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Systematic Review

Estimation and Prediction of Avoidable Health Care Costs of Cardiovascular Diseases and Type 2 Diabetes Through Adequate Dairy Food Consumption: A Systematic Review and Micro Simulation Modeling Study

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Abstract

Background: Recent evidence from prospective cohort studies show a relationship between consumption of dairy foods and cardiovascular diseases (CVDs) and type 2 diabetes mellitus (T2DM). This association highlights the importance of dairy foods consumption in prevention of these diseases and also reduction of associated healthcare costs. The aim of this study was to estimate avoidable healthcare costs of CVD and T2D through adequate dairy foods consumption in Iran.

Methods: This was a multistage modelling study. We conducted a systematic literature review in PubMed and EMBASE to identify any association between incidence of CVD and T2DM and dairy foods intake, and also associated relative risks. We obtained age- and sex-specific dairy foods consumption level and healthcare expenditures from national surveys and studies. Patient level simulation Markov models were constructed to predict the disease incidence, patient population size and associated healthcare costs for current and optimal dairy foods consumption at different time horizons (1, 5, 10 and 20 years). All parameters including costs and transition probabilities were defined as statistical distributions in the models, and all analyses were conducted by accounting for first and second order uncertainty.

Results: The systematic review results indicated that dairy foods consumption was inversely associated with incidence of T2DM, coronary heart disease (CHD) and stroke. We estimated that the introduction of a diet containing 3 servings of dairy foods per day may produce a $0.43 saving in annual per capita healthcare costs in Iran in the first year due to saving in cost of CVD and T2DM treatment. The estimated savings in per capita healthcare costs were $8.42, $39.97 and $190.25 in 5, 10 and 20-years' time, respectively. Corresponding total aggregated avoidable costs for the entire Iranian population within the study time horizons were $33.83, $661.31, $3,138.21 and $14,934.63 million, respectively.

Conclusion: Our analysis demonstrated that increasing dairy foods consumption to recommended levels would be associated with reductions in healthcare costs. Further randomized trial studies are required to investigate the effect of dairy foods intake on cost of CVD and T2DM in the population.

Keywords: Avoidable cost, Cardiovascular diseases, Dairy foods, Diabetes, Iran, Markov model

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Introduction

Healthcare costs have been growing rapidly over the last 3 decades in many countries including Iran, causing concern among governments, patients and insurance companies. Among the leading causes of mortality in Iran are cardiovascular diseases (CVDs), diabetes and cancer, which account for more than 70% of all deaths.[1] These diseases also impose a great burden on the country's economy in terms of healthcare costs and low productivity.[2–4] These diseases account for almost half of

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total healthcare expenditure in all countries.[5]

Results from the Global Burden of Disease (GBD) study show that unhealthy or poor diet is the leading risk factor for chronic diseases in many countries, including Iran.[6] But so far, little attention has been given to the possible effects of dietary food intake modifications on the risk of developing one or more aforementioned chronic diseases and their related healthcare costs. Data published in the past 2 decades from randomized controlled trials (RCTs) and prospective studies suggest that dairy foods are among the main food groups that can be used to reduce the burden of various medical conditions.[7–16] Recent studies have shown that the dietary approaches to stop hypertension (DASH), a dietary pattern which is high in fruit, vegetables, nuts, fish, and low-fat dairy foods, can reduce blood pressure effectively, which may in part be attributed to its relatively high content of low-fat dairy foods.[7,17,18] The mechanisms by which dairy foods affect CVD incidence are diverse and include both positive and negative influences. Dairy foods are rich in protein (casein and whey), vitamins (riboflavin and vitamin B-12) and minerals (calcium, potassium, and magnesium) that can have beneficial effects on CVD.[19] Saturated fat in dairy foods, on the other hand, can adversely influence coronary heart diseases (CHDs). In general, synthesis of the literature shows that dairy foods consumption may have protective effects on hypertension, CHD and stroke incidence.[14,16,20–25] Recent studies suggest that there is also a significant inverse association between intakes of dairy foods and type 2 diabetes mellitus (T2DM).[10,11,26]

