

- Manson JE, Aragaki AK, Rossouw JE et al. Menopausal hormone therapy and long-term all-cause and cause-specific mortality: the Women's Health Initiative Randomized Trials. *JAMA* 2017; 318(10): 927–938.
- Mikkola TS, Savolainen-Peltonen H, Tuomikoski P et al. Reduced risk of breast cancer mortality in women using postmenopausal hormone

therapy: a Finnish nationwide comparative study. *Menopause* 2016; 23(11): 1199–1203.

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### Reply to the letter to the editor 'European cancer mortality predictions for the year 2019 with focus on breast cancer, by Malvezzi M et al' by Marsden and Hamoda, On behalf of the British Menopause Society Medical Advisory Council

We agree with Dr Marsden and Dr Hamoda that the key determinant of the declines in breast cancer mortality across Europe has been improved management, including essentially better treatments, together with early diagnosis and organized screening [1].

We only mentioned in two lines a possible role of decrease in menopausal hormone use on national breast cancer rates [2]. Indeed, changes in hormonal replacement therapy (HRT) use had a relevant impact on incidence, but their influence on mortality is limited and not adequately quantified [3, 4].

Still, despite the better prognosis of breast cancer diagnosed in women using HRT [5], some rises in breast cancer incidence may well translate to an increase of mortality, though smaller than that of incidence. This remains unquantified, but in agreement with Dr Marsden and Dr Hamoda, is likely to have a limited impact as compared to the improvements in breast cancer management over the last few decades [6].

M. Malvezzi<sup>1</sup>, G. Carioli<sup>1</sup>, P. Bertuccio<sup>2</sup>, P. Boffetta<sup>3</sup>, F. Levi<sup>4</sup>,  
C. La Vecchia<sup>1\*</sup> & E. Negri<sup>2</sup>

Departments of <sup>1</sup>Clinical Sciences and Community Health; <sup>2</sup>Biomedical and Clinical Sciences, Università degli Studi di Milano, Milan, Italy; <sup>3</sup>Tisch Cancer Institute, Icahn School of Medicine at Mount Sinai, New York, USA; <sup>4</sup>Institute of Social and Preventive Medicine (IUMSP), Lausanne University Hospital, Lausanne, Switzerland  
(\*E-mail: carlo.lavecchia@unimi.it)

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### Disclosure

The authors have declared no conflicts of interest.

### References

- Marsden J, Hamoda H, On behalf of the British Menopause Society Medical Advisory Council. European cancer mortality predictions for the year 2019 with focus on breast cancer, by Malvezzi M et al. *Ann Oncol* 2019; 30(8): 1393–1394.
- Malvezzi M, Carioli G, Bertuccio P et al. European cancer mortality predictions for the year 2019 with focus on breast cancer. *Ann Oncol* 2019; 30(5): 781–787.
- Brewster DH, Sharpe KH, Clark DI, Collins J. Declining breast cancer incidence and decreased HRT use. *Lancet* 2009; 373(9662): 459–460. author reply 461.
- Pelucchi C, Levi F, La Vecchia C. The rise and fall in menopausal hormone therapy and breast cancer incidence. *Breast* 2010; 19(3): 198–201.
- La Vecchia C. Estrogen and combined estrogen-progestogen therapy in the menopause and breast cancer. *Breast* 2004; 13(6): 515–518.
- Carioli G, Malvezzi M, Rodriguez T et al. Trends and predictions to 2020 in breast cancer mortality in Europe. *Breast* 2017; 36: 89–95.

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### Extramural spread of rectal cancer and the AJCC Cancer Staging Manual 8th edition, 2017

Currently, management decisions in rectal cancer are largely based on the assessment of locoregional tumour spread by imaging. T3 tumours comprise the majority of all rectal cancers and are accurately visualised by pretreatment magnetic resonance imaging (MRI). Local recurrence and survival after treatment are highly related to the degree of extramural spread within the T3 category with a heterogeneity far greater than for any other T stage, with local recurrence ranging from less than 10% to over 20%. Histopathological analysis of cancer-specific end points within the T3 category has shown that its division into pT3a and

pT3b subgroups in which extramural spread is up to and including 5 mm in the former and more than 5 mm in the latter is the strongest locoregional prognostic factor of local recurrence and survival [1–3]. Staging pretreatment MRI now forms the basis for management planning for locoregional disease, including the decision to recommend chemoradiation and the subsequent assessment of tumour response when this is given.

The 7th edition of the AJCC Cancer Staging Handbook published in 2010 made no mention of the degree of extrarectal spread as a risk factor for local recurrence and survival, but in the 4th edition of the UICC TNM Supplement published 2 years later [3], a subdivision of the T3 category into T3a and T3b was proposed as an optional addition to the pT classification, based on a 5-mm point of subdivision. The quoted respective local