A Global Breast Cancer General Knowledge Test

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Abstract

Background: The late Hans Rosling has made the case that we are often wrong in our assessments of important global socioeconomic and health facts, and that beyond ignorance, unconscious and predictable biases account for this situation. To respond appropriately to the global challenges of poor outcomes for a large fraction of women with breast cancer, a correct knowledge base is essential.

Methods and results: After consultation with global breast cancer expert colleagues, I constructed a series of 14 questions covering a breadth of major population, economic, epidemiologic, diagnostic, treatment, and palliation breast cancer issues; documented the correct answers to these; and here briefly consider the implications of these answers.

Discussion: This exercise suggests that emphases other than on resources, education, and certain policies may be more important in contributing to better outcomes in global breast cancer, particularly in low- and middle-income countries.

Introduction

Most forcefully and completely in his book Factfulness, the late Hans Rosling has made the case that we are often wrong in our assessments of important global socioeconomic and health facts, and that beyond ignorance, unconscious and predictable biases account for this situation [1]. He presents a 13-item test he reports to have given to multiple international audiences of well-educated and presumably well-informed leaders, with repeatedly poor results.

The problems of cancer are increasing in low- and middle-income countries (LMICs), which now have significant majorities of the global case, morbidity and mortality burdens [2]. The professional oncology communities, particularly those in high-income countries, are being increasingly called upon to define pragmatic and realistic approaches to these problems [3]. For, in particular, academic medical cancer professionals, called upon or choosing to participate in activities directed to global breast cancer control, critical to exercising due diligence in such efforts is having a solid basic knowledge base. I surmised that for such professionals, defining such a limited base for breast cancer might serve to call attention to issues with important implications for interventions.

Methods

The author contacted several senior clinicians, seeking individuals in particular, with experience in the breadth of breast cancer challenges in low- and middle-income countries.

Based on discussions with these individuals, I constructed a series of 14 basic knowledge questions about global aspects of breast cancer covering a breadth of major population, socio-economic, epidemiologic, diagnostic, treatment, and palliation issues; documented the correct answers to these; and here briefly consider the implications of these answers
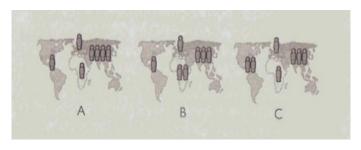
Results

Global Breast Cancer General Knowledge Test

Questions

1) Which map shows best where the 7 billion people in the world today live?

2) Among economic groups of countries-

A.   low,

B.   middle and

C   high-income- in which group does the majority of the world population live?

3) Globally, new cases of breast cancer each year are diagnosed in:

A.   More pre- than postmenopausal women

B.   Approximately equivalent numbers of pre- and postmenopausal women

C.   More post- than premenopausal women.

4) Because of changes in parity, in the coming decades the

standardized incidence of breast cancer globally is expected to:

A. Increase

B. Decrease

C. Remain stable.

5) Lactation for greater than 6 months is consistently associated with:

A. Decreased risk of breast cancer in premenopausal women.

B. Decreased risk of breast cancer in pre- and postmenopausal women.

C. Decreased risk of breast cancer in postmenopausal women.

6) Higher stage disease at diagnosis in low- and middle-income countries is most strongly associated with:

A. Educational level of women

B. Physician expertise in diagnosis

C. Affordability and accessibility of cancer care

7) Globally, among women with suspected breast cancer, the fraction that has a pathological/histological confirmed diagnosis and hormonal receptor testing is:

A. 85%

B. 70%

C. 50%

8) Globally, among women with operable breast cancer, the fraction that has primary surgery is:

A. >90%

B. 75%

C. 60%

9) Globally, among women with higher stage operable breast cancer, who could benefit from adjuvant radiation therapy, the fraction that actually receives such treatment is:

A. 80%

B. 50%

C. 25%

10) Globally, the most significant barriers to women receiving effective systemic therapies are:

A. The high costs of therapies and poverty

B. The limited knowledge of patients and physicians

C. Medical system governance and economic issues

11) Globally, in premenopausal women with operable hormonal receptor positive breast cancer, adjuvant hormonal therapy can increase absolute 10-year overall survival by:

A. 10%

B. 15%

C. 20%

12) At 5 years, among women in many populations appropriately prescribed adjuvant hormonal therapies, the fraction which has taken these treatments for the entire period is:

A. 80%

B. 65%

C. <50%

13) For women receiving adjuvant chemotherapy for breast cancer, impairment of cognitive function has been demonstrated in:

A. <10%

B. 25%

C. Half

14) In comprehensive evaluations of palliative care across many countries (such as the Economist Intelligence Unit Quality of Death Index report -4), opioid painkiller drugs are available and accessible in:

A. Most countries

B. More than half of countries

C. Less than half of countries

Answers

1.   This is one of Rosling's key questions (1). The correct answer is map A. The 2017 estimates for the four regions are the Americas 1.0 billion, Europe 0.84 billion, Africa 1.3 billion and Asia 4.4 billion according to the United Nations Population Division [5] (Figure 1).