Although dairy foods consumption, including milk, cheese, and yogurt, have been encouraged through the food-based dietary guidelines in Iran,[27] results from recent studies show that most people in Iran do not consume enough dairy foods. Based on the updated dietary guideline recommended intakes of dairy, including for those following a vegetarian eating pattern, are 3 daily servings for Americans nine and older, 2.5 servings for children ages 4 through 8 and 2 servings for children ages 2 through 3 years old. The Mediterranean eating pattern calls for only 2 servings of dairy for adults per day.[28] Special emphasis is placed on consuming more fat-free and low-fat milk and milk products in particular. Results from dietary surveys show that on average, people in Iran are consuming about 0.7 servings of milk, 0.9 servings of cheese and 1 servings of yogurt per day.[8,29,30] Dairy consumption decreases with age, and the gap between actual and recommended dairy consumption widens through adulthood with less than 1.5 dairy servings consumed by adults over the age of 50 years.

A reduction in the incidence of chronic diseases through adequate dairy consumption may improve population health and reduce healthcare costs. This may be considered improbable in the short term given the complex effects of dietary risk factors on diseases incidence. But results from prospective cohort studies show a significant association between certain medical conditions and dairy consumption.[7–9,16] Moreover, results from dose–response meta-analysis studies which provide vital information in judging the causal relationships when data from RCTs are sparse, suggest that the relationship between dairy consumption and T2DM and CVD are undeniable.[10,11,20] Up to now, efforts to increase consumption of dairy foods at the population-level have received little support from policy-makers. Unavailable or insufficient estimates of the mortality and economic burden of diseases due to low intake of dairy foods can partly explain the lack of attention to the above mentioned efforts. To address this important knowledge gap, we aimed to use the most recent epidemiological and economic data to estimate avoidable CVD and T2DM healthcare costs through increased dairy foods consumption.

Methods

Study Design

This is a modelling study and data from previous literature and national databases were used to present 2 disease models to estimate avoidable T2DM and CVD healthcare costs. First, a systematic literature review was conducted to identify any association between different levels of dairy foods consumption and incidence of CVD and T2DM, using dose response meta-analysis studies. Second, we obtained age- and sex-specific dairy foods consumption statistics from national studies. Third, healthcare expenditures associated with CVD and T2DM were obtained from national studies and health system registries. Finally, using all data from previous steps as well as other epidemiological data, a Markov model for each disease was constructed to estimate avoidable direct healthcare costs of CVD and T2DM through increased dairy consumption to optimum level (Figure 1). Below we have described details of the methods used in each step.

