

HRT and the likelihood of some medical conditions

A discussion aid for GPs and patients

Menopause: identification
and management
(NICE guideline NG23)

About this document

Introduction and contents

This discussion aid should be used alongside the [section on effects of hormone replacement therapy on specific health outcomes](#) in NICE's guideline on menopause.

In this document, the likelihood of having some medical conditions is provided for different age groups, as follows:

Women experiencing menopause aged **45 or over**:

Combined HRT

- [Cancer: breast](#)
- [Cancer: endometrial](#)
- [Cancer: ovarian](#)
- [Coronary heart disease](#)
- [Dementia](#)
- [Osteoporosis](#)
- [Stroke](#)

Oestrogen-only HRT

- [Cancer: breast](#)
- [Cancer: endometrial](#)
- [Cancer: ovarian](#)
- [Coronary heart disease](#)
- [Dementia](#)
- [Osteoporosis](#)
- [Stroke](#)

Women experiencing early menopause (**ages 40 to 44**):

Combined HRT

- [Cancer: breast](#)
- [Other medical conditions](#)

Oestrogen-only HRT

- [Cancer: breast](#)
- [Other medical conditions](#)

Moving around this document

If you are using this document digitally, you can click on any of the links above to go to that section. At the end of each section you can click on the 'home' icon to come back to this page.



What does this document cover?

The numbers presented are **absolute risks**. Duration and recency of HRT use are included where possible. Where they are not included, it is because the data was not available in the evidence we looked at for this guideline.

The benefits and risks of HRT described in this document only cover the use of HRT within the licensed dosages.

The graphs present:

- the number of women per 1,000 women experiencing menopause who have never taken HRT – this is the **baseline risk**, that is, the number of women per 1,000 that will experience the outcome anyway even if they do not take HRT
- the number of women per 1,000 who are expected to experience the outcome if they take HRT (**absolute risk**).

The numbers presented in this document are new cases of each of the outcomes (for example, a first fragility fracture or first-time breast cancer). The longest period over which risk is reported is 20 years (covering ages 50 to 69). For most outcomes, lifetime risk data was not available. The period of time over which risk is measured is provided for each outcome.

These **estimates** have been calculated to support GPs and their patients during discussions about how HRT may affect the likelihood of having some medical conditions. For more information, see the sections on [how we estimated the absolute risks](#) and [uncertainty around the data](#).

The committee discussed evidence that included a very large amount of data. Different data sources provided different level of detail and focused on different parameters. To make discussions and shared decision making easier, this document only presents the data that includes enough detail to support the recommendations, so the sources presented vary from outcome to outcome.

For each outcome:

- the numbers in this document are estimates that have been calculated based on data from sources listed in the relevant 'where the data comes from' section
- detailed calculations for the estimates can be found in [supplement 19: absolute calculations](#)
- data on other follow-up periods, duration of use, type of user (that is, current or past users), or age groups are included in the evidence review for each outcome – these can be from the same sources or from different sources, including different study types.

For each outcome, a link to the relevant evidence review and calculations can be found in the 'To find out more' sections.

Who is the data relevant for?

In line with [recommendation 1.8.1 in the section on starting hormone replacement therapy in NICE's guideline on menopause](#):


- people with a uterus (womb) should be offered combined HRT
- people who have had a total hysterectomy should be offered oestrogen-only HRT.

In some people who have had a hysterectomy, the choice of HRT may be influenced by an underlying condition. Only the sections on the type of HRT that they will be offered are relevant to each person.

Trans men and non-binary people registered female at birth

The estimates in this document only covers women, because there was no evidence available for trans men and non-binary people registered female at birth. However, the committee agreed that their conclusions from the available evidence could be extended to trans men and non-binary people registered female at birth who have never taken gender-affirming hormone therapy, so the data in this document can be used for making shared decisions with people in these groups.

The data does not cover people who have taken gender-affirming therapy in the past and the committee's conclusions cannot be extended to this group. For more information, see the [rationale and impact section in the guideline](#) related to the type of HRT being recommended and the age of the person.



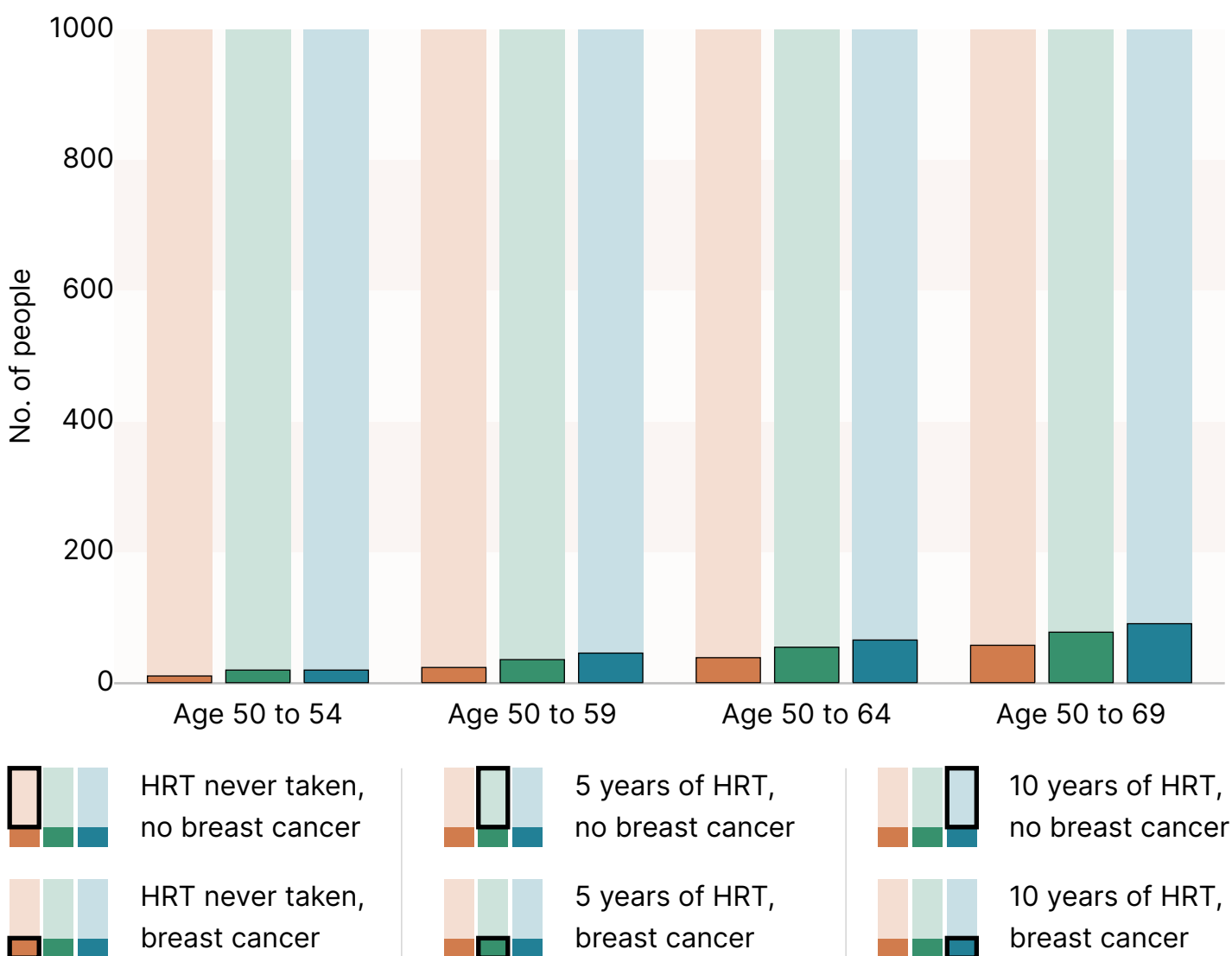
**Section 1:
Information for
women experiencing
menopause aged 45
or over**

Combined HRT: breast cancer

The risk of breast cancer in groups of 1,000 people for 4 successive periods of 5 years, starting when people are aged 50 and going all the way until they are 69, is presented in **Bar graph 1**. It shows the estimated risk for people who do not take HRT, for people who take combined HRT for the first 5 years (that is, from age 50 to 54), and for people who take combined HRT for the first 10 years (that is, from age 50 to 59).

Each bar in the graph represents 1,000 people, and is split into 2 parts. One part shows the number of people who develop breast cancer, the other part the number of people who do not.

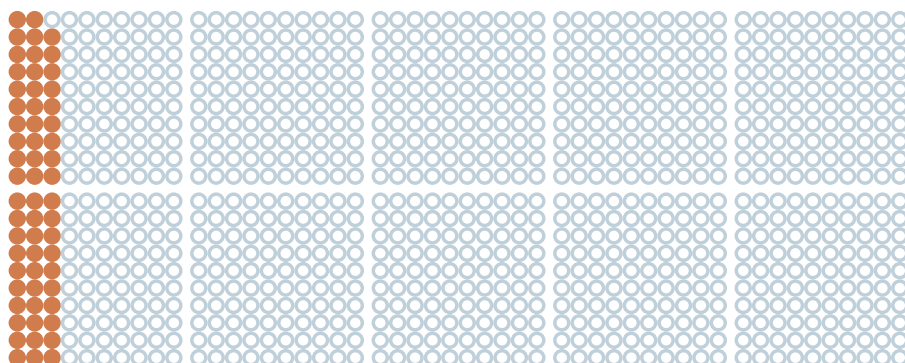
Bar graph 1: How cumulative risk of breast cancer changes as people age



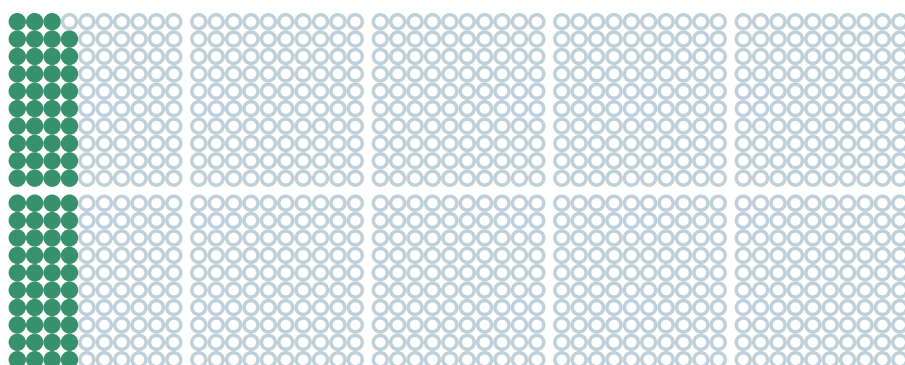
Bar graph 1 shows that breast cancer risk increases slowly as people age. This slow increase in risk takes place regardless of whether people take HRT. It increases slightly more for people who take combined HRT for 5 years than for people who never take HRT, and slightly more again for people who take combined HRT for 10 years. And so, after 20 years, the risks are as follows (see the graphs on the next page), depending whether people take or do not take HRT, and how long they take it for.

