Diet, Nutrition, Physical Activity and Cancer: a Global Perspective

Third Expert Report

Professor Martin Wiseman
WCRF International; and
University of Southampton
Outline

- WCRF network and the Continuous Update Project (CUP)
- Background to the subject
- Evidence on cancer incidence and survival
- Recommendations and policy implications
- Key points
- Conclusions
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The World Cancer Research Fund Network

World Cancer Research Fund International (est. 1999)

Leads and unifies a network of cancer charities with a global reach, dedicated to the prevention of cancer through diet, weight and physical activity.
Who we are

What we do

Fund research on the relationship of diet, nutrition, physical activity and body weight to cancer risk

Interpret the accumulated scientific literature to derive Cancer Prevention Recommendations

Educate people through our national Health Information programmes

Advocate effective policies to help people and populations to reduce their chances of developing cancer
The Continuous Update Project (CUP)

Continuous Update Project
The process we use to analyse worldwide research

- One central database for cancer prevention research
- Prepare protocols, conduct systematic reviews, analyse meta-data and update central database, prepare reports
- External review of protocols and reports
- Draw conclusions from the evidence; review Cancer Prevention Recommendations
- Use Panel conclusions and Cancer Prevention Recommendations to make public health recommendations and set research priorities

Scientists at Imperial College London: collate the worldwide evidence
Peer reviewers
CUP Panel (cancer experts from around the world) with support from WCRF/AICR Secretariat
World Cancer Research Fund Network

SECOND EXPERT REPORT 2007
CONTINUOUS UPDATE PROJECT 2018
THIRD EXPERT REPORT

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Migration data

Figure 1.2.20 Cancer incidence for selected cancers in Japanese women by generation in Hawaii and Japan, 1968–1977

- Stomach
- Colon, rectum
- Breast

Rate per 100,000

Japan (Miyagi) | Hawaii (1st generation) | Hawaii (2nd generation)

Age-adjusted to the World Standard Population
(From Kolonel et al, 1980)
Colorectal cancer incidence trends

Selected countries, men, 1975 to 2010
Hallmarks of cancer and enabling characteristics


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Nutrition, physical activity and the hallmarks of cancer

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The evidence for cancer risk: a summary matrix

<table>
<thead>
<tr>
<th>Year</th>
<th>Exposure Group Key</th>
<th>Conclusions Key</th>
</tr>
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<tbody>
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<td></td>
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</tr>
</tbody>
</table>

- Diet and Cancer Report
- World Cancer Research Fund International
- dietandcancerreport.org

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Abbreviation: SLR, systematic literature review.
### SUMMARY OF STRONG EVIDENCE ON DIET, NUTRITION, PHYSICAL ACTIVITY AND THE PREVENTION OF CANCER

To reference this matrix please use the following citation:

NUTRITION AND CANCERS

• ADIPOSITY
Breast (post); Colorectum; Endometrium; Oesophagus (a/c); Pancreas; Gallbladder; Kidney; Ovary; Prostate (advanced); Liver; Stomach (cardia); Mouth, pharynx, larynx (MPL)

• PHYSICAL (IN)ACTIVITY
Colon, Breast, Endometrium

• MEAT – RED AND PROCESSED
Colorectal

• ALCOHOL
MPL; Breast; Colorectum; Liver; Oesophagus (SCC)

• PLANT FOODS (F&V, PULSES, WHOLEGRAINS)
Aerodigestive cancers (MPL, nasopharynx, lung, oesophagus, stomach, colorectal)

• BREASTFEEDING
Breast (mother), Obesity (child)

• HEIGHT
Breast; Colorectal; Pancreas; Kidney; Ovary; Prostate; Endometrium; Melanoma
Diet, Nutrition, Physical Activity and Cancer: a Global Perspective