Step 1: Identification of Diseases Related to Dairy Consumption

We conducted a systematic literature review to identify studies which investigated the relationship between dairy consumption and several medical conditions. The medical conditions included were CHD, stroke and T2DM. We conducted our search in 2015, which was updated on February 07, 2016. We searched PubMed (1946 – Search Date) and EMBASE (1974–2016 February) via Ovid SP with no date/time, language, or document type limitation. Search terms were collected through experts'
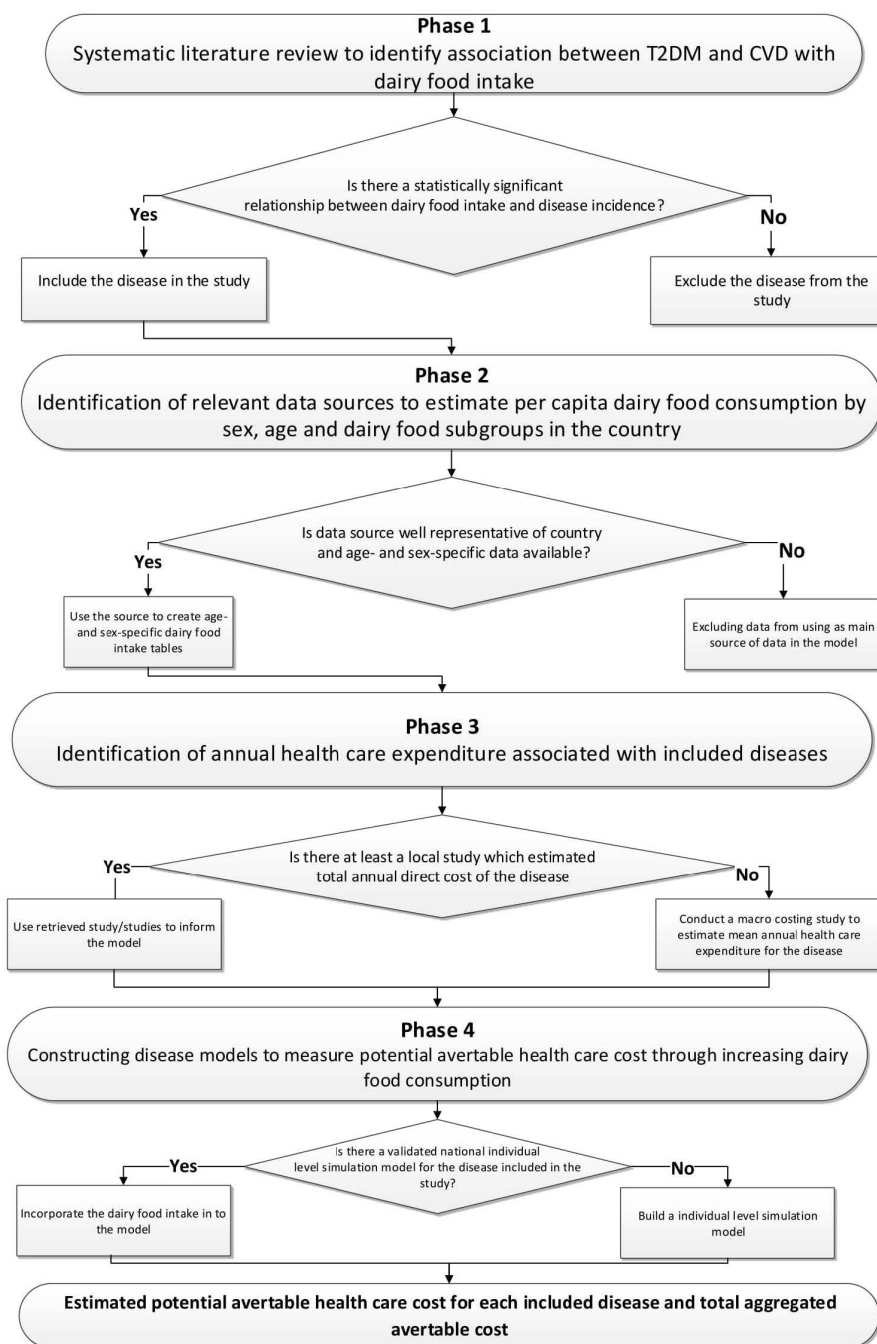
Figure 1. Study Phases' Flowchart.

opinion, literature review, and controlled vocabulary (Medical Subject Headings [MeSH] and Excerpta Medica Tree [EMTREE]). Search strategies developed by assistance of a medical information specialist. The review included secondary research (meta-analyses and pooled analyses) that investigated the relation between consumption of different types of dairy foods among adults and the elderly population and incidences of the included medical conditions. We excluded all non-human studies, narrative review articles, case reports, and editorials. Two methodologists selected the studies based on the study inclusion criteria. In case of disagreement, a third reviewer reconciled the decision to make the final

selection. We critically appraised the included studies using AMSTAR, a measurement tool to assess systematic reviews and meta-analysis studies. All included studies were summarized in narrative form and in summary tables that display the important features of the studies including: outcomes, sample sizes, and incidence summary measures (Table 1).

Step 2: Estimation of Per Capita Dairy Consumption by Sex, Age and Dairy Food Subgroups

Two important sources of data were identified to be used for estimating average per capita dairy consumption. The first one is a survey conducted by Statistical Centre

Table 1. Selected Studies That Reported a Significant Association Between Dairy Consumption and Incidence of T2DM and CVD Diseases

Outcome	Studies Included in Each Meta-Analysis	Unit of RR	RR (95% CI)	Source
CHD	7	For <1.5 servings/day	0·88 (0·80–0·96)	[20]
CHD	9	For 1.5–3 servings/day	0·93 (0·85–1·00)	[20]
CHD	5	For >3 servings/day	0·86 (0·79–0·94)	[20]
Stroke	15	For <1.5 servings/day	0·92 (0·89–0·96)	[20]
Stroke	10	For >1.5 servings/day	0·91 (0·88–0·95)	[20]
T2DM	13	Per 200 g/d	0.94 (0.91–0.97)	[20]

Abbreviations: RR, relative risk; CHD, coronary heart diseases; T2DM, type 2 diabetes mellitus; g/d, gram/day.