Combined HRT: breast cancer

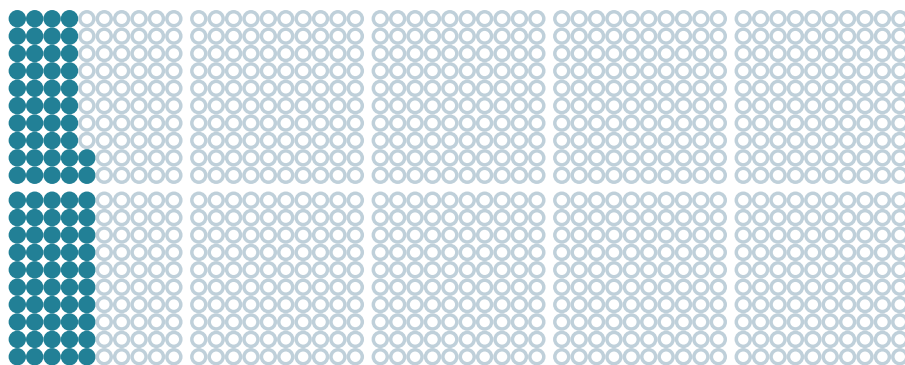
On average, between the ages of 50 and 69 (that is, when measuring over 20 years):



59 women out of 1,000 women who **never take HRT** develop breast cancer, 941 do not.



79 women out of 1,000 women who **take combined HRT for 5 years** from the age of 50 develop breast cancer, 921 do not. This is 20 more women, compared to women who do not take HRT.



92 women out of 1,000 women who **take combined HRT for 10 years** from the age of 50 develop breast cancer, 908 do not. This is 33 more women, compared to women who do not take HRT.

Note: These graphs cover continuous and sequential combined HRT together.

Where has the data come from?

The data used for the graphs in this section come from:

- the Office for National Statistics (ONS)
- information on prescriptions made for HRT on the NHS
- 24 observational studies.



To find out more

For the exact calculations, and to find out more about the data used in calculating our estimates and which bibliographic references it was taken from, see [supplement 19: absolute calculations](#).

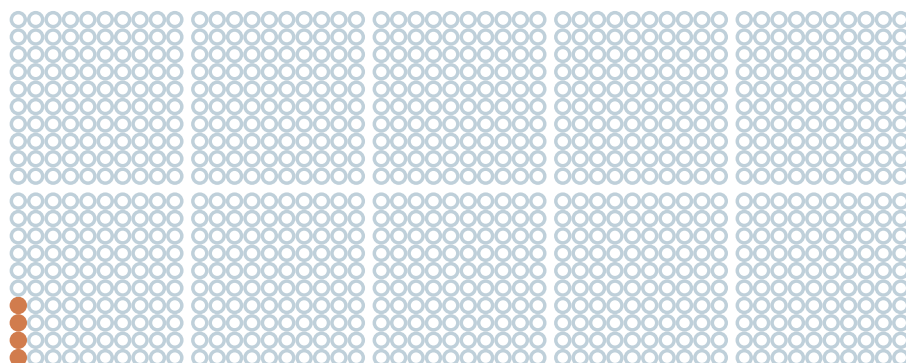
For information about uncertainty around the data, and for additional data, see [appendix L of evidence review D: breast cancer](#).

For full details of the committee discussions, see committee discussions and interpretation of the evidence in [evidence review D: breast cancer](#).

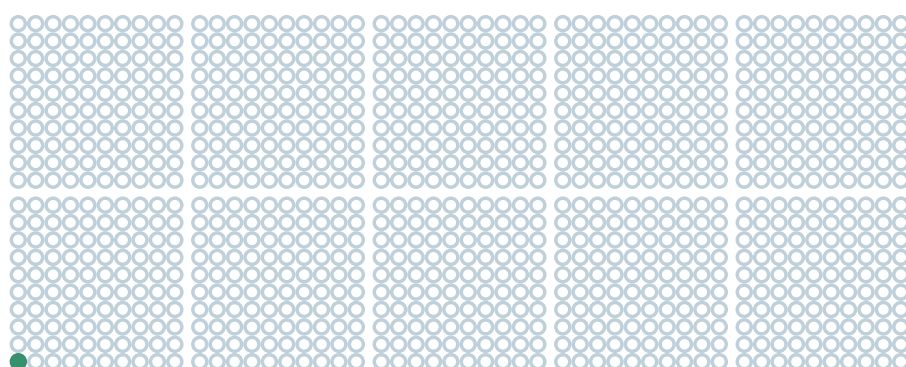


Combined HRT: endometrial cancer

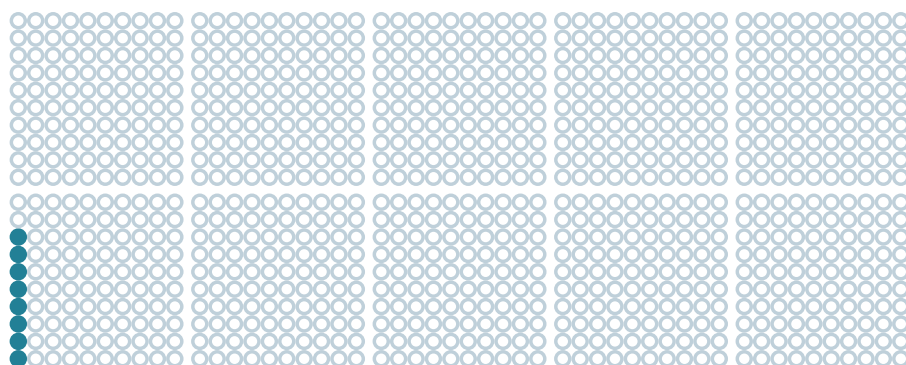
On average, between the ages of 50 and 54 (that is, when measuring over 5 years):



4 women out of 1,000 women who **never take HRT** develop endometrial cancer, 996 do not.



1 woman out of 1,000 women who take **continuous combined HRT** for an **unknown duration** from the age of 50 develop endometrial cancer, 999 do not. This is 3 fewer women, compared to women who never take HRT.



8 women out of 1,000 women who take **sequential combined HRT** from the age of 50 for an **unknown duration** develop endometrial cancer, 992 do not. This is 4 more women, compared to women who never take HRT.

Where has the data come from?

The data used for the graphs in this section comes from:

- the Office for National Statistics (ONS)
- information on prescriptions made for HRT on the NHS
- 2 observational studies.



To find out more

For the exact calculations, and to find out more about the data used in calculating our estimates and which bibliographic references it was taken from, see [supplement 19: absolute calculations](#).

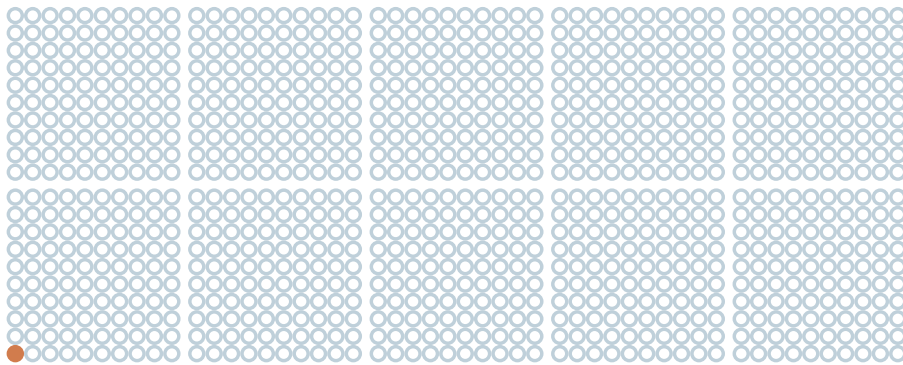
For information about uncertainty around the data, and for additional data, see [appendix M of evidence review E: endometrial cancer](#).

For full details of the committee discussions, see committee discussions and interpretation of the evidence in [evidence review E: endometrial cancer](#).

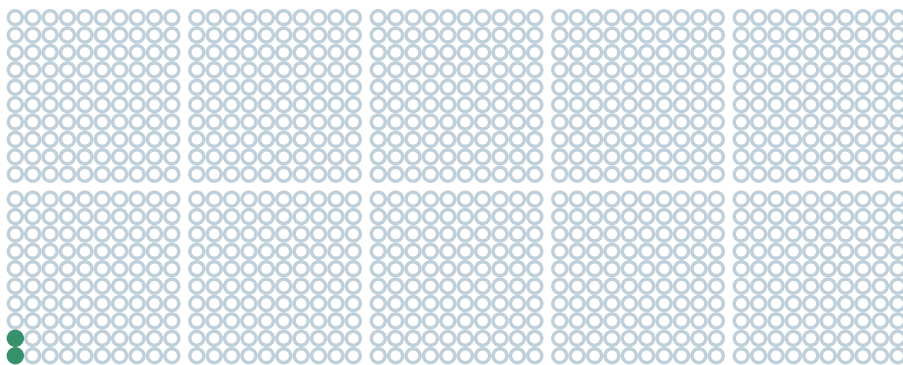


Combined HRT: ovarian cancer

On average, between the ages of 50 and 54 (that is, when measuring over 5 years):



1 woman out of 1,000 women who **never take HRT** develops ovarian cancer, 999 do not.



2 women out of 1,000 women who take **combined or oestrogen-only HRT** for an **unknown duration** from the age of 50 develop ovarian cancer, 998 do not. This is 1 more woman, compared to women who never take HRT.

Where has the data come from?

The data used for the graphs in this section comes from:

- the Office for National Statistics (ONS)
- information on prescriptions made for HRT on the NHS
- 17 observational studies.



To find out more

For the exact calculations, and to find out more about the data used in calculating our estimates and which bibliographic references it was taken from, see [supplement 19: absolute calculations](#).

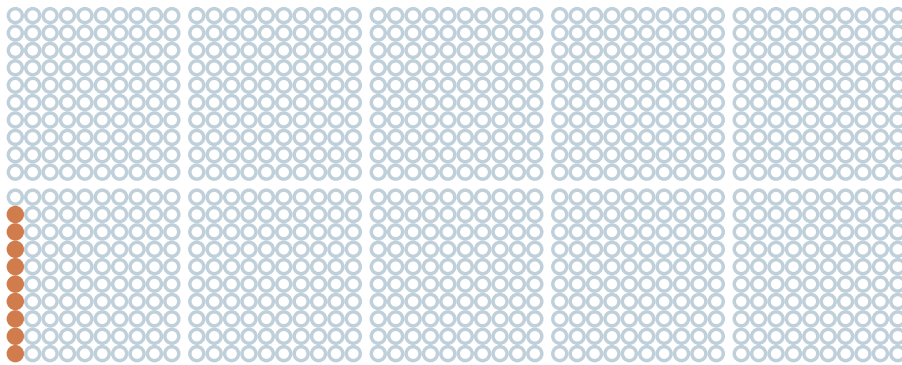
For information about uncertainty around the data, and for additional data, see [appendix L of evidence review F: ovarian cancer](#).

For full details of the committee discussions, see committee discussions and interpretation of the evidence in [evidence review F: ovarian cancer](#).

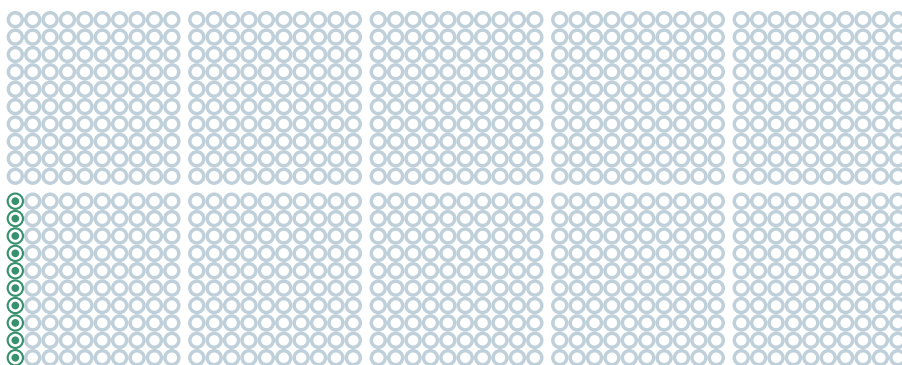


Combined HRT: coronary heart disease

On average, between the ages of 50 and 54 (that is, when measuring over 5 years):



9 women out of 1,000 women who **never take HRT** develop coronary heart disease, 991 do not.



