Supplementary Online Content

Du M, Griecci CF, Cudhea FF, et al; Food-PRICE Project. Cost-effectiveness analysis of nutrition facts added-sugar labeling and obesity-associated cancer rates in the US. *JAMA Netw Open*. 2021;4(4):e217501. doi:10.1001/jamanetworkopen.2021.7501

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This supplementary material has been provided by the authors to give readers additional information about their work.

eAppendix 1. Baseline cancer incidence and methods of cancer incidence projections for 13 types of cancer

We estimated the cancer incidence rate projections for the defined 32 demographic subgroups as inputs for the DiCOM model. We obtained age adjusted incidence rates, then projected rates based on historical trends, and then applied a cohort period age shifting method to calculate incidence rates for each of 32 subgroups over their lifetime.

We first obtained age-adjusted incidence rates for each year (2006-2015) from the United States Cancer Statistics which combines data from the Surveillance, Epidemiology, and End Results (SEER) database and the Centers for Disease Control and Prevention's National Program of Cancer Registries (NPCR) database.¹ An age-adjusted rate is a weighted average of the age-specific rates, where the weights are the proportions of persons in the corresponding age groups of a standard population. The potential confounding effect of age is reduced when comparing age-adjusted rates computed using the same standard population.

We then projected age-adjusted cancer incidence based on historical trends. We used the incidence data estimated from the most recent 10 years, 2006-2015, to predict the future 15 years, 2016-2030 and then held the incidence rate constant for all subsequent years.² To do so, we estimated the average annual percent change (AAPC) using age-adjusted incidence rates from 2006 to 2015, then applied it to the 2015 baseline incidence to project future incidence for each cancer type by subgroup.³ The estimated annual percent change was calculated for each cancer site and 32 subgroups by fitting a regression line to the natural logarithm of the age-adjusted rates (I) in years 2006 through 2015 (y). The equation for AAPC: $\ln(I) = \alpha + \beta$ y, where α and β were coefficients to be estimated and y is calendar year.^{2,3} The average annual percent change (AAPC) is a summary measure of the trend over a pre-specified fixed interval. It allows us to use a single number to describe the average APCs over a period of multiple years. It is valid even if the model indicates that there were changes in trends during those years. It is computed as a weighted average of the APCs, with the weights equal to the length of the APC interval.

We combined the AAPC projected incidence rates with the projected US population data and apply the cohortperiod method to estimate the "crude" projected cancer incidence in each of the 32 subgroups from 2016 and 2095 incidence rates that will be used in the DiCOM model. US population estimates by single year of age, race/ethnicity, and sex will be extracted from the National Interim Projections of the US population via the US Census Bureau website. The projections series use the official estimates of the resident population on July 1, 2016 as the base for projecting the U.S. population from 2017 to 2060.⁴ The series use the cohort-component method and historical trends in births, deaths, and international migration to project the future size and composition of the national population.

We have made two assumptions about this incidence rate. The population projection data are through year 2060 so we will assume incidence rates to be constant from year 2060 onward. We also assumed the population dies once they hit 100 years old and the model will then apply an incidence rate of 0 for any remaining years through year 2095. The DiCOM model will take into account the second assumption that death occurs at 100 years old.

eAppendix 2. Cancer survival for 13 types of cancer

We estimated the 5-year relative survival for the defined 32 demographic subgroups. We obtained five-year relative survival rates using the period analysis method from the United States Cancer Statistics which incorporates data from the Surveillance, Epidemiology, and End Results (SEER) database.¹ The five-year survival for 2014, which was the most recent available data at time of analysis, was used. These rates were extracted for each cancer type and by the defined 32 demographic subgroups for each cancer type. The rates will be on a scale 0-1.

Relative survival is a net survival measure representing cancer survival in the absence of other causes of death. Relative survival is defined as the ratio of the proportion of observed survivors in a cohort of cancer patients to the proportion of expected survivors in a comparable set of cancer free individuals.⁵ Relative survival is the preferred method to estimate survival from cancer registry data.