2.   This is also one of Rosling's major questions (1). The correct answer is B. World Bank data for 2015 show that the majority of people (76%!) live in middle-income countries, with the groups low (<$2), middle ($2-<32$) and high ($32 and >) daily income defined by gross national income per capita in current US dollars [6].

3.   The correct answer is B, but trending towards A. The critical, often unacknowledged, figures are the sizes of the annual pre- and post-menopausal global new case populations which are approximately equivalent. Using Globocan, projections are for almost 900,000 total new cases in low- and middle-income (LMIC) countries, and 720,000 in high-income countries in 2020 [7]. These estimates for total cases are the same as might be calculated with estimates of 3 billion women in LMICs and an adjusted incidence of 30/100,000/year (which figure is lower than is reported from the Shanghai registry currently -41.7 ASR-, and about what is reported from the Kolkata registry from a more than a decade ago, giving information for the two countries with the largest populations); and estimates of 0.8 billion women in high-income countries and an age adjusted incidence of 91/100,000/year [7-9]. Premenopausal cases in high-income countries account for approximately 25% of all cases or then 175,000 new annual cases [10]. The situation in LMIC generally is less certain. The age structure of most LMICs is wide-based, with much larger younger populations to be affected by breast cancer. In some countries, 2/3rds of new cases are in premenopausal women, which would then

mean that there are 600,000 new annual cases. 600,000 LMIC premenopausal cases and 175,000 high income country cases= 775,000 or approximately half of the estimated new cases.

4. The correct answer is B—incidence is projected to increase. Globally, in the last 50 years parity has been halved—it has fallen remarkably to 2.5 babies per woman. (1, p.84). This change is contributing to projections of increased future risk of breast cancer because of the association of increased parity with decreased breast cancer risk. For example, in a Swedish study, each additional birth conferred a 10% risk reduction [11]. In another investigation, as has also a meta-analysis, decreasing parity was found to have the determinant role in likely future breast cancer incidence [12,13].

5. The correct answer is B. While a sentinel study suggested that lactation is associated with reduced risk in only premenopausal women, a subsequent meta-analysis has shown reduced risk through life [13,14].

6. The correct answer is C affordability and accessibility of care. The consistent experience of clinicians in LMICs is that women are aware of serious signs of breast cancer in their breasts, but often feel that they have no choice to act on their concerns because affordable and accessible care is not within their reach. The strongest objective evidence in support of this conclusion comes from an IARC study of breast self-examination in the Philippines where, while smaller tumors were detected by women taught BSE, the study was abandoned because women did not act on their findings because of their beliefs that treatment care was out of their economic reach [15]. LMIC physicians trained in allopathic medicine very aware of the common signs of breast cancer.

7. The correct answer is B, but the 70% figure is really an estimate. A significantly lower figure could in fact be the true figure. For example, perhaps only 10% of patents in Nigeria have such surgical pathology studies. Access to surgical pathology services is limited in many countries. Human rights, economic issues, and educational issues for physicians in low- and middle-income countries also contribute to lower use of such services, especially hormone receptor testing.

8. The correct answer is A. In most countries in the world, hospitalization -requiring care and competent surgical care for breast cancer are generally available.

9. The correct answer is B, approximately 50%. There are data showing that approximately 1/3rd of annual global cancer cases have no access to radiation therapy [16]. Human rights and economic issues in low- and middle-income countries, where a majority of women needing such treatment live, account for additional cases in which such treatment is not given.

10. The correct answer is C. Specific basic drugs costs are in fact usually within reach of poorest families; patients and doctors are generally very aware and available to provide treatments. It is systems and ancillary costs, often for unneeded tests or magnified by corruption and medicine as primarily a commercial activity, which stand in the way of patients generally receiving systemic treatments.

