Daily Almond Consumption in Cardiovascular Disease Prevention via LDL-C Change in the U.S. Population: a Cost-Effectiveness Analysis

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Abstract

Background

Heart disease is the leading cause of death in the United States. The U.S. Food and Drug Administration approved the health claim that 1.5 oz. (42.5 g) nut intake may reduce the risk of cardiovascular disease (CVD). Previous studies have focused on the cost-effectiveness of other foods or dietary factors on primary CVD prevention, yet not in almond consumption. This study aimed to examine the cost-effectiveness of almond consumption in CVD prevention.

Methods

A decision model was developed for 42.5 g almond per day versus no almond consumption and CVD in the U.S. population. Parameters in the model were derived from the literature, which included the probabilities of increasing LDL-C, developing acute myocardial infarction (MI) and stroke, treating MI, dying from the disease and surgery, as well as the costs of the disease and procedures in the U.S. population, and the quality-adjusted life years (QALY). The cost of almonds was based on the current price in the U.S. market. Sensitivity analyses were conducted for the time of almond consumption, ten-year risk prevention, patients with or without CVD and using sex-specific probabilities for MI, and varying the costs of procedures and almonds.

Results

The almond strategy had $302 lower cost and 0.02 QALY gain compared to the non-almond strategy in the main analysis. The annual net monetary benefit (NMB) of almond consumption was $1,360 higher per person than no almond consumption, when the willingness to pay threshold was set at $50,000 for annual health care expenditure. Almond was more cost-effective than non-almond in CVD prevention in all the sensitivity analyses, except for the time of almond consumption as a morning or afternoon snack or when costs of almonds increased from $0.47 to $1.41 per day.

Conclusion

Consuming 42.5 g of almonds per day is a cost-effective approach to prevent CVD in the short term and potentially in the long term.

Background
Almonds contain a variety of bioactive components that have been individually related to cardiovascular health(1). Almonds, along with other tree nuts, are good sources of mono- and polyunsaturated fats that have been shown to lower blood lipid levels. The qualified health claim for tree nuts and heart health by the U.S. Food and Drug Administration states, “Scientific evidence suggests but does not prove that eating 1.5 ounces per day of most nuts, as part of a diet low in saturated fat and cholesterol, may reduce the risk of heart disease.”(2)

Cardiovascular disease (CVD) treatments are usually expensive, which include medications and invasive or non-invasive surgeries. Between 2014 and 2015, the estimated direct cost of CVD and stroke was $213.8 billion in the U.S.(3) Although some studies have been conducted to assess the cost-effectiveness of those treatments,(4) findings suggest that treatments such as statin medication are effective, but can have side-effects on health.(5)

In contrast, tree nuts as part of a healthy diet, typically does not have any side effects on consumers, with the exception of tree nut allergies.(6) Given the fact that nuts, including almonds, are relatively expensive, it is not clear whether consuming almonds on a daily basis would be a cost-effective way to prevent CVD. The purpose of this research is to determine whether the consumption of almonds is an economically preferred alternative for CVD prevention using both short-term base case analysis and 10-year risk prevention.

Methods

Base-case Decision Model

We developed a decision model for CVD prevention among adults with 42.5 g (1.5 oz.) almond consumption per day (almond strategy), as compared with no almond consumption (non-almond strategy) to project 1-year health outcomes and CVD-related costs (Figure 1). We referred to a previous paper to develop the model structure.(7) Our previous meta-analysis found a significant decrease in LDL-C (low-density lipoprotein cholesterol) among almond intervention groups, as compared with no almond controls.(8) Level of LDL-C was applied as the determinant for possible risk
for future CVD events. Individuals with lower or normal levels of LDL-C, who did not have CVD, started in the “disease-free” health state, either in the almond or non-almond strategy. We assumed that all the probabilities of CVD events were the same in the almond and non-almond strategy if their LDL-C increased. The probabilities of changes in LDL-C for the almond and non-almond strategy were obtained through contact with the study authors.(9) Transitions from the “disease-onset” health state to CVD events, including acute myocardial infarction (MI), stroke, and chronic heart disease (CHD) were based on probabilities derived from targeted literature reviews. After an acute MI event, health states were further classified as: 1) undergoing a procedure (coronary artery bypass graft (CABG), percutaneous transluminal coronary angioplasty (PTCA)), 2) no procedure (but managed medically), 3) having a MI-related death. After an event of stroke, health states were further classified as: 1) asymptomatic stroke, 2) recurrent stroke, and 3) death from stroke. Once in a CVD disease state, individuals could not transition back to a “disease-free” state. After an acute disease state, individuals transitioned to a CHD state.