Survivors of breast and other cancers
<table>
<thead>
<tr>
<th></th>
<th>DECREASES RISK</th>
<th></th>
<th>INCREASES RISK</th>
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<td>Exposure</td>
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<td>Timeframe</td>
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<td><strong>STRONG EVIDENCE</strong></td>
<td>Convincing</td>
<td></td>
<td>Strong</td>
<td></td>
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<tr>
<td></td>
<td>Probable</td>
<td></td>
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<tr>
<td><strong>LIMITED EVIDENCE</strong></td>
<td>Limited – suggestive</td>
<td>Physical activity</td>
<td>&gt;12 months after diagnosis</td>
<td>Body fatness</td>
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<tr>
<td></td>
<td></td>
<td>Foods containing fibre</td>
<td>Before diagnosis</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Fruits containing fibre</td>
<td>≥12 months after diagnosis</td>
<td>Total fat</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Foods containing soy</td>
<td>≥12 months after diagnosis</td>
<td>Saturated fatty acids</td>
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<tr>
<td><strong>STRONG EVIDENCE</strong></td>
<td>Substantial effect on risk unlikely</td>
<td></td>
<td>Strong</td>
<td></td>
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</tbody>
</table>

**STRONG**: Evidence strong enough to support a judgement of a convincing or probable causal relationship and generally justify making recommendations.

**LIMITED**: Evidence that is too limited to justify making specific recommendations.

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Recommendations
OUR CANCER PREVENTION RECOMMENDATIONS

Not smoking and avoiding other exposure to tobacco and excess sun are also important in reducing cancer risk. Following these Recommendations is likely to reduce intakes of salt, saturated and trans fats, which together will help prevent other non-communicable diseases.
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RECOMMENDATION

Be a healthy weight

Keep your weight within the healthy range\(^1\) and avoid weight gain in adult life

**GOAL**

Ensure that body weight during childhood and adolescence projects towards the lower end of the healthy adult BMI range

**GOAL**

Keep your weight as low as you can within the healthy range throughout life

**GOAL**

Avoid weight gain (measured as body weight or waist circumference)\(^2\) throughout adulthood

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\(^1\) The healthy (or, as defined by WHO, ‘normal’) range of BMI for adults is 18.5–24.9 kg/m\(^2\) [1]. Different reference ranges have been proposed for Asian populations [1]. Where these ranges differ from the WHO definition, they are to be used as the guide. Further research is required to establish appropriate thresholds in other ethnic groups. The healthy range for BMI during childhood varies with age [2].

\(^2\) WHO recommends keeping waist circumference below 94 cm (37 inches) in men and 80 cm (31.5 inches) in women (based on data from European people). These values are roughly equivalent to a BMI of around 25 kg/m\(^2\) [3]. For Asian populations, cut-offs for waist circumferences of 90 cm (35.4 inches) for men and 80 cm (31.5 inches) for women have been proposed [3]. Further research is required to establish appropriate waist circumference values for other ethnic groups.
RECOMMENDATION
Be physically active

Be physically active as part of everyday life – walk more and sit less

- **GOAL** Be at least moderately physically active\(^1\), and follow or exceed national guidelines
- **GOAL** Limit sedentary habits

\(^1\) Moderate physical activity increases heart rate to about 60 to 75 per cent of its maximum.
**RECOMMENDATION**

**Eat a diet rich in wholegrains, vegetables, fruit and beans**

Make wholegrains, vegetables, fruit, and pulses (legumes) such as beans and lentils a major part of your usual daily diet.

- **GOAL** Consume a diet that provides at least 30 grams per day of fibre from food sources.
- **GOAL** Include in most meals foods containing wholegrains, non-starchy vegetables, fruit and pulses (legumes) such as beans and lentils.
- **GOAL** Eat a diet high in all types of plant foods including at least five portions or servings (at least 400 grams or 15 ounces in total) of a variety of non-starchy vegetables and fruit every day.
- **GOAL** If you eat starchy roots and tubers as staple foods, eat non-starchy vegetables, fruit and pulses (legumes) regularly too if possible.

*Measured by the AOAC method.*
RECOMMENDATION

Limit consumption of ‘fast foods’ and other processed foods high in fat, starches or sugars

Limiting these foods helps control calorie intake and maintain a healthy weight

GOAL Limit consumption of processed foods high in fat, starches or sugars – including ‘fast foods’; many pre-prepared dishes, snacks, bakery foods and desserts; and confectionery (candy)

1 ‘Fast foods’ are readily available convenience foods that tend to be energy dense and are often consumed frequently and in large portions.
RECOMMENDATION

Limit consumption of red and processed meat

Eat no more than moderate amounts of red meat\(^1\), such as beef, pork and lamb. Eat little, if any, processed meat\(^2\)

**GOAL**
If you eat red meat, limit consumption to no more than about three portions per week. Three portions is equivalent to about 350 to 500 grams (about 12 to 18 ounces) cooked weight of red meat\(^3\). Consume very little, if any, processed meat.

