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Increased consumption of fruit and vegetables and future cancer incidence in selected European countries

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A B S T R A C T

Cancer is one of the major causes of death in western countries. Fruit and vegetable consumption may reduce the risk of cancers of the oropharynx, oesophagus, lung, stomach and colorectum. We investigated the potential effect of interventions aimed at increasing the intake of fruits and vegetables to the recommended level (500 g/d) on future cancer incidence in Europe. Data on cancer incidence and daily intake of fruit and vegetables were compiled for France, Germany, The Netherlands, Spain and Sweden. We also performed a meta-analysis of European observational studies to arrive at a quantitative estimate on the association between fruit and vegetable intake and cancer risk. Predictions on the future cancer incidence were modelled using PREVENT 3.01. Our study predicted 212,000 fruit- and vegetable-related cancer cases in these countries in 2050, out of which 398 (0.19%) might be prevented if the 500 g/d fruit and vegetable intake were achieved in the aforementioned countries. The largest absolute impact was observed for lung cancer with 257 (out of 136,517) preventable cases if the intervention was successfully implemented. Sweden would benefit the most from intervention to increase fruit and vegetable consumption with a 2% reduction in expected cases. Increasing fruit and vegetable consumption has a small impact on reducing the burden of cancer in Europe. Health impact assessment tools such as PREVENT can provide the basis for decision making in chronic disease prevention.

1. Introduction

Cancer remains a chronic disease causing major morbidity and mortality in Western countries. In Europe it was estimated that in the year 2008, 3.2 million new cancer cases were diagnosed.[1] Since lifestyle behaviours such as smoking, diet and physical activity have been identified as important and modifiable risk factors for various types of cancers, many cancer cases might be avoided by introducing lifestyle interventions.[2]

Earlier studies suggested that a large proportion (up to 23%) of cancers is preventable by increasing the population's fruit and vegetable intake.[3,4] Micronutrients present in fruit and vegetables such as antioxidant nutrients, dietary fibre

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and phytochemicals may potentially protect against cancer.[5] However, recent studies have reported substantially weaker relations between fruit and vegetable intake and cancer occurrence.[5,6] This might be explained by the hypothesis that the protective effect of fruit and vegetable on cancer risk is through moderating the effect of other risk factors such as smoking.[5] The recent decrease in cigarette smoking may have reduced the association between fruit and vegetables and cancer risk. In addition, others have proposed that total diet composition and dietary variation such as the Mediterranean diet may be more important in determining the risk of cancer rather than one component of the diet.[7]

No recent assessment of the potential impact of interventions aimed at increasing fruit and vegetable intake on cancer incidence is available. Therefore, in this study, we aimed to model the potential effect of different interventions to increase the intake of fruit and vegetables on the future incidence of cancers in five European countries with different dietary habits: France, Germany, The Netherlands, Spain and Sweden. In the analysis, we included cancers of the oral cavity, pharynx, oesophagus, stomach, colorectum and lung, based on the conclusions of two recent reviews[5,6] on the protective effect of fruit and vegetable consumption.

2. Materials and methods

In this study, we analysed data for five European countries, namely, France, Germany, The Netherlands, Spain and Sweden. For the analysis the following data were used for each of the five countries: (1) country- and sex-specific fruit and vegetable consumption patterns; (2) cancer incidence rates; (3) current and projected future population sizes (by age and sex groups); (4) risk functions for fruit and vegetable intake on cancer incidence and (5) expected effects of interventions on consumption of fruit and vegetables. We used PREVENT, a dynamic simulation model to integrate the data and evaluate the impact of increasing fruit and vegetable consumption on cancer risk.

2.1. Data collection

2.1.1. Fruit and vegetable consumption patterns

Data on average individual daily fruit and vegetable intake by sex in grams were abstracted from publications of the European Investigation into Cancer and Nutrition (EPIC) study.[8,9] We used EPIC data because this was the only source providing comparable data collection with estimates in the format as required by PREVENT. EPIC is a multi-centre prospective cohort study based in 22 collaborating centres in nine European countries. Data on individual fruit and vegetable intake were assessed through a validated, semi-quantitative food frequency questionnaire.[10] Regional data were weighted based on sample sizes to derive national data.

As a comparison we also used the national food consumption survey for France (Table 1).[8,9] Confidence intervals were calculated assuming a normal distribution covering 99.8% of the population within three standard deviations so that a minimum daily consumption of fruit and vegetable would not fall below 0.

Table 1 – Baseline fruit and vegetable intake (g/d) used as input for the modelling.

Countries	Gender	Daily fruit consumption Mean (SD)	Daily fruit vegetable consumption Mean (SD)
The Netherlands[a]	Male	168 (54)	137 (44)
	Female	197 (64)	130 (42)
Spain[a]	Male	365 (118)	222 (72)
	Female	316 (102)	174 (56)
Sweden[a]	Male	122 (39)	112 (36)
	Female	155 (50)	127 (41)
Germany[a]	Male	210 (68)	160 (51)
	Female	236 (76)	166 (53)
France[a]	Female	251 (81)	221 (71)
France[b]	Male	189 (61)	93 (30)
	Female	184 (59)	109 (35)

a Fruit consumption as reported by the European Prospective Investigation into Cancer and Nutrition (EPIC) cohorts.[8]
b Recent national French food and nutrient intake data.[9]

2.1.2. Incidence and demographic data

Data of newly diagnosed cases (by 5-year age groups and sex) for oral cavity, pharyngeal, oesophageal, lung, stomach and colorectal cancer were retrieved from national (the Netherlands and Sweden) or regional (Germany, France and Spain) cancer registries.[11–14]

Current and expected future population data (by age and sex) and population mortality data (by age, sex and calendar period) were collected from Eurostat.[15]

2.1.3. Estimating risk functions – meta-analysis: association between fruit and vegetable intake and cancer risk in Europe

Two large reviews reported a similar direction of results on the relation between fruit and vegetable consumption and cancers of the oropharynx, oesophagus, lung, stomach and colorectum.[5,6,16] Therefore, these cancer types were included in our modelling exercise. In order to obtain risk estimates describing the decrease in risk per unit increase in fruit and vegetable intake, a systematic search for publications giving estimates of relative risks or odds ratios on the association between fruit and/or vegetables consumption intake and cancer was performed.[17–46] We included only European studies published in English up to December 2008 (Appendix 1). We limited the meta-analysis to European studies because the differing prevalence of confounding risk factors (smoking, obesity, infections) in other continents may influence the reported risk estimates. For example, the role of fruit and vegetable in stomach cancer in Asian countries may be different to that in Europe because of other risk profiles: high consumption of salted foods, sour pancakes (China), mouldy grain (China) and mountain herbs (Japan).[47,48]

Articles were excluded from the meta-analysis for any one of the following reasons: (1) the article was a review paper; (2) the results from the same subjects had already been partially or completely published; (3) the article had insufficient data for determining an estimator of relative risk (RR), odds ratio

(OR), variance and quantitative intake of fruit/vegetable related to the reported estimators; (4) the results were on micronutrients and (5) the results were not cancer site specific.