11. The correct answer is C. The relative risk of 10-year death reduction with 5 years of tamoxifen in the EBCCTG was 0.25

and was equivalent in axillary node positive and negative populations of uncertain hormonal receptor status [17]. In the generally low-risk populations the EBCCTG data come from, the 10-year absolute survival was 69% in untreated and 77% in treated patients, while in a higher risk group from Vietnam and China treated with surgical oophorectomy and 5 years of tamoxifen, the absolute survival was 49% in untreated and 78% in treated hormone receptor positive patients (RR reduction for death 0.57), and 50% and 72% unselected for hormonal receptor status (RR reduction for death 0.44) respectively [18]. The suggestion that combined surgical oophorectomy/ovarian suppression plus tamoxifen has greater long-term impact than tamoxifen alone is supported by data from the SOFT trial [19]. If globally, premenopausal women with operable breast cancer, generally observed to be at greater risk for recurrence because of higher stage disease at diagnosis, have 10-year survival of 50% without any adjuvant treatment, and have optimal treatment relative risk reductions of 0.25, 0.44, and 0.57, the absolute increases in survival would be 12.5%, 22%, and 28% [17,18]. An estimate of 20% overall is reasonable based on the cited data.

12. The correct answer is C. The impact of effective hormonal therapies is significantly reduced by drop-out from treatment not an economic or side-effect issue, but a behavioral-health patient model issue [20-22]. The long-term lower adherence to therapy for breast cancer is very similar to that for other chronic disease interventions [23].

13. The correct answer is B. While the most compelling data to date have come from studies in women from high-income countries, their application to women worldwide is not in doubt [24,25].

14. The correct answer is C. As the 2015 Economist report states: "In only 33 of the 80 countries in the index are opioid painkillers freely available and accessible. In many countries access to opioids is still hampered by red tape and legal restrictions, lack of training and awareness, and social stigma" (4, p. 7).

Discussion

While the suggested questions may not raise all the most important issues, and the answers to some (particularly 6 through 10, concerning reasons for higher stage disease and lack of access to systemic therapies in LMICs, and global fractions with access to surgical pathology, surgery and radiation therapy services) may be considered poorly data-supported, the author believes that these questions and answers (and their implications) do highlight some very relevant issues in addressing global breast cancer more successfully. Specifically, first, the major case-burdens now and into the future, are increasing and in Asia, and in middle-income countries among premenopausal women and without resources to attack breast cancer. Affordability and access to care and medical systems their governance, associated corruption, organization and the commercialization of medicine, are majorly responsible for shortfalls in optimal care. New business models for radiotherapy in particular, are desperately needed. The beneficial effects of hormonal therapies are huge, but lost in practice. The toxicities of chemotherapies play a major role in their optimal application. Palliative care, particularly for women, is woefully inadequate. These questions

and their answers can serve to focus attention on how the world of medicine really works.

Resources (whose is unclear), education (patient and professional), costs of drugs, and policies (for screening as an example, an activity for breast cancer very unlikely in LMICs to have a meaningful impact, or for developing cancer registries, or for resource-stratified guidelines), are frequently offered as issues which should command attention in better addressing global breast cancer [4,26,27]. In some ways these are the kinds of simple solutions to complex challenges, about which Rosling warns we should beware [1]. The WHO Report of its Independent High-level Commission on Noncommunicable Diseases offers 16 "Best Buys", 15 of which are for policies, none of which directly or majorly affect breast cancer, the most common major malignancy in women worldwide [28]. The suggested questions and answers in this communication suggest different directions. As Rosling has suggested, getting our heads around important facts about global cancer, is where we have to start if we are going to successfully address global public health oncology, and unconscious and predictable biases may explain why we often get the facts wrong [1]. The late Jonathan Mann and the psychology and Marketing Professor Art Markman have emphasized that how you define the problem determines whether you solve it [29]. These 'test' questions and answers are a different start to meeting the broad challenges of better global breast cancer control.

As I have written: "We need to think hard, big, and deep about the social change involved in improving cancer outcomes for our fellow planet travelers" [30].

REFERENCES

1. Rosling H, Rosling O, Ronnlund AR (2018) Factfulness. Flatiron books, New York. 018.P. 276

2. Daniels ME, Donilon TE, Bollyky TJ (2014) The emerging global health care crisis. No communicable diseases in low and middle-income countries. Independent Task Force Report No. 72. Council on Foreign Relations. New York.

3. Farmer P, Frenk J, Knaul FM (2010) Expansion of cancer care and control of low-and middle-income: A call to action. Lancet 376: 1186-1193.

4. The Economist Intelligence Unit: The 2015 Quality of Death Index. London, The Economist, 2015.

5. UN Population Division. Population, medium fertility variant. World Population Prospects 2017. United Nations, Department of Economic and Social Affairs, Population Division.

