Quantifying the Utility of Taking Pills for Cardiovascular Prevention

Robert Hutchins, MD, MPH; Anthony J. Viera, MD, MPH; Stacey L. Sheridan, MD, MPH; Michael P. Pignone, MD, MPH

Background—The decrease in utility attributed to taking pills for cardiovascular prevention can have major effects on the cost-effectiveness of interventions but has not been well studied. We sought to measure the utility of daily pill-taking for cardiovascular prevention.

Methods and Results—We conducted a cross-sectional Internet-based survey of 1000 US residents aged ≥30 in March 2014. We calculated utility values, using time trade-off as our primary method and standard gamble and willingness-to-pay techniques as secondary analyses. Mean age of respondents was 50 years. Most were female (59%) and white (63%); 28% had less than a college degree; and 79% took ≥1 pills daily. Mean utility using the time trade-off method was 0.990 (95% confidence interval, 0.988–0.992), including ≥70% not willing to trade any amount of time to avoid taking a preventive pill daily. Using the standard gamble method, mean utility was 0.991 (0.989–0.993), with 62% not willing to risk any chance of death. Respondents were willing to pay an average of $1445 to avoid taking a pill daily, which translated to a mean utility of 0.994 (0.940–0.997), including 41% unwilling to pay any amount. Time trade-off–based utility varied by age (decreasing utility as age increased), sex, race, numeracy, difficulty with obtaining pills, and number of pills taken per day but did not vary by education level, literacy, or income.

Conclusions—Mean utility for taking a pill daily for cardiovascular prevention is ≈0.990 to 0.994. (Circ Cardiovasc Qual Outcomes. 2015;8:155-163. DOI: 10.1161/CIRCOUTCOMES.114.001240.)

Key Words: cost-utility analysis ■ prevention and control

In assessing the potential value of preventive services, including cardiovascular disease (CVD) prevention, cost-effectiveness analyses attempt to consider all the potential beneficial and detrimental effects of the service, including the effects of taking the medication daily on quality of life, apart from any specific adverse effects. In such studies, these effects are often represented by assigning a numeric value that represents the relative quality of life that a certain health state carries versus an ideal state of perfect health. This numeric value is termed a utility. Utilities usually range from 0 to 1, with 0 representing death and 1 representing perfect health. Using an accurate utility value can have large effects on the cost-effectiveness of the preventive service.

Many studies have attempted to quantify patient utilities for specific health conditions. There are several potential methods for quantifying a utility value. These methods include rating scale, standard gamble (SG), time trade-off (TTO), and willingness to pay (WTP). Each method differs in its feasibility and its connection to expected utility theory. The rating scale is easy to use but lacks theoretical justification under expected utility theory because it involves rating as opposed to choice under uncertainty. Conversely, the SG directly measures risk attitude and is considered the gold standard of health utility estimation. The TTO has some theoretical justifications and can be measured effectively with a brief interview. In contrast to SG, it does not directly assess the risk attitude of the respondent. It does, however, have direct application in calculating quality-adjusted life-years (QALYs) and can be a good method for cost-effectiveness analyses. Values determined by SG are often equivalent to, or higher than, the TTO, which may be primarily because of respondent risk aversion. WTP is less theoretically supported under expected utility theory but is supported by other economic theory and has the advantage of using units (dollars or other currency) with which participants are familiar.

Most previous studies have focused on valuing health states, but relatively few have attempted to measure the effects of processes of care (sometimes called process utility), including the effect of taking medications. Until recently, we were aware of only 1 study by Gage and colleagues, described in 2 publications, that attempted to quantify the utility value for taking pills.
WHAT IS KNOWN

• Little is known about the utility attributed to taking pills for cardiovascular prevention, which may have implications for cost-effectiveness of interventions.
• In a larger, more diverse sample of US adults than prior studies, we sought to measure the utility of daily pill-taking for cardiovascular prevention using time trade-off, standard gamble, and willingness-to-pay techniques.

WHAT THE STUDY ADDS

• We found the utility of taking a pill daily for cardiovascular prevention was 0.990 to 0.994, with consistency across utility methods.
• Approximately 70% of respondents indicated that they would not trade any time (ie, utility of 1.0) for daily pill-taking.
• These results may be useful for researchers and policymakers evaluating preventive interventions for cardiovascular disease.

of daily pill-taking, in this case for cardiovascular prevention with aspirin. In this study, 70 patients, mainly older white men within the Veterans Affairs system, were interviewed using the TTO method for their utility for taking a daily aspirin. They found a mean utility value of 0.998.

A recent study performed in London, UK, attempted to determine the utility of taking a pill daily by interviewing 360 people in public streets in North West London. In that study, participants answered a questionnaire to determine the amount of life they would need to gain to take a preventive pill for the rest of their life. The median increase required was 6 months, with an interquartile range from 1 to 36 months; 12% had extreme disutility (requiring more than a 10-year increase in life expectancy), whereas 34% required less than a month increase.

Given the small sample sizes, the use of single utility assessment methods, and the limited generalizability of prior studies, we sought to better understand the utility of pill-taking for CVD prevention. In our preliminary work, we conducted an Internet-based survey of 708 university healthcare employees in North Carolina, using modifications of the TTO method, SG, and WTP methods. We found the mean utility of taking a daily pill for prevention to be 0.997, similar to the value found by Gage and colleagues. However, our study population consisted of mainly highly educated healthcare workers, almost all of whom took ≥1 daily pills, and hence was also limited in its generalizability (Robert Hutchins, MPH, unpublished data, 2013).