Cost of Therapy

The cost of almonds was derived from a publicly available source as the current price of almonds in the U.S. market.(10) The annual cost was calculated based on the consumption of 42.5 g per day. The costs of CVD events and costs of treatments were derived from recent literature.(11-14) The costs of each procedure (i.e., CABG or PTCA) included procedural and physician fees as well as costs for hospital stays and ancillary services. For procedures following the CHD state, we considered costs for re-hospitalization, outpatient and rehabilitation services, medication, and physician fees.(12) The costs for medical therapy and emergency admission for MI were used for the “no procedure” outcome. For the costs for direct death due to MI, we included physician fees, hospital stay expenses and ancillary services.(11) We used the first-year follow-up costs for stroke medication and rehabilitation as the cost for recurrent stroke.(13) The five-day hospitalization cost for cerebrovascular disease was used as the cost for death from stroke since the average cost and the length of stay is similar between the two events.(14)
Quality-adjusted Life Year

Quality-adjusted life year (QALY) for each outcome was used as the effectiveness in the model. We assumed that the QALY of the disease-free stage was equal to 1. The input parameters in the model are listed in Table 1.

Sensitivity analyses

We performed several one-way sensitivity analyses. In the sensitivity analyses, the cost-effectiveness ratio was calculated by altering the probability of LDL-C response to almonds based on the time of day almonds were consumed. In the study by Tan et al., the LDL-C response varied by the time of day of almond consumption (i.e., morning, noon, or afternoon; with or without a meal).(9) The following parameters identified from targeted literature reviews were changed: 1) the probabilities of developing acute MI; 2) the probabilities of developing CVD in 10 years; 3) the costs of CABG and PTCA procedures; 4) the cost of almonds; and 5) the LDL response among participants with existing CVD. For the probability of developing acute MI, we tested sex-specific probabilities identified from the literature.

Preferred alternative was chosen based on the net monetary benefit (NMB):

\[ NMB = \frac{W}{\Delta_1} - \frac{C}{\Delta_2} \]

where is the maximum willingness to pay for health care, \( \Delta \) is the difference in the mean effectiveness of two strategies, and \( \Delta \) is the difference in the mean cost of two strategies.(15) TreeAge Pro 2018 was used to conduct the analyses and the willingness to pay for health care was set to $50,000 per year.

Results

Base-case Decision Model

The base-case decision model for one year showed that consuming 42.5 g of almonds was a preferable strategy to prevent CVD outcomes such as MI, CHD, and stroke (Table 2). The results showed that 42.5 g of almond consumption every day costs an individual $1,132/QALY and no almond consumption costs $1,480/QALY. The annual NMB was $46,869 and $45,509 for the almond and non-almond strategy, respectively, when the willingness to pay was $50,000 for individual health care.
expenditure every year. A negative incremental cost-effectiveness ratio (ICER) was obtained due to lower costs of almond consumption in relation to the higher amount of QALYs gained.

Sensitivity Analyses

When almonds were consumed during lunch, the cost was $19 less and the QALY gain were 0.01 more, resulting in an NMB of $45,951, which indicated that almond strategy was better than the non-almond strategy. In this scenario, the non-almond strategy was dominated. The NMB for non-almond remained the same as in the main analysis. However, the non-almond was a more preferred strategy compared to the almond-strategy when almonds were consumed either as a morning snack or as an afternoon snack. The non-almond strategy cost $581 less with a gain of 0.02 more QALYs compared to the almond strategy when almonds were consumed as a morning snack. The non-almond strategy cost $139 less with the same QALYs gained compared to the almond strategy when almonds were consumed as an afternoon snack. The NMB was $44,012 and $45,441 when almonds were consumed as a morning snack and as an afternoon snack, respectively. When consuming almonds as a morning snack, the almond strategy was dominated.