Period analysis is a method which enhances up-to-date monitoring of survival.^{6,7} In contrast to traditional cohort analysis of survival, period analysis derives long-term survival estimates exclusively from the survival experience of patients within some recent calendar period.^{6,7} Three-year intervals were chosen which results in years 2008-2014 used to calculate 5year survival. Using seven years of data to calculate 5-year survival is standard method used by SEER and used in SEER publications.⁸

The first interval will contribute to the one year survival and will use cases diagnosed in 2012-2014, the second interval will contribute to the two year survival and will use cases diagnosed in 2011-2013, the third interval will contribute to the three year survival and will use cases diagnosed in 2010-2012, the fourth interval will contribute to the four year survival and will use cases diagnosed in 2009-2011 and the fifth interval will contribute to the five year survival and will use cases diagnosed in 2008-2010.

This analysis therefore used 2008-2014 diagnoses to calculate for 5-year relative survival for 2014. The highlighted orange boxes represent survival contributions for each year of diagnosis and year of follow-up (e**Table 1**). The annual probability of death was calculated as 1-exp[ln(5-year relative survival)/5].

eTable 1. Period method for five-year relative survival for 2014

eAppendix 3. Methods of estimating health related quality of life among 13 types of cancer

Health utility values range from 0 (dead) to 1 (perfect health and were assigned for each cancer type and by phase of care (initial, continuous, end of life), if available. We first searched databases for systematic reviews pertaining to utility weights or HRQOL measures for each cancer type of interest separately. We started with PubMed and searched Google Scholar if needed. The following search string was used for each cancer type: ("health related quality of life" OR "HRQOL" OR "quality of life" OR "QOL" OR "preference weight*" OR "utility weight*" OR "health state utilit*" OR "health utility*") AND ("cancer of interest") AND ("cancer" OR "neoplasm*") AND ("review" OR "systematic review").

When an appropriate systematic review was identified, we read the articles included in the review and determined if the paper met the following data needs. Data Extraction Hierarchy: 1) cancer type specific to the type of interest; 2) consistent in instrument used, prefer EQ-5D whenever available; 3) US samples preferred; 4) phase of care (assume same utility weights by phase if phase of care data were not available). If no systematic reviews available, we searched for individual studies about the utility weights of the cancer of interest. Additionally, check how often the paper is cited to see if it is a frequently used utility weight.

eAppendix 4. Estimate the association between added sugar labeling policy and added sugar intake

In order to understand the impact of the Nutrition Facts added sugar labeling policy, we must understand how both consumers and industry will respond to the policy as illustrated by the logical framework.

Because there is no much literature on the impact of added sugar labeling specifically, some assumptions must be made using the best available evidence from a mixture of sources. In Huang et al., the authors used the association estimate of calorie labeling, a reduction of intake by 6.6% (95% CI: 4.4% to 8.8%), as a proxy for added sugar labeling impact.^{9,10} This policy impact estimate was chosen to represent a more conservative estimate than the larger impact observed from labeling on other dietary constituents such as sodium and *trans fat*. ⁹ This impact on consumer behavior alone was assumed to take effect during the first year of implementation and no further reduction thereafter. For industry reformulation, Huang et al. assumed no reformulation in the first year of labeling implementation, then 8.25% (95% CI: 7.5% to 9.0%) of the sugarcontaining products would be reformulated each of years 2 to 5 during the intervention period to achieve 25% reduction in added sugar content in these products, with no additional reformulation thereafter.¹⁰⁻¹² In sum, this represents an 8.25% x 4 years x $25\% = 8.25\%$ net reduction in added sugar amounts of U.S. sugar-containing products over the intervention period.¹⁰

eAppendix 5. Methods of estimating policy implementation costs

We estimated the costs of implementing the Nutrition Facts added sugar labeling for both government and industry, including government administration cost, monitoring and evaluation costs, industry compliance costs and reformulation costs, based on FDA's budget report, ¹³ the Nutrition Review Project report, ¹⁴ and FDA's RIA¹¹ (e**Table 2**).

eTable 2. Implementation cost estimates for the Nutrition Facts added sugar labeling policy (in 2015 US dollars)

^aPolicy intervention costs were inflated to 2015 US (December) dollars using the Consumer Price Index.