Additional studies reference a utility value for taking pills for cardiovascular prevention, although most of these studies seem to have chosen values based mainly on expert opinion or by citing the studies by Gage and colleagues. In these prior studies, the range of utility values for aspirin ranged from 0.996 to 1.0; for statins, it ranged from 0.999 to 1.0; and for antihypertensives, it ranged from 0.95 to 1.0. Many of these studies included sensitivity analyses that extended the lower end of the range of utility values and often found that small differences in utility had important effects on cost-effectiveness.

To address the limitations of previous studies and to better inform future cost-effectiveness analyses, we conducted a nationwide, Internet-based survey to quantify the utility of taking pills for the purpose of trying to prevent a heart attack or stroke, using the same 3 methods: TTO, SG, and WTP.

Methods

Survey Overview

We conducted a cross-sectional study using an Internet-based survey to collect data that would allow us to calculate respondents’ utilities for taking a pill for cardiovascular prevention. It was granted exempt status by the Institutional Review Board of the University of North Carolina.

Our survey (Appendix in the Data Supplement), which was administered online through Survey Sampling International (SSI), consisted of a total of 20 items. After an introductory page that explained our research topic and obtained informed consent, initial items asked about the respondent’s demographics, followed by questions regarding a respondent’s personal pill-taking regimen.

Subsequent sections elicited utilities via the 3 methods of interest: TTO, SG, and WTP. Traditional utility assessment involves a ping-pong interview method, in which different trade-offs are offered until a state of indifference is reached. We modified our assessments to use individual, multiple-choice questions for ease of survey administration.

For our assessments, we asked participants to assume the pills had no side effects and no costs; thus, we were explicitly testing the isolated utility of taking pills. We made this choice because side effects and costs can (and should) be dealt with separately in cost-effectiveness or cost-utility analyses. We also included questions to ascertain the numeracy and literacy level of each respondent, followed by a final section asking for remaining demographic data.

Participant Selection

Participants were recruited online in March 2014 by SSI using their database consisting of people who agree in general to be contacted about surveys. Our only eligibility criterion was age ≥30. To better capture a more representative sample, we also requested that SSI recruit ≥20% of respondents who took no pills and ≥20% of respondents who had less than a college education. Once a sufficient number of respondents was recruited within a category, the quota for that category was considered closed. As per usual SSI policy, respondents were offered a small cash reward, such as $0.50 to $1.00, or entry into sweepstakes for prize drawings. As a quality assurance measure, SSI tracks and removes respondents who completed the survey in less than one-third of the median response time (ie, speeders) and those who respond in a uniform pattern (eg, always selecting the same option).

Measures

Our main outcome was mean utility value for taking 1 pill per day, using TTO. We also examined utility for taking 1 pill per day using SG and a modified WTP method and examined the utility of taking 2 pills daily or 1 pill twice per day using TTO method as well. For WTP, we used both an open-ended and a closed-ended question.

Participants rated difficulty obtaining medications and difficulty paying for medications on a scale from 1 to 5. For analysis, these difficulty levels were then combined into 3 categories: not difficult, neutral, and difficult. In addition, numeracy was assessed using 2 questions from a standard numeracy questionnaire, and literacy was assessed using a 1-question literacy screener. Respondents who indicated that they felt extremely comfortable or quite a bit comfortable filling out medical forms by themselves were considered as having adequate literacy, whereas those who indicated somewhat comfortable, a little bit comfortable, or not comfortable were classified as having inadequate literacy.

Utility Calculation

The TTO utility value was derived by dividing the maximum amount of time each respondent was willing to give up at the end of their life to avoid having to take a medication (determined via a single
multiple-choice question), by the mean amount of time each respondent had remaining in his or her life (using an average life expectancy of 78 years) and subtracting it from 1. Potential responses for the single question included none, 1 week, 2 weeks, 1 month, 3 months, 6 months, 9 months, 12 months, 18 months, or 24 months.

The utility value for SG was calculated as 1 minus the maximum risk of death the participant was willing to accept to avoid taking medications daily, again assessed via a single, multiple-choice question. Potential responses included 0, 1, 10, 100, 1000, 10,000, or 100,000, with a constant denominator of 1000000.

For the WTP method, the respondent was asked the amount he or she was willing to pay to not have to take a pill daily while still receiving the benefits of the medication. Responses for the close-ended question included 50, 10, 50, 100, 250, 500, 1000, 2500, 5000, 10,000, or 25,000 dollars.

The utility value using WTP was derived by dividing the amount a participant was willing to pay (to not have to take a pill daily) by their total estimated earnings through an average retirement age of 65 years and subtracting it from 1. We used the middle value from the income category the participant selected for annual household income. Because this method required estimation of income to age 65 years, we could not calculate a WTP utility for respondents older than age 65 years.

Participant responses to TTO, SG, and WTP questions were converted to utility values using Microsoft Excel (Mac 2011, version 14.1.0., Redmond, WA), after which an analysis was performed using STATA 12 (StataCorp. 2011, Stata Statistical Software: Release 12, College Station, TX).

We describe basic participant demographics and utility values using proportions with 95% confidence intervals or means with standard deviations. All utility values were rounded to 3 decimal places. The utility values are not normally distributed (with median values of 1), but we report means, which is consistent with prior literature. Because of the distribution of the data, we used bootstrapping methods to calculate confidence intervals. Kruskal–Wallis tests were used to compare utility values by participant characteristics and pill-taking experience.