of Iran (SCI) for the last 2 decades. The SCI survey provides annual average dairy consumption. The dataset is nationally representative and presents the information on all different types of dairy foods including milk, cheese, butter, yogurt and other forms of dairy foods consumed in rural and urban households. Although the SCI food database provides detailed information on dairy consumption, it does not provide age- and sex-specific statistics on food consumption at the household-level. The second data source was a study conducted within the framework of the Tehran Lipid and Glucose Study (TLGS), a large prospective cohort study that used a representative sample of the Iranian urban population.[31] In the TLGS study, normal dietary intake was assessed using a 168-item food-frequency questionnaire (FFQ). The FFQ consists of a list of foods with a standard serving size. All participants in the study were asked to report the frequency of consumption of different types of foods during previous year on a daily, weekly and monthly basis. Dairy foods were classified into 3 groups including milk, yogurt and cheese according to the US Food Guide

Pyramid. Since FFQ provides reasonably valid measures of dairy consumption compared to the questionnaire used in the SCI survey, and given that data from the SCI is provided at the household-level while data from TLGS provides age- and sex specific data, we used the second dataset to estimate average per capita dairy consumption. Since the selected dataset is only representative of the urban population (~70% of all population), we adjusted the mean per capita dairy consumption in urban areas using the relative consumption reported in the SCI survey to estimate mean consumption level for rural population. Average dairy food consumption by sex, age and food are presented in Table 2.

Step 3: Direct Healthcare Expenditure Associated With Included Diseases

We obtained direct healthcare expenditure associated with diseases included in this study from previous local studies and medical expenditure registries in Iran. To estimate annual cost of patients with T2DM, we used the most recent estimates by Javanbakht et al.[4] They performed a

Table 2. Dairy Foods Intake Per Person (g/d)

Age Group	Sex	Milk*		Yogurt*		Cheese*	
		Mean	SD	Mean	SD	Mean	SD
1–9	Male	269.7	341.6	189.1	245.8	22.1	24.6
	Female	264.6	335.1	222.1	265.1	21.8	21.2
10–19	Male	252.4	341.1	224.9	291.1	26.2	27.5
	Female	213.4	322.7	231.2	300.9	23.0	24.7
20–29	Male	169.0	254.9	228.7	281.5	24.5	26.0
	Female	168.4	273.4	208.2	263.8	21.9	24.1
30–39	Male	151.9	233.3	210.0	249.7	23.8	24.6
	Female	180.1	279.2	211.8	257.9	25.1	24.2
40–49	Male	136.5	220.6	201.1	238.1	24.8	21.4
	Female	155.7	243.3	202.3	243.9	25.3	19.9
50–59	Male	133.5	215.5	201.5	241.6	24.9	22.0
	Female	164.7	264.5	195.8	231.3	24.7	18.9
60–69	Male	147.1	232.5	187.7	213.7	24.9	21.2
	Female	158.7	267.2	198.3	234.7	24.7	21.2
70+	Male	170.1	259.6	198.0	229.6	26.4	23.5
	Female	146.7	226.0	182.7	200.0	25.4	20.0

* Includes all types of milk (i.e. low fat and high fat milk and chocolate milk); all types of yogurt; all types of cheese.

systematic literature review and Bayesian meta-analysis to estimate the cost of patients with T2DM in Iran. They concluded that in 2009, the mean annual direct cost of patients with T2DM was US$556 (posterior standard deviation [PSD]: 221).

To estimate the cost associated with CVD, a macro-costing approach was taken because no national study was found in our search. Firstly, we defined relevant specific disease conditions that are included under the umbrella term CVD based on the International Disease Classification (ICD-10). These codes were (I20- I25) for CHD, (I10-I15) for hypertension and (I60-I69) for stroke. Secondly, using hospital information system registries, 12 506 medical record files were extracted for patients who were admitted from March 2014 – September 2014 in 6 main hospitals in 4 different provinces of Iran (Tehran, Esfahan, Fars and Kurdistan, which account for 33% of the entire population in Iran). Thirdly, since our aim was to estimate the real cost of healthcare from public and private perspective, and given that all selected hospitals were in the public sector (90% of all hospital beds belong to public sector in Iran), we adjusted all hospital charges to reflect the real cost of care. Fourthly, we calculated mean cost of each episode of hospitalization for each health condition using hospital admissions registry. A total annual inpatient cost was estimated separately for CHD, stroke and hypertension. Finally, as we aimed to estimate annual direct health expenditure per patient, we used the ratio of inpatient cost to total direct cost to estimate total annual direct cost. Costs of other diseases included in the study were obtained from previous studies (Table S1, Supplementary Materials). After summarizing the estimated average cost of diseases, all costs were converted to US$ using an exchange rate (1$ equal to 32 000 Iranian Rial), and inflated to 2016 price using consumer price index in Iran.[32]

