

Peer Review File

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Reviewer A

This is a review article on an overview of epidemiological aspects of breast cancer in older adults worldwide. I think that the idea is interesting and well written with oversight aspects.

Comment 1: In minor points, I think key papers on CGA as below are not referred.

1. Hurria A, Mohile S, Gajra A, Klepin H, Muss H, Chapman A, Feng T, Smith D, Sun CL, De Glas N, Cohen HJ, Katheria V, Doan C, Zavala L, Levi A, Akiba C, Tew WP (2016) Validation of a Prediction Tool for Chemotherapy Toxicity in Older Adults With Cancer. *J Clin Oncol* 34:2366-2371. doi: 10.1200/JCO.2015.65.4327
2. Mohile SG, Dale W, Somerfield MR, Schonberg MA, Boyd CM, Burhenn PS, Canin B, Cohen HJ, Holmes HM, Hopkins JO, Janelins MC, Khorana AA, Klepin HD, Lichtman SM, Mustian KM, Tew WP, Hurria A (2018) Practical Assessment and Management of Vulnerabilities in Older Patients Receiving Chemotherapy: ASCO Guideline for Geriatric Oncology. *J Clin Oncol* 36:2326-2347. doi: 10.1200/jco.2018.78.8687

Reply 1: Thank you for the suggestions, we have added the articles mentioned above (ref. 86 and 91), without adapting the text

Changes in the text: page 9: An important reason to perform a comprehensive geriatric assessment is to detect unidentified problems and risks to guide integrated geriatric and supportive care interventions (85, 86). Another reason for performing a geriatric assessment is the ability to get a better impression about possible treatment outcomes, such as side effects (85, 87). A comprehensive geriatric assessment also gives a better estimation of the expected life expectancy taking the competing risks into account (85). Despite the evidence of the beneficial effect of geriatric assessments regarding decision-making, treatment outcomes and treatment adherence, their current use in daily practise is still limited (88, 89). This might be due to the inability to interpret a geriatric assessment (90). Moreover, a geriatric assessment is time consuming. There are also other interesting tools specifically designed to predict treatment outcomes, such as the chemotherapy toxicity tool developed by Hurria et al. on chemotoxicity in patients with cancer (87, 91).

Reviewer B

Comment 1: Manuscript could be shortened and made more succinct, especially focusing on breast cancer and elderly patients.

Reply 1: we have deleted several parts of the manuscript, especially those not focusing on breast cancer and elderly patients.

Changes in the text: see main document.

Comment 2: Title needs to be improved to ensure readers know what the article is about. For example, it is not clear the focus of the paper is about breast cancer in elderly patients (>70 years) and discrepancy between countries/socioeconomic differences.

Reply 2: Thank you for the suggestion. Since this is an invited article, we were given this title by the guest editor. However, the guest editor agreed to change the title and use the current title as a subtitle, resulting in the following title: Breast cancer in the Older population: A global challenge – an epidemiological perspective.

Comment 3: Typo on line 65.

Reply 3: we replaced HER2neu negative into HER2-negative

Changes in the text: this change resulted in the following sentence on page 4: Tumours in the older population are more often hormone receptor-positive and HER2-negative (80% in patients aged ≥ 75 years and 65% in patients < 50 years) and less often triple negative than tumours in younger patients (9% and 15% in patients aged ≥ 75 years and < 50 years, respectively) (10-12).

Comment 4: Line 77 does not make sense. Needs to be clearer.

Reply 4: We have deleted the first sentence of line 77 on page 5: “In older patients, breast cancer occurs to the background of ageing.”, which results in a more logical paragraph.

Changes in the text: see above.