# The epidemiology of breast cancer, a summary overview

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In the European Union (EU), overall breast cancer mortality rates (world standard) declined from 17.9/100,000 in 2002 to 15.2 in 2012. The predicted 2020 rate is 13.4/100,000. The falls were largest in young women (20-49 years, -22% between 2002 and 2012). About 32,500 breast cancer deaths will be avoided in 2020 in the EU as compared to the peak rate of 1989, and a total of 475,000 breast cancer deaths over the period 1990-2020 [1], again as compared to the peak rate of the late 1980's.

Likewise, breast cancer mortality trends were favourable in North America and Oceania over the last three decades, and a further 10% reduction in their overall rates is predicted for 2020, to reach values of 11-12/100,000 women, i.e. about 50% lower than their top rates in the later 1980's [2].

In Europe, the lifetime probability of developing breast cancer varies from about 5% for a woman with no family history and low lifetime risk profile to over 30% for a woman with young family history and high lifestyle risk profile. Strong familial and genetic factors are restricted to a minority of women (though milder genetic predisposition is common), thus an appreciable proportion of breast cancers is in principle preventable through intervention on lifestyle factors.

## REPRODUCTIVE, MENSTRUAL AND HORMONAL FACTORS

There are several indications that breast cancer incidence and risk are associated to menstrual and reproductive factors which influence endogenous female hormones [3]. Thus, breast cancer risk is inversely related to parity, age at menarche and directly related to age at first birth and at menopause. The excess breast cancer risk for each year of delay of menopause (about 2.5%) is similar to that for one year use of hormone replacement therapy (HRT) in menopause [4].

Breast cancer risk is also directly related to overweight and obesity in postmenopause, and this is interpreted in terms of increased estrogen levels and availability in overweight post-menopausal women [5].

Cohort studies measuring endogenous hormone levels in postmenopausal women also indicate that breast cancer risk is directly related to various measures of estrogens and androgens, and inversely to sex hormone binding globulines (SHBG), hence pointing to free available hormones as key risk determinants.

Current and recent use of oral contraceptives (OC) and HRT (mainly combination estrogen–progestin HRT) is also related to increased breast cancer risk. However, the relative risk (RR) appears to decline in the short term after stopping OC and HRT use. This indicates that exogenous hormones have a short term effect on breast cancer risk, and appreciably reduce the public result implications of OC, but not necessarily of HRT, which are used in middle age women, where breast cancer rates are high [6].

Timing of endogenous hormone exposure is however more difficult to define, and hence the time-risk relation remains less clearly defined – although it is now established that long-term overweight and obesity are associated to greater breast cancer risk, while the RR levels off in post-menopausal women who lose weight [3, 5].

## LIFESTYLE HABITS

The best established lifestyle factors for breast cancer are overweight and obesity, HRT in post-menopause, and alcohol consumption both in pre-and post-menopause. The RRs for overweight, obesity and HRT approach 1.5 to 2; about 40% of European women are overweight in post-menopause and 10% long term users of HRT. Thus, control of long-term (mainly combined estrogen and progestin) HRT use, and reduction of overweight and obesity in post–menopausal women could avoid 15 to 20% post-menopausal breast cancers. The RR for alcohol drinking increased by about 5% per drink per day, and up to 30 to 40% of women in selected European countries drink alcohol regularly [7]. Thus, reduction of alcohol drinking could avoid 5% of breast cancers in Europe - and in selected countries, up to 10%. A favorable influence of physical activity and selected aspects of diet on breast cancer risk is also possible, though definition of these factors and their quantification remains uncertain [8]. Still, assuming a RR of 0.8 for regular physical activity and a proportion inactive women of 50%, up to 10% of breast cancers could be avoided by widespread adoption of physical activity. A similar proportion could be avoided by a diet rich in vegetables and poor in animal fats, again assuming a RR of 0.8 for a favourable diet [9]. In a case-control study conducted in Italy and Switzerland, and including 3034 breast cancer cases and 3392 controls, adherence to the Mediterranean diet was quantitatively measured through a Mediterranean Diet Score (MDS) summarizing the major characteristics of the dietary pattern and ranging from 0 (lowest adherence) to 9 (highest adherence). Compared to MDS of 0-3, the odds ratios of breast cancer were 0.86 (95% confidence interval, CI, 0.76-0.98) for MDS of 4-5 and 0.82 (95% CI, 0.71-0.95) for MDS of 6-9. Similar results were found in premenopausal and postmenopausal women [10, 11]. Lactation has a protective effect on breast cancer, but given the limited number of births per woman in Europe, even long-term lactation would have a modest impact on lifetime breast cancer risk. Likewise, breast cancer risk could be reduced by earlier first birth and increased number of births, but – though in principle modifiable – these factors imply complex and difficult to adopt societal changes.

In any case, modification of selected lifestyle factors would have a substantial impact – up to 40% - in reducing the breast cancer burden in Europe [3].

### References

1. Carioli G, Malvezzi M, Rodriguez T, Bertuccio P, Negri E, La Vecchia C. Trends and predictions to 2020 in breast cancer mortality in Europe. Breast 2017; 36: 89-95.
2. Carioli G, Malvezzi M, Rodriguez T, Bertuccio P, Negri E, La Vecchia C. Trends and predictions to 2020 in breast cancer mortality: Americas and Australasia. Breast 2018; 37: 163-169.
3. Boffetta P, Boccia S, La Vecchia C. Cancer of the breast. In A quick guide to cancer epidemiology. Cham, New York: Springer 2014; 46-51.
4. Rosato V, Bosetti C, Negri E et al. Reproductive and hormonal factors, family history, and breast cancer according to the hormonal receptor status. Eur J Cancer Prev 2014; 23: 412-417.
5. La Vecchia C, Giordano SH, Hortobagyi GN, Chabner B. Overweight, obesity, diabetes, and risk of breast cancer: interlocking pieces of the puzzle. Oncologist 2011; 16: 726-729.
6. Cibula D, Gompel A, Mueck AO et al. Hormonal contraception and risk of cancer. Hum Reprod Update 2010; 16: 631-650.
7. Seitz HK, Pelucchi C, Bagnardi V, La Vecchia C. Epidemiology and pathophysiology of alcohol and breast cancer: Update 2012. Alcohol Alcohol 2012; 47: 204-212.
8. D'Avanzo B, Nanni O, La Vecchia C et al. Physical activity and breast cancer risk. Cancer Epidemiol Biomarkers Prev 1996; 5: 155-160
9. Mezzetti M, La Vecchia C, Decarli A, Boyle P, Talamini R, Franceschi S. Population attributable risk for breast cancer: diet, nutrition, and physical exercise. J Natl Cancer Inst 1998; 90: 389-394.
10. Giacosa A, Barale R, Bavaresco L et al. Cancer prevention in Europe: the Mediterranean diet as a protective choice. Eur J Cancer Prev 2013; 22: 90-95.
11. Turati F, Carioli G, Bravi F et al. Mediterranean Diet and Breast Cancer Risk. Nutrients 2018; 10(3) pii: E326. doi: 10.3390/nu10030326.

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