Step 4: Modelling

After identifying the diseases that are significantly related to dairy consumption and estimating annual per capita cost, we built a Markov micro simulation (MM) model to predict the incidence of each disease at current and optimal levels of dairy consumption. The MM model is a computer modelling technique that simulates individual lives. The model uses person-level features including a unique identifier and a set of associated attributes such as age, sex, level of dairy consumption and disease condition. We applied a set of transition probabilities and costs inputs in the models. The models used all the defined parameters and transition probabilities over many time steps and simulated individuals through the model one at a time and generated individual life histories of a simulated population.[33,34]

CVD Model

We constructed our CVD MM model with 7 health states named: Healthy, hypertension, post stroke, CHD, CVD-related death, net emigration and death from background mortality. Figure S1 (see online Supplementary Materials) shows the structure of the CVD MM model. CHD health state includes patients with myocardial infarction and angina. A Markov model is a stochastic model describing a sequence of possible events in which the probability of each event depends only on the state attained in the previous event. Individual populations were simulated to pass through the model one at a time where they may exit because of CVD-related or background death or net emigration. If a case develops CVD, the model tracks disease progression in a cohort based on the defined transition probabilities.[4] We obtained distribution of Iranian population in different age groups from the latest national census database.[35] The most recent Iranian life table was used to estimate age- and sex-specific probability of death from background mortality.[36] Age- and sex-specific prevalence of CVD and hypertension were taken from national health surveys and used as the initial distribution of the simulated cohort in the Markov states.[37–40] We used recent data provided by the national surveillance of risk factors of non-communicable diseases (SRFND) and other national studies to obtain age- and sex-specific incidence of CVD.[38,41] To estimate CVD incidence in the second arm (optimal dairy consumption), we linked the incidence rates to consumption level of various dairy foods (Table S1, Supplementary Materials). Results from dose-response meta-analysis provided us with RR of CVD incidence for different levels of dairy consumption. We assumed that dairy consumption was protective if only they were taken up to their recommended levels.

When a CVD event happened, it was either fatal or non-fatal. We obtained age- and sex-specific probabilities of having a fatal CVD event from an Iranian population-based cohort study (population-based Isfahan Cohort Study (ICS)) which has reported fatal and nonfatal incidence rates of IHD and stroke in a cohort of population in Iran based on 32,893 person-years of follow-up.[41] We assumed that transitions across health states occur annually. The relevant annual costs assigned to each health state were based on the findings from phase 3 of the study. As we aimed to estimate total avoidable healthcare cost, we simulated a representative cohort sample of entire Iranian male and female population from 2016. We estimated the expected avoidable cost using 1, 5, 10 and 20 years' time-horizons.

CVD Model Validation

To assess validity of the model, we followed the

International Society for Pharmacoeconomics and Outcomes Research (ISPOR) task force guideline.[42] To validate the structure of the CVD model, the models as well as input data and results were presented to an expert group of health professionals to determine face validity. The group was asked to evaluate the model structure and assumptions in comparison to real world circumstances. We conducted a wide series of sensitivity analyses to evaluate internal validity of the CVD model. We assigned some null and extreme values for input parameters such as zero unit cost or probabilities and ran simulations separately for each validation scenario to compare results with base case values and to test the robustness of the outputs.

T2DM Model

To estimate total avoidable healthcare cost associated with T2DM, we used the model which was already developed by the current study's team. All details of the model have been described elsewhere,[4] in brief, the T2DM MM model contained 6 health states: Healthy, undiagnosed diabetes, diagnosed diabetes, net migration, diabetes-related death and death from background mortality (Figure S2, Supplementary Materials). As per the CVD model, we linked the incidence of T2DM to dairy foods consumption data which were incorporated into the T2DM MM model to estimate avoidable healthcare cost.