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\(^1\) The term ‘red meat’ refers to all types of mammalian muscle meat, such as beef, veal, pork, lamb, mutton, horse and goat.

\(^2\) The term ‘processed meat’ refers to meat that has been transformed through salting, curing, fermentation, smoking or other processes to enhance flavour or improve preservation.

\(^3\) 500 grams of cooked red meat is roughly equivalent to 700–750 grams of raw meat, but the exact conversion depends on the cut of meat, the proportions of lean meat and fat, and the method and degree of cooking.
RECOMMENDATION

Limit consumption of sugar sweetened drinks

Drink mostly water and unsweetened drinks

GOAL  Do not consume sugar sweetened drinks¹

¹ Sugar sweetened drinks are defined here as liquids that are sweetened by adding free sugars, such as sucrose, high fructose corn syrup and sugars naturally present in honey, syrups, fruit juices and fruit juice concentrate. This includes, among others, sodas, sports drinks, energy drinks, sweetened waters, cordials, barley water, and coffee- and tea-based beverages with sugars or syrups added. This does not include versions of these drinks which are ‘sugar free’ or sweetened only with artificial sweeteners.
RECOMMENDATION

Limit alcohol consumption

For cancer prevention, it’s best not to drink alcohol
RECOMMENDATION

Do not use supplements for cancer prevention

Aim to meet nutritional needs through diet alone

GOAL: High-dose dietary supplements are not recommended for cancer prevention – aim to meet nutritional needs through diet alone.

1 A dietary supplement is a product intended for ingestion that contains a ‘dietary ingredient’ intended to achieve levels of consumption of micronutrients or other food components beyond what is usually achievable through diet alone.
RECOMMENDATION

For mothers: breastfeed your baby, if you can

Breastfeeding is good for both mother and baby

GOAL: This recommendation aligns with the advice of the World Health Organization, which recommends infants are exclusively breastfed\(^1\) for 6 months, and then up to 2 years of age or beyond alongside appropriate complementary foods.

\(^1\) ‘Exclusive breastfeeding’ is defined as giving a baby only breastmilk (including breastmilk that has been expressed or is from a wet nurse) and nothing else – no other liquids or solid foods, not even water [1]. It does, however, allow the infant to receive oral rehydration solution, drops or syrups consisting of vitamins, minerals, supplements or medicines [1].

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RECOMMENDATION

After a cancer diagnosis: follow our Recommendations, if you can

Check with your health professional what is right for you

**GOAL**

All cancer survivors\(^1\) should receive nutritional care and guidance on physical activity from trained professionals

**GOAL**

Unless otherwise advised, and if you can, all cancer survivors are advised to follow the Cancer Prevention Recommendations as far as possible after the acute stage of treatment

\(^1\) Cancer survivors are people who have been diagnosed with cancer, including those who have recovered from the disease.

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Adherence to the 2007 Recommendations

Results shown for women

Cox regression model stratified by centre and age, and adjusted by level of school, smoking status, smoke intensity, and menopausal status

Romaguera et al (2012), AJCN

Vergnaud et al (2013), AJCN

Cancer risk

Score constructed to measure adherence to WCRF/AICR Cancer Prevention Recommendations

Total mortality

P for trend <0.0001
OUR CANCER PREVENTION RECOMMENDATIONS

Not smoking and avoiding other exposure to tobacco and excess sun are also important in reducing cancer risk. Following these Recommendations is likely to reduce intakes of salt, saturated and trans fats, which together will help prevent other non-communicable diseases.

1. **Eat a diet rich in wholegrains, vegetables, fruit and beans**
2. **Be physically active**
3. **Be a healthy weight**
4. **Limit consumption of red and processed meat**
5. **Limit consumption of fast foods and other processed foods high in fat, starches or sugars**
6. **Limit sugar-sweetened drinks**
7. **Limit alcohol consumption**
8. **Do not use supplements for cancer prevention**
9. **For mothers: Breastfeed your baby, if you can**
10. **After a cancer diagnosis: Follow our recommendations, if you can**

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The influence of nutrition through the life course