^b Given no range of uncertainty was provided in source materials, we assumed 20% uncertainty around these costs.

Added sugar labeling is one of many provisions in FDA's rule to update the Nutrition Facts label. The cost of implementing all provisions is fixed for government (administration and monitoring and evaluation) and industry compliance. Therefore, we attributed 50% of the costs for implementing the entire labeling policy to the costs of added sugar labeling for government administration (#1), government monitoring and evaluation (#2), and industry compliance cost (#3) as this approach generated more conservative estimates. Uncertainty for the costs associated with government administration (41) and government monitoring and evaluation (42) was not provided in the source materials.^{13,14} We assumed that uncertainty is 20% around these costs.

For annual costs, namely the government monitoring and evaluation cost (#2) and the industry reformulation cost (44) , we applied 3% discounting rate recommended by the Second Panel on cost-effectiveness in health and medicine¹⁵ to reflect the present value of future costs of government monitoring and evaluation and industry reformulation. The model is a closed cohort model, so we computed the discounted present value of per-person costs and total national costs for persons alive at implementation who remained alive in each subsequent year (not for the larger total US population in each year, which also has growth from immigration and new persons reaching the threshold age). The year-specific discounting factor is estimated by $1/(1+3\%)^{(t-1)}$ (t is number of years of policy intervention, $t=1, 2, 3, \ldots$, lifetime) (e**Table 3**):

eTable 3. Discounting factor in each year over a lifetime

As our model estimated the costs and health outcomes based on a closed cohort and the population size decline over time, we need to express the annual costs in proportion to the population at risk. The population at risk was estimated based on the proportion of death (P_{dt} , $t=1, 2, 3, ...$) in each year. We first obtained the proportion of people who are alive at each year by calculating 1-P_{dt} (t=1, 2, 3, ...). Then we multiplied the baseline population size of 235 million by the proportion of people who are alive in each year (e**Table 4**).

eTable 4. Population size of people who are alive in each year over a lifetime (in millions)

We then estimated the per-person annual cost for cost categories #2 and #4, by dividing the annual cost estimated in the second year of implementing the policy among all US population by the population size in the second year. Specifically, for government monitoring and evaluation, the per person annual cost is estimated \$251,824/233,719,989=\$0.00108, and that for industry reformulation is \$44,550,571/233,719,989=\$0.190615. Taken together, to estimate the discounted annual cost of #2 and #4, we multiplied the population at risk, the per person annual cost estimated at year-2, and the year-specific discounting factor, using: discounted annual cost = population at risk x per-person annual cost x $1/(1+3%)^{(t-1)}$.

eAppendix 6. Annual health-related costs among cancer patients and the general population without cancer

The annual health-related costs data include: 1) medical expenditure, 2) productivity loss form missed work days or disability, and 3) patient time cost associated with receiving care for cancer survivors by age (under 65 vs. above 65 years old) and phase of care (initial, continuing, end-year of life); 4) medical expenditure, 5) productivity loss, and 6) patient time cost for individuals without cancer by age and status of end year of life. The description of data source and data structure were provided in e**Table 5**.

eTable 5. Description of Data Source of Health-Related Expenditures

^a The definition of phases of care: 1) initial phase, defined as the first 12 months following diagnosis, 2) end-year of life phase, defined as the final 12 months of life, and 3) the continuing phase, defined as all the months between the initial phase and the end-year of life. The costs of end-year of life varied by cause of death, either cancer-specific death or death due to other causes.

b Weighted means were calculated based on sample sizes and strata means.

We extracted the raw data for each of the costing component from the published literatures.^{2,16-20} The overall assumptions for data extraction include: 1) health-related costs for breast cancer among post-menopausal females, advanced prostate cancer, esophageal adenocarcinoma, and stomach cardia cancer, by age, sex, and phase of cancer care, were the same as those for breast cancer, prostate cancer, esophagus cancer, and stomach cancer; 2) if no data available for a specific cancer type, we assumed the costs for that cancer type were the same as the estimates of costs for all-cancer sites, e.g., medical expenditure for all-cancer sites were used to replace the medical expenditures for multiple myeloma, gallbladder, liver, and thyroid cancers; 3) we extracted the costs for end-year of life due to cancer death and assumed that death due to other causes is not a competing outcome; 4) we assumed that the end-year life medical expenditure for individuals without cancer does not vary by the 32 subgroups.

