Fruits and vegetables in the prevention of cancer and cardiovascular disease†

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Abstract

Objective: We quantified the public health benefit of fruits and vegetables on the prevention of cancer and cardiovascular disease (CVD), using currently available human data.

Design: We reviewed over 250 observational studies on cancer and CVD. Relative risks (RRs) for high versus low intake of fruits and vegetables were obtained. The preventable proportion of chronic diseases, i.e. the per cent of cases attributable to low consumption of fruits and vegetables, was estimated using three scenarios: best guess, optimistic (using stronger RRs) and conservative (using weaker RRs and eliminating the contribution of smoking and/or drinking). The preventable proportion was calculated for increasing average intake from the current 250 g day\(^{-1}\) to the recommended 400 g day\(^{-1}\) among the general Dutch population.

Results: It is estimated that in the Netherlands cancer incidence could be reduced by 19% (12,000 cases annually, best guess), ranging from 6% (conservative) to 28% (optimistic). Cardiovascular deaths could be reduced by 16% (8,000 deaths annually, best guess), ranging from 6% to 22%. Evidence is most abundant for gastrointestinal cancers, followed by hormone-related cancers, but limited for other sites and CVD.

Conclusions: Increasing consumption of fruits and vegetables carries a large public health potential. Population trials and biological mechanisms should eventually provide scientific proof of their efficacy. The available evidence is sufficient to justify public health education and promotion aimed at a substantial increase in the consumption of fruits and vegetables.

Keywords

Cancer Cardiovascular disease Fruit Vegetables Public health

High consumption of fruits and vegetables is generally considered to be beneficial to health. Based on abundant literature, the potential public health importance of increased consumption of fruits and vegetables has been widely recognized, both for cancer\(^1,2\) and CVD\(^1\).

Bioactive compounds are held responsible for the benefits, e.g. dietary fibre, vitamin C, carotenoids and components such as glucosinolates, folic acid and (iso)flavonoids\(^3\). In chemoprevention, their mode of action, efficacy and importance to public health has been evaluated\(^6\). Unfortunately, overall testing of the efficacy of fruits and vegetables in population trials is hampered because of methodological factors like blinding, compliance and study duration. This, however, should not distract our attention from the public health impact that can be obtained given the epidemiological evidence already available. To substantiate this, we aimed to quantify the public health benefits of increased consumption of fruits and vegetables for the general Dutch population, taking into account scientific uncertainties by using different scenarios.

Methods

Literature searches and calculations have been described in detail\(^7\). We included analytical epidemiological studies on chronic diseases, published up to early 1998\(^7\). We abstracted results from 269 analyses on cancer sites (195 case–control; 74 prospective, some from the same cohort), and from 14 analyses on CVD (three case–control; 11 prospective).

Depending on study design and analysis, odds ratios or RRs were obtained. These usually represented risk for subjects in the highest versus the lowest category of intake of fruits and vegetables, which reflects a difference of about 1.5–2 servings or about 150 g day\(^{-1}\). Abstracted RRs were adjusted for potential confounders like smoking,
alcohol intake and other factors, as considered relevant in the original papers. Some studies reported RRs for the intake of specific subgroups of fruits and/or vegetables only, and not for their total intake; therefore, our results are based on 217 studies on the disease endpoints shown in Table 1.

To calculate the preventable proportion of chronic diseases, i.e. the per cent of cases attributable to low intake of fruits and vegetables, the desired increase in consumption was set to 150 g day\(^{-1}\) for the population as a whole. The model assumes that the distribution of intake remains similar and is just shifted 150 g day\(^{-1}\) upward. This should result in the current average intake of about 250 g day\(^{-1}\), based on the Dutch Food Consumption Survey (vegetables 128 g day\(^{-1}\), excluding potatoes; fruits 114 g day\(^{-1}\))\(^8\) increasing to the recommended intake (400 g day\(^{-1}\), excluding potatoes). Like most of the abstracted RRs, these figures do not include potatoes, since they are not perceived as vegetable food in the Netherlands and they are bulk food in the traditional hot meal (average intake 118 g day\(^{-1}\))\(^8\).