10 women out of 1,000 women who **take combined HRT for 5 years** from the age of 50 develop coronary heart disease, 990 do not.

There is a very small difference between the group that took combined HRT and the group that never took HRT. This difference is shown to be down to chance (in scientific terms, this is called [not statistically significant](#)).

Where has the data come from?

The data used for the graphs in this section comes from:

- hospital episode statistics
- information on prescriptions made for HRT on the NHS
- 2 randomised controlled trials.



To find out more

For the exact calculations, and to find out more about the data used in calculating our estimates and which bibliographic references it was taken from, see [supplement 19: absolute calculations](#).

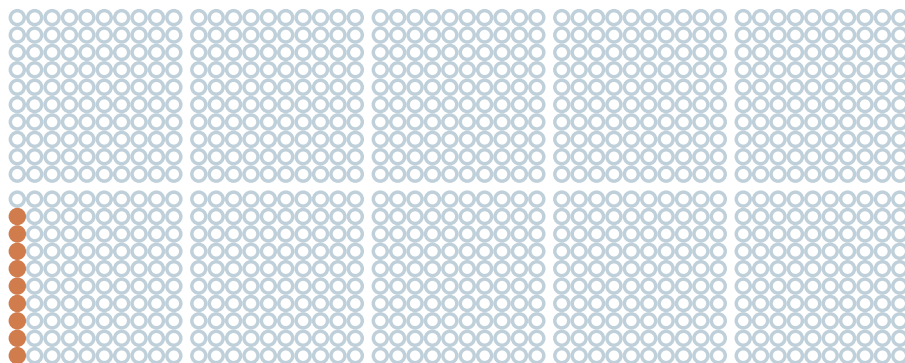
For information about uncertainty around the data, and for additional data, see [appendix L of evidence review C: cardiovascular disease](#).

For full details of the committee discussions, see committee discussions and interpretation of the evidence in [evidence review C: cardiovascular disease](#).

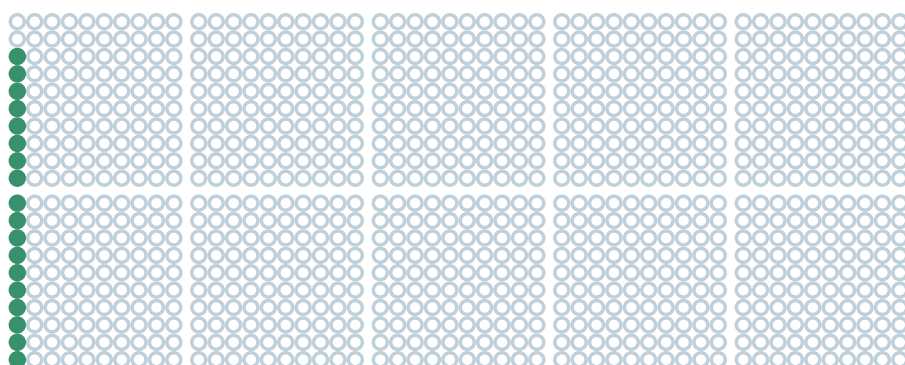


Combined HRT started after 65: dementia

On average, over a 4-year period starting when they are age 65 or over:



9 women out of 1,000 women who **never take HRT** develop dementia, 991 do not.



18 women out of 1,000 women who **take combined HRT for 4 years, starting at age 65 or over**, develop dementia over the same 4-year period, 982 do not. This is 9 more women, compared to women who never take HRT.

Note: most women who take HRT for menopause-associated symptoms start it before the age of 65, in their 50s, but data for that age group was inconclusive.

See [NICE's guideline on menopause](#) for more information.

Where has the data come from?

The data used for the graphs in this section comes from 1 randomised controlled trial covering women with an intact uterus.



To find out more

For the exact calculations, and to find out more about the data used in calculating our estimates and which bibliographic references it was taken from, see [supplement 19: absolute calculations](#).

For information about uncertainty around the data, and for additional data, see [appendix L of evidence review G: dementia](#).

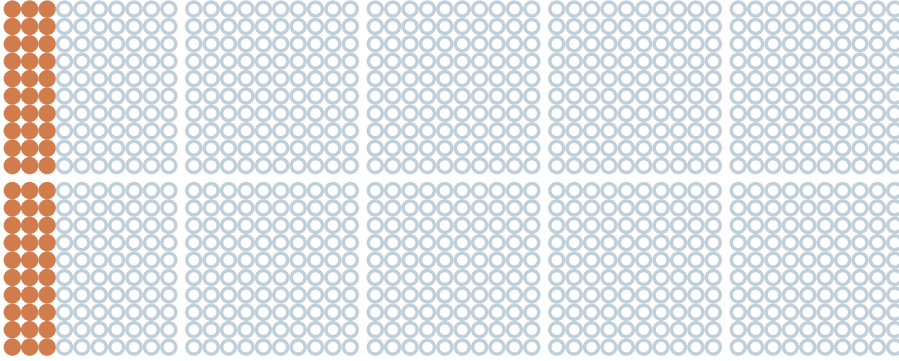
For full details of the committee discussions, see committee discussions and interpretation of the evidence in [evidence review G: dementia](#).



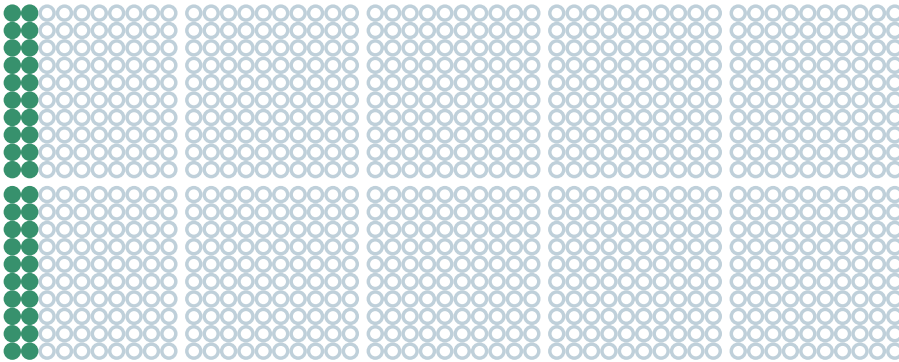
Combined HRT: osteoporosis

In this section, fragility fractures are used as a marker of osteoporosis.

On average, between the ages of 50 and 54 (that is, when measuring over 5 years):

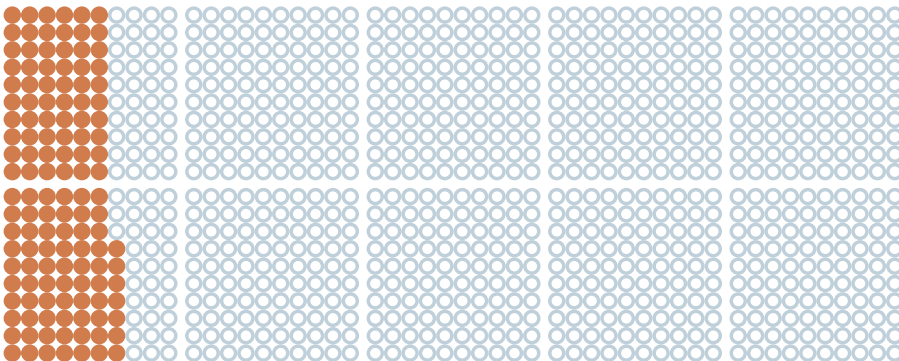


60 women out of 1,000 women who **never take HRT** experience a fragility fracture, 940 do not.

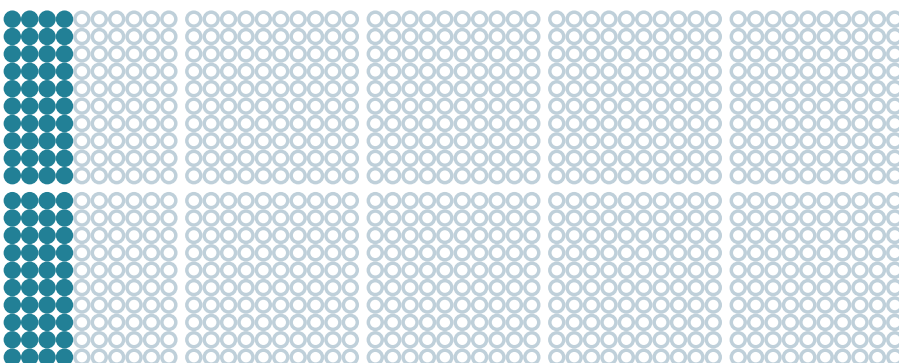


40 women out of 1,000 women who **take HRT for 5 years** from the age of 50 experience a fragility fracture, 960 do not. This is 20 fewer women, compared to women who never take HRT.

On average, between the ages of 50 and 59 (that is, when measuring over 10 years):



127 women out of 1,000 women who **never take HRT** experience a fragility fracture, 873 do not.



80 women out of 1,000 women who **take HRT for 10 years** from the age of 50 experience a fragility fracture, 920 do not. This is 47 fewer women, compared to women who never take HRT.

i The evidence on fragility fractures, as reported in the 2015 NICE guideline, does not distinguish between combined and oestrogen-only HRT. It has been included in both the combined and oestrogen-only HRT sections of this document to better support discussions.

Where has the data come from?

The data used for the graphs in this section comes from 1 observational study.

i To find out more

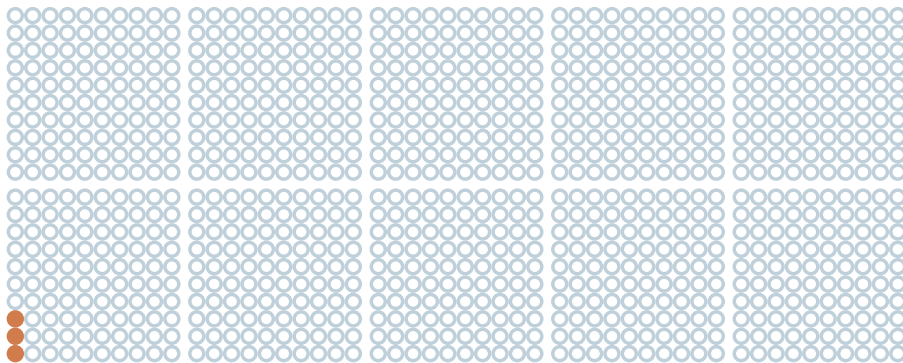
For the exact calculations, and to find out more about the data used in calculating our estimates and which bibliographic references it was taken from, see [supplement 19: absolute calculations](#).

For information about uncertainty around the data, and for additional data, see the [2015 full guideline](#).