6. World Bank. Population of Country Income Groups in 2015-Population total.

7. Ferlay J, Soerjomataram I, Dikshit R (2015) Cancer incidence and mortality worldwide: Sources, methods and major patterns in GLOBOCAN 2012. Int J Cancer 13(5): E359–E386.

8. Huang Z, Wen W, Zheng Y (2016) Breast cancer incidence and mortality: trends over 40 years among women in Shanghai, China. Annals of Oncology 27(6):1129-1134.

9. Sen U, Sankaranarayanan R, Mandal S (2002) Cancer patterns in Eastern India: The first report of the Kolkata Cancer Registry. Int J Cancer 100 (1):86–91.

10. American Cancer Society. Breast Cancer Facts & Figures 2017-2018. Atlanta: American Cancer Society, Inc. 2017.

11. Lambe M (1996) Parity, age at first and last birth and risk of breast cancer. Breast Cancer Res Treat. 38:305-311.

12. You WP, Symonds I, Rühli FJ, Henneberg M (2018) Decreasing birth rate determining worldwide incidence and regional variation of female breast cancer. Adv in Breast Cancer Res. 7:1-14.

13. Collaborative Group on Hormonal Factors in Breast Cancer. Breast cancer and breastfeeding: collaborative reanalysis of individual data from 47 epidemiological studies in 30 countries, including 50,302 women with breast cancer and 96,973 women without the disease. Lancet. 2002;360: 187-195

14. Newcombe PA, Storer BE, Longnecker MP (1994) Lactation and reduced risk of premenopausal breast cancer. N Engl J Med. 330:81-87.

15. Pisani P, Parkin DM, Ngelangel C (2006) Outcome of screening by clinical examination of the breast in a trial in the Philippines. Int J Cancer. 118(1):149-154.

16. Mei LY, Eduardo Z, Freddie B, Jacques F, Michael B (2016) Global Access to Radiotherapy Services: Have We Made Progress During the Past Decade? J Global Oncology 2:4, 207-215

17. Early Breast Cancer Trialists' Collaborative Group: effects of chemotherapy and hormonal therapy for early stage breast cancer on recurrence 15-year survival: An overview of randomized trial. Lancet 2005. 365:1687-1717.

18. Love RR, Van Dinh N, Quy TT (2008) Survival after adjuvant oophorectomy and tamoxifen in operable breast cancer in premenopausal women. J Clin Oncol. 26(2):253-7.

19. Francis PA, Pagani O, Fleming GF (2018) Tailoring adjuvant endocrine therapy for premenopausal breast cancer. New Engl J Med 379:122–137.

20. Chlebowski RT, Kim J, Haque R (2014) Adherence to Endocrine Therapy in Breast Cancer Adjuvant and Prevention Settings. Cancer Prev Res 7(4):378-87.

21. Partridge AH, Wang PS, Winer EP, Avorn J (2003) Non-adherence to adjuvant tamoxifen therapy in women with primary breast cancer. J Clin Oncol. 21:602–6.

22. van Herk-Sukel MP, van de Poll-Franse LV, Voogd CA (2010) Half of breast cancer patients discontinue tamoxifen and any endocrine treatment before the end of the recommended treatment period of 5 years: A population-based analysis. Breast Cancer Res Treat 122:843–51.

23. Nieuwlaat R, Wilczynski N, Navarro T, Hobson N, Jeffery R, et al. (2014) Interventions for enhancing medication adherence. Cochrane Database of Systematic Reviews 11

24. Matsuda T, Takayama T, Tashiro M, Nakamura Y, Ohashi Y, et al. (2005) Mild cognitive impairment after adjuvant chemotherapy in breast cancer patients evaluation of

appropriate research design and methodology to measure symptoms. Breast Cancer 12(4): 279–287

25. Lera AT, Fede AB, Miranda MC (2010) Cognitive dysfunction (chemobrain) in breast cancer patients receiving adjuvant therapy: A meta-analysis. j Clinical Oncology 28 (15)

26. Daniels ME, Donilon TE, Bollyky TJ (2014) The Emerging Global Health Crisis Noncommunicable Diseases in Low- and Middle-Income Countries. Independent Task Force Report No. 72. Council on Foreign Relations, New York.

27. Anderson BO (2008) Guideline implementation for breast healthcare in low-income and middle-income countries. Cancer 13:2221-43.

28. Time to Deliver: Report of the WHO Independent High-level Commission on Noncommunicable Diseases. Geneva: World Health Organization, 2018.

29. Markman A (2019) How you define the problem determines whether you solve it. Harv Bus Rev 10:29-30,

30. Love RR (2019) Improving cancer outcomes in low- and middle-income countries. J Global Oncology 5:1-3.

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