case-control studies, and the mechanistic evidence is speculative. There is limited evidence that greater adult attained height, or the factors that lead to it, are a cause of endometrial cancer. The causal factor is unlikely to be tallness itself, but factors that promote linear growth in childhood.

7.12.5.7 Other exposures

Other exposures were evaluated. However, the data were either of too low quality, too inconsistent, or the number of studies too few to allow conclusions to be reached. These were as follows: cereals (grains) and their products; fruits; pulses (legumes); tofu and soya; poultry; fish; eggs; milk and dairy products; coffee; alcohol; carbohydrates; dietary fibre; total fat; animal fats; saturated fatty acids; cholesterol; protein; retinol; beta-carotene; vitamin C; vitamin E; energy intake; and lactation.

7.12.6 Comparison with previous report

7.12.6.1 General

See 7.1.6.1, and box 3.8 in chapter 3.

7.12.6.2 Specific

The finding here on physical activity is new. The evidence on body fatness and on abdominal fatness (not considered separately in the previous report's matrices) has strengthened.

7.12.7 Conclusions

The Panel concludes:
The evidence that body fatness is a cause of cancer of the endometrium is convincing; abdominal fatness is probably also a cause.

Physical activity probably protects against this cancer.

There is limited evidence suggesting that non-starchy vegetables protect against endometrial cancer, and that red meat, and also the factors that lead to greater adult attained height, or its consequences, are causes of this cancer.

7.13 Cervix

Cervical cancer is the second most common cancer in women worldwide. Around half a million cases were recorded in 2002, accounting for around 10 per cent of all new cases of cancer in women (5 per cent overall). It is most common in Africa, some parts of Asia including India, and in Latin America. It is most common in relatively young women. Five-year survival rates are around 50 per cent. It is the third most common cause of cancer death in women.

Overall, *the Panel notes* that food and nutrition and associated factors are not significant factors in modification of the risk of cancer of the cervix, although general nutritional status may affect a woman's vulnerability to infection.

Life events that protect against cervical cancer include having relatively few sexual partners. The reverse also applies. Infection with HPV is a necessary cause of this cancer, and smoking tobacco increases risk.

***The Panel judges* as follows:**
There is limited evidence suggesting that carrots protect against cervical cancer.

In final summary, there is no strong evidence, corresponding to judgements of "convincing" and "probable", to conclude that any aspect of food, nutrition, and physical activity modifies the risk of cervical cancer.

The cervix is the neck of the womb. The part of the cervix inside the cervical canal is called the endocervix. The part on the outside is the ectocervix. Most cervical cancers start where these two parts meet. There are two main types, squamous cell carcinoma and adenocarcinoma. Occasionally, mixed carcinomas, with features of both types, occur. Approximately 80 per cent of cervical cancers are squamous cell carcinomas, with most of the rest being adenocarcinomas.[265] Both types of cervical cancer are covered in this Report.

7.13.1 Trends, incidence, and survival

Age-adjusted rates of cervical cancer are decreasing, particularly in high- and middle-income countries, although there are insufficient data to derive trends in low-income countries. In high-income countries, the incidence of adenocarcinomas has increased since the 1970s, both absolutely and relative to squamous cell carcinomas. The prevalence appears to be increasing disproportionately in young women.[266]

Cervical cancer is predominantly a disease of low-income countries, with overall rates nearly twice as high in middle- to low- as in high-income countries. Around the world, age-adjusted incidence rates range from more than 40 per 100 000 women in parts of Africa, South America, and Melanesia, to less than 10 per 100 000 in North America and parts of Asia. However, rates are relatively high elsewhere

FOOD, NUTRITION, PHYSICAL ACTIVITY, AND CANCER OF THE CERVIX

In the judgement of the Panel, the factors listed below modify the risk of cancer of the cervix. Judgements are graded according to the strength of the evidence.

	DECREASES RISK	INCREASES RISK
Convincing		
Probable		
Limited — suggestive	Carrots[1]	
Limited — no conclusion	Non-starchy vegetables; fruits; milk; retinol; vitamin E; alcoholism[2]; body fatness; adult attained height.	
Substantial effect on risk unlikely	None identified	

1 Judgements on vegetables and fruits do not include those preserved by salting and/or pickling.
2 Although data suggest that alcoholism is related to increased risk, *the Panel concludes* that this is likely to be due to factors other than alcohol intake itself.

For an explanation of all the terms used in the matrix, please see chapter 3.5.1, the text of this section, and the glossary.

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in Asia, for example in India and Bangladesh. In the USA, rates are higher among both African-American and Hispanic-American women than in white women. The incidence of many cancers rises with age, but cervical cancer peaks in younger women, between the ages of 30 and 45.[6] However, mortality does not follow the same pattern, and rises with age. Most women in high-income countries, and to varying degrees in other countries, have access to preventive screening programmes that are designed to detect precancerous lesions. If these are identified and removed, the incidence of this cancer is reduced. After a screening programme was implemented in the UK in 1988, cervical cancer incidence (age-standardised rate) has fallen by nearly 60 per cent.[6] It is generally well accepted that better access to cervical screening programmes worldwide would decrease both the incidence and mortality rates for this cancer.[267] More recently vaccination against HPV has become a preventive option.

The overall 5-year survival rate is approximately 50 per cent: 61 per cent in high-income countries compared with 41 per cent in middle- to low-income countries.[124] This cancer accounts for somewhat over 4 per cent of all cancer incidence (around 10 per cent in women) but only around 4 per cent of all cancer deaths (just over 9 per cent in women). Also see box 7.1.1.

