

# Prevention of cervical and breast cancer mortality in low- and middle-income countries: a window of opportunity

This article was published in the following Dove Press journal:  
*International Journal of Women's Health*

Silvia de Sanjose  
Vivien D Tsu

Sexual and Reproductive Health, PATH,  
Seattle, WA, USA

**Abstract:** Breast and cervical cancer are the two most common women's cancers worldwide. Countries have invested for decades in early detection programs for breast and cervical cancer through screening, community education, and opportunistic case detection by health professionals. However, effectiveness in low- and middle-income countries (LMICs) has been limited due to low coverage, insufficient laboratory capacities for diagnosis, health information systems (HIS) that are not designed to track patients or monitor program performance, barriers that inhibit women's uptake of services, and inadequate treatment options. Even where some screening activities exist, there has not been sufficient attention to ensuring completion of appropriate diagnosis and treatment after women receive a positive screening test result or report symptoms suggesting cervical or breast cancer. Because of this failure to provide adequate follow-up care, these women miss the potential benefit from early detection and have a higher than average risk to develop cancer or progress to more advanced cancer stages that could have been avoided. There are several critical steps in a woman's journey from good health to elevated cancer risk, then to cancer prevention or diagnosis, and finally to treatment. There is a window of opportunity that extends from the time a positive finding is identified—by a cervical or breast screening test or recognition of a breast abnormality—to the point when cervical precancer treatment is delivered or a treatment plan for diagnosed breast cancer is initiated. Building on existing health systems and adapting measurable, affordable, and culturally acceptable interventions can achieve a lasting impact. If women can successfully navigate this window of opportunity, they can avoid progression to cervical cancer or greatly reduce the need for invasive treatments for breast cancer and improve their chances for survival and improved quality of life. We propose several actions that can lead us on the path towards reduction of this cancer burden.

**Keywords:** screening, self-exam, prevention, impact, cervical cancer, breast cancer

## Introduction

### Breast and cervical cancer burden

Breast and cervical cancer are the two most common cancers in low- and middle-income countries (LMICs), both sexes combined. Breast cancer represents 27.3% of all cancers in women in LMICs, with an age-standardized incidence rate of 31.3 per 100,000, representing over half a million new cases every year. Nearly half of affected women will die from breast cancer.<sup>1</sup> Cervical cancer accounts for

Correspondence: Silvia de Sanjose  
PATH, 2201 Westlake Avenue, Suite 200,  
Seattle, WA 98121, USA  
Tel +1 206 285 3500  
Fax +1 206 285 6619  
Email [sdesanjose@path.org](mailto:sdesanjose@path.org)

15.9% of the total cancer burden in women living in LMICs with around 300,000 new cases every year. The age-standardized incidence rate is 15.9 per 100,000. Over 87% of these women will likely die from the disease.<sup>2</sup>

Although breast cancer has been regarded as a disease of industrialized geographies and cervical cancer as a cancer of low-resource settings, we are now being confronted with a steady increase in breast cancer incidence in the same areas where cervical cancer used to be the predominant cancer. Breast cancer in LMICs is probably the cancer with the highest increase in incidence in recent years, largely attributable to a transition towards westernized lifestyles that include demographic, reproductive, diet, and physical activity changes.<sup>2</sup>

On the other hand, downward trends in cervical cancer incidence are being observed in selected LMICs, particularly in the Americas,<sup>3</sup> yet rates remain high in many countries, especially for a cancer that could be largely preventable.<sup>4</sup> The burden of both cancers is high in LMICs where access to advanced treatment is clearly limited<sup>5</sup> and will be so for many years to come.

How can countries develop strategies that are feasible and affordable? Analysis of the best-value-for-money strategies indicates that vaccination against human papillomavirus (HPV) and cervical screening at least once in a lifetime together with an opportunistic clinical breast exam (CBE) are strategic actions that could reduce the burden of both diseases, if followed by appropriate management.<sup>6</sup>