### Outliers and Inconsistencies

As supplemental analyses to our main results, we used 2 alternate approaches to account for potential outliers and inconsistent responses. First, we reanalyzed our data with values <0.95 truncated to 0.95.

Inconsistent responses (eg, a respondent having a higher utility for taking pills twice per day than for once per day) among the TTO utilities were not uncommon (≈10%) in our data. To adjust for this, we graded the consistency of each respondent’s answers from 0 to 3 based on whether the utility they assigned, using TTO, was less for 1 pill than either 2 pills or 1 pill twice daily (1 point each), or whether 2 pills than 1 pill twice daily (1 point). Respondents were given 3 points for the most consistency and 0 for the least consistency. Secondary analysis was performed with the responses with a consistency score <2 defined as inconsistent and removed.

### Results

#### Characteristics of Respondents

A total of 18780 e-mail invitations were sent by SSI to potentially eligible participants, of which 3069 were opened. Overall, 1726 people were screened out for one of the following: not fulfilling eligibility criteria (1342), hitting a closed quota (362), duplicate attempts (22), or attempted survey on an unsupported device (18). Of the 1325 eligible respondents remaining, 27 dropped out on their own after the introduction, 115 dropped out on their own at some other point in the survey, 103 were classified as speeders, and 80 were noted to respond in a uniform pattern. Thus, the rate of completion was 1000/1325 (75.5%).

Participant characteristics are shown in Table 1. Mean age of respondents was 50 years. Most participants were female (59%) and white (62.9%), and most participants had health insurance (81.4%). Almost a quarter (22%) had incomes <$25000, whereas 26% had annual household incomes >$75000. In terms of education, 28% had less than a college

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>n</th>
<th>No. (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean age, y</td>
<td>1000</td>
<td>50</td>
</tr>
<tr>
<td>Age group, y</td>
<td>1000</td>
<td></td>
</tr>
<tr>
<td>30–50</td>
<td>505</td>
<td>(50.5)</td>
</tr>
<tr>
<td>51–65</td>
<td>366</td>
<td>(36.6)</td>
</tr>
<tr>
<td>&gt;65</td>
<td>129</td>
<td>(12.9)</td>
</tr>
<tr>
<td>% Female</td>
<td>1000</td>
<td></td>
</tr>
<tr>
<td></td>
<td>590</td>
<td>(59.0)</td>
</tr>
<tr>
<td>Race*</td>
<td>1000</td>
<td></td>
</tr>
<tr>
<td>White</td>
<td>629</td>
<td>(62.9)</td>
</tr>
<tr>
<td>Black</td>
<td>159</td>
<td>(15.9)</td>
</tr>
<tr>
<td>Other</td>
<td>212</td>
<td>(21.2)</td>
</tr>
<tr>
<td>Income</td>
<td>1000</td>
<td></td>
</tr>
<tr>
<td>&lt;$25000</td>
<td>224</td>
<td>(22.4)</td>
</tr>
<tr>
<td>$25000–$7500</td>
<td>516</td>
<td>(51.6)</td>
</tr>
<tr>
<td>&gt;$75000</td>
<td>260</td>
<td>(26.0)</td>
</tr>
<tr>
<td>&lt; College degree</td>
<td>1000</td>
<td></td>
</tr>
<tr>
<td></td>
<td>284</td>
<td>(28.4)</td>
</tr>
<tr>
<td>Numeracy</td>
<td>1000</td>
<td></td>
</tr>
<tr>
<td>0 correct</td>
<td>202</td>
<td>(20.2)</td>
</tr>
<tr>
<td>1 correct</td>
<td>288</td>
<td>(28.8)</td>
</tr>
<tr>
<td>2 correct</td>
<td>510</td>
<td>(51.1)</td>
</tr>
<tr>
<td>Literacy†</td>
<td>1000</td>
<td></td>
</tr>
<tr>
<td>Inadequate</td>
<td>284</td>
<td>(28.4)</td>
</tr>
<tr>
<td>Adequate</td>
<td>716</td>
<td>(71.6)</td>
</tr>
<tr>
<td>Health‡</td>
<td>1000</td>
<td></td>
</tr>
<tr>
<td>Poor</td>
<td>38</td>
<td>(3.8)</td>
</tr>
<tr>
<td>Fair</td>
<td>196</td>
<td>(19.6)</td>
</tr>
<tr>
<td>Good</td>
<td>387</td>
<td>(38.7)</td>
</tr>
<tr>
<td>Very good</td>
<td>291</td>
<td>(29.1)</td>
</tr>
<tr>
<td>Excellent</td>
<td>88</td>
<td>(8.8)</td>
</tr>
<tr>
<td>% Insured</td>
<td>1000</td>
<td></td>
</tr>
<tr>
<td></td>
<td>814</td>
<td>(81.4)</td>
</tr>
<tr>
<td>No. of pills taken per day</td>
<td>1000</td>
<td></td>
</tr>
<tr>
<td>0</td>
<td>209</td>
<td>(20.9)</td>
</tr>
<tr>
<td>1</td>
<td>99</td>
<td>(9.9)</td>
</tr>
<tr>
<td>2</td>
<td>153</td>
<td>(15.3)</td>
</tr>
<tr>
<td>3+</td>
<td>539</td>
<td>(53.9)</td>
</tr>
<tr>
<td>No. of times pills taken per day</td>
<td>791</td>
<td></td>
</tr>
<tr>
<td>1</td>
<td>335</td>
<td>(42.4)</td>
</tr>
<tr>
<td>2</td>
<td>341</td>
<td>(43.1)</td>
</tr>
<tr>
<td>3+</td>
<td>115</td>
<td>(14.5)</td>
</tr>
<tr>
<td>Difficulty obtaining pills$</td>
<td>791</td>
<td></td>
</tr>
<tr>
<td>Somewhat difficult</td>
<td>77</td>
<td>(9.7)</td>
</tr>
<tr>
<td>Very difficult</td>
<td>14</td>
<td>(1.8)</td>
</tr>
<tr>
<td>Difficulty paying for pills$</td>
<td>791</td>
<td></td>
</tr>
<tr>
<td>Somewhat difficult</td>
<td>166</td>
<td>(21.0)</td>
</tr>
<tr>
<td>Very difficult</td>
<td>39</td>
<td>(4.9)</td>
</tr>
</tbody>
</table>