As shown in Table 2, the preventable proportion was calculated using three scenarios – ‘best guess’, ‘optimistic’ and ‘conservative’ – each representing a different set of assumptions or interpretations of the scientific evidence. Calculations differed with respect to the site-specific RRs used (Table 1). Furthermore, for the ‘conservative’ scenario for cancer we subtracted cases attributable to smoking and alcohol prior to the calculations, using published site-specific estimates\(^9\); for CVD, we assumed an RR of 2.0 for smoking and 1990 figures for smoking prevalence\(^10\), resulting in 26% of cases attributable to smoking. To calculate the preventable proportion, the disease-specific RRs for each scenario (Table 1) were applied to cancer incidence and CVD mortality in the Netherlands\(^10,11\). The results section provides an example.

### Results

Table 1 presents RRs of cancer and CVD for high versus low intake of fruits and vegetables as used in the three scenarios. With respect to the studies identified, gastrointestinal cancer sites are most frequently studied (41% of 205 cancer studies), followed by the respiratory tract (25%) and hormone-dependent cancers (20%). Regarding cancer incidence in the Netherlands, hormone-related cancers are highly relevant (28% of all incident cases), followed by gastrointestinal and respiratory tract cancers (17% each). For CVD, over 50% of deaths are due to coronary heart disease and stroke, but the number of studies that addressed fruits and vegetables is disproportionately low as compared to cancer (6% of all 217 studies mentioned).

Using the RRs from Table 1, we calculated the number of cases attributable to low consumption of fruits and vegetables, for each of the three scenarios. For example, for oesophageal cancer, the ‘best guess’ RR for high versus low fruit and vegetable intake is 0.54; thus, if the population increases fruit and vegetable consumption by 150 g day\(^{-1}\) on average, the oesophageal cancer incidence would decrease by 46%. As oesophageal cancer represents 1.5% of the total cancer incidence in the Netherlands...

### Table 1 The main data used for the calculation of the preventable proportion of chronic diseases

<table>
<thead>
<tr>
<th></th>
<th>Proportion of total cancer incidence/CVD mortality (%)(^*)</th>
<th>Number of studies used for estimation†</th>
<th>RR for scenario‡</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td>Best guess</td>
</tr>
<tr>
<td><strong>Cancer</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Upper respiratory tract</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Oral cavity, pharynx</td>
<td>1.1</td>
<td>6</td>
<td>0.52</td>
</tr>
<tr>
<td>Larynx</td>
<td>1.9</td>
<td>10</td>
<td>0.45</td>
</tr>
<tr>
<td>Lung</td>
<td>13.9</td>
<td>35</td>
<td>0.58</td>
</tr>
<tr>
<td>Gastrointestinal</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Oesophagus</td>
<td>1.5</td>
<td>23</td>
<td>0.54</td>
</tr>
<tr>
<td>Stomach</td>
<td>3.7</td>
<td>26</td>
<td>0.49</td>
</tr>
<tr>
<td>Colon/rectum</td>
<td>11.3</td>
<td>36</td>
<td>0.63</td>
</tr>
<tr>
<td><strong>Hormone-related</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Breast</td>
<td>15.9</td>
<td>20</td>
<td>0.84</td>
</tr>
<tr>
<td>Endometrium</td>
<td>2.2</td>
<td>5</td>
<td>0.78</td>
</tr>
<tr>
<td>Prostate</td>
<td>9.9</td>
<td>16</td>
<td>0.93</td>
</tr>
<tr>
<td><strong>Other</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pancreas</td>
<td>2.1</td>
<td>15</td>
<td>0.62</td>
</tr>
<tr>
<td>Bladder</td>
<td>3.2</td>
<td>7</td>
<td>0.65</td>
</tr>
<tr>
<td>Kidney (renal cell)</td>
<td>1.8</td>
<td>6</td>
<td>0.80</td>
</tr>
<tr>
<td><strong>Cardiovascular disease</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Coronary heart disease</td>
<td>39.6</td>
<td>8</td>
<td>0.70</td>
</tr>
<tr>
<td>Stroke</td>
<td>24.1</td>
<td>4</td>
<td>0.85</td>
</tr>
</tbody>
</table>

\(^*\)Total incidence of cancer and total mortality of cardiovascular disease (CVD) was set to 100%.