The non-almond strategy was always dominated when varying the probability of MI from 0.56% to 0.96%. By using sex-specific MI probabilities, we found that among men in the almond strategy, it cost $1,154/QALY per year in CVD prevention, while the cost increased to $1,515/QALY among men in the non-almond strategy. For women, it cost $1,139/QALY and $1,490/QALY in the almond strategy and non-almond strategy, respectively. For both men and women, the NMB was higher in the almond strategy ($46,838 for almond vs. $45,461 for non-almond in men; $46,860 for almond vs. $45,495 for non-almond in women).

When we expanded the time horizon to ten years, the almond strategy cost $30 more, but gained 0.02 QALYs more than the non-almond strategy. The cost per QALY was $1,829 and $1,841 for almond and non-almond, respectively. The NMB for almond was $1,098 higher than the non-almond strategy.

In the sensitivity analyses, the non-almond strategy continued to be dominated even when different costs of procedures were input. The two strategies cost the same amount of money per QALY to
prevent CVD and both resulted in the same NMB. As the price of almond increased, it cost more money per QALY to prevent CVD by consuming almonds, and the non-almond strategy became more financially viable. With the price of organic almonds, it cost $1,488/QALY for almond consumption with an NMB of $46,527.

For secondary prevention, the almond strategy cost $994/QALY compared with $1,161/QALY for the non-almond strategy, and had a higher NMB ($47,278 for almond vs. $46,428 for non-almond).

Discussion
This study assessed the cost-effectiveness of almond consumption in the short term and up to 10 years for CVD prevention. We found that consuming almonds is a cost-effective way to prevent CVD in the short term and potentially in the long term. In the sensitivity analyses, consuming almonds is also a financially viable way to prevent CVD. The non-almond strategy was only preferred when almonds were consumed as a snack (in the morning or in the afternoon) or when organic almonds (higher cost) were consumed.

Heart disease is the leading cause of death in the United States, with over 630,000 deaths in 2015 and over 140,000 stroke-related deaths in the same year.(16) The disease also lays a huge economic burden in the US. Between 2014 and 2015, the estimated annual cost of CVD in the United States was $351.2 billion. The projected total costs of CVD until 2035 will continue to increase for people in all age groups.(3) Under such disease and economic burden, cost-effective primary prevention strategies for CVD are imperative for the population.

Our recent meta-analysis showed a reduction in CVD risk factors, such as LDL-C, total cholesterol, body weight, and apolipoprotein B with almond consumption.(8) Almonds contain phytochemicals such as proanthocyanidins, hydrolysable tannins, fat-soluble bioactives including vitamin E and phytosterols, and antioxidants that are cardio-beneficial. Other macro- and micro-nutrient components in almonds, including omega-3 fatty acids, selenium, magnesium, copper, potassium, and -sitosterol, are also potentially cardio-protective.(1)

Previous studies have focused on the cost-effectiveness of other foods or dietary factors on primary CVD prevention, (17-20) but little is known about the cost-effectiveness of almonds. To our best
knowledge, this is the first cost-effectiveness study for CVD prevention using an almond strategy. In this study, we conducted a base-case model and several sensitivity analyses to assess the cost-effectiveness in the short term and the long term. The results of this study may provide some insights on individual level healthy dietary behaviors as well as population level benefits of consuming almonds.

Our models had a few limitations. For example, the focus of this study was on the U.S. population using the costs of medical treatments and the probabilities of developing diseases from studies conducted in the U.S. Therefore, the results may not be generalizable to populations in other countries. Furthermore, unlike medical or surgical therapies, there are no serious side effects for consuming almonds, except for tree nut allergies. Thus, our models do not take into consideration any serious side effects, which may be related to the preference of the almond strategy. Lastly, we were not able to use total cholesterol/high-density lipoprotein ratio as a mediator due to the lack of data.