*Self-reported.
†Based on single-item literacy screener 5-point scale of comfort filling out medical forms.
‡Self-reported; rated on 5-point scale.
degree. Approximately 20% answered 0 of 2 numeracy questions correctly, and 29% had inadequate literacy. Health status was mixed: 38% rated their health as either very good or excellent. Approximately 54% took ≥3 pills per day, whereas 21% took no pills per day.

TTO Utility Value
The number of weeks of life that participants were willing to trade to avoid taking a pill daily are shown in Figure 1. Approximately 70% of respondents indicated that they would not trade any time (ie, utility of 1.0), with the remainder of responses distributed across the range of potential responses, and 8.2% were willing to trade 2 years of their time. The mean response was 12.3 weeks (SD=30), which translates to a utility of 0.990 (Table 2). The mean utility value was statistically significantly lower for older age, male sex, non-white race, those with lower numeracy levels, those reporting more difficulty with obtaining pills, and those taking ≥3 pills per day (Table 3).

When outliers <0.95 were truncated to 0.95, the mean utility for taking 1 pill daily was 0.994. When consistency scores <2 were removed, the mean utility for taking 1 pill daily using the TTO method was 0.992.

SG Utility Value
For the SG method, the maximum chance of death participants who were willing to risk avoid taking a pill daily is shown in Figure 2: 62.1% were not willing to trade any risk of immediate death (utility value 1.0), 12.8% were only willing to risk the smallest amount of time offered (0.0001%), and 9% were reported as being willing to risk a 10% chance (utility 0.90), the largest option offered. The mean risk that death respondents were willing to accept was 0.9%, which translated to a mean utility of 0.991 (Table 2).

Mean utility values by SG were lower for those aged 30 to 50, women, non-whites, those with difficulty obtaining pills, and those who reported taking ≥1 pills daily.

When consistency scores <2 were removed, the mean utility for taking 1 pill daily by SG remained 0.991.

WTP Utility Value
The distribution of responses for the closed-end WTP questions is shown in Figure 3. Approximately 43% were not willing to pay any amount (utility value of 1.0) with other responses distributed across the range of response options presented, but only 2.8% were willing to pay the largest amount ($25,000). On average, respondents were willing to pay $1445 to not have to take 1 pill daily for the rest of their life. Values from the open-ended question differed slightly: 37% were unwilling to pay any amount, and the mean amount across respondents was $2452. Based on these WTP values, the overall average utility for taking one pill daily was 0.994 (95% confidence interval, 0.990–0.997) for the closed-ended question and 0.994 (95% confidence interval, 0.990–0.997) for the free response question, respectively (Table 2).

Men had lower mean utility values; there were no consistent differences for the other patient characteristics examined (Table 4). When consistency scores <2 were removed, the mean utility for taking 1 pill daily using the WTP method was 0.993.

Discussion
In this large, national sample, we found the utility of taking a pill daily for CVD prevention to be 0.990 to 0.994. This relatively narrow range of values seems to hold across multiple utility methods, each with its own theoretical strengths and weaknesses. We observed some differences in utilities across demographic groups, but these differences were generally small and not consistent across methods.

Our mean utility values are slightly lower but otherwise similar to those obtained by Gage and colleagues using TTO

<table>
<thead>
<tr>
<th>Assessment Method</th>
<th>Utility Value (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Time trade-off</td>
<td></td>
</tr>
<tr>
<td>1 pill daily</td>
<td>0.990 (0.987–0.992)</td>
</tr>
<tr>
<td>2 pills daily</td>
<td>0.990 (0.988–0.992)</td>
</tr>
<tr>
<td>1 pill twice a day</td>
<td>0.990 (0.989–0.992)</td>
</tr>
<tr>
<td>Standard gamble</td>
<td></td>
</tr>
<tr>
<td>1 pill daily</td>
<td>0.991 (0.989–0.992)</td>
</tr>
<tr>
<td>Willingness to pay</td>
<td></td>
</tr>
<tr>
<td>1 pill daily (multiple choice)</td>
<td>0.994 (0.990–0.997)</td>
</tr>
<tr>
<td>1 pill daily (free response)</td>
<td>0.994 (0.990–0.997)</td>
</tr>
</tbody>
</table>

CI indicates confidence interval.
Table 3. Mean Utility Values by Participant Characteristics*