We pooled the risk estimates reported in Appendix 1 to derive the average reduction in cancer risk related to a 1-g increase in fruit/vegetable intake. We did this by first converting risk estimates and confidence intervals into relative risks/odds ratios per gram of daily fruit or vegetable intake. Then, the risk estimates were pooled using 'Episheet', a spreadsheet-based analytical package designed for the analysis of epidemiological data.[37,49]

2.1.4. Intervention effect sizes

We modelled an intervention resulting in a recommended level of daily population consumption (average: 300 g fruits and 200 g vegetables). The standard deviation was set to be 25 g. This was done so that the counterfactual has a standard deviation of 50 g for fruit and vegetable consumption (together), as suggested by WHO[50] or the World Cancer Research Fund.[5] An exception to this scenario was Spain because the average daily fruit and vegetable consumption for the Spanish EPIC population was higher than the recommended level. Therefore, we used the observed mean intake for Spain and modelled the impact of change because of the smaller standard deviation.

In addition, we added two country-specific scenarios as follows:

1. France: we analysed the impact of intervention using the average intake of fruit/vegetables reported by the national survey. This scenario gives an estimate of the difference in expected outcome when a different source of data on fruit/vegetable intake was used.
2. Spain: a study has reported a 25% decrease in fruit consumption over the past 10 years in this country.[51] Therefore, we modelled a pessimistic scenario for Spain to calculate the impact on cancer incidence if this trend continued until Spain reached the level of intake in Sweden, the country with the lowest consumption in the present study.

2.2. Statistical analysis

2.2.1. Modelling the outcomes for the two intervention scenarios

To model different scenarios for the future fruit and vegetable intake, we used the simulation model software PREVENT 3.01. Detailed description of the mathematical calculation of PREVENT is described in another article in this issue.[52] In short, PREVENT 3.01 compares the projected future incidence without interventions with the projected future incidence after successful implementation of an intervention. In this study, the intervention was applied at the baseline + 1 year. Thereafter, the fruit and vegetable consumption remained constant until 2050. The base-years for each country are as follows: year 2000 for France, 2002 for Germany and Spain, 2003 for the Netherlands and 2005 for Sweden.

We assumed that after a change in fruit/vegetable consumption a period of 5 years was needed until the first changes in the population cancer incidence rates occurred (latency time). In addition, a lag time of 15 years was applied. Lag time is defined as the period of time from the first change in disease risk until the full impact of intervention is achieved. We assumed an exponential trajectory of changes over the lag time.

Compared with other risk factors, such as smoking, fruit and vegetable intake influences cancer risk only moderately. Hence, we expected trends in other risk factors to have a substantial effect on the incidence trends. We therefore assumed the 'autonomous trends' to be equal to the estimated annual percentage change in incidence over the past decade.[53] Because cancer incidence trends would not eternally proceed as they have in the past, we allowed for a dampening in the future trends. We applied a 5-yearly reduction of 25% in the autonomous trends that were used, as proposed by Moller et al.[54]

2.3. Sensitivity analysis

We repeated the main analysis using two different assumptions as follows:

1. Lag time of 10 years instead of 15 years.
2. A linear change in the effect of fruit/vegetable consumption over the lag time, instead of an exponential one.

3. Results

3.1. Daily intake of fruit and vegetables

Individual daily fruit intake reported from EPIC was highest for Spain (365 g/d for men and 316 g/d for women) and lowest for Swedish men (122 g/d) and Dutch women (155 g/d) (Table 1). The highest individual daily vegetable intake was observed in Spain: 222 g/d for men and in France for women (221 g/d). Lowest intakes were observed among the Swedes (112 g/d for men and 127 g/d for women; Table 1).

3.2. Relative risk per gram increase in daily fruit and vegetable intake

The results of the meta-analysis suggested a small protective effect of fruit and vegetable consumption. For colorectal cancer our pooled estimate no longer reached statistical significance (pooled relative risk for fruit: [1.00 0.99–1.001] and vegetables: [0.99 0.97–1.00]). Based on this finding, colorectal cancer was excluded from further analyses. A significant inverse association was found for fruit intake and cancers of the oropharynx, oesophagus, stomach and lung, with pooled relative risk of 0.995, 0.994, 0.9981 and 0.999 per gram increase in intake per day, respectively. For vegetables, a significant effect was found for cancers of the oropharynx, oesophagus and stomach, with regression coefficients of 0.986, 0.996 and 0.996 per gram increase of intake per day, respectively (Table 2). Although vegetable consumption was not significantly related to a decrease in lung cancer risk, we modelled the impact of intervention with vegetables on lung cancer risk,

Table 2 – Change in cancer risk per gram increase in daily consumption of fruit and vegetables.

Cancer type	Pooled relative risk per gram increase in: Fruit intake	95% CI[a]	Vegetable intake	95% CI[a]
Oesophageal cancer	0.995	0.994–0.997	0.996	0.994–0.998
Oropharyngeal cancer	0.994	0.992–0.997	0.986	0.979–0.992
Colorectal cancer[b]	1.00	0.99–1.00	0.999	0.997–1.00
Lung cancer[c]	0.999	0.998–0.999	0.998	0.997–1.00
Stomach cancer	0.998	0.9976–0.9995	0.996	0.994–0.998

[a] 95% CI: 95% Confidence Interval.
[b] Excluded from further analysis.
[c] Vegetable intake did not show a significant (positive or negative) relation to lung cancer risk, but was still included in the analysis because intervention was modelled for both fruit and vegetable intake.

because we modelled the intervention for fruit and vegetable intake together.

3.3. *Number of new cancer cases*

Without intervention, we expected 118,958 fruit- and vegetable-related cancers in 2050. Under our assumptions, increasing the mean population's fruit and vegetable intake to 500 g/d would prevent 221 and 177 new cases of stomach, lung, oesophageal and oropharyngeal cancer, in men and women, in our studied countries for the year 2050.

The magnitude of decrease in new cancer cases if interventions were successful varied by cancer types and countries. Interventions to increase fruit and vegetable intake were related to the largest relative decrease in oesophageal cancer (0.29%). In absolute terms the largest benefits were found for lung cancer, causing a reduction of 257 cases in the countries under study. In Sweden the benefit of increasing intake was the highest (1.72% reduction in all fruit- and vegetable-related cancers; Tables 3 and 4).

3.4. *Cancer incidence rate*

Increasing the average population fruit intake had a small impact on incidence rates. No effect was observed in France and Spain (Table 5). In the other countries, the impact was largest for men and lung cancer, e.g. among Swedish men we predicted 30.3/100,000 person-years in 2050 under the baseline scenario and 29.6/100,000 person-years under the intervention scenario.

3.5. *Additional scenarios: new cancer cases in France and Spain*

The French national survey reported much lower fruit and vegetable intake than the EPIC study (Table 1), with an average intake of fruit and vegetable of 184 and 109 g/d versus 251 and 221 g/d, respectively. As expected, the modelled impact of an intervention is larger if we use the average consumption as reported by the national survey, i.e. 691 fewer

Table 3 – Number of cancer cases in men by country in the base year, expected number of cases in 2050 with and without intervention[a] and time needed to achieved preventable cases under intervention B to increase fruit and vegetable intake.