The interpretation of our results requires more caution. First, our study was based on input from published literature instead of primary data from an intervention cohort. Thus, the inputs were constrained by the study design of the literature, especially the probabilities. As a result, we made three assumptions in the models: 1) changes in LDL-C can lead to a difference in CVD risk in one year in the main analysis; 2) changes in LDL-C caused by almonds remained consistent in the ten-year sensitivity analysis; and 3) costs of almonds and procedures over time remained consistent in the ten-year sensitivity analysis. More data may be needed to estimate the costs of almonds and procedures over time.

Conclusion
Consuming almonds 42.5 g per day is a cost-effective approach to prevent CVD in the short term and potentially up to 10 years. Given the fact that the American population consumed an average of 2.93 g almonds daily in the 2017-2018 crop year, (21) the potential benefits of increasing the almond consumption to the recommended level could be significant.

List Of Abbreviations
CABG = coronary artery bypass graft; CHD = chronic heart disease; CVD = cardiovascular disease;
ICER = incremental cost-effectiveness ratio; LDL-C = low-density lipoprotein cholesterol; MI = myocardial infarction; NMB = net monetary benefit; PTCA = percutaneous transluminal coronary angioplasty; QALY = quality-adjusted life years.

Declarations

Ethics approval and consent to participate
Not applicable

Consent for publication
Not applicable

Availability of data and material
All data analyzed during this study are included in these published articles (Table 1)

Competing interests
G.R. was a consultant for Porter Novelli and E.J.J. had additional funds from the Almond Board of California for a clinical trial at the time of the study. Other authors declare that they have no competing interests.

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Authors’ contributions
G.R. and E.J.J. conceived and designed the experiments; J.W. and M.A.L.B. synthesized the data; J.W. performed the analyses; J.W., G.R., E.J.J., M.A.L.B. wrote the paper. G.R. and E.J.J. had primary responsibility for final content. All authors read and approved the final manuscript.

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Not applicable

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Tables

Table 1. Input Parameters in the Decision-making Model and Source

| Parameter                              | Value                  | Source                      |
|----------------------------------------|------------------------|-----------------------------|
| Probability                            |                        |                             |
| Increase in LDL-C                      | 29% (almond)           | Tan et al.(9)               |
|                                        | 44% (non-almond)       | Tan et al.(9)               |
| Developing MI                          | 0.38% (one year)       | Pikula et al.(22)           |
|                                        | 3.75% (ten year)       | Pikula et al.(22)           |
| Death due to MI                        | 14%                    | Benjamin et al.(23)         |
| Taking CABG                            | 0.11%                  | Epstein et al.(24)          |
| Death due to CABG                      | 1.85%                  | Eisenberg et al.(25)        |
| Taking PTCA                            | 0.37%                  | Epstein et al.(24)          |
| Death due to PTCA                      | 1.82%                  | Benjamin et al.(23)         |
| Developing stroke                      | 0.25%                  | Pikula et al.(22)           |
|                                        | 2.46% (ten year)       | Pikula et al.(22)           |
| Recurrent stroke                        | 30.33%                 | Benjamin et al.(23)         |
| Death due to stroke                    | 21.82%                 | Benjamin et al.(23)         |
| Cost                                   |                        |                             |
| Almond (one year)                      | $170.75b               | Trader Joe’s(10)            |
| CABG Procedure                         | $33,254                | Cohen et al.(11)            |
| Follow-up of CABG                      | $6,143                 | Cohen et al.(11)            |
| Failure to Rescue after CABG           | $5,091c                | Cohen et al.(11)            |
| PCI Procedure                          | $27,560                | Cohen et al.(11)            |
| Follow-up of PCI                       | $8,426                 | Cohen et al.(11)            |
| Failure to Rescue after PCI            | $8,208c                | Cohen et al.(11)            |
| Treatment to Acute MI                  | $13,051                | Cohen et al.(11)            |
| Treatment to Chronic Heart Disease     | $3,069                 | Caruba et al.(12)           |
| Recurrent Stroke                        | $51,760                | Engel-Nitz et al.(13)       |
| Death due to Stroke                    | $9,500                 | Russo & Andrews(14)         |
| Effectivenessd                         |                        |                             |
| Successful CABG                        | 0.82 QALY              | Elizabeth et al.(26)        |
| Successful PCI                         | 0.85 QALY              | Elizabeth et al.(26)        |
| Chronic Heart Disease                  | 0.86 QALY              | Bakhai et al.(27)           |
| Recurrent Stroke                       | 0.48 QALY              | Nelson et al.(28)           |