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>1 Pill Daily</th>
<th>2 Pills Daily</th>
<th>1 Pill Twice Daily</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Mean</td>
<td>P Value†</td>
<td>Mean</td>
</tr>
<tr>
<td>Age, y</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>30–50</td>
<td>0.992</td>
<td>0.993</td>
<td>0.993</td>
</tr>
<tr>
<td>51–64</td>
<td>0.990</td>
<td>0.990</td>
<td>0.990</td>
</tr>
<tr>
<td>≥65</td>
<td>0.978</td>
<td>0.981</td>
<td>0.981</td>
</tr>
<tr>
<td>Sex</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Female</td>
<td>0.991</td>
<td>0.991</td>
<td>0.991</td>
</tr>
<tr>
<td>Male</td>
<td>0.988</td>
<td>0.990</td>
<td>0.990</td>
</tr>
<tr>
<td>Race</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Black</td>
<td>0.989</td>
<td>0.989</td>
<td>0.989</td>
</tr>
<tr>
<td>White</td>
<td>0.990</td>
<td>0.991</td>
<td>0.991</td>
</tr>
<tr>
<td>Other</td>
<td>0.988</td>
<td>0.990</td>
<td>0.990</td>
</tr>
<tr>
<td>Education level</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;College degree</td>
<td>0.986</td>
<td>0.988</td>
<td>0.988</td>
</tr>
<tr>
<td>College or graduate degree</td>
<td>0.991</td>
<td>0.991</td>
<td>0.991</td>
</tr>
<tr>
<td>Income</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;$25,000</td>
<td>0.985</td>
<td>0.2267</td>
<td>0.987</td>
</tr>
<tr>
<td>$25,000–$75,000</td>
<td>0.990</td>
<td>0.991</td>
<td>0.991</td>
</tr>
<tr>
<td>&gt;$75,000</td>
<td>0.994</td>
<td>0.993</td>
<td>0.993</td>
</tr>
<tr>
<td>Health rating</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;Very good</td>
<td>0.990</td>
<td>0.0762</td>
<td>0.991</td>
</tr>
<tr>
<td>≥Very good</td>
<td>0.989</td>
<td>0.989</td>
<td>0.989</td>
</tr>
<tr>
<td>Numeracy level‡</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>0 correct</td>
<td>0.987</td>
<td>0.0010</td>
<td>0.987</td>
</tr>
<tr>
<td>1 correct</td>
<td>0.988</td>
<td>0.990</td>
<td>0.990</td>
</tr>
<tr>
<td>2 correct</td>
<td>0.992</td>
<td>0.992</td>
<td>0.992</td>
</tr>
<tr>
<td>Literacy level§</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Inadequate</td>
<td>0.993</td>
<td>0.9857</td>
<td>0.994</td>
</tr>
<tr>
<td>Adequate</td>
<td>0.988</td>
<td>0.989</td>
<td>0.989</td>
</tr>
<tr>
<td>Difficulty obtaining pills</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Not difficult</td>
<td>0.991</td>
<td>0.0003</td>
<td>0.991</td>
</tr>
<tr>
<td>Neutral</td>
<td>0.987</td>
<td>0.990</td>
<td>0.990</td>
</tr>
<tr>
<td>Difficult</td>
<td>0.985</td>
<td>0.989</td>
<td>0.989</td>
</tr>
<tr>
<td>Difficulty paying for pills</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Not difficult</td>
<td>0.989</td>
<td>0.1433</td>
<td>0.989</td>
</tr>
<tr>
<td>Neutral</td>
<td>0.994</td>
<td>0.994</td>
<td>0.994</td>
</tr>
<tr>
<td>Difficult</td>
<td>0.986</td>
<td>0.990</td>
<td>0.990</td>
</tr>
<tr>
<td>No. of times pills taken per day</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;2</td>
<td>0.990</td>
<td>0.5006</td>
<td>0.990</td>
</tr>
<tr>
<td>≥2</td>
<td>0.990</td>
<td>0.991</td>
<td>0.991</td>
</tr>
<tr>
<td>No. of pills taken per day</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>0</td>
<td>0.991</td>
<td>0.0008</td>
<td>0.990</td>
</tr>
<tr>
<td>1</td>
<td>0.990</td>
<td>0.990</td>
<td>0.990</td>
</tr>
<tr>
<td>2</td>
<td>0.993</td>
<td>0.993</td>
<td>0.993</td>
</tr>
<tr>
<td>3+</td>
<td>0.988</td>
<td>0.990</td>
<td>0.990</td>
</tr>
</tbody>
</table>

*Utilities derived using time trade-off technique.
†P values based on 1-way analysis of variance.
‡Based on number of answers correct from numeracy screener.
§Based on response to single-question literacy screener.
interviews among a small sample of mostly older, male VA patients in Northern California in the context of decision making about aspirin use (mean, 0.998) and our prior pilot study in a sample of university healthcare employees in North Carolina (mean, 0.997; Robert Hutchins, MPH, unpublished data, 2013). They are also similar to the median value (6 months of additional life expectancy required) found using a modified TTO in younger (mean age, 38) citizens of London, only 22% of whom were current daily medication takers.