If a specific costing component was not reported directly in the raw data, we calculated the cost for that component based on available data. For example, the annual productivity loss for colorectal cancer were reported as a percentage of total health-related costs.²⁰ We multiplied the percentage and the total health-related costs to obtain the productivity loss for colorectal cancer. We also performed data imputation for unavailable data. For instance, the annual productivity loss for allcancer sites was reported by time interval since cancer diagnosis (diagnosed within one year vs. diagnosed greater than one year).¹⁶ To obtain this costing component by the defined phases of care, we calculated the weighted means which was used as the annual productivity loss for continuing phase. We then assumed that the productivity loss in the initial phase and end-oflife phase of cancer care are 1.3 times and 4 times to the mean estimates based on available data for other cancers.^{2,16} For individuals without cancer, we assumed that the end-of-life productivity loss is 4 times to the mean estimate of the productivity loss. The same rules applied to data imputation for patient time costs.

We then applied the age shifting to keep the expenditures consistent within each age group. Starting from 2021, individuals in the cohort of 55-64 years old will turn into the cohort of 65 years and older. Therefore, we assumed that starting from 2021, the heath-related expenditures for individuals who were in the cohort of 55-64 years old would be the same as those for individuals who were in the cohort of 65 years and older at the beginning of the DiCOM model. Based on the same assumption, starting from 2031 and 2047, the health-related expenditures for the cohort of 45-54 years old and those for the cohort of 20-44 years old were projected to be the same as those for the cohort of 65 years and older, respectively. We followed the same rule and applied the age shifting for the health-related expenditures for individuals without cancer. All estimations and projections were performed in SAS 9.4. All health-related expenditures were inflated to 2015 US dollars using the Personal Health Care (PHC) index.

Subgroups	Age	Sex	Race/Ethnicity
1	20-44y	Female	NHW
$\overline{2}$	20-44y	Female	NHB
3	20-44y	Female	HISP
$\overline{4}$	20-44y	Female	OTH
5	$\overline{2}0 - 44y$	Male	NHW
$\overline{\mathbf{6}}$	$20 - 44y$	Male	NHB
$\overline{\mathbf{7}}$	20-44y	Male	HISP
8	20-44y	Male	OTH
9	45-54y	Female	NHW
10	45-54y	Female	NHB
11	$45 - 54y$	Female	HISP
12	45-54y	Female	OTH
13	45-54y	Male	NHW
$\overline{14}$	45-54y	Male	$\overline{\text{NHB}}$
$\overline{15}$	45-54y	Male	HISP
16	45-54y	Male	OTH
17	55-64y	Female	NHW
18	55-64y	Female	$\overline{\mathsf{N}}$ HB
19	55-64y	Female	HISP
$\overline{20}$	55-64y	Female	OTH
21	55-64y	Male	NHW
22	55-64y	Male	NHB
23	55-64y	Male	HISP
24	55-64y	Male	OTH
25	$65 + y$	Female	NHW
26	$65 + y$	Female	NHB
27	$65 + y$	Female	HISP
28	$\overline{6}5+y$	Female	OTH
29	$65 + y$	Male	NHW
30	$65 + y$	Male	NHB
$\overline{31}$	$65 + y$	Male	HISP
32	$65 + y$	Male	OTH

eTable 6. Defining population and 32 subgroups

eTable 7. Characteristics of US adults aged 20 years or older participated in the NHANES, 2013-2016

eTable 8. Consumption of added sugar from foods and beverages among US adults participated in 2013-2016 NHANES, by 32 subgroups

eTable 9 Relative risk estimates of etiologic relationships between body mass index (BMI) and cancer

eTable 10. Health-related quality of life among US cancer patients aged 20 years or older, by cancer type and phase of care

eTable 11. Baseline medical costs, productivity loss, and patient time costs among US cancer patients aged 20 years or older, by cancer type

eTable 12. Baseline medical costs, productivity loss, and patient time costs among general population aged 20 years or older in the US, by 32 subgroups

eTable 13. Estimated changes in health-related costs associated with Nutrition Facts added sugar labeling on reducing cancer burdens in the US over a lifetime, by cancer type^a