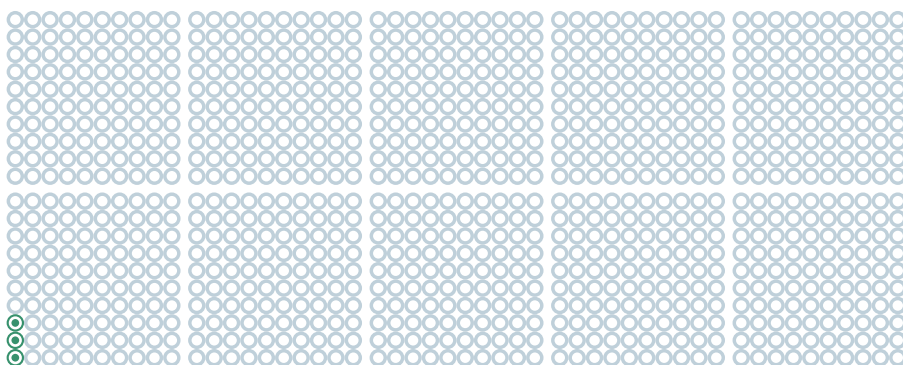


Combined HRT: stroke

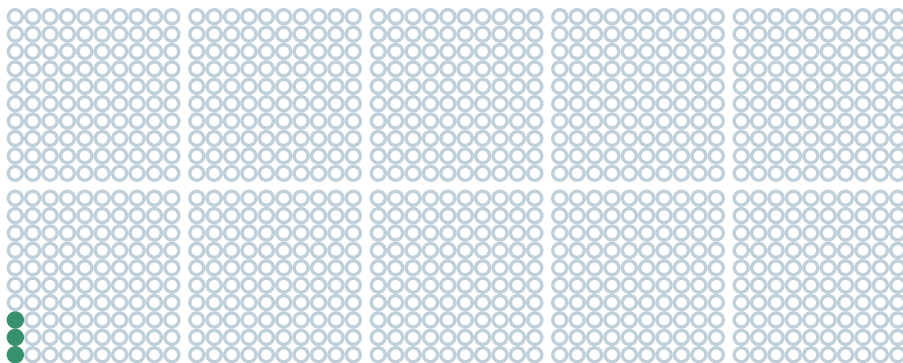
On average, between the ages of 50 and 54 (that is, when measuring over 5 years):



3 women out of 1,000 women who **never take HRT** have a stroke, 997 do not.



The numbers are similar for women who take **combined HRT with transdermal oestrogen** (oestrogen taken through the skin) for an **unknown duration** from the age of 50.



The numbers are also similar for women who take **combined HRT with oral oestrogen** (oestrogen taken by mouth) for an **unknown duration** from the age of 50.

For this outcome, there is a very small difference in numbers of first-time stroke between each of the groups that took HRT and the group that never took HRT, but it is too small to be apparent in groups of 1,000 women. Additionally:

- for **transdermal oestrogen** (oestrogen absorbed through the skin), it is shown to be down to chance (in scientific terms, this is called [not statistically significant](#))
- for **oral oestrogen** (oestrogen taken by mouth), it is shown not to be down to chance (in scientific terms, this is called [statistically significant](#)).

Where has the data come from?

The data used for the graphs in this section comes from:

- hospital episode statistics
- information on prescriptions made for HRT on the NHS
- 1 randomised controlled trial, for combined HRT with oral oestrogen
- 1 observational study, for combined HRT with transdermal oestrogen.



To find out more

For the exact calculations, and to find out more about the data used in calculating our estimates and which bibliographic references it was taken from, see [supplement 19: absolute calculations](#).

For information about uncertainty around the data, and for additional data, see [appendix L of evidence review C: cardiovascular disease](#).

For full details of the committee discussions, see committee discussions and interpretation of the evidence in [evidence review C: cardiovascular disease](#).

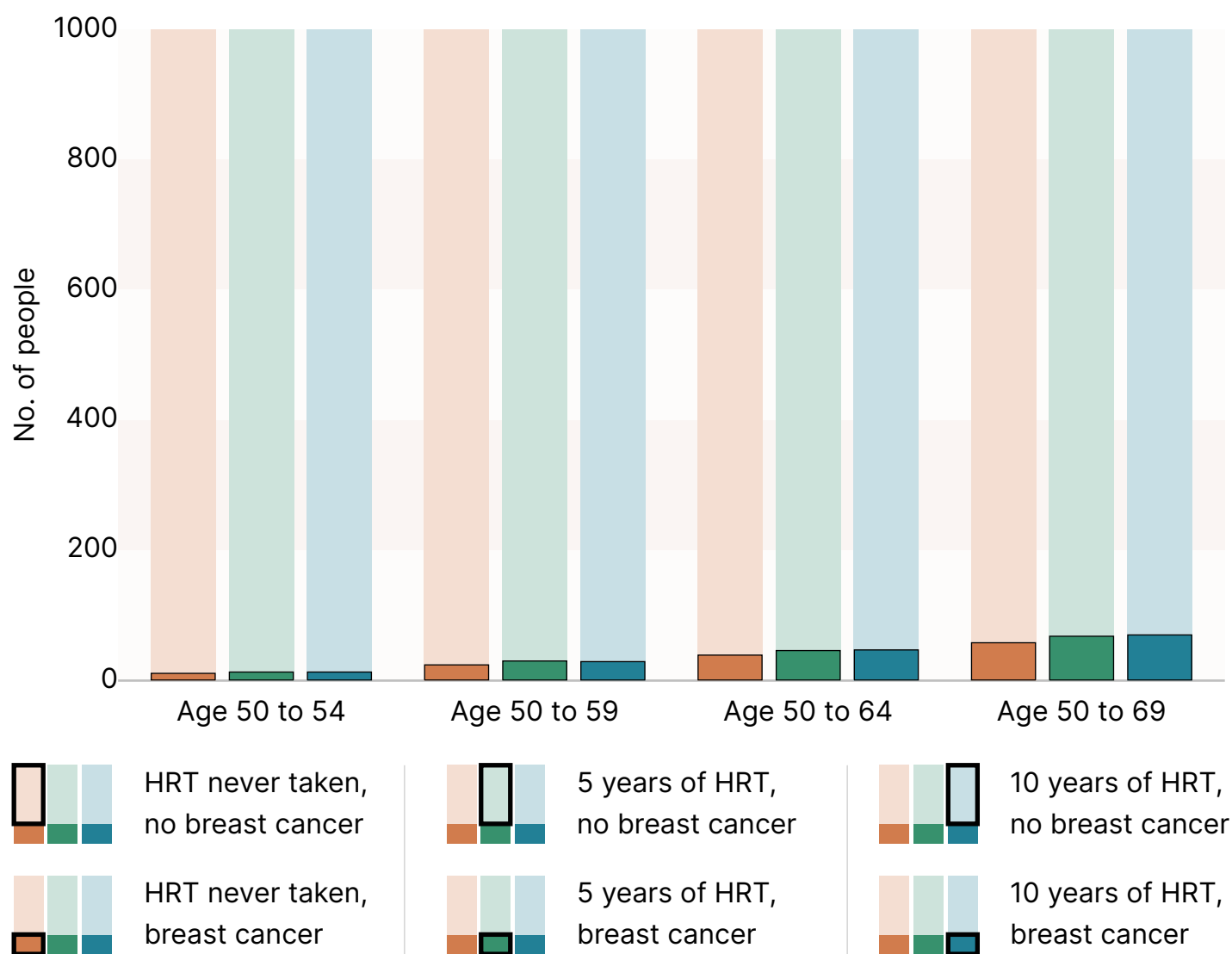


Oestrogen-only HRT: breast cancer

The risk of breast cancer in groups of 1,000 people for 4 successive periods of 5 years, starting when people are aged 50 and going all the way until they are 69, is presented in **Bar graph 2**. It shows the estimated risk for people who do not take HRT, for people who take oestrogen-only HRT for the first 5 years (that is, from age 50 to 54), and for people who take oestrogen-only HRT for the first 10 years (that is, from age 50 to 59).

Each bar in the graph represents 1,000 people, and is split into 2 parts. One part shows the number of people who develop breast cancer, the other part the number of people who do not.

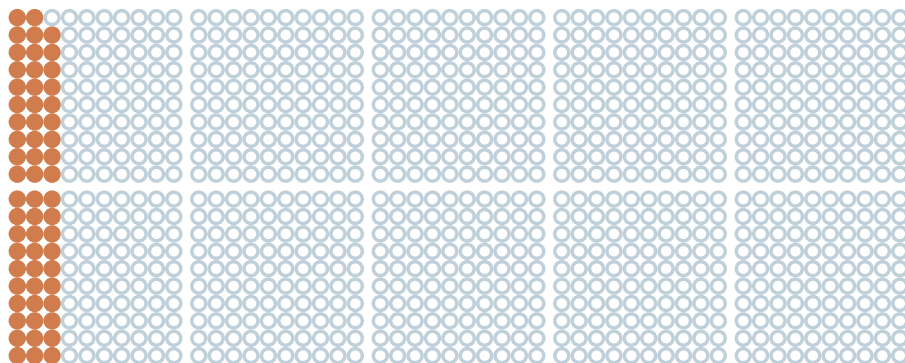
Bar graph 2: How cumulative risk of breast cancer changes as people age



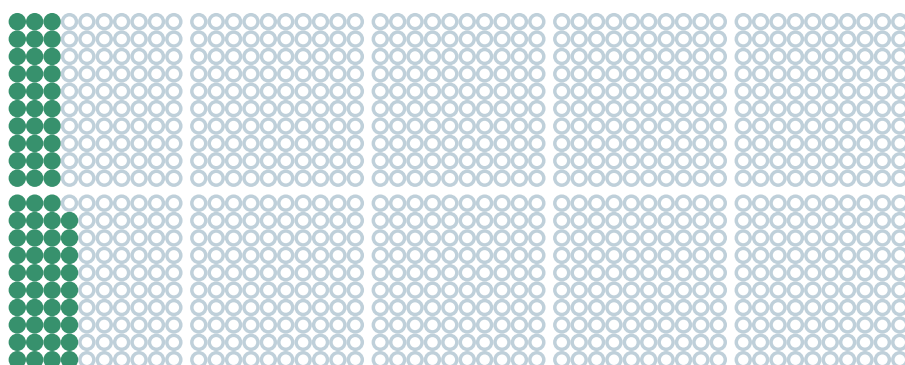
Bar graph 2 shows that breast cancer risk increases slowly as people age. This slow increase in risk takes place regardless of whether people take HRT. It increases slightly more for people who take oestrogen-only HRT for 5 years than for people who never take HRT, and slightly more again for people who take oestrogen-only HRT for 10 years. And so, after 20 years, the risks are as follows (see the graphs on the next page), depending whether people take or do not take HRT, and how long they take it for.

Oestrogen-only HRT: breast cancer

On average, between the ages of 50 and 69 (that is, when measured over 20 years):

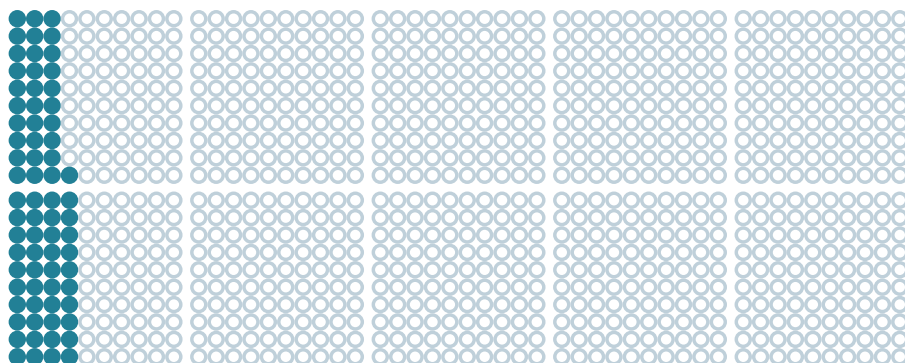


59 women out of 1,000 women who **never take HRT** develop breast cancer, 941 do not.



69 women out of 1,000 women who **take oestrogen-only HRT for 5 years** from the age of 50 develop breast cancer, 931 do not.

This is 10 more women, compared to women who do not take HRT.



71 women out of 1,000 women who **take oestrogen-only HRT for 10 years** from the age of 50 develop breast cancer, 931 do not.

This is 12 more women, compared to women who do not take HRT.

Where has the data come from?