The utility value of taking a pill daily can have an important effect on cost-effectiveness analyses for CVD prevention, even for small decrements in utility such as those found in this study. For example, one study examined whether cost-effectiveness of aspirin for women was sensitive to the assigned utility value of taking the pill. The base case used a utility value of 1.0; the authors then examined the cost per QALY gained across a variety of utility values for taking aspirin. In that analysis, using any utility value below ~0.9996 caused a large increase in the cost per QALY, above the arbitrary but commonly used threshold of $50000/QALY for patients at relatively modest baseline CVD risk. By lowering it to 0.995, the authors found that the cost per QALY had exceeded $200000. A second study used a base case utility value of 0.999 for taking statins for prevention and found a cost/QALY of $34995 for a 55-year-old man. Assuming no disutility from taking a pill and altering that utility value to only 1.0, the cost/QALY decreases ~25% to $26394. A third study examined the cost-effectiveness of the management of chronic nonvalvular atrial fibrillation with no treatment, aspirin, or warfarin. Although the authors used a base case utility value of 0.99 for warfarin, they performed a 1-way sensitivity analysis by varying that utility value from 0.95 to 1.0. The authors found that the results were sensitive to the assigned utility of taking warfarin. During that range, the outcome varied from making warfarin the most favored strategy to the least favored strategy (compared with aspirin). Such analyses highlight the importance of having an accurately measured utility value for pill-taking rather than simply relying on arbitrary levels or expert opinion, as has often been previously done.

We are aware of ≥17 additional studies that use a utility value of taking pills in their analyses. All these studies cited values between 0.95 and 1.0, depending on the type of pill and whether or not side effects and monitoring were considered. A strength of our study is that we assessed the disutility of pill-taking apart from the costs, monitoring, or
<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Standard Gamble</th>
<th>Willingness to Pay†</th>
<th>Willingness to Pay† (Free Response)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>n</td>
<td>Mean</td>
<td>P Value‡</td>
</tr>
<tr>
<td>Age, y</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>30–50</td>
<td>505</td>
<td>0.989 &lt;0.0001</td>
<td></td>
</tr>
<tr>
<td>51–64</td>
<td>366</td>
<td>0.993</td>
<td></td>
</tr>
<tr>
<td>≥65</td>
<td>129</td>
<td>0.991</td>
<td></td>
</tr>
<tr>
<td>Sex</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Female</td>
<td>539</td>
<td>0.990 &lt;0.0001</td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>461</td>
<td>0.992</td>
<td></td>
</tr>
<tr>
<td>Race</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Black</td>
<td>159</td>
<td>0.987 0.0001</td>
<td></td>
</tr>
<tr>
<td>White</td>
<td>629</td>
<td>0.992</td>
<td></td>
</tr>
<tr>
<td>Other</td>
<td>212</td>
<td>0.989</td>
<td></td>
</tr>
<tr>
<td>Education level</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt; College degree</td>
<td>284</td>
<td>0.989 0.6026</td>
<td></td>
</tr>
<tr>
<td>College or graduate degree</td>
<td>716</td>
<td>0.991</td>
<td></td>
</tr>
<tr>
<td>Income level</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;$25000</td>
<td>224</td>
<td>0.985 0.0340</td>
<td></td>
</tr>
<tr>
<td>$25000–$75000</td>
<td>516</td>
<td>0.992</td>
<td></td>
</tr>
<tr>
<td>&gt;$75000</td>
<td>260</td>
<td>0.992</td>
<td></td>
</tr>
<tr>
<td>Health rating</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt; Very good</td>
<td>621</td>
<td>0.989 0.3176</td>
<td></td>
</tr>
<tr>
<td>≥ Very good</td>
<td>379</td>
<td>0.994</td>
<td></td>
</tr>
<tr>
<td>Numeracy level§</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>0 Correct</td>
<td>202</td>
<td>0.983 0.0004</td>
<td></td>
</tr>
<tr>
<td>1 Correct</td>
<td>288</td>
<td>0.988</td>
<td></td>
</tr>
<tr>
<td>2 Correct</td>
<td>510</td>
<td>0.995</td>
<td></td>
</tr>
<tr>
<td>Literacy level¶</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Inadequate</td>
<td>284</td>
<td>0.989 0.0190</td>
<td></td>
</tr>
<tr>
<td>Adequate</td>
<td>716</td>
<td>0.991</td>
<td></td>
</tr>
<tr>
<td>Difficulty obtaining pills</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Not difficult</td>
<td>564</td>
<td>0.991 0.0084</td>
<td></td>
</tr>
<tr>
<td>Neutral</td>
<td>136</td>
<td>0.987</td>
<td></td>
</tr>
<tr>
<td>Difficult</td>
<td>91</td>
<td>0.988</td>
<td></td>
</tr>
<tr>
<td>Difficulty paying for pills</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Not difficult</td>
<td>396</td>
<td>0.991 0.1499</td>
<td></td>
</tr>
<tr>
<td>Neutral</td>
<td>190</td>
<td>0.990</td>
<td></td>
</tr>
<tr>
<td>Difficult</td>
<td>204</td>
<td>0.989</td>
<td></td>
</tr>
<tr>
<td>No. of times pills taken per day</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;2</td>
<td>544</td>
<td>0.990 0.0896</td>
<td></td>
</tr>
<tr>
<td>≥2</td>
<td>456</td>
<td>0.991</td>
<td></td>
</tr>
<tr>
<td>No. of pills taken per day</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>0</td>
<td>209</td>
<td>0.994 0.0002</td>
<td></td>
</tr>
<tr>
<td>1</td>
<td>99</td>
<td>0.987</td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>153</td>
<td>0.989</td>
<td></td>
</tr>
<tr>
<td>3+</td>
<td>539</td>
<td>0.991</td>
<td></td>
</tr>
</tbody>
</table>

*Utilities derived using standard gamble method or willingness-to-pay method, as indicated.
†Participants with age ≥65 years (n=129) removed before calculating mean and P value.
‡P values based on 1-way analysis of variance.
§Based on number of answers correct from numeracy screener.
¶Based on response to single-question literacy screener.
the harms from treatment-related adverse effects. Such effects ideally should be accounted for separately in cost-effectiveness analyses. Most of the previously published cost-effectiveness analysis studies used a value of 1.0 as their base case and then performed a sensitivity analysis to analyze a range. The lower end of the range of most sensitivity analyses was generally lower than the values that we obtained in this study.