Cancer site		Germany	Spain	Sweden	The Netherlands	Total
Stomach	Base year (cases)	11,059	4440	574	1252	17,325
	Trend only in 2050 (cases)	14,183	5230	542	1179	21,134
	Intervention in 2050 (cases)	14,167	5227	533	1178	21,105
	Preventable cases (%)	16 (0.1)	3 (0.1)	9 (1.7)	1 (0.1)	299 (0.1)
Lung	Base year (cases)	32,255	17,587	1910	6062	57,814
	Trend only in 2050 (cases)	33,928	35,547	2716	5417	77,608
	Intervention in 2050 (cases)	33,872	35,526	2668	5407	77,473
	Preventable cases (%)	56 (0.2)	21 (0.1)	48 (1.8)	10 (0.2)	135 (0.2)
Oesophagus	Base year (cases)	3655	1773	323	1006	6757
	Trend only in 2050 (cases)	2981	2353	662	2827	8823
	Intervention in 2050 (cases)	2973	2350	649	2820	8792
	Preventable cases (%)	8 (0.3)	3 (0.1)	13 (2.0)	7 (0.3)	31 (0.4)
Oropharynx	Base year (cases)	7727	3858	333	962	12,880
	Trend only in 2050 (cases)	7668	2046	412	1267	11,393
	Intervention in 2050 (cases)	7654	2043	405	1265	11,367
	Preventable cases (%)	14 (0.2)	3 (0.2)	7 (1.7)	2 (0.2)	26 (0.2)
Total	Expected cases in 2050	58,760	45,176	4332	10,690	118,958
	Preventable cases (%)	94 (0.2)	30 (0.1)	77 (1.8)	20 (0.2)	221 (0.2)

[a] Intervention: increase fruit consumption to 300 g/d and vegetables to 200 g/d, with standard deviation 25 g. If base intake is higher than the aforementioned goal (see Table 1) then the intervention was to reduce standard deviation to 25 g.

Table 4 – Number of cancer cases in women by country in the base year, expected number of cases in 2050 with and without intervention[a] and time needed to achieved preventable cases under intervention B to increase fruit and vegetable intake.

Cancer site		France	Germany	Spain	Sweden	The Netherlands	Total
Stomach	Base year (cases)	2308	8213	3056	337	693	14,607
	Trend only in 2050 (cases)	2680	6008	6540	287	747	16,262
	Intervention in 2050 (cases)	2678	6001	6535	283	746	16,243
	Preventable cases (%)	2 (0.1)	7 (0.1)	5 (0.1)	4 (1.4)	1 (0.1)	19 (0.1)
Lung	Base year (cases)	4683	12,416	2119	1517	2868	23,603
	Trend only in 2050 (cases)	15,096	27,845	5445	3179	7344	58,909
	Intervention in 2050 (cases)	15,087	27,804	5440	3126	7330	58,787
	Preventable cases (%)	9 (0.1)	41 (0.2)	5 (0.1)	53 (1.7)	14 (0.2)	122 (0.2)
Oesophagus	Base year (cases)	875	1038	380	106	415	2814
	Trend only in 2050 (cases)	2307	2182	1401	154	753	6797
	Intervention in 2050 (cases)	2304	2177	1399	151	751	6782
	Preventable cases (%)	3 (0.1)	5 (0.2)	2 (0.1)	3 (2.0)	2 (0.3)	15 (0.2)
Oropharynx	Base year (cases)	2337	2582	914	207	526	6566
	Trend only in 2050 (cases)	4611	3725	1169	345	932	10,782
	Intervention in 2050 (cases)	4605	3719	1168	339	930	10,761
	Preventable cases (%)	6 (0.1)	6 (0.2)	1 (0.1)	6 (1.7)	2 (0.2)	21 (0.2)
Total	Expected cases in 2050	24,694	39,760	14,555	3965	9776	92,750
	Preventable cases (%)	20 (0.1)	59 (0.2)	13 (0.1)	66 (1.7)	19 (0.2)	177 (0.2)

[a] Intervention: increase fruit consumption to 300 g/d and vegetables to 200 g/d, with standard deviation 25 g. If base intake is higher than the aforementioned goal (see Table 1) then the intervention was to reduce standard deviation to 25 g.

Table 5 – Incidence rates (European standardised, per 100,000) by sex and country in 2050 with and without interventions to increase fruit and vegetable intake.

Cancer site	Rates in 2050	France[a]	Germany		Spain		Sweden		The Netherlands	
		Female	Male	Female	Male	Female	Male	Female	Male	Female
Stomach	Trend only	3.0	17.2	6.1	10.8	10.3	5.4	2.6	7.5	4.1
	Intervention	3.0	17.2	6.1	10.8	10.3	5.3	2.6	7.4	4.1
Lung	Trend only	25.6	45.2	38.4	82.5	11.2	30.3	38.5	37.2	58.5
	Intervention	25.6	45.0	38.4	82.4	11.2	29.6	37.9	37.1	58.4
Oesophageal	Trend only	3.4	4.7	2.7	6.1	2.7	7.8	1.4	20.4	4.3
	Intervention	3.4	4.7	2.7	6.1	2.7	7.7	1.3	20.3	4.3
Oropharynx	Trend only	8.8	14.6	5.6	3.6	1.4	2.3	2.5	6.9	5.0
	Intervention	8.8	14.6	5.6	3.6	1.4	2.2	2.4	6.9	5.0

[a] Prevalence of fruit and vegetable consumption was only available for female subjects.[8]

new cancer cases versus 20 if modelling were based on the EPIC data (Table 6).

If the fruit intake in Spain were to decrease by 25% every 10 years until the average population intake was 150 g/d in men and 130 g/d in women, we would expect 11,492 additional new cancer cases compared with the baseline scenario (10,191 in men and 1301 in women, Table 6). The additional cases were mostly for lung cancer (8015 in men and 483 in women).

3.6. *Sensitivity analyses*

Both sensitivity analyses resulted in the same number of prevented cases and projected incidence rates in the year 2050 (Table 7). Compared with the main analysis, differences were observed in the time period needed to achieve the intervention goal. For example, changing the lag time into a linear one rather than exponential (main analysis) would result in achieving the intervention goal 0–4 years earlier than the main intervention scenario.

4. Discussion

This study demonstrated small decreases in the total number of cases and incidence rates of the cancers studied if interventions to increase fruit and vegetable consumption were to be successfully implemented and adopted by the population. Assuming that the specified goal of 500 g/d of fruit and vegetable intake were achieved, about 398 out of 211,708 fruit- and vegetable-related cancer cases would probably be prevented in 2050 in the countries included in this study.[53] The largest impact of increasing fruit and vegetable intake was

Table 6 – Number of cancer cases by sex and country in the base year and in 2050 with or without intervention under an optional scenario on fruit and vegetable intake.