Sensitivity Analysis

To explore parameter uncertainty in the model, we conducted probabilistic sensitivity analysis (PSA). To conduct PSA, we defined input parameters including costs and transition probabilities as statistical distributions in the model. Ranges and distributional assumptions for input parameters were based on the literature and nature of the parameters. We ran the base-case analysis as probabilistic with a generation of 1000 trials within each individual level simulation. In other words, the model repeated the simulation 1000 times for each individual. Each time, the analysis drew the model parameters from the pre-specified probability distributions. We assigned beta distribution for transition probabilities, gamma distribution for cost, and log-normal distribution for RRs (Table S1, Supplementary Materials). We used TreeAge Pro 2014 software to construct and run all the models and the simulations.

Results

There were 287 records from PubMed and 429 records from EMBASE. After removing 181 duplicates, 2 researchers screened 535 records based on title and abstract. 452 studies were excluded during screening,

because they were irrelevant to our research question. Eighty-four studies were selected for full text assessment using inclusion and exclusion criteria. Finally 12 studies including 4 studies for diabetes.[10,43–45] and 8 for CVD,[20,22,46–51] were included and appraised using AMSTAR tool. Process of selection of studies is shown in PRISMA flow diagram (Figure 2). Results from our systematic review indicated that T2DM, CHD and stroke were significantly associated with level of dairy foods consumption.

T2DM

After assessing all included studies for T2DM using the AMSATR tool, a study conducted by Gao et al[10] was used to inform the T2DM model. Results from the T2DM model revealed a per capita savings of $0.20, $5.93, $30.57 and $142.56 within 1, 5, 10 and 20 years' time horizon, respectively, due to a reduction in T2DM incidence by increasing dairy foods consumption to its optimum level. Total avoidable costs for all Iranian populations within the modelling time horizons were estimated to be $15.64, $465.78, $2400.13 and $11191.16 million, respectively.

CVD

Among included studies regarding relationship between CVD and dairy foods consumption, Alexander et al[20] was selected based on the AMSATR tool to inform the CVD model. The results showed that average avoidable per capita healthcare costs were $0.23, $2.49, $9.40 and $47.69 in 1, 5, 10 and 20-years' time horizon, respectively, and corresponding total estimated avoidable costs among entire Iranian population were $18.19, $195.53, $738.08 and $3743.47 million, respectively.

Total Avoidable Costs

Including all avoidable costs from T2DM and CVD revealed that the introduction of a diet containing 3 servings of dairy foods/day may produce a $0.43 saving in annual per capita healthcare cost in Iran in the first year. The estimated savings in per capita health cost were $8.42, $39.97 and $190.25 in 5, 10 and 20-years' time horizon, respectively. Corresponding total aggregated avoidable cost for entire Iranian population within the study time horizons were $33.83, $661.31, $3138.21 and $14934.63 million, respectively. A summary of the estimations for all diseases can be found in Table 3.

Discussion

Our analysis demonstrates significant reductions in healthcare cost that could be achieved by increasing consumption of dairy foods to the recommended levels. Doidge et al[52] conducted a study to estimate the