**Strengths and Limitations**

To our knowledge, this is the largest study to date that quantifies the utility of pill-taking. Although our survey population was not perfectly representative of the US population >30 years, the large sample and rigorous measurement of covariates allowed us to examine multiple subgroups, an important strength of our study compared with previous work. An important additional strength of our study is its use of 3 different utility assessments, and although our SG and TTO assessments were modified versions of the typical interview-based assessments, all 3 methods of our methods converged on a similar result.

We found that at least some participants were willing to make trade-offs (ie, had utility values other than 1.0) by each of the methods, including ≈60% of participants with WTP. The low number of people who would not trade any amount is a strength of WTP and provides indirect support for using it. We had hypothesized that WTP may be a particularly good method for this type of utility assessment because it involves a nonrisk-based decision and is expressed in units (dollars) that may be more familiar to participants. Our findings suggest promise for its use in other situations requiring the measurement of small decrements in utility.

It is also important to note that the use of categories for TTO and SG, although helpful in terms of survey administration, produce utilities that are potentially less precise than traditional interview-based methods and are dependent on the percentage of respondents choosing the highest response category because they might have expressed even more disutility if other, larger responses were available. We were reassured by the fact that the percentage of people choosing the largest value was small: <10% for the SG and TTO, and only 2.8% for the WTP. The WTP questions were especially helpful in this regard because we included an open-ended question along with the categorical, close-ended question. Although the average open-ended response was larger (as in past studies with this method), it produced similar utilities to the closed-ended question.

We also acknowledge other limitations. This survey could only gather data on hypothetical scenarios. The ideal study would be prospective, with actual patients making the decision about initiating preventive therapies and then tracking their pill-taking behavior. It is possible that those who express high levels of disutility would be less likely to initiate and adhere to pill-taking regimens, but this needs to be studied empirically.

To make our survey feasible and increase the chance of yielding accurate results, we modified the administration of utility assessment methods. This adapted methodology may affect our utility estimates. The questions we used to assess utility using the TTO and SG used set intervals in a multiple-choice format rather than using open-ended questions and an interview format with multiple questions until indifference. However, the options we provided were within a reasonable range of the magnitude of answers we were expecting based on our prior work and literature review. We estimated utilities for TTO based on average life expectancy; using individuals’ actual life expectancy, based on health status, may yield different results.

We did not assess test-retest reliability. Utility values may fluctuate over time as individuals adapt to a given health state. Our survey only measured individuals’ preferences at 1 point in time; however, we did not see large differences in results based on current pill-taking, giving us confidence that this effect is probably not large.

Although we stipulated in our survey instrument that participants would not have to pay for pills and to ignore any potential side effects, we cannot be certain that these issues did not have an effect on participants’ responses, which could have introduced some error in our utility estimates. We did not ask whether respondents took pills specifically for CVD prevention or whether they had experienced any CVD event in the past. Utility values may vary based on these factors and should be examined in future surveys.

Finally, we and others have focused this work on the disutility of pill-taking for CVD prevention in general. People may have different utilities for preventive medications used for specific cardiovascular risk factors or for other health purposes, such as cancer prevention or prevention of osteoporotic fractures. Again, future surveys should examine utility in the context of other conditions.

**Conclusion**

The mean utility value of taking a pill daily for CVD prevention is ≈0.990 to 0.994. Knowing this value and the distribution of responses may be useful for researchers and policymakers evaluating preventive interventions for CVD that include taking pills, including the decision about taking aspirin or statins, and should be considered in addition to information about the decrements in utility from adverse outcomes such as gastrointestinal bleeding or myopathy.

**Acknowledgments**

Dr Hutchins had full access to all the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis. Mark Weaver provided assistance with the bootstrapping analyses and calculation of the nonparametric statistics. All authors helped in study concept and design, analysis and interpretation of data, and critical revision of article. Drs Hutchins, Viera, and Pignone helped in acquisition of data, drafting of article, and statistical analysis. Dr Pignone obtained financial support (K05 CA129166; Pignone [PI]; September 30, 2008, to August 31, 2014). Drs Viera and Pignone helped in study supervision. Exempt status is granted by IRB (13 to 1403).

**Sources of Funding**

Funding was provided by a K05 grant from the National Cancer Institute (K05 CA129166; Pignone [PI]). The funding source had no role in trial design, data analyses, article preparation, or the decision to submit the article for publication.

**Disclosures**

None.

**References**


Quantifying the Utility of Taking Pills for Cardiovascular Prevention
Robert Hutchins, Anthony J. Viera, Stacey L. Sheridan and Michael P. Pignone

Circ Cardiovasc Qual Outcomes. 2015;8:155-163; originally published online February 3, 2015;
doi: 10.1161/CIRCOUTCOMES.114.001240
Circulation: Cardiovascular Quality and Outcomes is published by the American Heart Association, 7272
Greenville Avenue, Dallas, TX 75231
Copyright © 2015 American Heart Association, Inc. All rights reserved.
Print ISSN: 1941-7705. Online ISSN: 1941-7713

The online version of this article, along with updated information and services, is located on the
World Wide Web at:
http://circoutcomes.ahajournals.org/content/8/2/155

Data Supplement (unedited) at:
http://circoutcomes.ahajournals.org/content/suppl/2015/02/09/CIRCOUTCOMES.114.001240.DC1

Permissions: Requests for permissions to reproduce figures, tables, or portions of articles originally published
in Circulation: Cardiovascular Quality and Outcomes can be obtained via RightsLink, a service of the
Copyright Clearance Center, not the Editorial Office. Once the online version of the published article for
which permission is being requested is located, click Request Permissions in the middle column of the Web
page under Services. Further information about this process is available in the Permissions and Rights
Question and Answer document.