Cancer site		France: National data[a]			Spain: decrease fruit intake[b]		
		Male	Female	Total	Male	Female	Total
Stomach	Base year	4326	2308	6634	4440	3056	7496
	Trend only in 2050 (cases)	5822	2680	8502	5230	6540	11,770
	Intervention in 2050 (cases)	5666	2609	8275	6413	7129	13,542
	Preventable in 2050 (cases)[c]	156	71	227	–1183	–589	–1772
Lung	Base year	23,056	4683	27,739	17,587	2119	19,706
	Trend only in 2050 (cases)	40,834	15,096	55,930	35,547	5445	40,992
	Intervention in 2050 (cases)	39,594	14,665	54,259	43,562	5928	49,490
	Preventable in 2050 (cases)[c]	1240	431	1671	–8015	–483	–8498
Oesophagus	Base year	3967	875	4842	1,773	380	2153
	Trend only in 2050 (cases)	3969	2307	6276	2353	1401	3754
	Intervention in 2050 (cases)	3849	2241	6090	2884	1526	4410
	Preventable in 2050 (cases)[c]	120	66	186	–531	–125	–656
Oropharynx	Base year	12,872	2337	15,209	3858	914	4772
	Trend only in 2050 (cases)	14,635	4611	19,246	2046	1169	3215
	Intervention in 2050 (cases)	14,242	4488	18,730	2508	1273	3781
	Preventable in 2050 (cases)[c]	393	123	516	–462	–104	–566
Total		1909	691	2600	–10191	–1301	–11492

[a] Fruit and vegetable consumption from recent national French food and nutrient intake data was used.[9]
[b] Decrease fruit intake by 25%[51] every 10 years until the intake level was similar to the lowest in the European countries included in this study (Sweden).
[c] Negative value of preventable cases: additional cases at the end of simulation.

Table 7 – Sensitivity analyses.

Countries	Cancer cases in 2005	10-year lag-time			Linear lag-time		
		Male	Female	Total	Male	Female	Total
France	With intervention[a]	–	24,674	24,674	–	24,674	24,674
	Preventable (%)	–	20 (0.1)	20 (0.1)	–	20 (0.1)	20 (0.1)
Germany	With intervention[a]	58,666	39,701	98,367	58,666	39,701	98,367
	Preventable (%)	94 (0.2)	59 (0.2)	153 (0.2)	94 (0.2)	59 (0.2)	153 (0.2)
Spain	With intervention[a]	45,146	14,542	59,688	45,146	14,542	59,688
	Preventable (%)	30 (0.1)	13 (0.1)	43 (0.1)	30 (0.1)	13 (0.1)	43 (0.1)
Sweden	With intervention[a]	4255	3899	8,154	4255	3899	8154
	Preventable (%)	77 (1.8)	66 (1.7)	143 (1.7)	77 (1.8)	66 (1.7)	143 (1.7)
The Netherlands	With intervention[a]	10670	9,757	20,427	10,670	9757	20,427
	Preventable (%)	20 (0.2)	19 (0.2)	39 (0.2)	20 (0.2)	19 (0.2)	39 (0.2)

[a] Intervention: increase fruit consumption to 300 g/d and vegetables to 200 g/d, with standard deviation 25 g. If base intake is higher than the aforementioned goal (see Table 1) then intervention was to reduce the standard deviation to 25 g.

on reducing the rate of oesophageal cancer. In absolute terms the largest benefits were found for lung cancer, for which a reduction of 257 cases was observed in the studied countries.

Interventions aimed at increasing fruit and vegetable consumption had the largest potential impact on reducing cancer incidence in Sweden because of the low baseline of fruit and vegetable intake. On the other hand, in Spain where fruit and vegetable intake is high, interventions should be aimed at maintaining the high intake levels. Reduction in fruit consumption may markedly increase the number of cancer cases. Because Spanish males had the highest incidence of lung cancer,[55] the scenario with the decline in fruit and vegetable intake had such a large impact, stressing the importance of other risk factors such as smoking. This is also true for other cancer risk factors (e.g. excess weight, alcohol consumption) that are more common in Spain.[55]

We modelled the effects of increasing fruit and vegetable intake and did not include other risk factors that might be modified by fruit and vegetable intake. The anti-cancer effects of fruit and vegetable intake are likely due to anti-oxidant, antibacterial and antiviral effects.[5] The magnitude of these effects therefore depends on the exposure to other risk factors. If those carcinogens (largely) disappear, their effects may diminish. For example, the benefit of fruit or vegetable intake against lung cancer has been reported to be apparent among smokers only.[40,56] In Spain where the proportion of smokers in the population is high, the benefit of fruit and vegetable intake may be under-estimated in our analysis. This may also apply to other risk factors such as alcohol intake or excess weight. Conversely, the effects in Sweden might be overestimated since many of the other risk factors have a relatively low prevalence in this country. It should be noted that vegetable intake did not show a significant relationship to lung cancer risk, so for the modelling the effects on lung cancer risk were entirely attributable to changes in fruit consumption. To include interrelation between risk factors demands detailed data on many risk factor associations that are not available, and hence were not modelled.

4.1. *Limitations*

PREVENT is a programme that predicts future cancer burden, which is important for health planners to optimise resources. However, it cannot be used as an exact predictor of future cancer incidence. As with any prediction method, PREVENT makes several assumptions and relies heavily on underlying input data. Since all these input data and assumptions were the same for the different scenarios, the different interventions can be compared with each other. Furthermore, baseline data including incidence, prevalence and population data were derived from comparable and established resources and are assumed to be reliable.

Therefore, limitations of this study are mainly due to the fact that modelling is inevitably based on a number of assumptions. In this study, we took a (simplified) assumption that the whole population responded equally to the intervention. We are aware of the studies that reported a different effect of intervention programmes on different sub-groups, such as by socio-economic status.[57] To model impact of intervention by subpopulation would necessitate data for all subgroups, e.g. incidence and prevalence data and population forecasts that are not readily available. Therefore, we assumed equal effects of the intervention on fruit and vegetable consumption in this study. Second, we assumed that the association of fruit and vegetable intake on cancer risk would be the same in all population groups. Anti-cancer effects of fruit and vegetables are likely to be different among subgroups (smokers, drinkers or those with excess weight) depending on their underlying cancer risks.[5] Because of the lack of detailed data needed, we did not include this in the modelling of the current study.

Data on fruit and vegetable consumption were taken from the reported study of the EPIC cohort.[8] This probably resulted in an overestimation of fruit and vegetable intake at baseline, since subjects that participate in cohort studies are often more health conscious than the general population. For example, the French EPIC cohort was based on female school teachers with a mean fruit intake of 251 g/d and vegetable intake of 221 g/d.[8] Another source (national survey) for fruit and vegetable intake in France reported much lower consumption (average fruit intake among women: 184 g/d, vegetables intake: 109 g/d).[9] As expected, using the prevalence rates of fruit and vegetable consumption as reported in EPIC resulted in a smaller impact of intervention on cancer incidence. The second issue of using the EPIC data pertains to the fact that the data on the fruit and vegetable intake of this cohort were collected in the early 1990s.[8,9] Since then consumption may have changed. Yet, we assumed ‘status quo’, because the direction of change in fruit and vegetable intake is not easily predicted. Martin-Moreno and colleagues reported either similar or increasing consumption in western and northern Europe over time or a decreasing trend in southern European countries.[55] Yet in western or northern European countries, consumption is still much lower than the recommended level, leaving ample room for interventions. As for southern Europe decreased consumption may lead to underestimation in the estimated impact of prevention in our modelling.