## Ongoing progress

LMICs have invested—at modest levels—for decades in early detection activities, particularly for pre-cancerous lesions of the cervix, through screening, and occasionally through opportunistic case detection by health professionals of early breast cancer.<sup>7</sup> However, effectiveness has been limited due to low coverage, insufficient laboratory capacities for diagnosis, health information systems (HIS) that are not designed to track patients or monitor program performance, barriers that inhibit women's uptake of services, and inadequate treatment options.<sup>8</sup> Recently, LMICs have been building resources to monitor non-communicable diseases (NCDs) and to control cervical cancer through vaccination.<sup>9</sup> Few currently have national programs to support screening, but many are moving towards accelerating strategies that will ultimately reduce the burden of cervical disease among unvaccinated women.<sup>10,11</sup> Secondary prevention of breast cancer in LMICs is clearly in its early stages, as access to the best available tool for

tumor detection—mammography—is still limited due to its cost and complexity; more basic options like CBE are the only cost-effective approach in LMICs for the time being.<sup>12,13</sup> Although recommendations have been previously presented that integrate the different actors in cancer prevention, the path is clearly unfinished.<sup>6,14,15</sup>

## Window of opportunity

Even those countries that do offer basic screening services often fail to follow up a positive finding with adequate treatment. Complex follow-up regimens that require multiple visits can inhibit adequate management, while more streamlined approaches that reduce visits and utilize affordable technologies can enhance it. In Peru, for example, CBE may be the best early detection option in rural environments when access to mammograms is limited. Adding ultrasound to CBE and fine needle aspiration (FNA) biopsy may overcome barriers and improve downstaging by reducing visits and providing care closer to where women live.<sup>16</sup> In Colombia, women involved in breast cancer early detection underwent up to five visits between the initial screening visit and beginning treatment, if breast cancer were diagnosed.<sup>17</sup> Breast cancer survival rates at 5 years may go from 70% in Ecuador as compared to 90% in the USA; 5-year survival for cervical cancer can be of 23 points difference in Asian cancer registries (ie, Korea 78%, Thailand 55%) or 35 points difference in the few African cancer registries (72% in Algeria, 38% in South Africa).<sup>2</sup> Differences may be attributable to late-stage diagnosis and to limited access to treatment.<sup>2,18</sup>

Many LMICs worldwide have now a cancer plan that includes cervical and breast cancer strategies for screening and early detection, generally on an opportunistic basis.<sup>19</sup> However, it is important that any new population intervention promoting screening or early detection provide an adequate system for follow-up. For example, HPV screening tests are slowly being introduced in LMICs as national programs.<sup>20</sup> Women with a positive test may need to go for a triage test and treatment. Organizing these sequential visits may result in a considerable loss to follow-up. This is why a country may decide on optimal solutions of screen and treat in one single visit. Even women who have received treatment should get a follow-up visit a year later to ensure adequate treatment success and program quality. Thus, registration of screening and treatment interventions is necessary for an adequate continuum of care and is rarely available.<sup>21–24</sup>

The point of this paper is to raise awareness of the need to follow those women who, after accessing a secondary prevention exam or reporting potential symptoms, turn out

to have a positive test. These women are likely to be at higher risk of cancer than the general population and may require additional tests to confirm diagnosis. At this stage there is a window of opportunity that extends from the time a positive finding is identified—by a cervical or breast screening test or recognition of a breast abnormality—to the point when cervical precancer treatment is delivered or a treatment plan for diagnosed breast cancer is initiated, during which prompt and appropriate intervention can prevent the development of cervical cancer or late stage presentation of breast cancer (Figure 1).<sup>21</sup>

We think that by focusing on four critical areas in a structured manner, countries could gain the necessary momentum to reach vulnerable populations with effective services during this window of opportunity.

1. Identify and track women with a positive screening test or clinical finding of cervical or breast cancer by strengthening the HIS and increase the use of HIS outputs by health workers.