\(^†\)Most studies addressed incidence; for CVD, mortality figures were used instead.
Public health impact of fruits and vegetables

(Table 1), the latter would reduce by 46% of 1.5% = 0.7%.

Since 75% of oesophageal cancer incidence has been attributed to smoking and/or alcohol, we restricted the calculations in the conservative scenario (RR = 0.61, see Table 1) to the 25% of cases not attributable to smoking and/or drinking. Thus, in this scenario, the preventable proportion by increased fruit and vegetable consumption would only be 39% times 25% times 1.5%, i.e. 0.1% of total cancer incidence. These calculations were repeated for all the disease endpoints mentioned and the results were added to obtain the total preventable proportion for each scenario. For CVD, similar procedures were followed; however, mortality figures were used instead, as reliable incidence data of CVD were not available for the Netherlands.

Based on the above calculations, we estimated that an increase in the consumption of fruits and vegetables of 150 g day\(^{-1}\) on average, will eventually reduce cancer incidence by 19% (best guess), ranging from 6% (conservative) to 28% (optimistic). In the Netherlands, this would result in 12 000 preventable cases (best guess), ranging from 4500 (conservative) to 17 500 on an annual basis (optimistic). For CVD, the proportion of preventable deaths is estimated at 16% (8000 deaths year\(^{-1}\)) for the best guess, ranging from 6% (3000 deaths year\(^{-1}\)) to 22% (11 500 deaths year\(^{-1}\)). Figure 1 shows the projected cancer incidence and cardiovascular deaths as a function of intake of fruits and vegetables, taking the current intake of 250 g day\(^{-1}\) as the starting point. Figure 1 makes clear that our calculations assume linearity of the dose–response relation for fruits and vegetables. Within the range presented, one can read the preventable proportion in similar populations for each scenario.

**Discussion**

We quantified the potential impact of increased consumption of fruits and vegetables in the prevention of major types of cancer and CVD, estimating that 6–28% of cancer incidence and 6–22% of CVD mortality may be preventable if the Dutch population adheres to the national dietary guidelines, that is if they increase fruit and vegetable intake by 1–2 servings per day. Because these estimates are based on observational studies, they represent the overall effect of beneficial and adverse

### Table 2 Data sources and calculation of the preventable proportion of cancer and cardiovascular disease according to three scenarios

<table>
<thead>
<tr>
<th>Scenario</th>
<th>Calculation of RRs for Table 1</th>
<th>Data source of RRs</th>
</tr>
</thead>
<tbody>
<tr>
<td>Best guess</td>
<td>Mean disease-specific summary RR of the three landmark reviews and the midpoint RR of recent studies, weighed by the number of studies</td>
<td>For cancer, three landmark review papers† each provided their own best estimate site-specific RRs based on all the studies they reviewed. For more recent studies on cancer, and for the studies on CVD, we ranked the site-specific RRs and excluded outliers.</td>
</tr>
<tr>
<td>Optimistic</td>
<td>Lowest* disease-specific summary RR from each of the three landmark reviews and the lowest RR of recent studies (excluding outliers), weighed by the number of studies</td>
<td></td>
</tr>
<tr>
<td>Conservative</td>
<td>Highest* disease-specific summary RR from each of the three landmark reviews and the highest RR of recent studies (excluding outliers), weighed by the number of studies. In addition, cases attributable to alcohol (cancer endpoint) and smoking (cancer and CVD) were eliminated before calculating the preventable proportion</td>
<td></td>
</tr>
</tbody>
</table>

\*Because of the protective effect, a lower RR indicates a stronger inverse association and a higher RR reflects a weaker association, closer to the null hypothesis RR = 1.