5. Conclusions

The results of our modelling show that increasing fruit and vegetable consumption had only a small effect on cancer occurrence in Europe. This effect is larger in countries where baseline fruit and vegetable intake was low. However, fruit and vegetables also have positive health effects on chronic conditions such as heart disease and stroke.[58] In addition, a balanced diet high in fruit and vegetables reduces excess weight that has been linked to increased risk of cancer.[5] Because modifying lifestyle is difficult, a combination of strategies and interventions carefully targeting diverse population groups is warned. To increase fruit and vegetable consumption face-to-face interventions and computer-tailored nutrition education have been reported to be effective.[59] Yet, at a population level policy-orientated intervention is more visible to implement and may reach a larger population size.[60]

Conflict of interest statement

None declared.

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Appendix 1. European studies on fruit consumption and its impact on the risk of oropharyngeal, oesophageal, stomach, colorectal and lung cancer

A. Fruit consumption and risk of cancer

Table 1.A.1. Fruit consumption and oropharyngeal cancer.

Author, year, country	Study design, participants	RR/OR (95% CI)	Adjustment
Tavani et al. (2001),[25] Note: Italy Note: data collected in 1996–1999, in North-east Italy	Case-control Cases: 132 Controls: 148	Fruit portions/week 7–13: 0.51 (0.22–1.21) >13: 0.34 (0.13–0.87)	Age, sex, number or portions, smoking, alcohol. Reference <7 portions/week
Sanchez et al. (2003),[27] Spain	Case-control Cases: 375 Controls: 375	Fruit portions/week 7–10: 0.54 (0.37–1.32) ⩾11: 0.52 (0.34–0.79)	Age, sex, hospital, education, smoking, alcohol. Reference ⩽6 portions/week
Franceschi et al. (1999),[24] Italy Note: data collected in 1992–1997, in Pordenone, Rome and Latina	Case-control Cases: 598 Controls: 1491	Fruit servings/week 4–5: 0.9 (0.7–1.1) ⩾6: 0.6 (0.4–0.9)	Age, sex, study centre, years of education, smoking, alcohol, total energy intake. Reference <4 servings/week
Negri et al. (1991),[19] Italy Note: data collected in 1983–1990, in northern Italy	Case-control Cases: 119 Controls: 6147 (hospital based)	Fruits portions/week 7–13: 0.6 (0.4–0.8) ⩾14: 0.2 (0.1–0.3)	Age, education, area of residence, smoking, sex. Reference <7 consumption/week

Table 1.A.2. Fruit consumption and oesophageal cancer.

Author, year, country	Study design	RR/OR	Adjustments
Sharp et al. (2001),[17] England and Scotland	Case-control (women) Cases, squamous cell carcinoma: 159 Control: 159	Total fruit times/week 12.01–18.04: 0.72 (0.35–1.49) 18.05–25.72: 0.81 (0.37–1.80) ⩾25.73: 0.64 (0.25–1.67)	Slimming diet, breakfast, salad (for fruit), years smoking, regular use of aspirin, centre, temperature tea/coffee. Age matched. Reference ⩽12.00 times/week
Launoy et al. (1998),[18] France	Case-control (male) Cases (Squamous Cell Carcinoma): 208 Control: 399	Fresh fruits g/d 60–120: 0.83 (0.48–1.49) 120–180: 0.49 (0.27–0.84) >180: 0.59 (0.35–1.00)	Age, interviewer, smoking, beer, aniseed aperitifs, hot calvados, whisky, total alcohol, total energy intake and other significant food groups. Reference <60 g/d
Negri et al. (1991),[19] Italy	Case-control Cases: 294 Controls: 6147 (hospital based)	Fruits portions/week 7–13: 0.5 (0.4–0.7) ⩾14: 0.3 (0.2–0.4)	Age, education, area of residence, smoking, sex. Reference <7 portions/week
Terry et al. (2001),[38] Sweden	Case-control Cases: Adenocarcinoma: 185 Squamous cell carcinoma: 165 Control: 1123	Adenocarcinoma Fruit servings/d 0.6: 0.8 (0.5–1.2) 1: 0.7 (0.4–1.1) 2: 0.7 (0.4–1.1) Squamous cell carcinoma Fruit servings/d 0.6: 0.7 (0.4–1.2) 1: 0.8 (0.5–1.3) 2: 0.6 (0.4–1.1)	Age, gender, total energy intake, body mass index, gastro-oesophageal reflux symptoms, cigarette smoking. Reference 0.2 servings/d.

Table 1.A.2. (*continued*)

Author, year, country	Study design	RR/OR	Adjustments
Anderson et al. (2007),[41] Ireland	Case control (population-based) Cases: Adenocarcinoma: 225 Control: 257	Fruit portions/week 5–20: 0.52 (0.32–0.85) >20: 0.47 (0.28–0.80)	Sex, age at interview, smoking, alcohol, energy intake, BMI (5 years prior to interview), education and job type. Reference < 5 portions/week
Gonzalez et al. (2006),[42] Europe (EPIC)	Cohort study Cohort: 481,518 Cases (adenocarcinoma): 65	Fresh fruit g/d 130–263: 0.67 (0.37–1.22) ⩾264: 0.94 (0.49–1.80)	Stratified by centre and age. Adjusted by sex, height, weight, education, smoking, smoking intensity, physical activity, alcohol, energy intake, red meat and processed meat intake. Reference <130 (average men and women)

Table 1.A.3. Fruit consumption and stomach cancer.

Author, year, country	Study design	RR/OR	Adjustment
Botterweck et al. (1998),[26] The Netherlands	Case cohort Cases: 282 Cohort (fruit): 3123	Median fruit intake g/d 109: 0.92 (0.64–1.32) 157: 0.88 (0.61–1.27) 216: 0.74 (0.50–1.09) 325: 0.83 (0.56–1.23)	Age, sex, level of education, stomach disorders, family history of stomach cancer, smoking status, fruit consumption (in the case of vegetable analyses), and vegetable consumption (in the case of fruit analyses). Reference 46 g/d
Ramon et al. (1993),[37] Spain	Case-control Cases: 117 Controls: 234	Fruits g/d 355.7–408.4: 1.08 (0.62–2.31) 408.5–461.4: 0.97 (0.41–1.87) >461.4: 0.85 (0.21–1.11)	All foods listed, sex, age, education and cigarettes/d Vegetables results did not report confidence interval
La Vecchia et al., 1997,[35] Italy	Case-control Cases: 746 Control: 2053	Fruit servings/week 2: 0.8 (0.6–1.0) ⩾3: 0.6 (0.5–0.8)	Age, sex, education, area of residence, family history of gastric cancer, body mass index, total energy intake Reference <2 servings/week
Ekström et al. (2000),[31] Sweden	Case-control Cases: 505 Controls: 1116	Fruit intake/week 20 years prior to interview Cardia 3–5: 0.7 (0.4–1.3) 6–7: 0.5 (0.2–0.9) >1/d: 0.5 (0.2–1.0) Non-cardia 3–5: 0.8 (0.6–1.2) 6–7: 0.6 (0.4–0.8) >1/d: 0.6 (0.4–0.8)	Age, sex, total caloric intake, tobacco use, BMI, geographic risk area, number of siblings, socioeconomic status, number of meals/d, multivitamin supplements, salt use, urban environment. Reference ⩽2 intake/week

(*continued on next page*)

Table 1.A.3. (*continued*)