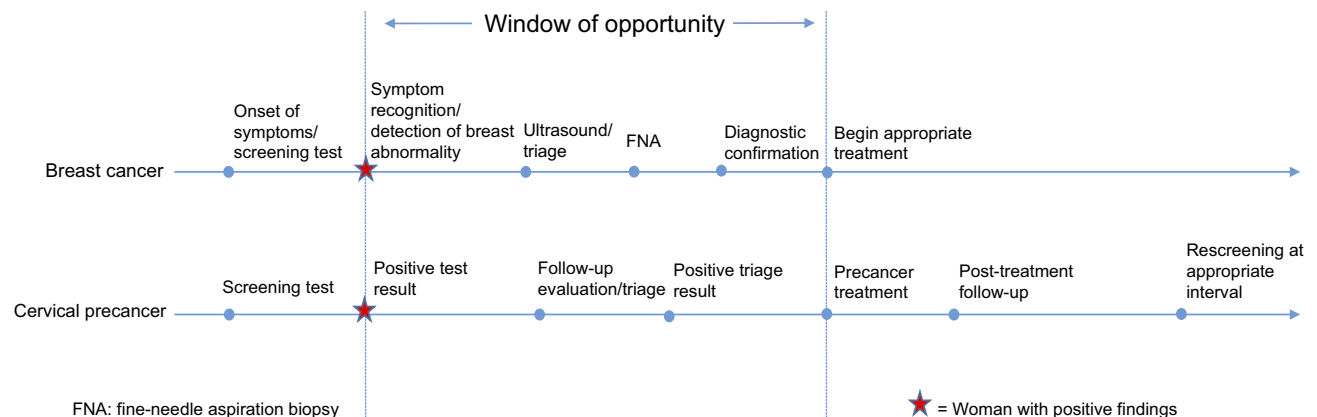
HIS in LMICs are generally designed for program monitoring using aggregated service data—often with different systems for different facility levels and poor or nonexistent linkages between the systems—that makes tracking of individual clients nearly impossible.<sup>25</sup> The systems often rely on women to manage their own follow-up or depend on individual health care worker initiative to seek out women overdue for recommended care. In a recent WHO review of eHealth challenges in the Americas, PAHO concluded that—despite considerable progress—lack of unique patient identifiers, inadequate mechanisms for exchange of clinical data between systems, and absence of legal frameworks to facilitate data exchange

remain as significant problems.<sup>26</sup> Although several countries, especially in Africa, have adopted electronic platforms like the District Health Information Software 2 (DHIS2), it does not allow longitudinal tracking; in addition, limited human resources for data entry, inadequate training, and equipment limitations can lead to incomplete or incorrect data entry.<sup>25</sup> Even when using a single-visit approach to cervical cancer screening, traceability is still required for women not eligible for ablative treatment and for confirmation of cure one year afterwards for all treated women.

Assessing the existing data flow contained in each health system and enforcing registration of basic data can facilitate traceability for women needing follow-up. Countries can then determine what changes are needed and whether additional computer-assisted and eHealth solutions are feasible and effective in reaching women needing follow-up.

2. Strengthen the availability and quality of diagnostic and treatment services for breast abnormalities and cervical precancer by evaluating current service availability, increasing capacity where needed, and measuring adherence to quality standards.

Taking the example of Peru, a model program to improve early detection of breast cancer was developed to be a more resource-appropriate alternative to the standard national guidelines and is currently being scaled up.<sup>16,27</sup> In Guatemala and Nicaragua, where HPV testing has been introduced in selected departments, new patient treatment algorithms were implemented to govern triage testing and treatment options after a positive HPV test result.<sup>8,28</sup> However, there is preliminary evidence that different algorithms are being applied, and the quality of screening outcomes is not uniformly good.<sup>29</sup> There



**Figure 1** Window of opportunity in continuum of care for breast and cervical cancer prevention.

is a need for expert review of these algorithms, their corresponding national guidelines, and how they are being implemented. A careful review can generate the recommendations for adjustments that are needed in practice. Remedial training to address weaknesses can be offered where needed, and innovative quality assurance mechanisms to strengthen capacity and quality can be applied.

3. Identify potential barriers and facilitators affecting traceability, mitigate the barriers, and expand on patient navigation services.

Whenever there is an intervention in asymptomatic populations, it is important to identify barriers that may limit a full uptake of provided services.<sup>30–33</sup> It is important to explore the usefulness, feasibility, and acceptability of interventions and solutions to mitigate barriers, such as use of mobile phones or text messages.<sup>34–36</sup> Patient navigation programs can help to shorten the time from initial presentation to final diagnosis and entry to treatment.<sup>37</sup> Community health workers are also an important resource that can provide insight into the needs of women and potential misunderstandings of health-related issues.<sup>38</sup> Workshops including community stakeholders can contribute to tailoring interventions and implementing solutions to reduce the barriers to service uptake.

4. Generate country-specific evidence on the effectiveness of the interventions, costs of inputs, and value for money (cost-effectiveness).

Finally, it is important to evaluate each intervention in terms of value-for-money towards the ultimate goal of reductions in incidence (cervical cancer) and mortality (both cancers). Data on incremental use of follow-up services, health impact, and costs of new interventions can be used to construct disease-outcome models to estimate the value-for-money and the anticipated national budget impact of the different approaches. In-depth evaluation of all process activities (ie, providers person-time at the clinic; resources to introduce data; time and services for follow-up; task shifting) may help the system to refine service flows and eliminate unnecessary costs.<sup>39</sup>

We call for a multidisciplinary and multisectoral approach to this window of opportunity that can ensure that women with breast abnormalities or with a positive cervical

screening test receive the full spectrum of care needed to follow-up, clarify their diagnosis, and, if necessary, treat their condition in a timely way.