The data used for the graphs in this section come from:

- the Office for National Statistics (ONS)
- information on prescriptions made for HRT on the NHS
- 24 observational studies.



To find out more

For the exact calculations, and to find out more about the data used in calculating our estimates and which bibliographic references it was taken from, see [supplement 19: absolute calculations](#).

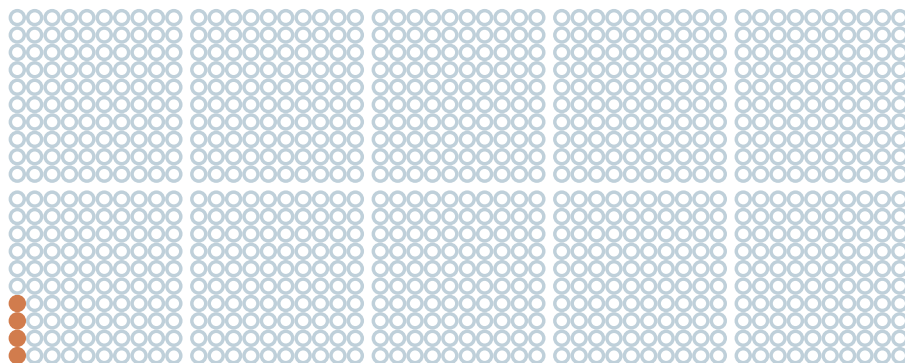
For information about uncertainty around the data, and for additional data, see [appendix L of evidence review D: breast cancer](#).

For full details of the committee discussions, see committee discussions and interpretation of the evidence in [evidence review D: breast cancer](#).

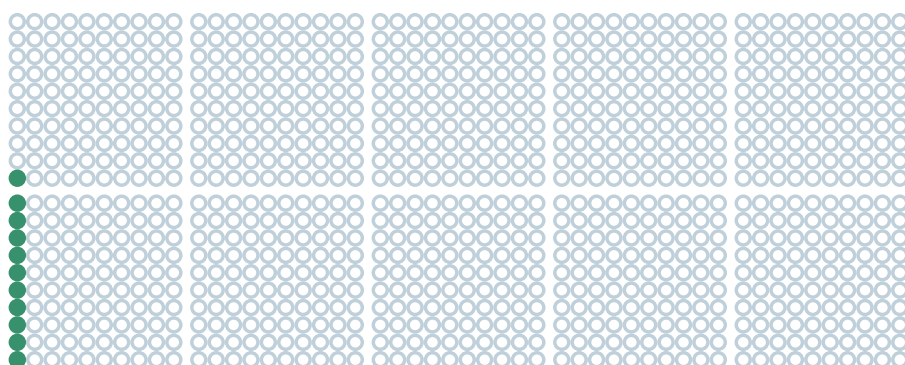


Oestrogen-only HRT: endometrial cancer

On average, between the ages of 50 and 54 (that is, when measuring over 5 years):



4 women out of 1,000 women with a uterus who **never take HRT** develop endometrial cancer, 996 do not.



11 women out of 1,000 women with a uterus who take **oestrogen-only HRT** from the age of 50 for an **unknown duration** develop endometrial cancer, 989 do not. This is 7 more women, compared to women who never take HRT.

Where has the data come from?

The data used for the graphs in this section comes from:

- the Office for National Statistics (ONS)
- information on prescriptions made for HRT on the NHS
- 1 observational study.



To find out more

For the exact calculations, and to find out more about the data used in calculating our estimates and which bibliographic references it was taken from, see [supplement 19: absolute calculations](#).

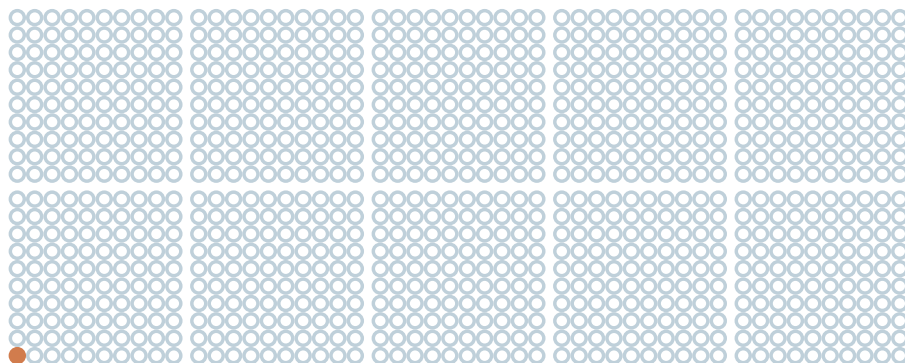
For information about uncertainty around the data, and for additional data, see [appendix M of evidence review E: endometrial cancer](#).

For full details of the committee discussions, see committee discussions and interpretation of the evidence in [evidence review E: endometrial cancer](#).

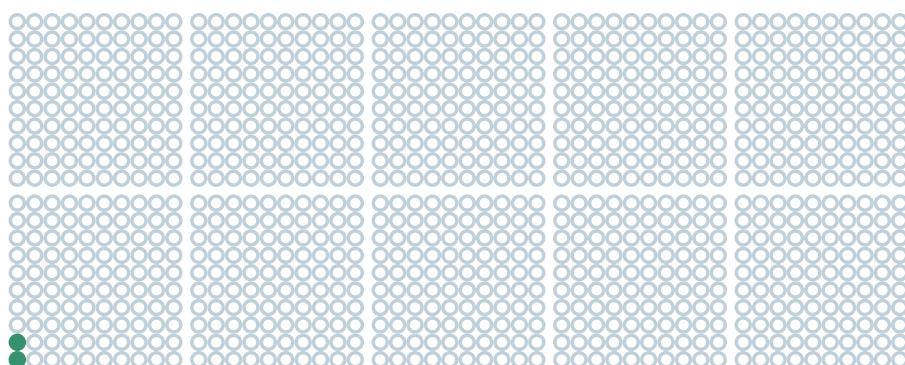


Oestrogen-only HRT: ovarian cancer

On average, between the ages of 50 and 54 (that is, when measuring over 5 years):



1 woman out of 1,000 women who **never take HRT** develops ovarian cancer, 999 do not.



2 women out of 1,000 women who take **oestrogen-only HRT** from the age of 50 for an **unknown duration** develop ovarian cancer, 998 do not. This is 1 more woman, compared to women who never take HRT.

Where has the data come from?

The data used for the graphs in this section comes from:

- the Office for National Statistics (ONS)
- information on prescriptions made for HRT on the NHS
- 17 observational studies.



To find out more

For the exact calculations, and to find out more about the data used in calculating our estimates and which bibliographic references it was taken from, see [supplement 19: absolute calculations](#).

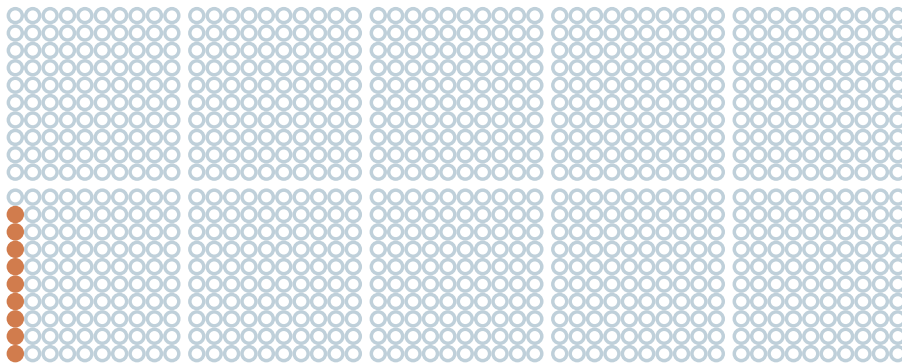
For information about uncertainty around the data, and for additional data, see [appendix L of evidence review F: ovarian cancer](#).

For full details of the committee discussions, see committee discussions and interpretation of the evidence in [evidence review F: ovarian cancer](#).

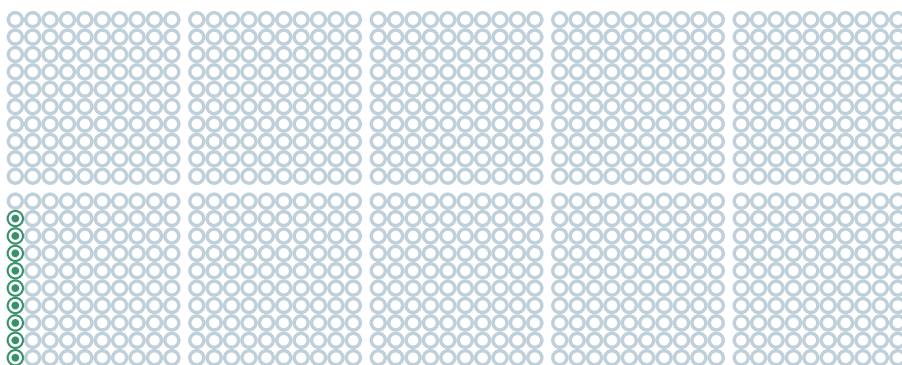


Oestrogen-only HRT: coronary heart disease

On average, between the ages of 50 and 54 (that is, when measuring over 5 years):



9 women out of 1,000 women who **never take HRT** develop coronary heart disease, 991 do not.



The numbers are similar for women who take **oestrogen-only HRT** between the ages of 50 and 54.

For this outcome, there is a very small difference between the group that took HRT and the group that never took HRT, but it is too small to be apparent in groups of 1,000 women. This difference is shown to be down to chance (in scientific terms, this is called [not statistically significant](#)).

Where has the data come from?

The data used for the graphs in this section comes from:

- hospital episode statistics
- information on prescriptions made for HRT on the NHS
- 1 randomised controlled trial.



To find out more

For the exact calculations, and to find out more about the data used in calculating our estimates and which bibliographic references it was taken from, see [supplement 19: absolute calculations](#).

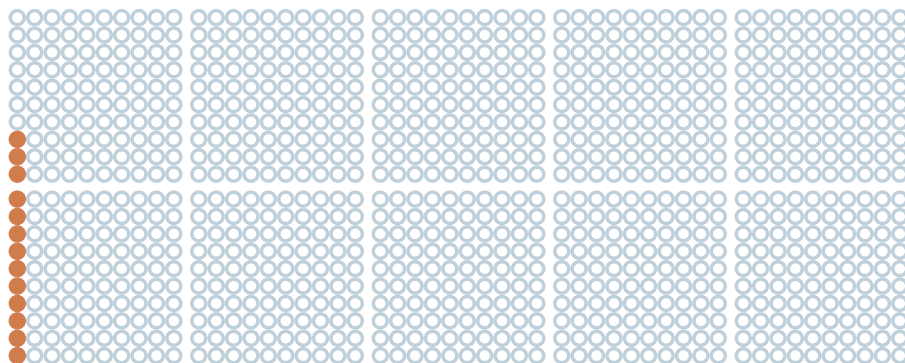
For information about uncertainty around the data, and for additional data, see [appendix L of evidence review C: cardiovascular disease](#).

For full details of the committee discussions, see committee discussions and interpretation of the evidence in [evidence review C: cardiovascular disease](#).