Author, year, country	Study design	RR/OR	Adjustment
Terry et al. (2001),[38] Sweden	Case-control Case (gastric cardia): 258 Control: 1123	Fruit servings/d 0.6: 1.0 (0.7–1.4) 1: 0.9 (0.6–1.3) 2: 1.0 (0.6–1.4)	Age, gender, total energy intake, body mass index, gastro-oesophageal reflux symptoms, cigarette smoking. Reference: 0.2 servings/d
Lucenteforte et al. (2008),[43] Italy	Case-control Case: 230 Control: 547	Fruit servings/week 8.7–13.6: 0.79 (0.47–1.33) 13.6–17.4: 0.73 (0.43–1.23) 17.4–24.5: 0.89 (0.53–1.48) 24.5–55.3: 0.53 (0.30–0.93)	Sex, age, education, year of interview, body mass index, tobacco smoking, family history, total energy intake. Reference (upper limit): 8.7 servings/week
Larsson et al. (2006),[44] Sweden	Population-based cohort study Women: 36,664 Men: 45,338 Cases: 139	Fruit servings/d 1.0–1.4: 0.93 (0.58–1.49) 1.5–2.4: 0.86 (0.55–1.36) $\geqslant$2.5: 0.86 (0.52–1.43)	Age, sex, education, smoking and pack years of smoking, diabetes, total energy intake, alcohol and processed meat intake. Reference 1 serving/d
Lunet et al. (2007),[45] Portugal	Case control Cases: 305 Control: 1129	Fruit servings/d Cardia 1.6–2.5: 0.63 (0.32–1.23) $\geqslant$2.6: 0.47 (0.21–1.05) Non-cardia 1.6–2.5: 0.86 (0.60–1.22) $\geqslant$2.6: 0.53 (0.35–0.80) Not classified 1.6–2.5: 1.01 (0.33–3.10) $\geqslant$2.6: 1.65 (0.57–4.76)	Sex, age, education level, total caloric intake, vegetable consumption. Reference $\leqslant$1.5 servings/d
Gonzalez et al. (2006),[42] Europe (EPIC)	Cohort study Cohort: 481,518 Cases (adenocarcinoma): 330	Fresh fruit g/d 170: 1.17 (0.87–1.58) 239: 0.85 (0.61–1.19) 337: 0.99 (0.68–1.42)	Stratified by centre and age. Adjusted by sex, height, weight, education, smoking, smoking intensity, physical activity, alcohol, energy intake, red meat and processed meat intake. Reference (cut-off) 93 g/d (average men and women)

Table 1.A.4. Fruit consumption and colorectal cancer.

Author, year, country	Study design	RR/OR	Adjustment
Pietinen et al. (1999),[39] Finland	Primary prevention trial (case-cohort) Cases: 185 Non-cases: 26926	Fruits g/d 30–82: 1.0 (0.6–1.4) 83–132: 0.9 (0.6–1.4) 133–216: 1.1 (0.8–1.7)	Age, smoking years, BMI, alcohol, education, physical activity at work, calcium intake. Reference: <30 g/d
Voorrips et al. (2000),[30] The Netherlands	Case-cohort Cases: Men, colon: 313 Men, rectal: 201 Cohort, men: 1456 Cases: Women, colon: 274 Women, rectal: 122 Cohort, women: 1497	Men, fruit g/d, colon: 91: 1.40 (0.95–2.06) 136: 0.91 (0.60–1.38) 187: 1.29 (0.87–1.90) 286: 1.33 (0.90–1.97) Women, fruit g/d, colon 124: 0.95 (0.62–1.45) 177: 0.78 (0.50–1.22) 237: 0.91 (0.60–1.38) 343: 0.73 (0.48–1.11) Men, fruit g/d, rectal: 91: 0.99 (0.64–1.52) 136: 0.65 (0.40–1.05) 187: 0.84 (0.54–1.31) 286: 0.85 (0.55–1.32) Women, fruit g/d, rectal: 124: 0.95 (0.48–1.87) 177: 1.31 (0.70–2.48) 237: 1.30 (0.69–2.41) 343: 0.67 (0.34–1.33)	Age, family history of colorectal cancer, category of alcohol intake. Reference (men) 34 g/d. Reference (women) 65 g/d
Terry et al. (2001),[20] Sweden	Cohort Cases: 460 Cohort: 61463	Fruit servings/d 1.0–1.5: 0.68 (0.53–0.87) 1.5–2.0: 0.74 (0.58–0.96) >2.0: 0.68 (0.52–0.89)	Age, consumption of red meat and dairy products, total calories. Reference <1 servings/d
Kampman et al. (1995)[34]	Case-control: Colon, Cases: 232 Controls: 259 population-based	Fruits g/d 125–198: 0.97 (0.58–1.53) 199–288: 0.79 (0.46–1.63) >288: 0.82 (0.84–1.41)	Age, gender, urbanisation level, total energy intake, alcohol use, cholecystectomy, family history of colon cancer. Reference <125 g/d
Negri et al. (1991),[19] Italy	Case-control: Colon Cases: 673 Controls: 6147 (hospital-based)	Fruit portions/week 7–13: 1.0 (0.8–1.2) ⩾14: 0.6 (0.5–0.7)	Age, education, area of residence, smoking, sex Reference <7 portions/week
Negri et al. (1991),[19] Italy	Case-control: Rectum, Cases: 406 Controls: 6147 (hospital-based)	Fruit portions/week 7–13: 1.3 (1.0–1.7) ⩾14: 0.9 (0.7–1.3)	Age, education, area of residence, smoking, sex Reference <7 portions/week

Table 1.A.5. Fruit consumption and lung cancer.

Author, year, country	Study design	RR/OR	Adjustment
Voorrips et al. (2000),[30] The Netherlands	Case-cohort Cases: 963 Cohort: 2953	Fruit g/d (median) 109: 0.7 (0.6–1.0) 157: 0.6 (0.5–0.8) 216: 0.6 (0.4–0.8) 325: 0.8 (0.6–1.1)	Age, sex, family history of lung cancer, highest education level, current smoker, years of smoking, number of cigarettes/d. Reference 46 g/d
Jansen et al. (2001)[33]	Cohort (Only male)		Age, number of cigarettes smoked, cohort (for Finland & Italy), energy intake, vegetable intake
Finland	Cases: 85 Cohort: 1288	Fruit g/d (median) 118.1: 0.63 (0.34–1.14) 289.1: 0.82 (0.45–1.50)	Reference 44.4 g/d
Italy	Cases: 41 Cohort: 1207	Fruit g/d (median) 100: 0.79 (0.33–1.89) 247.5: 1.08 (0.45–2.62)	Reference 5 g/d
The Netherlands	Cases: 61 Cohort: 613	Fruit g/d (median) 130: 0.33 (0.16–0.70) 241.5: 0.35 (0.16–0.74)	Reference 43 g/d
Holick et al. (2002),[32] Finland	Cases: 1644 Cohort: 27,084	Fruit g/d 116–176: 0.91 (0.79–1.05) 177–241: 0.95 (0.82–1.10) 242–332: 0.82 (0.71–0.96) >332: 0.73 (0.62–0.86)	Age, years smoked, cigarettes per d, intervention, supplement use, energy intake, cholesterol and fat. Reference <116 g/d
Dosil-Diaz et al. (2008),[46] Spain	Case-control Cases: 295 Controls: 322	Fruit times/week 1–6: 1.85 (0.96–3.59) 7: 1.49 (0.81–2.73)	Sex, age, smoking, employment in risk occupations. Reference <1 time/week

B. Vegetables consumption and risk of cancer

Table 1.B.1. Vegetables consumption and oropharyngeal cancer.

