduction benefits and side effects are based on published data from randomized trials, 10 years of follow-up for the benefits and side effects were not available. Data are not currently available on the risk reduction benefits of polypills and, thus, the potential benefits relied on previously published meta-analyses. NHANES 2007-2008 provides nationally representative estimates for the civilian non-institutionalized US population but it does not have data on CHD and stroke incidence. Therefore, we used data from three large cohort studies. Although these cohorts are population-based and maintain active follow-up and adjudication of incident fatal and non-fatal CVD events, they are not based upon nationally representative samples.

Several polypills aimed at CVD reduction are currently under development and being evaluated in randomized controlled trials. While the CVD risk reduction benefits of polypills still need to be determined in randomized controlled trials, the use of polypills among US adults at high risk for CVD has the potential to prevent millions of CHD and stroke events.

Reference List


Figure 1.
Percentage (top panel) and number (bottom panel) of US adults expected to have a coronary heart disease event (left panels) or stroke (right panels) over the next 10 years with and without use of polypills.

History of cardiovascular disease (CVD) Includes individuals with a history of myocardial infarction, coronary heart disease, or stroke

Without Polypill – Numbers are the product of the population size, estimated from NHANES 1999-2004, times the 10-year coronary heart disease incidence rates estimated using participants in the population-based Framingham Offspring Study, Atherosclerosis Risk in Communities study (ARIC) and the Cardiovascular Health Study (CHS) meeting the listed criteria.

With Polypill – Calculated as the observed coronary heart disease and stroke event rates in the Framingham Offspring Study, ARIC and CHS multiplied by the event reductions associated with the polypill medications as described in the methods section.
### Table 1

Characteristics of US adults ≥ 55 years of age and those with a history of cardiovascular disease.

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>US adults ≥ 55 years (n=2554)</th>
<th>History of Cardiovascular Disease† (n=592)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean (SD) age, years</td>
<td>66.9 (0.3)</td>
<td>65.1 (0.8)</td>
</tr>
<tr>
<td>Male sex, %</td>
<td>43.9%</td>
<td>54.7%</td>
</tr>
<tr>
<td>Race-ethnicity</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Non-Hispanic white, %</td>
<td>78.0%</td>
<td>75.8%</td>
</tr>
<tr>
<td>Non-Hispanic black, %</td>
<td>9.6%</td>
<td>11.6%</td>
</tr>
<tr>
<td>Mexican-American, %</td>
<td>7.7%</td>
<td>6.8%</td>
</tr>
<tr>
<td>Cigarette smoking, %</td>
<td>12.7%</td>
<td>21.7%</td>
</tr>
<tr>
<td>Mean (SD) systolic BP, mmHg</td>
<td>131.5 (0.7)</td>
<td>130.3 (1.1)</td>
</tr>
<tr>
<td>Mean (SD) diastolic BP, mmHg</td>
<td>68.9 (0.6)</td>
<td>68.1 (1.1)</td>
</tr>
<tr>
<td>Hypertension, %</td>
<td>60.1%</td>
<td>69.3%</td>
</tr>
<tr>
<td>Mean (SD) HDL-cholesterol, mg/dL</td>
<td>53.8 (0.6)</td>
<td>49.3 (0.6)</td>
</tr>
<tr>
<td>Mean (SD) LDL-cholesterol, mg/dL</td>
<td>116.5 (1.9)</td>
<td>102.9 (3.1)</td>
</tr>
<tr>
<td>High LDL-cholesterol, %</td>
<td>63.7%</td>
<td>88.3%</td>
</tr>
<tr>
<td>Diabetes mellitus, %</td>
<td>10.3%</td>
<td>15.6%</td>
</tr>
<tr>
<td>History of myocardial infarction, %</td>
<td>8.2%</td>
<td>46.0%</td>
</tr>
<tr>
<td>History of coronary heart disease, %</td>
<td>8.7%</td>
<td>45.5%</td>
</tr>
<tr>
<td>Angina, %</td>
<td>5.3%</td>
<td>20.9%</td>
</tr>
<tr>
<td>History of stroke, %</td>
<td>7.4%</td>
<td>44.1%</td>
</tr>
</tbody>
</table>

Abbreviations: SD – standard deviation; BP – blood pressure.

n represents number of participants in NHANES 2007-2008.

† Includes a history of myocardial infarction, coronary heart disease, or stroke.

LDL-cholesterol is based on 977 participants ≥ 55 years and 240 participants with a history of cardiovascular disease and fasting samples.
Table 2

Current guideline recommendations and actual use of aspirin, antihypertensive medications and statins among US adults ≥ 55 years of age and those with a history of cardiovascular disease.