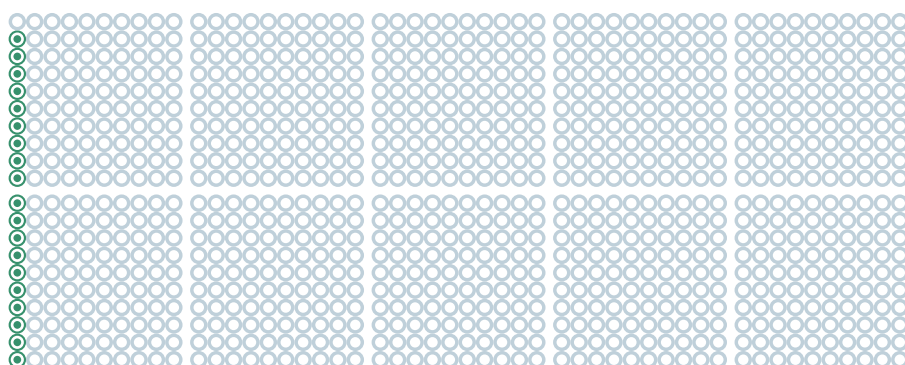


Oestrogen-only HRT started after 65: dementia

On average, over a 5-year period, starting when they are age 65 or over:



13 women out of 1,000 women who **never take HRT** develop dementia, 987 do not.



19 women out of 1,000 women who **take oestrogen-only HRT** for 5 years from the age of 65 develop dementia over the same 5-year period, 981 do not.

For this outcome, there is a small difference between the group that took oestrogen-only HRT and the group that never took HRT. This difference is shown to be down to chance (in scientific terms, this is called [not statistically significant](#)).

Where has the data come from?

The data used for the graphs in this section comes from 1 randomised controlled trial.



To find out more

For the exact calculations, and to find out more about the data used in calculating our estimates and which bibliographic references it was taken from, see [supplement 19: absolute calculations](#).

For information about uncertainty around the data, and for additional data, see [appendix L of evidence review G: dementia](#).

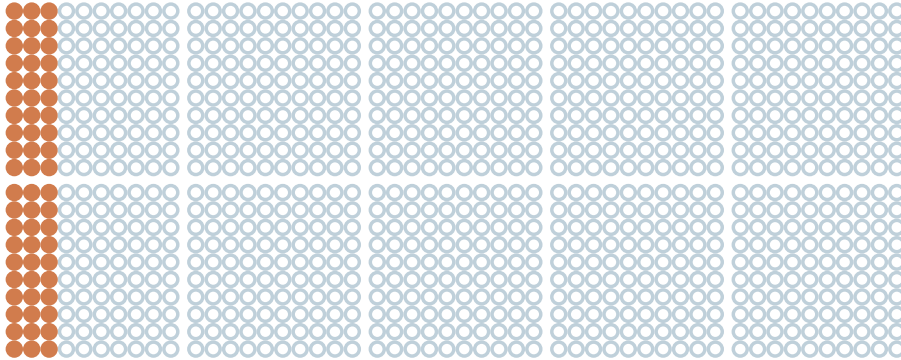
For full details of the committee discussions, see committee discussions and interpretation of the evidence in [evidence review G: dementia](#).



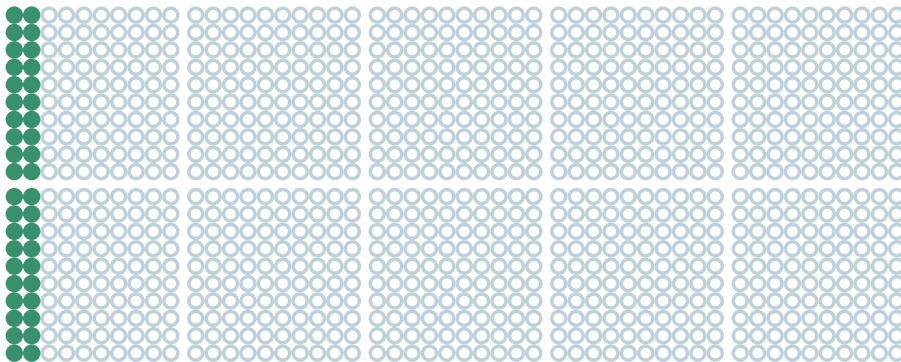
Oestrogen-only HRT: osteoporosis

In this section, fragility fractures are used as a marker of osteoporosis.

On average, between the ages of 50 and 54 (that is, when measuring over 5 years):

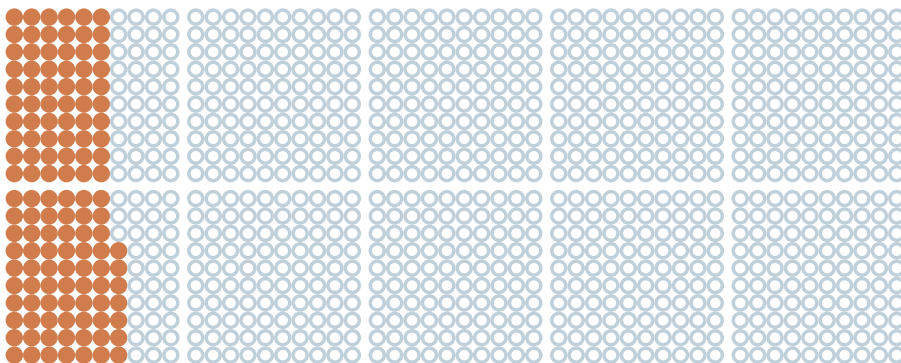


60 women out of 1,000 women who **never take HRT** experience a fragility fracture, 940 do not.

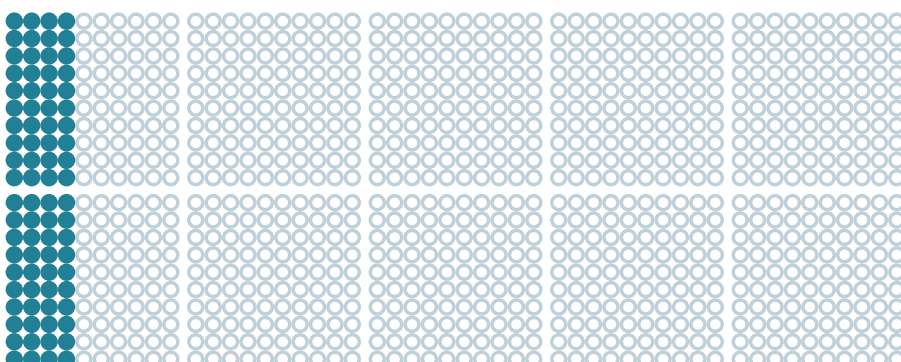


40 women out of 1,000 women who **take HRT** for 5 years from the age of 50 experience a fragility fracture, 960 do not. This is 20 fewer women, compared to women who never take HRT.

On average, between the ages of 50 and 59 (that is, when measuring over 10 years):



127 women out of 1,000 women who **never take HRT** experience a fragility fracture, 873 do not.



80 women out of 1,000 women who **take HRT** for 10 years from the age of 50 experience a fragility fracture, 920 do not. This is 47 fewer women, compared to women who never take HRT.

i The evidence on fragility fractures, as reported in the 2015 NICE guideline, does not distinguish between combined and oestrogen-only HRT. It has been included in both the combined and oestrogen-only HRT sections of this document to better support discussions.

Where has the data come from?

The data used for the graphs in this section comes from 1 observational study.

i To find out more

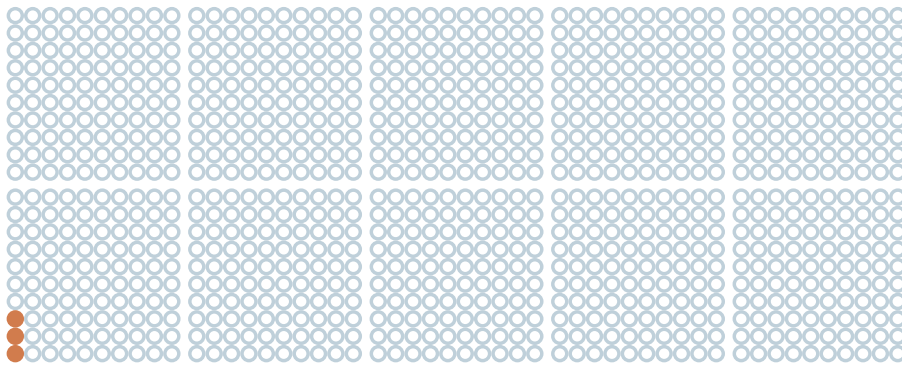
For the exact calculations, and to find out more about the data used in calculating our estimates and which bibliographic references it was taken from, see [supplement 19: absolute calculations](#).

For information about uncertainty around the data, and for additional data, see the [2015 full guideline](#).

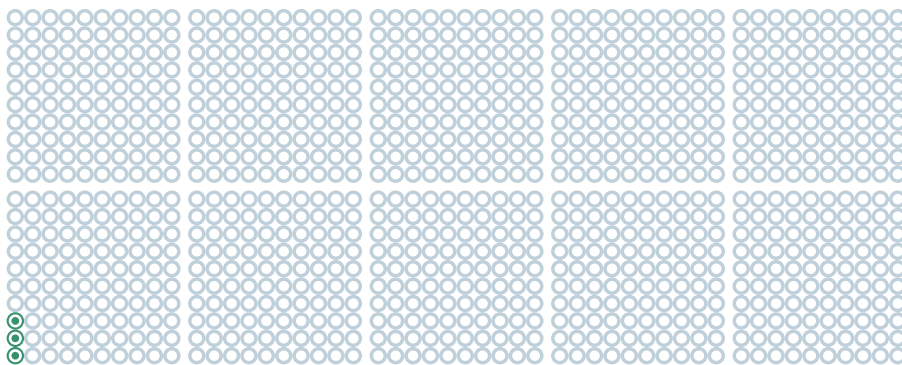


Oestrogen-only HRT: stroke

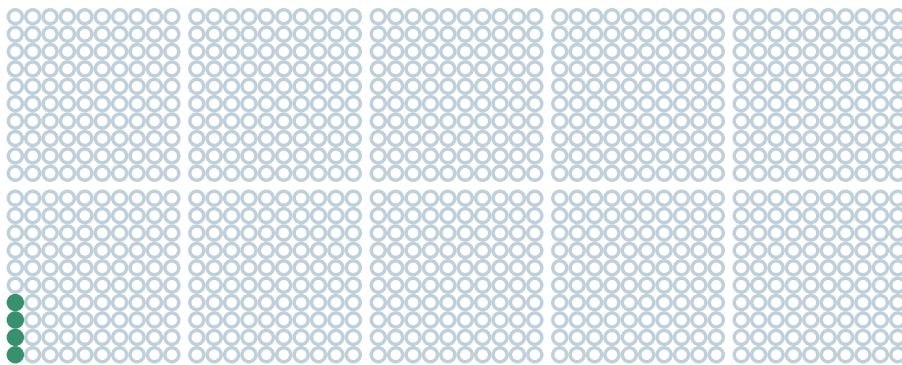
On average, between the ages of 50 and 54 (that is, when measuring over 5 years):



3 women out of 1,000 women who **never take HRT** have a stroke, 997 do not.



The numbers are similar for women who take **transdermal oestrogen-only HRT** for an unknown duration from the age of 50, and for women who never take HRT.



4 women out of 1,000 women who take **oral oestrogen-only HRT** from the age of 50 for an unknown duration have a stroke between the ages of 50 and 54, 996 do not.

This is 1 more woman, compared to women who never take HRT.

There is a very small difference between the group that took transdermal oestrogen-only HRT and the group that never took HRT, but it is too small to be apparent in groups of 1,000 women. This difference is shown to be down to chance (in scientific terms, this is called [not statistically significant](#)).

Where has the data come from?

The data used for the graphs in this section comes from:

- hospital episode statistics
- information on prescriptions made for HRT on the NHS
- 1 randomised controlled trial, for oral oestrogen-only HRT
- 2 observational studies, for transdermal oestrogen-only HRT.




To find out more

For the exact calculations, and to find out more about the data used in calculating our estimates and which bibliographic references it was taken from, see [supplement 19: absolute calculations](#).