Author, year, country	Study design, participants	RR/OR (95% CI)	Adjustment
Tavani et al. (2001),[25] Note: Italy Note: data collected in 1996–1999, in North-east Italy	Case-control Cases: 132 Controls: 148	Vegetables portions/week: 7–13: 0.30 (0.15–0.60) >13: 0.37 (0.16–0.88)	Age, sex, number or portions, smoking, alcohol. Reference < 7 portions/week
Sanchez et al. (2003),[27] Spain	Case-control Cases: 375 Controls: 375	Vegetables portions/week: 4–7: 0.92 (0.63–1.32) ⩾8: 0.54 (0.34–0.87)	Age, sex, hospital, education, smoking, alcohol. Reference ⩽3 portions/week
Franceschi et al. (1999),[24] Italy Note: data collected in 1992–1997, in Pordenone, Rome and Latina	Case-control Cases: 598 Controls: 1491	Vegetables portions/week: 4–6: 0.7 (0.5–0.9) ⩾7: 0.5 (0.3–0.8)	Age, sex, study centre, years of education, smoking, alcohol, total energy intake. Reference <4 servings/week.
Negri et al. (1991),[19] Italy Note: data collected in 1983–1990, in northern Italy	Case-control Cases: 119 Controls: 6147 (hospital-based)	Vegetables portions/week: 7: 0.6 (0.4–0.9) >7: 0.3 (0.1–0.5)	Age, education, area of residence, smoking, sex. Reference <7 portions/week

Table 1.B.2. Vegetable consumption and oesophageal cancer.

Author, year, country	Study design	RR/OR	Adjustments
Sharp et al. (2001),[17] England and Scotland	Case-control (women) Cases, squamous cell carcinoma: 159 Control: 159	All salad times/week 6.45–11.46: 0.87 (0.46–1.67) 11.47–17.11: 0.28 (0.12–0.68) ⩾17.12: 0.42 (0.20–0.92)	Slimming diet, breakfast, salad (for fruit), years smoking, regular use of aspirin, centre, temperature tea/ coffee. Age matched. Reference ⩽6.45 times/week
Launoy et al. (1998)[18]	Case-control (male) Cases (Squamous Cell Carcinoma): 208 Control: 399	Vegetables g/d 200–300: 0.95 (0.56–1.63) 300–400: 0.63 (0.34–1.18) >400: 0.24 (-0.11–0.55)	Age, interviewer, smoking, beer, aniseed aperitifs, hot calvados, whisky, total alcohol, total energy intake and other significant food groups. Reference <200g/d
Negri et al. (1991)[19]	Case-control Cases: 294 Controls: 6147 (hospital based)	Vegetables portions/week: 7: 0.5 (0.4–0.6) >7: 0.2 (0.1–0.3)	Age, education, area of residence, smoking, sex. Reference <7 portions/week
Terry et al. (2001)[38]	Case-control Cases: Adenocarcinoma: 185 Squamous cell carcinoma: 165 Control: 1123	Adenocarcinoma Vegetable servings/d 1.6: 0.7 (0.4–1.0) 2.2: 0.6 (0.4–0.9) 3.3: 0.5 (0.3–0.8) Squamous cell carcinoma Vegetable servings/d 1.6: 0.8 (0.5–1.3) 2.2: 0.6 (0.3–0.9) 3.3: 0.6 (0.4–1.0)	Age, gender, total energy intake, body mass index, gastro-oesophageal reflux symptoms, cigarette smoking. Reference 1.1 servings/d
Anderson et al. (2007),[41] Ireland	Case control (population-based) Cases: Adenocarcinoma: 224 Control: 257	Vegetable portions/week 12–17: 1.13 (0.68–1.86) >17: 1.38 (0.84–2.28)	Sex, age at interview, smoking, alcohol, energy intake, BMI (5 years prior to interview), education and job type. Reference < 12 portions/ week
Gonzalez et al. (2006),[42] Europe (EPIC)	Cohort study Cohort: 481,518 Cases (adenocarcinoma): 65	Fresh vegetable g/d 129–232: 0.88 (0.48–1.63) ⩾233: 0.71 (0.34–1.48)	Stratified by centre and age. Adjusted by sex, height, weight, education, smoking, smoking intensity, physical activity, alcohol, energy intake, red meat and processed meat intake. Reference (cut-off) <129 g/d (average men & women)

Table 1.B.3. Vegetable consumption and stomach cancer.

Author, year, country	Study design	RR/OR	Adjustment
Botterweck et al. (1998),[26] The Netherlands	Case cohort Cases: 282 Cohort (vegetables): 2953 and (fruit): 3123	Vegetables g/d (median) 145: 0.76 (0.52–1.09) 178: 0.47 (0.31–0.72) 217: 0.64 (0.43–0.95) 286: 0.79 (0.55–1.14)	Age, sex, level of education, stomach disorders, family history of stomach cancer, smoking status, fruit consumption (in the case of vegetable analyses), and vegetable consumption (in the case of fruit analyses). Reference 190 g/d.
La Vecchia et al., 1997,[35] Italy	Case-control Cases: 746 Control: 2053	Vegetables servings/week: 5: 0.8 (0.6–1.0) 6: 0.8 (0.6–1.0) ⩾7: 0.5 (0.4–0.7)	Age, sex, education, area of residence, family history of gastric cancer, body mass index, total energy intake Reference <5 servings/week
Hansson et al., 1993,[28] Sweden	Case-control Cases: 338 Controls: 669	Vegetables times/month Adolescence 2.1–5: 0.61 (0.43–0.86) 5–15: 0.68 (0.48–0.97) >15: 0.58 (0.37–0.89) 20 years prior to interview: 2.1–5: 0.65 (0.46–0.93) 5–15: 0.71 (0.50–1.01) >15: 0.50 (0.32–0.78)	Age, gender, SES. Reference: <2.1 times/month. Fruits results only, fruit-specific.
Ekström et al. (2000),[31] Sweden	Case-control Case: 505 Control: 1116	Vegetables intake/week 20 years prior to interviewCardia 6–8: 0.5 (0.3–1.0) 9–13: 0.4 (0.2–0.8) ⩾2/d: 0.5 (0.3–1.1) Non-cardia 6–8: 1.0 (0.7–1.4) 9–13: 0.8 (0.6–1.1) ⩾2/d: 0.7 (0.5–1.0)	Age, sex, total caloric intake, tobacco use, BMI, geographic risk area, number of siblings, socioeconomic status, number of meals/d, multivitamin supplements, salt use, urban environment. Reference ⩽5 intake/week.
Terry et al., 2001,[38] Sweden	Case control Case (gastric cardia): 258 Control: 1123	Vegetable servings/d 0.6: 1.3 (0.9–1.9) 1 1.2 (0.8–1.8) 2: 0.8 (0.6–1.3)	Age, gender, total energy intake, body mass index, gastro-oesophageal reflux symptoms, cigarette smoking. Reference 0.2 servings/d.
Lucenteforte et al. (2008), Italy	Case-control Case: 230 Control: 547	Vegetable servings/week 5.4–7.7: 0.73 (0.44–1.21) 7.7–10.5: 0.80 (0.49–1.32) 10.5–13.7: 0.55 (0.32–0.96) 13.7–33.2: 0.47 (0.27–0.81)	Sex, age, education, year of interview, body mass index, tobacco smoking, family history, total energy intake. Reference (upper limit): 5.4 servings/week
Larsson et al. (2006), Sweden	Population-based cohort study Women: 36,664 Men: 45,338 Cases: 139	Vegetable servings/d 1.0–1.4: 0.66 (0.36–1.21) 1.5–2.4: 0.67 (0.41–1.11) ⩾ 2.5: 0.56 (0.34–0.93)	Age, sex, education, smoking and pack years of smoking, diabetes, total energy intake, alcohol and processed meat intake. Reference 1 serving/d.