<table>
<thead>
<tr>
<th></th>
<th>Age ≥ 55 years (n=2,554)</th>
<th>History of Cardiovascular Disease† (n=592)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Recommended use‡</td>
<td>Actual use</td>
</tr>
<tr>
<td>Aspirin, %</td>
<td>84.2%</td>
<td>31.6%</td>
</tr>
<tr>
<td>Antihypertensives, %</td>
<td>60.1%</td>
<td>47.8%</td>
</tr>
<tr>
<td>Statins, %</td>
<td>63.7%</td>
<td>37.3%</td>
</tr>
</tbody>
</table>

n - number of NHANES 2007-2008 participants. Statin use is based on 977 participants ≥ 55 years and 240 participants with a history of cardiovascular disease who fasted prior to their study visit.

† Includes individuals with a history of myocardial infarction, coronary heart disease, or stroke

‡ Recommended use is based on the American Heart Association guidelines for aspirin, the National Heart, Lung, and Blood Institute’s JNC-7 guidelines for antihypertensive medication, and the National Cholesterol Education Program’s Third Adult Treatment Panel guidelines for statins.
Table 3

Percentage and number of US adults expected to have coronary heart disease and stroke events over 10 years with and without the use of a polypill.

<table>
<thead>
<tr>
<th></th>
<th>US adults ≥ 55 years</th>
<th>History of CVD†</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Worst case</td>
<td>Best case</td>
</tr>
<tr>
<td>10 year event rates</td>
<td>CHD</td>
<td>CHD</td>
</tr>
<tr>
<td>Without polypill</td>
<td>10.7%</td>
<td>10.7%</td>
</tr>
<tr>
<td>With polypill</td>
<td>8.8%</td>
<td>4.5%</td>
</tr>
<tr>
<td>% reduction</td>
<td>18%</td>
<td>58%</td>
</tr>
<tr>
<td>Events, millions</td>
<td>Without polypill</td>
<td>7.2</td>
</tr>
<tr>
<td></td>
<td>With polypill</td>
<td>5.9</td>
</tr>
<tr>
<td>Prevented events</td>
<td>1.3</td>
<td>4.2</td>
</tr>
</tbody>
</table>

CVD – cardiovascular disease, CHD – coronary heart disease

† Includes individuals with a history of myocardial infarction, coronary heart disease, or stroke

Worst case scenario reflects the minimal expected benefit and best case scenario reflects the maximum expected benefit from prior meta-analyses of the individual polypill components (see methods for additional details).
Table 4

Sensitivity analyses showing the percentage and number of US adults expected to have coronary heart disease and stroke events over 10 years with and without the use of a polypill assuming only persons currently antihypertensive medications or statins will take the polypill.

<table>
<thead>
<tr>
<th></th>
<th>US adults ≥ 55 years</th>
<th>History of CVD†</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of US adults, millions</td>
<td>67.6</td>
<td>15.4</td>
</tr>
<tr>
<td>Number on antihypertensive or statin medication, millions</td>
<td>41.8</td>
<td>12.0</td>
</tr>
<tr>
<td>10-year event rates</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Without polypill</td>
<td>10.7%</td>
<td>6.7%</td>
</tr>
<tr>
<td></td>
<td>18.3%</td>
<td>10.6%</td>
</tr>
<tr>
<td>With polypill</td>
<td>7.8%</td>
<td>5.2%</td>
</tr>
<tr>
<td></td>
<td>13.8%</td>
<td>8.1%</td>
</tr>
<tr>
<td>% reduction</td>
<td>27%</td>
<td>22%</td>
</tr>
<tr>
<td></td>
<td>25%</td>
<td>24%</td>
</tr>
<tr>
<td>Events, millions</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Without polypill</td>
<td>7.2</td>
<td>4.5</td>
</tr>
<tr>
<td></td>
<td>2.8</td>
<td>1.6</td>
</tr>
<tr>
<td>With polypill</td>
<td>5.3</td>
<td>3.5</td>
</tr>
<tr>
<td></td>
<td>2.1</td>
<td>1.2</td>
</tr>
<tr>
<td>Prevented events</td>
<td>1.9</td>
<td>1.0</td>
</tr>
<tr>
<td></td>
<td>0.7</td>
<td>0.4</td>
</tr>
</tbody>
</table>

CVD – cardiovascular disease, CHD – coronary heart disease

† Includes individuals with a history of myocardial infarction, coronary heart disease, or stroke