How nutrition, at all stages of the life course and cancer journey, influences the risk of developing cancer, as well as the resilience to cancer and response to treatment.
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Public health and policy implications
The NOURISHING framework

| N | Nutrition label standards and regulations on the use of claims and implied claims on food |
| O | Offer healthy food and set standards in public institutions and other specific settings |
| U | Use economic tools to address food affordability and purchase incentives |
| R | Restrict food advertising and other forms of commercial promotion |
| I | Improve nutritional quality of the whole food supply |
| S | Set incentives and rules to create a healthy retail and food service environment |
| H | Harness food supply chain and actions across sectors to ensure coherence with health |
| I | Inform people about food and nutrition through public awareness |
| N | Nutrition advice and counselling in health care settings |
| G | Give nutrition education and skills |

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A new policy framework to address diet, physical activity, breastfeeding and alcohol consumption
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The key messages are robust

- Be active, and don’t be sedentary – and keep it up as long as possible
- Eat enough but not too much – don’t get too thin or fat
- Eat food not pills
- Mostly from plants, emphasise wholegrains and pulses
- Avoid highly processed energy dense foods and sugar sweetened beverages (and alcohol, processed meat and salty foods)
- Grow appropriately from conception to adulthood
- Get your mother to be well nourished before getting pregnant. And to breastfeed you.
For cancer survivors...

• If you already have a diagnosis of cancer, the evidence on nutrition and outcome is not as strong, but the best advice is to follow (as far as possible) the recommendations for cancer prevention.
Outline

• WCRF network and the Continuous Update Project (CUP)
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• Key points
• Conclusions
• The evidence is good enough to justify action
  Evidence for nutrition and cancer
  Evidence for effective interventions

• The recommendations come as a whole package

• Action needs leadership from government and health professionals
For more information contact ri@wcrf.org

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wcrf.org/blog
GLOBAL CANCER DATA 2018

**Global cancer incidence**

- **18.1 million new cancer cases**
  - The Americas: 21.0%
    - Number of cases: 3,792,000
  - Europe: 23.4%
    - Number of cases: 4,250,000
  - Asia: 48.4%
    - Number of cases: 8,751,000
  - Africa: 5.8%
    - Number of cases: 1,055,000
  - Oceania: 1.4%
    - Number of cases: 252,000

**Global cancer mortality**

- **9.6 million cancer deaths**
  - The Americas: 14.4%
    - Number of deaths: 1,321,000
  - Europe: 20.3%
    - Number of deaths: 1,943,000
  - Asia: 57.3%
    - Number of deaths: 5,477,000
  - Africa: 7.3%
    - Number of deaths: 693,000
  - Oceania: 0.7%
    - Number of deaths: 70,000

*Estimated number of incident cases, both sexes, all cancers including non-melanoma skin cancer, for all ages, worldwide*

*Data source: GLOBOCAN 2018
Available at Global Cancer Observatory (http://gco.iarc.fr)*

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Genetic damage and cancer

Association between the WCRF/AICR score and total cancer risk

Men

Women

Cox regression model stratified by centre and age, and adjusted by energy intake, level of school, smoking status, presence of chronic diseases at baseline, ever use of contraceptive pills, ever use of HRT, age at first menarche, age at first pregnancy, and menopausal status

Romaguera D et al, AJCN 2012
Association between the WCRF/AICR score and total mortality

Cox regression model stratified by centre and age, and adjusted by level of school, smoking status, smoke intensity, and menopausal status

Vergnaud AC et al, AJCN 2013
Adult height, weight and ranges of body mass index (BMI)

Body mass index (BMI) is a simple index of weight-for-height used to classify underweight, healthy weight and overweight in adults. BMI is defined as weight in kilograms divided by the square of height in metres (kg/m²).

It is not possible to specify a single BMI goal that applies to all people, because healthy people vary in their proportion of lean to fat tissue at any BMI. We recommend that people aim to keep their BMI as low as possible within the healthy BMI range. People who have gained weight, even within the healthy range, are advised to aim to return to their original weight.