^aValues are the median estimates (95% uncertainty intervals) of each distribution of 1000 simulations.

bHealth-related costs were inflated to 2015 US dollars using the Personal Health Care (PHC) index. Negative costs represent savings. Costs are medians from 1000 simulations so may not add up to totals.

eTable 14. Estimated new cancer cases averted by Nutrition Facts added sugar labeling policy in the US by age, gender, race/ethnicity, and cancer type over a lifetime (US population=235,162,844)^a

^a Values are the median estimates (95% uncertainty intervals) of each distribution of 1000 simulations.

eTable 15. Estimated cancer deaths reduced by Nutrition Facts added sugar labeling policy in the US by age, gender, race/ethnicity, and cancer type over a lifetime (US population=235,162,844)^a

^a Values are the median estimates (95% uncertainty intervals) of each distribution of 1000 simulations.

eTable 16. Estimated health gains and costs associated with Nutrition Facts added sugar labeling on reducing cancer burdens in the US over 10 years (US population=235,162,844)^a

Abbreviations: ICER, Incremental Cost-Effectiveness Ratio; QALY, quality-adjusted life years.

a Values are the median estimates (95% uncertainty intervals) of each distribution of 1000 simulations.

["] Values are the median estimates (90% directionly intervals) or each distinguation of 1999 simulations.
^b Health-related costs were inflated to 2015 US dollars using the Personal Health Care (PHC) index. Policy interv were inflated to 2015 US dollars using the Consumer Price Index. Negative costs represent savings.

 \textdegree Costs are medians from 1000 simulations so may not add up to totals.

^d Net costs were calculated as policy costs minus health-related costs from reduced cancer burdens. Societal perspective includes healthcare cost, patient time costs, productivity costs, and policy implementation costs; government perspective included policy costs relevant to policy implementation and program monitoring and evaluation and medical costs. e ICER threshold was evaluated at \$150 000/QALY.

eTable 17. Estimated health gains and costs associated with Nutrition Facts added sugar labeling on reducing cancer burdens in the US over a lifetime, 1-way sensitivity analyses at 50% of the policy impact and the diet-BMI association (US population=235,162,844)^a

Abbreviations: ICER, Incremental Cost-Effectiveness Ratio; QALY, quality-adjusted life years.

a Values are the median estimates (95% uncertainty intervals) of each distribution of 1000 simulations.

b Health-related costs were inflated to 2015 US dollars using the Personal Health Care (PHC) index. Policy intervention costs were inflated to 2015 US dollars using the Consumer Price Index. Negative costs represent savings.

^cCosts are medians from 1000 simulations so may not add up to totals.

d Net costs were calculated as policy costs minus health-related costs from reduced cancer burdens. Societal perspective includes healthcare cost, patient time costs, productivity costs, and policy implementation costs; government perspective included policy costs relevant to policy implementation and program monitoring and evaluation and medical costs. ^e ICER threshold was evaluated at \$150 000/QALY.

eTable 18. Estimated health gains and costs associated with Nutrition Facts added sugar labeling on reducing cancer burdens in the US over a lifetime, threshold analyses on policy impact (US population=235,162,844)^a

Abbreviations: ICER, Incremental Cost-Effectiveness Ratio; QALY, quality-adjusted life years.

a Values are the median estimates (95% uncertainty intervals) of each distribution of 1000 simulations.

b Health-related costs were inflated to 2015 US dollars using the Personal Health Care (PHC) index. Policy intervention costs were inflated to 2015 US dollars using the Consumer Price Index. Negative costs represent savings.

^cCosts are medians from 1000 simulations so may not add up to totals.