For information about uncertainty around the data, and for additional data, see [appendix L of evidence review C: cardiovascular disease](#).

For full details of the committee discussions, see committee discussions and interpretation of the evidence in [evidence review C: cardiovascular disease](#).





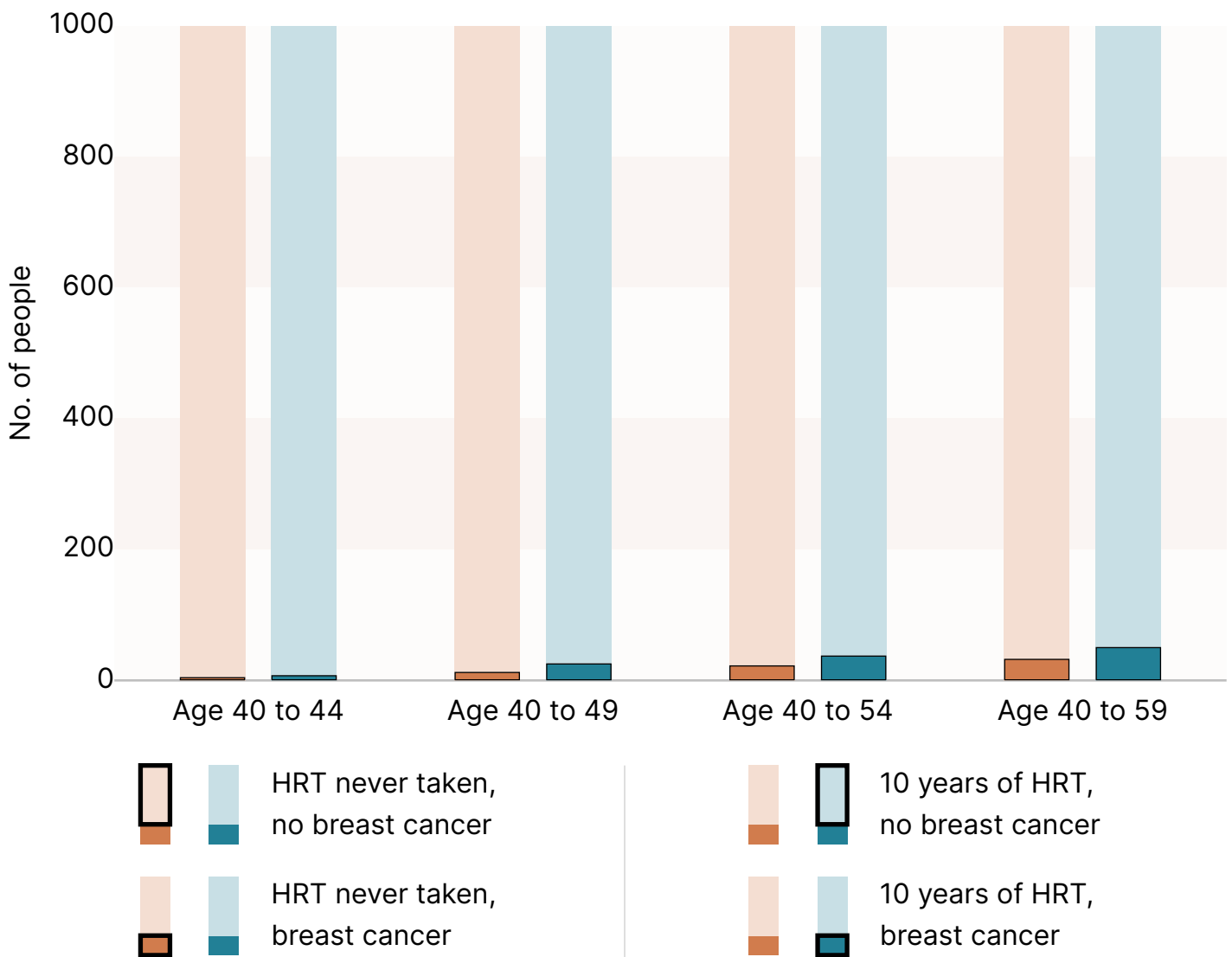
**Section 2:
Information for
women experiencing
early menopause
(aged 40 to 44)**

Combined HRT: breast cancer

Bar graph 3 presents the estimated risk of breast cancer in groups of 1,000 people for 4 successive periods of 5 years, starting when people are aged 40 and going all the way until they are 59. It shows the risk for people who do not take HRT and for people who take combined HRT for the first 10 years (that is, from age 40 to 49).

Each bar in the graph represents 1,000 people, and is split into 2 parts. One part shows the number of people who develop breast cancer, the other part the number of people who do not.

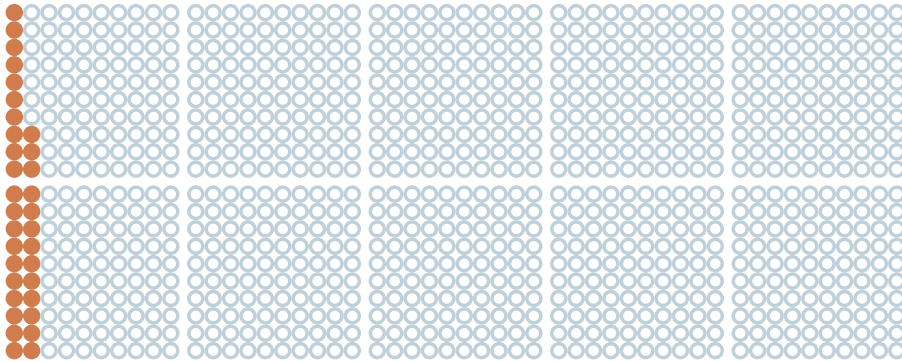
Bar graph 3: How cumulative risk of breast cancer changes as people age



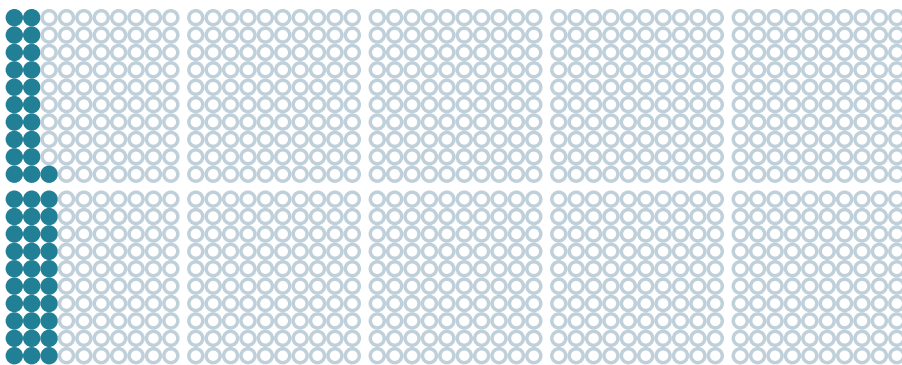
Bar graph 3 shows that breast cancer risk increases slowly as people age. This slow increase in risk takes place regardless of whether people take HRT. It increases slightly more for people who take combined HRT for 10 years than for people who never take HRT. And so, after 20 years, the risks are as follows (see the graphs on the next page), depending whether people take or do not take HRT, and how long they take it for.

Combined HRT: breast cancer

On average, between the ages of 40 and 59 (that is, when measuring over 20 years):



33 women out of 1,000 women who **never take HRT** develop breast cancer, 967 do not.



51 women out of 1,000 women experiencing early menopause who **take combined HRT for 10 years from the age of 40** develop breast cancer, 949 do not. This is 18 more women, compared to women who do not take HRT.

Where has the data come from?

The data used for the graphs in this section come from:

- the Office for National Statistics (ONS)
- information on prescriptions made for HRT on the NHS
- 24 observational studies.



To find out more

For the exact calculations, and to find out more about the data used in calculating our estimates and which bibliographic references it was taken from, see [supplement 19: absolute calculations](#).

For information about uncertainty around the data, and for additional data, see [appendix L of evidence review I: early menopause](#).

For full details of the committee discussions, see committee discussions and interpretation of the evidence in [evidence review I: early menopause](#).



Combined HRT: other medical conditions

No evidence was identified on the benefits and risks of either taking or not taking combined HRT relating to osteoporosis, risk of fractures or cardiovascular outcomes, or endometrial or ovarian cancer in people experiencing early menopause (people aged 40 to 44).

The committee agreed that taking HRT in early menopause may affect the risk of different health outcomes in different ways (that is, it may decrease some risks and increase others), as it does for people with primary ovarian insufficiency (POI) and for people experiencing menopause at age 45 or over.

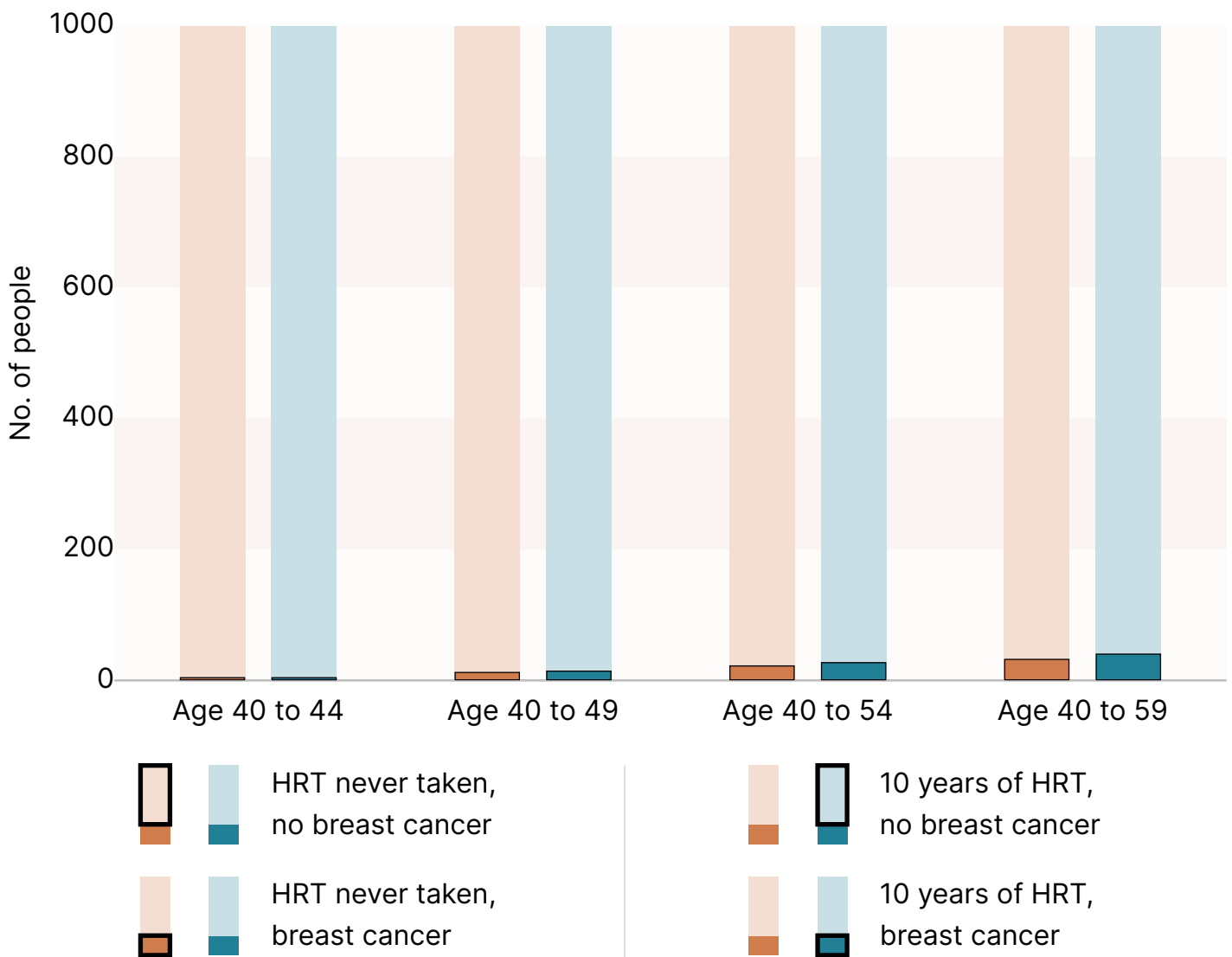


Oestrogen-only HRT: breast cancer

Bar graph 4 presents the estimated risk of breast cancer in groups of 1,000 people for 4 successive periods of 5 years, starting when people are aged 40 and going all the way until they are 59. It shows the risk for people who do not take HRT and for people who take oestrogen-only HRT for the first 10 years (that is, from age 40 to 49).