Adults above the healthy range of BMI are recommended to lose weight to approach the healthy range; general information is available from several reliable sources, such as government guidelines and the WCRF Network, but individually tailored advice is best sought from appropriately qualified professionals.
Obesity, physical activity and the hallmarks of cancer

Altered mitochondrial function; increased nutrient uptake in obesity-associated tumours

Insulin, PI3K, mTOR

Adipose stromal cells influence peritumoural vascularisation and inflammation

Oestrogen, MAPK, ERK

Adipose tissue-associated inflammation, leptin, STAT

Sustaining proliferative signalling
Evading growth suppressors
Avoiding immune destruction
Enabling replicative immortality
Tumor-promoting inflammation
Inducing angiogenesis
Activating invasion & metastasis
Enabling characteristics

Resisting cell death
Deregulating cellular energetics
Genome instability & mutation

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Evolution of cancer survivorship, England, 1970s to present

- All adults
- Male
- Female

Period of diagnosis:
- 1970-72
- 1980-81
- 1990-91
- 2000-01
- 2005-06
- 2010-11

5-year net survival %
- 20
- 30
- 40
- 50
- 60

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Lifestyle and the cancer process

- The cancer process is the result of a complex interaction involving diet, nutrition and physical activity, and other lifestyle and environmental factors, with host factors that are related both to inheritance and to prior experience, possibly through epigenetic change.

- Nutrition is important as part of a healthy lifestyle and plays a key role in reducing the risk of cancer.

- Nutrition is an important determinant of wellbeing after a cancer diagnosis, as well as a predictor of response to therapy and survival.
Cells of the tumour microenvironment


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Stages of cancer development and the hallmarks of cancer


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<table>
<thead>
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<th>Exposure</th>
<th>Systemic impact</th>
<th>Cell function</th>
<th>Hallmarks possibly affected</th>
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<tr>
<td>Greater body fatness</td>
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<tr>
<td>Hyperinsulinemia</td>
<td>mTOR/PI3K/AKT, MAPK</td>
<td>Reduced apoptosis; increased proliferation, genome instability</td>
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<tr>
<td>Increased oestriadiol</td>
<td>MAPK/ERK/PI3K</td>
<td>Increased proliferation in ER+ tissues; genome instability</td>
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<td>Inflammation</td>
<td>STAT3/NF-κB</td>
<td>Reduced apoptosis, increased cell division, altered macrophage function, etc.; genome instability</td>
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<td>E.g. WNT, P53</td>
<td>E.g. cellular energetics, etc.</td>
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<td>Lower fruit and vegetable intake</td>
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<td>Folate deficiency</td>
<td>DNA uracil misincorporation</td>
<td>Genome instability</td>
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<td>Low dietary fibre intake</td>
<td>Low butyrate</td>
<td>Reduced apoptosis; increased proliferation</td>
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<td>Low levels of carotenoids, vitamin A, C, E</td>
<td>Oxidative stress, inflammation</td>
<td>Increased inflammation, genomic instability, reduced apoptosis; increased proliferation</td>
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<td>Greater intake of red and processed meat</td>
<td>Elevated exposure to nitrates; endogenous N-nitroso compound formation</td>
<td>DNA adduct formation -&gt; mutations in p53, KRAS, etc.</td>
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<td>Greater Intake of dairy foods</td>
<td>Higher IGF-1</td>
<td>mTOR/PI3K/AKT, MAPK</td>
<td>Reduced apoptosis; increased proliferation</td>
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<td>Greater alcohol Intake</td>
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<tr>
<td>Elevated acetaldehyde</td>
<td>Oxidative stress, lipid peroxidation</td>
<td>Increased inflammation, genomic instability</td>
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<td>Increased oestriadiol</td>
<td>MAPK/ERK/PI3K</td>
<td>Increased proliferation in ER+ tissues</td>
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<td>Reduced apoptosis, increased cell division, altered macrophage function, etc.</td>
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<td>E.g. folate deficiency; interference with 1-carbon metabolism</td>
<td>DNA uracil misincorporation</td>
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<tr>
<td>Greater physical activity</td>
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<tr>
<td>Reduction in insulin</td>
<td>mTOR/PI3K/AKT, MAPK</td>
<td>Increased apoptosis; reduced proliferation, less genome instability</td>
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<td>MAPK/ERK/PI3K</td>
<td>Reduced proliferation in ER+ tissues; reduced genome instability</td>
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<tr>
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<td>STAT3/NF-κB</td>
<td>Increased apoptosis, increased cell division, altered macrophage function etc; reduced genome instability</td>
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<td>Reduced apoptosis; increased proliferation</td>
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Obesity and the hallmarks of cancer

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