^d Net costs were calculated as policy costs minus health-related costs from reduced cancer burdens. Societal perspective includes healthcare cost, patient time costs, productivity costs, and policy implementation costs; government perspective included policy costs relevant to policy implementation and program monitoring and evaluation and medical costs. e ICER threshold was evaluated at \$150 000/QALY.

eFigure 1. Diet and Cancer Outcome Model (DiCOM)

The model consists of four general health states: (a) healthy without cancer (healthy state); (b) initial cancer diagnosis (initial state) for each cancer type *i*; (c) continuing care (continuing state) for each cancer type *i*; and (d) death state. Transitions between states are based on national cancer incidence and cancer-specific mortality rates from SEER (for individual with cancer) and lifetable-based mortality rates (for individuals without cancer). The model simulates the policy impact on the number of new cases and deaths of 13 obesity-associated cancers, health-related quality of life (HRQOL), and health-related costs among U.S. adults over a lifetime by comparing a policy scenario (added sugar label) to a non-policy scenario (status quo).

eFigure 2. Estimated reduced new cancer cases and deaths associated with Nutrition Facts added sugar labeling policy in the US by age, gender, race/ethnicity, and cancer type over a lifetime

Cancer Deaths Averted

eFigure 3. Estimated life years and QALYs gained associated with Nutrition Facts added sugar labeling policy in the US by age, gender, and race/ethnicity over a lifetime

Consumer Behavior Consumer Behavior + Industry Response

eFigure 4. Estimated changes of heath-related costs associated with Nutrition Facts added sugar labeling policy in the US by age, gender, race/ethnicity and cancer type over a lifetime

Consumer Behavior + Industry Response

Medical Cost (\$, millions) **Medical Cost (\$, millions)**

Consumer Behavior

Consumer Behavior + Industry Response

Productivity Loss (\$, millions) **Productivity Loss (\$, millions)**

Consumer Behavior

Consumer Behavior + Industry Response

Patient Time Cost (\$, millions) **Patient Time Cost (\$, millions)**

(C)

eFigure 5. Estimated net costs from societal and healthcare perspectives associated with Nutrition Facts added sugar labeling policy in the US by age, gender, and race/ethnicity over a lifetime

Net Costs (\$ millions)

eFigure 6. **One-way sensitivity analysis of net costs of Nutrition Facts added sugar label and obesity-associated cancer rates to varying assumptions of key input parameters from (A) societal perspective and (B) healthcare perspective**

Societal Perspective

1a) conservative policy impact assumed half of the base-case policy impact (consumer behavior: -3.3%; industry reformulation: -4.13%); 1b) optimistic policy impact assumed two times of the base-case policy effect (consumer behavior: -13.0%; industry reformulation: -16.5%); 2a) weaker diet-BMI association assumed half of the base-case diet-BMI association (healthy-weight: 0.05 kg/m²; overweight/obese: 0.12 kg/m²); 2b) stronger diet-BMI association assumed two times of the base-case diet-BMI association (healthy-weight: 0.20 kg/m²; overweight/obese: 0.46 kg/m²); 3) 2% annual increase in medical expenditure on cancer care; 4a) lower policy implementation costs assumed 25% of the total costs for implementing the Nutrition Facts label; 4b) higher policy implementation costs assumed 75% of the total costs for implementing the Nutrition Facts label; 5a) lower discounting rate assumed 0% discounting rate; and 5b) higher discounting rate assumed 5% discounting rate. Under base-case scenario (policy effect assumed consumer behavior: -6.6%, and industry reformulation: -8.25%; diet-BMI association assumed healthy-weight: 0.1 kg/m2, and overweight/obese: 0.23 kg/m2; medical expenditure on cancer care assumed 0% annual increase; policy implementation costs assumed 50% of the total costs for implementing the Nutrition Facts label; discounting rate assumed 3%), the policy was cost-saving from both societal and healthcare perspectives. The policy remained cost-saving for all sensitivity analyses from the healthcare perspective and from societal perspective with additional industry reformulation. With consumer behavior alone, the policy was cost-saving when under 1b, 2b, 3, 4a, and 5b and was cost-effective under 1a (ICER: \$8330/QALY), 2a (\$8320/QALY), 4b (\$933/QALY), and 5b (\$1680/QALY).

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