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┌─────────────┐
│ Identification │   ┌─────────────────────────┐
└─────────────┘   │ Records identified through │
                  │    database searching       │
                  │       (n = 716 )            │
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│  Screening  │   │ Records after duplicates removed │
└─────────────┘   │       (n = 181 )            │
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                  │   Records screened        │──▶│ Records excluded (title  │
                  │       (n = 535 )          │   │ and abstract screening)  │
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┌─────────────┐   ┌─────────────────────────┐   ┌─────────────────────────┐
│ Eligibility │   │ Full-text articles assessed │──▶│ 72 full-text articles    │
└─────────────┘   │    for eligibility          │   │ excluded                 │
                  │       (n = 84 )             │   │ Not reporting association │
                  └─────────────────────────┘   │ between dairy products   │
                               │                 │ and including diseases,  │
                               ▼                 │ Editorials, letter to    │
                  ┌─────────────────────────┐   │ editors, Conference      │
                  │ 12 studies included in    │   │ abstracts, review articles │
                  │ study and assessed with   │   │    (n = 72 )             │
                  │ AMSTAR tool               │   └─────────────────────────┘
                  │ 8 CVD and hypertension    │
                  │ 4 T2DM                    │
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│  Included   │   │ 2 studies that were reported a │
└─────────────┘   │ significant association between │
                  │ dairy products consumption and  │
                  │ incidence of T2DM and CVD       │
                  │ were selected to inform the     │
                  │ disease models                  │
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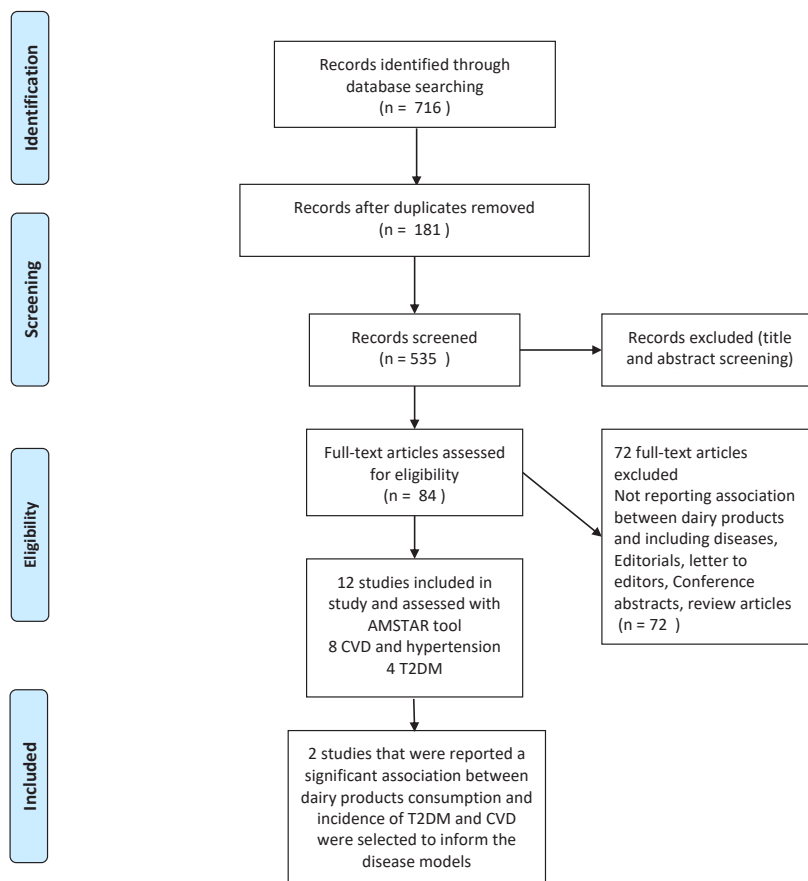
Figure 2. PRISMA Flow Diagram.

direct healthcare expenditure and burden of disease (disability-adjusted life years [DALY]) attributable to low consumption of dairy products in Australia. They found that in 2010–2011 financial year, AUD$2.0 billion (USD$2.1 billion, €1.6 billion, or 1.7% of direct healthcare expenditure) and loss of 75,012 DALY were attributable to low dairy products consumption. McCarron et al[53] also undertook another study to estimate healthcare cost

Table 3. Avoidable CVD and T2DM Healthcare Cost Through Adequate Dairy Intake in Iran

Time Horizon	Average Per Capita Cost (US$)			Total Cost of Iranian Population (Million US$)		
	Current Intake Mean	Optimum Intake Mean	Difference	Current Intake Mean	Optimum Intake Mean	Difference
T2DM						
1-year	95.32	95.12	0.2	7482.73	7467.10	15.64
5-years	507.53	501.59	5.93	39840.78	39375.00	465.78
10-years	1120.87	1090.29	30.57	87988.27	85588.14	2400.13
20-years	2690.25	2547.69	142.56	211184.96	199993.80	11191.16
CVD						
1-year	28.14	27.91	0.23	2209.03	2190.84	18.19
5-years	176.32	173.83	2.49	13840.98	13645.45	195.53
10-years	438.68	429.27	9.4	34436.04	33697.96	738.08
20-years	1078.05	1030.37	47.69	84627.12	80883.65	3,743.47
Total aggregated						
1-year	123.46	123.03	0.43	9691.76	9657.94	33.83
5-years	683.85	675.42	8.42	53681.76	53020.45	661.31
10-years	1559.55	1519.56	39.97	122424.31	119286.10	3138.21
20-years	3768.30	3578.06	190.25	295812.08	280877.45	14934.63

Abbreviations: CVD, cardiovascular disease; T2DM, type 2 diabetes mellitus.

savings associated with adequate dairy foods intake in the United States. The results revealed that if Americans increase their intake of dairy foods to the currently recommended 3 to 4 servings/d, the projected first year savings would be approximately $26 billion, and 5-year cumulative savings would be in excess of $200 billion.