Abbreviations: CABG = coronary artery bypass graft; LDL-C = low-density lipoprotein cholesterol; MI = myocardial infarction; PCI = percutaneous coronary intervention; PTCA = percutaneous transluminal coronary angioplasty. Note that PTCA and PCI were used interchangeably in data collection. aData is obtained from the request to author. bCost of almond was calculated based on the price of $4.99/lb. and consuming 42.5 g almond every day. The cost in 10-year sensitivity model was the 10 times of one-year cost. cFailure to rescue after procedures includes the cost of re-hospitalizations, physician fees, outpatient services, and medication cost. dEffectiveness of no cardiovascular event and death was set as 1 and 0, respectively.
Table 2. Results of Decision Model and Sensitivity Analyses

| Decision model | Cost  | Outcome (QALYs) | ICER   | NMB    |
|----------------|-------|-----------------|--------|--------|
| Almond         | $1,085| 0.96            |        | $46,869|
| Non-almond     | $1,388| 0.94            | Dominated | $45,509|
| Sensitivity-time of consumption<sup>a</sup> |       |                 |        |        |
| Morning snack  | $1,968| 0.92            | Dominated | $44,012|
| Lunch<sup>b</sup> | $1,369| 0.95            |        | $45,951|
| Afternoon snack| $1,527| 0.94            |        | $98,641|
| Sensitivity-sex-specific MI probability |       |                 |        |        |
| Men            |       |                 |        |        |
| Almond         | $1,107| 0.96            |        | $46,838|
| Non-almond     | $1,420| 0.94            | Dominated | $45,461|
| Women          |       |                 |        |        |
| Almond         | $1,092| 0.96            |        | $46,860|
| Non-almond     | $1,398| 0.94            | Dominated | $45,495|
| Sensitivity-10-year model |       |                 |        |        |
| Almond         | $1,750| 0.96            |        | $1,341 |
| Non-almond     | $1,719| 0.93            |        | $46,071|
| Sensitivity-cost of procedure |       |                 |        |        |
| Almond         | $1,085| 0.96            |        | $46,869|
| Non-almond     | $1,388| 0.94            | Dominated | $45,509|
| Sensitivity-cost of almond<sup>a</sup> |       |                 |        |        |
| Higher cost of almond | $1,427| 0.96            |        | $1,875 |
| Sensitivity-CVD patients |       |                 |        |        |
| Almond         | $959  | 0.96            |        | $47,278|
| Non-almond     | $1,104| 0.95            | Dominated | $46,428|

Abbreviations: ICER = incremental cost-effectiveness ratio; NMB = net monetary benefit; QALY = quality-adjusted life years. <sup>a</sup>Results of almond strategy in sensitivity analyses were reported. The result of non-almond strategy remained the same as in main analysis. <sup>b</sup>Non-almond strategy was dominated in the model.

Figures
Figure 1

Decision-making model The blue square is the decision node. Green circles are chance nodes. Red triangles are terminal nodes. CABG = coronary artery bypass graft; CHD = chronic heart disease; LDL-C = low-density lipoprotein cholesterol; MI = myocardial infarction; PTCA = percutaneous transluminal coronary angioplasty.

Supplementary Files
This is a list of supplementary files associated with this preprint. Click to download.
Net Monetary Benefit (NMB) formula.JPG