Reprints: Information about reprints can be found online at:
http://www.lww.com/reprints

Subscriptions: Information about subscribing to Circulation: Cardiovascular Quality and Outcomes is online
at:
http://circoutcomes.ahajournals.org//subscriptions/
Appendix. Survey Items.

Most adults will face the decision about whether to take some type of pill for preventive reasons at some point in their lives. When people take pills, they go through a process that involves, but is not limited to, obtaining the pills, ingesting the pills, and remembering to take the pills. Our research team is conducting a study to better understand how taking pills for preventive purposes affects people’s quality of life. Please answer all questions as accurately and honestly as possible."

What is your age? ______

What is your gender?
   o Male
   o Female

What best describes your race/ethnicity?
   o African American
   o Asian
   o Caucasian
   o Native American
   o Pacific Islander
   o Hispanic / Latino
   o Other/None of the above

What is your highest level of education completed?
   o Less than high school
   o High school or GED
   o Some college
   o College degree
   o Graduate or professional degree

We’d like to start by asking you a few questions about taking pills, which includes capsules, tablets, or gelcaps.

How many pills do you take each day? (Include vitamins and prescription medications you take daily but not pills you take only once in a while)
   o 0      (skip next three items)
   o 1
   o 2
   o 3
   o 4
   o 5
   o 6 or more

How many different times a day do you regularly take pills?
How difficult is it for you to pay for your pills?
- Very difficult
- Somewhat difficult
- Neutral
- Not very difficult
- Not difficult at all

How difficult is it for you to obtain your pills?
- Very difficult
- Somewhat difficult
- Neutral
- Not very difficult
- Not difficult at all

Please read the following carefully:

The next set of questions pertains to taking a pill to PREVENT a heart attack and stroke. Assume that by taking this pill you will live your life free of heart attack and stroke. Assume this pill does not cause any side effects and is free of charge. However, you do have to obtain a prescription from your doctor in order to get it, fill the prescription at the pharmacy, remember to take the pill every day, and physically swallow the pill.

Now assume that you have a choice. Instead of taking the pill every day, you could give up time at the end of your life and also be guaranteed to live a life free of heart attacks and stroke.

Approximately how much of your remaining life would you give up in order to NOT have to take this 1 pill every day for the rest of your life?
- None
- 1 week
- 2 weeks
- 1 month
- 3 months
- 6 months
- 9 months
- 12 months
- 18 months
- 24 months

How about if you were taking two such pills, at the same time of day (for example: 2 pills in the morning)?
How about if you were taking two such pills, at two DIFFERENT times of day (for example: 1 pill in the morning, 1 pill at night)?

Imagine that you have been diagnosed with a health condition that, if not treated, will limit the quality and length of your life. The physician who diagnoses you tells you that there are two known treatments, both of which will cure you completely.

**Treatment 1** is a one-time treatment that cures you but happens to also have the potential to cause immediate death.

**Treatment 2** is a pill you have to take once a day every day for the rest of your life. There is 0% risk of death from this pill.

Approximately what chance of immediate death are you willing to risk to take Treatment 1 one time instead of taking Treatment 2 every day for the rest of your life?

- 100,000 in 1,000,000
- 10,000 in 1,000,000
- 1,000 in 1,000,000
- 100 in 1,000,000
- 10 in 1,000,000
- 1 in 1,000,000
- 0 in 1,000,000
You can get treatment 1 for a one-time payment. Approximately how much would you be willing to pay to receive Treatment 1 one time instead of taking Treatment 2 every day for the rest of your life?

$__________

You can get treatment 1 for a one-time payment. Approximately how much would you be willing to pay to receive Treatment 1 one time instead of taking Treatment 2 every day for the rest of your life given the following options?

- $0
- $10
- $50
- $100
- $250
- $500
- $1,000
- $2,500
- $5,000
- $10,000
- $25,000

Next, we would like to ask you a few questions about chance and working with numbers. For each question, please give us your best estimate, even if you think your estimate is only a guess.

A person taking Drug A has a 1% chance of having an allergic reaction. If 1,000 people take Drug A, how many people would you expect to have an allergic reaction?

# of people = ________

The next question asks how many times something would happen in 1,000 tries.

Example: Imagine picking a jelly bean from a jar filled with an equal number of 4 different colored jelly beans (red, black, blue and green). Out of 1,000 tries, how many times would you expect to pick a red jelly bean?

Answer: 250 times out of 1,000

Now you try: Imagine that we flip a coin 1,000 times. What is your best guess about how many times the coin would come up heads in 1,000 flips?

# heads in 1,000 flips = ___________

How confident are you filling out medical forms by yourself?

- Not at all
- A little bit
Just a few final questions…

How would you rate your overall health?
- Poor
- Fair
- Good
- Very Good
- Excellent

Do you have health insurance?
- No
- Yes

What is your total household income?
- <$10,000
- $10,000-$24,999
- $25,000-$49,999
- $50,000-$74,999
- $75,000-$99,999
- $100,000-$150,000
- >$150,000