Table 1.B.3. (*continued*)

Author, year, country	Study design	RR/OR	Adjustment
Lunet, et.al., 2007,[45] Portugal	Case control Cases: 305 Control: 1129	Vegetable servings/d Cardia 1.4–2.3: 0.91 (0.48–1.73) ⩾2.4: 0.59 (0.26–1.35) Non-cardia 1.4–2.3: 0.83 (0.58–1.19) ⩾2.4: 0.85 (0.58–1.26) Not classified 1.4–2.3: 0.72 (0.26–1.96) ⩾2.4: 0.54 (0.17–1.68)	Sex, age, education level, total caloric intake, fruit consumption. Reference ⩽1.3 servings/d
Gonzalez et al. (2006),[42] Europe (EPIC)	Cohort study Cohort: 481,518 Cases (adenocarcinoma): 330	Vegetable g/d 152: 1.14 (0.85–1.52) 187: 0.82 (0.58–1.16) 244: 1.15 (0.78–1.70)	Stratified by centre and age. Adjusted by sex, height, weight, education, smoking, smoking intensity, physical activity, alcohol, energy intake, red meat and processed meat intake. Reference 113 g/d (average men & women)

Table 1.B.4. Vegetable consumption and colorectal cancer.

Author, year, country	Study design	RR/OR	Adjustment
Pietinen et al. (1999),[39] Finland	Primary prevention trial (case-cohort) Cases: 185 Non-cases: 26926	Vegetables g/d 44–81: 1.3 (0.8–1.9) 82–120: 1.1 (0.7–1.7) 121–191: 1.2 (0.8–1.9)	Age, smoking years, BMI, alcohol, education, physical activity at work, calcium intake. Reference <44 g/d
Voorrips et al. (2000),[30] The Netherlands	Case-cohort Cases: Men, colon: 313 Men, rectal: 201 Cohort, men: 1456 Cases: Women, colon: 274 Women, rectal: 122 Cohort, women: 1497	Men, vegetables, colon, median intake g/d 144: 0.96 (0.65–1.42) 175: 0.92 (0.62–1.36) 214: 0.98 (0.66–1.44) 285: 0.85 (0.57–1.27) Women, vegetables g/d, colon 147: 0.83 (0.54–1.26) 181: 0.95 (0.64–1.42) 220: 0.79 (0.52–1.20) 293: 0.83 (0.54–1.26) Men, vegetables, rectal, median intake g/d 144: 0.89 (0.56–1.43) 175: 0.88 (0.55–1.41) 214: 0.87 (0.54–1.39) 285: 0.88 (0.55–1.41) Women, vegetables g/d, rectal: 147: 1.56 (0.81–2.99) 181: 1.35 (0.69–2.61) 220: 1.60 (0.84–3.06) 293: 1.78 (0.94–3.38)	Age, family history of colorectal cancer, category of alcohol intake. Reference (men) 100 g/d. Reference (women) 107 g/d

(*continued on next page*)

Table 1.B.4. (*continued*)

Author, year, country	Study design	RR/OR	Adjustment
Terry et al. (2001),[20] Sweden	Cohort Cases: 460 Cohort: 61463	Vegetables servings/d 1.0–1.5: 0.87 (0.67–1.12) 1.5–2.0: 0.92 (0.72–1.19) >2.0: 0.84 (0.65–1.09)	Age, consumption of red meat and dairy products, total calories. Reference <1 servings/d
Kampman et al. (1995)[34]	Case-control: colon, Cases: 232 Controls: 259 population-based	Vegetables g/d 142–191: 0.73 (0.45–1.21) 192–247: 0.53 (0.32–0.89) >247: 0.40 (0.23–0.69)	Age, gender, urbanisation level, total energy intake, alcohol use, cholecystectomy, family history of colon cancer. Reference <142 g/d
Negri et al. (1991),[19] Italy	Case-control: colon Cases: 673 Controls: 6147 (hospital-based)	Vegetables portions/week 7: 1.0 (0.8–1.2) >7: 0.5 (0.4–0.6)	Age, education, area of residence, smoking, sex Reference <7 portions/week
Negri et al. (1991),[19] Italy	Case-control: rectum, Cases: 406 Controls: 6147 (hospital-based)	Vegetables portions/week 7: 1.0 (0.8–1.2) >7: 0.6 (0.4–0.8)	Age, education, area of residence, smoking, sex Reference <7 portions/week

Table 1.B.5. Vegetable consumption and lung cancer

Author, year, country	Study design	RR/OR	Adjustment
Voorrips et al. (2000),[30] The Netherlands	Case-cohort Cases: For vegetables: 929 For fruit: 963 Cohort: 2953	Vegetables g/d (median) 145: 1.1 (0.8–1.5) 178: 1.0 (0.7–1.3) 217: 1.0 (0.7–1.3) 286: 0.7 (0.5–1.0)	Age, sex, family history of lung cancer, highest education level, current smoker, years of smoking, number of cigarette/d. Reference 103 g/d
Jansen et al. (2001)[33]	Male cohort		Age, number of cigarettes smoked, cohort (for Finland & Italy), energy intake, fruit intake
Finland	Cases: 85 Cohort: 1288	Vegetables g/d 62.4: 0.69 (0.38–1.27) 131: 0.99 (0.56–1.78)	Reference 25.7 g/d
Italy	Cases: 41 Cohort: 1207	Vegetables g/d (median) 55: 0.83 (0.36–1.90) 98: 1.05 (0.47–2.35)	Reference 18 g/d
The Netherlands	Cases: 61 Cohort: 613	Vegetables g/d (median) 175: 0.82 (0.40–1.66) 223: 0.88 (0.43–1.82)	Reference 126.5 g/d
Holick et al. (2002),[32] Finland	Cases: 1644 Cohort: 27,084	Vegetables g/d 52–79: 1 (0.87–1.16) 80–109: 0.93 (0.80–1.08) 110–156: 0.83 (0.71–0.96) >156: 0.75 (0.63–0.88)	Age, years smoked, cigarettes per d, intervention, supplement use, energy intake, cholesterol and fat. Reference <52 g/d
Dosil-Diaz et al. (2008),[46] Spain	Case-control Cases: 295 Controls: 322	Vegetable times/week 5–6: 0.35 (0.17–0.70) 7: 0.50 (0.50–0.83)	Sex, age, smoking, employment in risk occupations. Reference <1 time/week

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