Other studies have reported associations between dairy consumption and incidence of some risk factors including hypertension[12] and obesity,[26,54] while we included only T2DM and CVD in our modeling. We included only direct medical cost in our estimations even though there are other indirect costs and health benefits to dairy consumption. However, including them would have increased the estimated avoidable cost. The indirect costs are related to increased productivity from a healthier workforce. Sensitivity analysis revealed that the results are more sensitive to mean annual cost of diseases, diseases incidence rates and RR of diseases incidence for different levels of dairy foods intake.

Like with all studies, several limitations exist that should be considered when interpreting the results. Firstly, due to limited longitudinal data, we assumed that some of the parameters used in our models were fixed over time, including disease incidence and dairy foods consumption. However, as time passes in the models, the cohorts become older and are at greater risk of developing diseases. Moreover the base-case estimation was based on the PSA which means to estimate results we have accounted for any uncertainty in the parameters used in the models. Second, prediction of avoidable future healthcare costs is related to current rates of healthcare utilization and costs. In our model, we used the most recent estimates of per capita cost rates for modelled diseases. However, per capita healthcare cost and utilization may change over time, and future changes may influence the estimations. Third, although all included meta–analyses used analytical models that were harmonised based on similar exposures and similar outcome classifications, the data used in these studies were generated from observational studies. Therefore, the validity of these meta-analyses is not guaranteed and may be biased, particularly because they are based on nutritional epidemiological studies where information bias is a dominant concern. Fourth, to present our models we classified different types of dairy foods into 3 main groups (milk, yogurt and cheese). Due to insufficient data, splitting results into high- and low-fat dairy foods was not possible, and this could be a source of bias as quality of dairy foods might be different across different countries. In addition, we did not have the distribution of dairy consumption by age-sex in rural areas. We assumed that the distribution is the same as that of the urban areas. However there might be some differences between age and sex pattern of dairy

foods intake in the country. Given that rural population constitutes less than 30% of the population in Iran, and it is unlikely that the pattern is hugely different from the urban areas, therefore we believe this could have minimal effect on the estimated costs. Finally, as we have modelled each disease separately, it is not possible to account for competing risks. Competing risks occur when patients can experience one or more events or outcomes which 'compete' with the other outcomes of interest. For example CVD patients that die due to a fatal CVD event have no chance for T2DM incidence; therefore there is no potential for saving T2DM healthcare cost through increased dairy consumption for those cases, though we believe this would have a minor effect on our estimations. Despite these limitations, using a systematic approach to find the most appropriate evidence and using local cost and sex- and age-specific epidemiologic and dairy consumption data in our analysis has made our results more applicable to local health policy-makers. We believe this method is the most solid and straightforward approach to assess the cost consequences of reducing disease incidence through improved healthy diet which could be utilized to study similar research questions in other disease and risk factor areas.

In conclusion, 2 of the main questions that health policy-makers are faced with are how much health resources should be allocated to encourage the adoption of a healthier diet and also what are the societal costs of current deviations from the recommended diet. Estimation of attributable cost to suboptimal dietary intake can help health policy-makers to understand where effective interventions might yield good returns and which policies and programs are cost effective that should be considered when defining a comprehensive and optimal plan of care to control chronic diseases. Our findings strongly suggest that increasing dairy foods consumption to recommended levels would be associated with significant reductions in CVD and T2DM healthcare cost. Public health nutrition strategies should be directed to encourage people to consume more dairy foods. Also it should be mentioned that the analysis does not suggest that the entire Iranian population should consume the recommended levels of dairy foods; it simply provides an estimate of avoidable CVD and T2DM health care cost by increasing dairy consumption to the recommended levels.

Supplementary Materials

Online Supplementary data contain Table S1 and Figures S1-S2.

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