7.13.2 Pathogenesis

Virtually all cervical cancers are associated with HPV infection (see box 7.13.1), and a woman's nutrition status may influence her susceptibility to this infection.[268] However, the majority of women with HPV do not develop cervical cancer. Therefore, HPV infection is a necessary but not a sufficient cause of cervical cancer. Women become susceptible to developing cervical cancer following HPV infection, but other environmental factors are required for the cancer to develop.

These factors may include toxins such as polycyclic aromatic hydrocarbons (see box 4.3.4) from tobacco smoke, food, or other environmental sources, which have been found in the mucus lining the cervix.[269]

Box 7.13.1 Human papilloma viruses

Human papilloma viruses (HPVs) are common. They infect squamous epithelia and generate warts. They are passed by direct contact; genital HPV infections are sexually transmitted. HPV infection rates are higher in women who have had a higher number of sexual partners (particularly male partners); do not use barrier methods of contraception; and who started having sex at a younger age.

There are more than 100 types of HPV. All can interfere with host-cell machinery that prevents cells from growing and replicating excessively, which are some of the cellular mechanisms that help protect the body against cancer development. Low-risk HPVs cause genital warts; high-risk HPVs cause squamous intra-epithelial lesions that can progress to invasive squamous cell carcinoma. The majority of human cervical cancers are associated with high-risk HPV infections. Four subtypes of this virus account for 80 per cent of all cervical cancer.

HPV infection tends to remain dormant, and with repeated infection, the HPV genome becomes integrated within the host cell genome and some cells may become cancerous.

Most HPV infections do not become persistent, and most persistent HPV infections do not lead to cancer. However, HPV infection is demonstrably present in 99 per cent of women with cervical cancer, and may be present but undetected in the remainder. HPV is a necessary while not sufficient cause of cervical cancer.

There are several stages at which foods or nutrition status could influence progression. Dietary factors influence susceptibility to infection; infection can alter nutrition status; diet may affect the likelihood of infections becoming persistent; and dietary factors have been shown to alter DNA stability and repair. Unfortunately, there is a shortage of epidemiological evidence specific to HPV at each of these stages. There is some limited evidence that eating vegetables and fruits can protect against persistence.[268] There is also evidence that folate can reduce persistence and independently reduce the risk of precancerous lesions in high-risk-HPV infected women.[270-272]

7.13.3 Other established causes

(Also see chapter 2.4 and 7.1.3.1.)

Life events. Early sexual experience and a relatively high number of sexual partners increase the risk and severity of HPV infection, and may be seen as indirect causes of cervical cancer.[220 222]

Tobacco use. Smoking tobacco makes a woman twice as likely to develop cervical cancer.[10] Tobacco by-products have been found in the cervical mucus of women who smoke. The effect of smoking is independent of that of viral infection.[10 273]

Infectious agents. HPV infection (see box 7.13.1) is a necessary but not sufficient cause of cervical cancer.[273 274]

Medication. Dethylstilboestrol (a synthetic oestrogen, now withdrawn) used by women during pregnancy is a cause of vaginal and cervical clear-cell adenocarcinoma in their daughters.[275]

7.13.4 Interpretation of the evidence

7.13.4.1 General

For general considerations that may affect interpretation of the evidence, see chapters 3.3 and 3.5, and boxes 3.1, 3.2, 3.6 and 3.7.

'Relative risk' is used in this Report to denote ratio measures of effect, including 'risk ratios', 'rate ratios', 'hazard ratios', and 'odds ratios'.

7.13.4.2 Specific

Considerations specific to cancer of the cervix include:

Confounding. High-quality studies adjust for HPV infection. Early studies that failed to adjust for HPV status have reduced validity.

7.13.5 Evidence and judgements

In total, 154 publications were included in the SLR for cervical cancer. Fuller summaries of the epidemiological, experimental, and mechanistic evidence are to be found in Chapters 4–6.

The full SLR is contained on the CD included with this Report.

7.13.5.1 Carrots

(Also see chapter 4.2.5.1.3.)

Five case-control studies and one ecological study investigated carrots. All of the case-control studies showed decreased risk for the highest levels of intake compared with the lowest, statistically significant in three. The case-control studies all used hospital-based controls and none adjusted for HPV status. The single ecological study showed non-significant increased risk with high intake of carrots.

Some carotenoids, including beta-carotene and alpha-carotene, which are found at high levels in carrots, are precursors of vitamin A. They also have properties independent of their pro-vitamin A activity. Carotenoids are recognised antioxidants, and low blood levels of dietary antioxidants are associated with HPV persistence.[276]

The evidence, from case-control studies only, is sparse but consistent. There is limited evidence suggesting that carrots protect against cervical cancer.

7.13.5.2 Other exposures

Other exposures were evaluated. However, the data were either of too low quality, too inconsistent, or the number of studies too few to allow conclusions to be reached. These were as follows: non-starchy vegetables; fruits; milk; retinol; vitamin E; alcoholism; body fatness; and adult attained height.

Although data suggest that alcoholism is related to increased risk, *the Panel concludes* that this is likely to be due to factors other than alcohol intake itself.

7.13.5.3 Exposures as related to non-invasive cancer outcomes

The following exposures were evaluated. However, the data were either too sparse, too inconsistent, or the number of studies too few to allow conclusions to be reached: vitamin A (as beta-carotene, alpha-carotene, or retinol); folate; vitamin C; vitamin E; and lycopene.

7.13.6 Comparison with previous report

7.13.6.1 General

See 7.1.6.1, and box 3.8 in chapter 3.

7.13.6.2 Specific

The previous report found that vegetables and fruits, and carotenoids (not carrots specifically), and also vitamins C and E possibly protect against cervical cancer.

7.13.7 Conclusions

The Panel concludes:

There is limited evidence suggesting that carrots protect against cervical cancer. The evidence is too limited to conclude that any aspect of food, nutrition, and physical activity directly modifies the risk of this cancer.