Each bar in the graph represents 1,000 people, and is split into 2 parts. One part shows the number of people who develop breast cancer, the other part the number of people who do not.

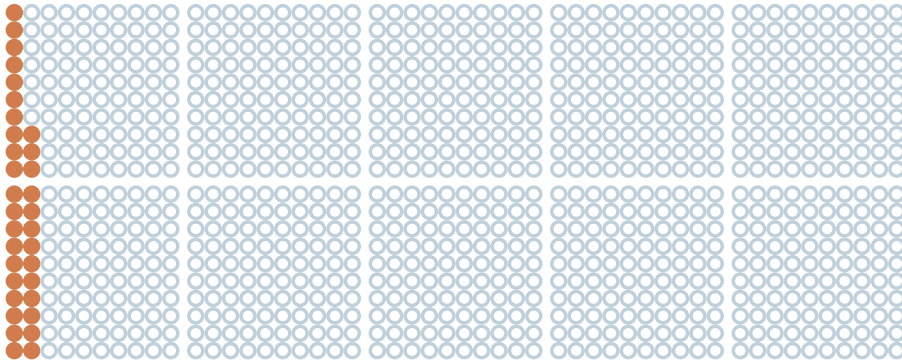
Bar graph 4: How cumulative risk of breast cancer changes as people age



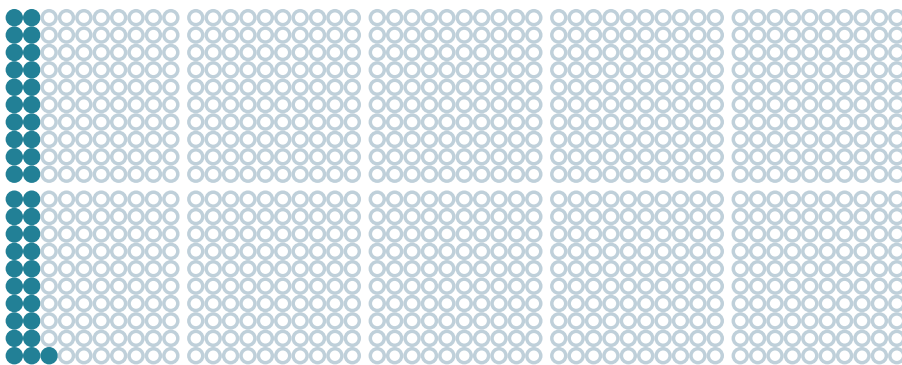
Bar graph 4 shows that breast cancer risk increases slowly as people age. This slow increase in risk takes place regardless of whether people take HRT. It increases slightly more for people who take oestrogen-only HRT for 10 years than for people who never take HRT. And so, after 20 years, the risks are as follows (see the graphs on the next page), depending whether people take or do not take HRT, and how long they take it for.

Oestrogen-only HRT: breast cancer

On average, between the ages of 40 and 59 (that is, when measuring over 20 years):



33 women out of 1,000 women who **never take HRT** develop breast cancer, 967 do not.



41 women out of 1,000 women experiencing early menopause who **take oestrogen-only HRT for 10 years from the age of 40** develop breast cancer, 959 do not. This is 8 more women, compared to women who do not take HRT.

Where has the data come from?

The data used for the graphs in this section come from:

- the Office for National Statistics (ONS)
- information on prescriptions made for HRT on the NHS
- 24 observational studies.



To find out more

For the exact calculations, and to find out more about the data used in calculating our estimates and which bibliographic references it was taken from, see [supplement 19: absolute calculations](#).

For information about uncertainty around the data, and for additional data, see [appendix L of evidence review I: early menopause](#).

For full details of the committee discussions, see committee discussions and interpretation of the evidence in [evidence review I: early menopause](#).



Oestrogen-only HRT: other medical conditions

No evidence was identified on the benefits and risks of either taking or not taking oestrogen-only HRT relating to osteoporosis, risk of fractures or cardiovascular outcomes, or endometrial or ovarian cancer in people experiencing early menopause (people aged 40 to 44).

The committee agreed that taking HRT in early menopause may affect the risk of different health outcomes in different ways (that is, it may decrease some risks and increase others), as it does for people with primary ovarian insufficiency (POI) and for people experiencing menopause at age 45 or over.



Making decisions based on this data

The committee agreed that all outcomes (medical conditions) covered in this document were serious, so any difference that was not caused by chance alone was considered meaningful enough to influence decision making. For more details, see [supporting document 1 - methods](#).

Statistical significance

Why do we check for statistical significance?

Every person's physical and physiological make-up is unique. And so, when comparing 2 random groups of people, even if the groups are created in a way that means that the people included have similar characteristics, differences will often still be observed between the 2 groups. These differences may also affect people's health and how their bodies react to diseases and treatments. If, in addition, 1 group uses a treatment and the other does not use the treatment, there will very often be some differences in health outcomes between the 2 groups. These may be linked to:

- differences between individuals (that is, differences down to chance), or
- the treatment taken by people in 1 of the 2 groups.

Scientific studies are planned and structured so that results are unlikely to be affected by chance or by a factor other than the treatment.

We can make a calculation that tells us whether a certain difference between the 2 groups is likely to be due to chance or not. If it is not, we say that the result is statistically significant. That then means that the observed difference is likely to be related to the treatment taken by people in 1 of the 2 groups.

Statistical significance is always calculated with a specific level of certainty. That level is most often set at 95% which is the level we used in this document.

**In short, if a result observed is statistically significant,
then it is unlikely to happen because of chance**

When results are statistically significant in this document

In most cases, we do not say when a difference is statistically significant; we only say when it is not statistically significant.

In some instances, a difference is statistically significant even when the numbers in the graphs are the same for women who take, or have taken, HRT and those who have never taken HRT. This is because the difference is too small to be apparent when expressed per 1,000 women.

When results are not statistically significant in this document

In some parts of the document, some results are referred to as not statistically significant. This means that for the outcome presented, any difference between women who take or have taken HRT, and women who have never taken HRT, is very likely to be due to chance alone.

Uncertainty around the data

How is uncertainty measured?

When we do not know the true value of something, we can estimate it. This is what we have done in this document.

An interval is a range of values. It is described by giving the minimum and maximum value in the range.

When we have estimated a value, we can also calculate an interval around the estimate that gives us a range of values within which the true value is likely to be found. The interval gives us a margin of error around the estimate. The smaller that margin, the more precise the estimate is. This is called a confidence interval.

Confidence intervals are also linked to the idea of statistical significance: if the confidence interval includes the value that shows no difference between 2 different groups, then the result is not statistically significant.

How uncertain are the estimates in this document?

The numbers in this document are all best estimates. With all estimates, there is a level of imprecision and uncertainty.

Here, what we are estimating is the risk of a specific health outcome in women who take or have taken HRT, and the risk of that same outcome in women who have never taken HRT. The imprecision is around how small or large any difference in risk between the 2 groups might be. The uncertainty, when present, relates to whether there is a decrease, no change or an increase in risk when taking HRT.

We have calculated confidence intervals for the estimates. Based on these, we can say that, for the estimates presented, the uncertainty does not affect the type of effect observed (which is either a reduction or increase in risk). That is, the estimate shows a similar effect to the effect that would be observed with any value in the confidence interval.

For full detail of the confidence intervals, statistical significance and imprecision ratings for any of the data in this document, see the [relevant evidence review for each outcome](#).

Why present absolute risks?

In clinical practice, the absolute effect provides more context regarding the risk of a particular outcome than the relative effect.

The calculations for each of the outcomes can be found in [supporting document 19](#).

A relative effect may show that someone is, for example, twice as likely to die following the use of a certain drug, which may seem a cause for concern. But in absolute terms, the risk may only be a small increase from 1 in 1,000 to 2 in 1,000 people.

Evidence (AAFP 2018) shows that health professionals and patients both have a similar level of understanding of absolute and relative risks (Cochrane 2011). However, it also shows that:

- change in risk seem larger (Cochrane 2011) and risk reduction is seen more positively (Journal of the National Cancer Institute 2011) when expressed as relative risks than as absolute risks
- using absolute risks maximises accuracy and is less likely to influence people's decision to accept therapy than using relative risks is (Ann Intern Med 2014).

It is therefore best practice to present risks as absolute risks.

In this document, rates have been presented as natural frequencies (number of cases per 1,000 women) rather than in percentages, because natural frequencies are considered easier to understand (Cochrane 2011).

How we estimated the absolute risks

It is important to bear in mind that the risks presented are at a population rather than an individual level. To estimate the absolute risks for people who take or have taken HRT:

- the relative effects as presented in the evidence reviews were applied to the absolute risk of each outcome for women who have never taken HRT
- confidence intervals were also applied to the effect estimates to give an indication of how close to the 'true' value the estimate lies.

To calculate the absolute risk of one outcome for women who have never taken HRT (or baseline absolute risk) in a given age group, we used the:

- proportion of women in the entire age group who have never taken HRT
- incidence of the outcome over the entire age group
- relative risk of the outcome in current users of HRT in that age group.

The formula which was used to do the calculations can be found in the appendix of the evidence review relevant to each outcome.

(Continued on next page.)

For some subgroups of people, the evidence only reported a relative effect, and NICE did not have information on the background risk of the outcome for that group. As a result, we could not deduce the absolute values for those subgroup populations.

For people experiencing menopause at age 45 or over, we did the calculations using data on people starting HRT at age 50, as an example. This is because the average age of menopause is 50 years old in the UK. Although data has been calculated in this way, it can be used to discuss benefits and risks with anyone aged 45 or over.

For people experiencing early menopause, we calculated the estimates using data for the relevant age range, that is, 40 to 44 years old.

References for the section on 'Why present absolute risks?'

- Schragger S (2018) [Five Ways to Communicate Risks So That Patients Understand](https://www.aafp.org/pubs/fpm/issues/2018/1100/p28.html#fpm20181100p28-b8). Fam Pract Manag 25(6): 28-31. <https://www.aafp.org/pubs/fpm/issues/2018/1100/p28.html#fpm20181100p28-b8>
- Akl EA, Oxman AD, Herrin J, et al. (2011) [Using alternative statistical formats for presenting risks and risk reductions](#). Cochrane Database Syst Rev. 2011(3):CD006776.
- Fagerlin A, Zikmund-Fisher BJ, Ubel PA (2011) [Helping patients decide: ten steps to better risk communication](#). J Natl Cancer Inst 103(19):1436-43.
- Zipkin DA, Umscheid CA, Keating NL, et al. (2104) Evidence-based risk reduction: a systematic review. Ann Int Med 161(4):270-280.