Interventions to improve traceability, increase access to quality diagnostic and treatment services, and facilitate women's ability and willingness to complete follow-up care, combined with careful analysis of cost-effectiveness, should be available to all women regardless of residence or socioeconomic status. Building on existing health systems and adapting measurable, affordable, and culturally acceptable modifications can achieve a lasting impact in low-resource settings. If women can successfully navigate this window of opportunity, they can avoid progression to cervical cancer or greatly reduce the need for invasive treatments for breast cancer and improve their chances for survival and improved quality of life.

## Acknowledgments

We are grateful to Carolyn Bain, Francesca Holme, and Rose Slavkovsky at PATH for their contributions to the early development of these ideas.

## Disclosure

This manuscript is based on research funded in part by the Bill & Melinda Gates Foundation. The findings and conclusions contained within are those of the authors and do not necessarily reflect positions or policies of the Bill & Melinda Gates Foundation. The authors report no other conflicts of interest in this work.

## References

1. Bray F, Ferlay J, Soerjomataram I, Siegel RL, Torre LA, Jemal A. Global cancer statistics 2018: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. *CA Cancer J Clin.* 2018;68(6):394–424. doi:10.3322/caac.21492
2. Allemani C, Matsuda T, Carlo VD, et al. Global surveillance of trends in cancer survival 2000–14 (CONCORD-3): analysis of individual records for 37 513 025 patients diagnosed with one of 18 cancers from 322 population-based registries in 71 countries. *Lancet.* 2018;391(10125):1023–1075. doi:10.1016/S0140-6736(17)33326-3
3. Vaccarella S, Laversanne M, Ferlay J, Bray F. Cervical cancer in Africa, Latin America and the Caribbean and Asia: regional inequalities and changing trends. *Int J Cancer.* 2017;141(10):1997–2001. doi:10.1002/ijc.30901
4. Schiffman M, Doorbar J, Wentzensen N, et al. Carcinogenic human papillomavirus infection. *Nat Rev Dis Primer.* 2016;2:16086. doi:10.1038/nrdp.2016.86
5. Vanderpuye V, Grover S, Hammad N, et al. An update on the management of breast cancer in Africa. *Infect Agent Cancer.* 2017;12(1). doi:10.1186/s13027-017-0124-y