†The reviews used were by Steinmetz and Potter, Block et al., and Margetts et al.\(^3\).
properties of fruits and vegetables in the amounts and
diversity as prepared by and consumed in the general
population.

An important issue is the internal validity of the
underlying observational studies, which relates to pub-
lication bias and study design. After the cancer-reducing
effects of fruits and vegetables were put forward by three
landmark reviews1–3, it may have become easier to publish
less favourable results thereafter. Indeed, we observed that
results from studies on cancer published after 1994 tended
to be somewhat weaker. This, however, is not due to
methodologically stronger studies becoming available
since the proportion of cohort studies was similar and
there were no major differences with case–control studies.
Furthermore, there was no obvious shift towards other
cancer sites that could be less strongly related to diet, since
the proportion of studies on gastrointestinal, hormone-
related and lung cancers remained similar. Thus, we
cannot exclude some publication bias in the older
studies on major cancer sites and on disease endpoints
of recent interest. Therefore, future studies might require
us to adapt the preventable proportion for CVD and some
cancer sites. It seems unlikely, however, that the
preventable proportion for total cancer would be
materially different since epidemiological studies have
addressed the role of fruit and vegetables in the major
cancer sites for a long time.

Apart from fruits and vegetables, cigarettes and alcohol
need attention as major risk factors. Although this was
taken into account in most of the studies, the inverse
associations for fruits and vegetables might partially result
from insufficient statistical adjustment in the original
studies. We assumed that other potentially relevant
confounders, e.g. socioeconomic status, were taken into
account in the original publications, if necessary. To a
large extent, however, such confounding will have been
accounted for already by adjustment for smoking and
drinking habits. Since some residual confounding by
smoking and drinking cannot be excluded, our
conservative estimate excluded all cases attributable to
smoking and/or drinking, based on independent estimates
of their RRs5. These methodological considerations should
discount the public health potential of fruit and
vegetables, however. Beyond that, public health campa-
igans should not ignore increasing fruit and vegetable
consumption until other risk factors have been eliminated.
The best guess and optimistic scenario take cigarette
smoking as an unfortunate fact of life among the Dutch
population, and the conservative scenario serves as a
reasonable lower limit for our calculations.

The time-lag between increasing intake of fruits and
vegetables and the emergence of the full public health
effect may span many years. If increased consumption of
fruits and vegetables reduces early disease stages, like
initiation of cancer or the emergence of fatty streaks, it will
take decades before disease rates are affected. If late stages
of disease are involved, e.g. in cancer suppression or
haemostatic factors, the time frame may be much shorter.
This can be studied in relatively short-term primary or
secondary prevention trials, which use metabolic effects
and intermediary or early clinical risk markers as the
endpoints. These additional pieces of evidence will be
complementary to the apparent ‘black box’ approach in
observational studies. The full public health effect may
take even longer to emerge, since health education
programmes and adaptation of food supplies also takes
time to be implemented in society. Moreover, CVD may
at first be partly replaced by cancer, and subsequently by
other diseases that occur at still older ages. Probably only
future generations will be able to see whether this
epidemiological transition has indeed occurred.

In the 1980s, Doll and Peto12 estimated that 35% (range
10–70%) of cancer in the USA could be diet related. Our
estimate of 19% (6–28%) is lower because it applies
specifically to increasing consumption of fruit and
vegetables rather than optimizing all dietary factors.
Although other countries may have different targets for
increasing fruits and vegetables and different mortality
patterns because of different smoking and drinking
habits, we expect that the main message for western
countries will largely be unaffected by such factors – that
is ‘Eat a variety of fruits and vegetables each day, at least
400 g’. Increasing consumption of fruits and vegetables in
the general population requires a clear and uniform
message from all parties involved in public health
education and promotion. Of course, population trials
and elucidation of biological mechanisms should even-
tually provide scientific proof of the efficacy of fruits and
vegetables. However, the data available already justify
public health action to increase fruit and vegetable
consumption.

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