6. Ginsburg O, Bray F, Coleman MP, et al. The global burden of women's cancers: a grand challenge in global health. *Lancet Lond Engl*. 2017;389(10071):847–860. doi:10.1016/S0140-6736(16)31392-7
7. Sankaranarayanan R. Screening for cancer in low- and middle-income countries. *Ann Glob Health*. 2014;80(5):412. doi:10.1016/j.aogh.2014.09.014
8. Holme F, Kapambwe S, Nessa A, Basu P, Murillo R, Jeronimo J. Scaling up proven innovative cervical cancer screening strategies: challenges and opportunities in implementation at the population level in low- and lower-middle-income countries. *Int J Gynaecol Obstet*. 2017;138(Suppl 1):63–68. doi:10.1002/ijgo.12185
9. World Health Organization (WHO). Noncommunicable diseases country profiles 2018. WHO. <http://www.who.int/nmh/publications/ncd-profiles-2018/en/>. Accessed March 5, 2019.
10. Luciani S, Bruni L, Agurto I, Ruiz-Matus C. HPV vaccine implementation and monitoring in Latin America. *Salud Pública México*. 2018;60(6,nov–dic):683. doi:10.21149/9090
11. Bruni L, Barrionuevo-Rosas L, Albero G, et al. ICO/IARC information centre on HPV and cancer (HPV information centre). Human papillomavirus and related diseases in the world. Summary Report. 2017 July 27 .
12. Horton S, Gauvreau CL. Cancer in low- and middle-income countries: an economic overview. In: Gelband H, Jha P, Sankaranarayanan R, Horton S, editors. *Cancer: Disease Control Priorities, Third Edition (Volume 3)*. Washington (DC): The International Bank for Reconstruction and Development/The World Bank; 2015. Available from: <http://www.ncbi.nlm.nih.gov/books/NBK343620/>. Accessed February 25, 2019.
13. Murillo R, Díaz S, Perry F, et al. Increased breast cancer screening and downstaging in Colombian women: a randomized trial of opportunistic breast-screening: downstaging with opportunistic screening for breast cancer in Colombia. *Int J Cancer*. 2016;138(3):705–713. doi:10.1002/ijc.29801
14. Harford JB, Otero IV, Anderson BO, et al. Problem solving for breast health care delivery in low and middle resource countries (LMCs): consensus statement from the breast health global initiative. *Breast Edinb Scotl*. 2011;20(Suppl 2):S20–S29. doi:10.1016/j.breast.2011.02.007
15. Denny L, de Sanjose S, Mutebi M, et al. Interventions to close the divide for women with breast and cervical cancer between low-income and middle-income countries and high-income countries. *Lancet Lond Engl*. 2017;389(10071):861–870. doi:10.1016/S0140-6736(16)31795-0
16. Bain C, Constant TH, Contreras I, Vega AMB, Jeronimo J, Tsu V. Model for early detection of breast cancer in low-resource areas: the experience in Peru. *J Glob Oncol*. 2018;4(4):1–7. doi:10.1200/JGO.17.00006
17. Alba LH, Díaz S, Gamboa O, et al. Accuracy of mammography and clinical breast examination in the implementation of breast cancer screening programs in Colombia. *Prev Med*. 2018;115:19–25. doi:10.1016/j.ypmed.2018.08.005
18. Jedy-Agba E, McCormack V, Adebamowo C, dos-Santos-Silva I. Stage at diagnosis of breast cancer in sub-Saharan Africa: a systematic review and meta-analysis. *Lancet Glob Health*. 2016;4(12):e923–e935. doi:10.1016/S2214-109X(16)30259-5
19. International Cancer Control Partnership. About the international cancer control partnership. International cancer control partnership. <https://www.iccp-portal.org/what>. Accessed February 28, 2019.
20. Cervical Cancer Action. Visual inspection (VIA) for cervical cancer screening. Cervical cancer action. <http://www.cervicalcanceraction.org/comments/map-slideshow-via.php>. Accessed February 28, 2019.
21. O'Neil DS, Keating NL, Dusengimana JM, et al. Quality of breast cancer treatment at a rural cancer center in Rwanda. *J Glob Oncol*. 2018;4(4):1–11. doi:10.1200/JGO.2016.008672
22. Toliman PJ, Kaldor JM, Badman SG, et al. Performance of clinical screening algorithms comprising point-of-care HPV-DNA testing using self-collected vaginal specimens, and visual inspection of the cervix with acetic acid, for the detection of underlying high-grade squamous intraepithelial lesions in Papua New Guinea. *Papillomavirus Res*. 2018;6:70–76. doi:10.1016/j.pvr.2018.10.009
23. Espina C, McKenzie F, dos-Santos-Silva I. Delayed presentation and diagnosis of breast cancer in African women: a systematic review. *Ann Epidemiol*. 2017;27(10):659–671.e7. doi:10.1016/j.annepidem.2017.09.007
24. Arrossi S, Thouyaret L, Laudi R, et al. Implementation of HPV-testing for cervical cancer screening in programmatic contexts: the Jujuy demonstration project in Argentina. *Int J Cancer*. 2015;137(7):1709–1718. doi:10.1002/ijc.29530
25. Drummond JL, Were MC, Arrossi S, Wools-Kaloustian K. Cervical cancer data and data systems in limited-resource settings: challenges and opportunities. *Int J Gynecol Obstet*. 2017;138:33–40. doi:10.1002/ijgo.12192
26. Pan American Health Organization (PAHO). PAHO eHealth: eHealth strategy and plan of action (2012–2017). Pan American Health Organization/World Health Organization. [Published November 8, 2011]. [https://www.paho.org/ict4health/index.php?option=com\\_content&view=article&id=54:estrategia-y-plan-de-accion-sobre-esalud-2012-2017&Itemid=146&lang=en](https://www.paho.org/ict4health/index.php?option=com_content&view=article&id=54:estrategia-y-plan-de-accion-sobre-esalud-2012-2017&Itemid=146&lang=en). Accessed February 25, 2019.
27. Dickerson LK, Rositch AF, Lucas S, Harvey SC. Pilot educational intervention and feasibility assessment of breast ultrasound in rural South Africa. *J Glob Oncol*. 2017;3(5):502–508. doi:10.1200/JGO.2016.008086
28. Jeronimo J, Holme F, Slavkovsky R, Camel C. Implementation of HPV testing in Latin America. *J Clin Virol*. 2016;76(Suppl 1):S69–S73. doi:10.1016/j.jcv.2015.11.035
29. PATH. Ongoing PATH analysis of country data collected in Guatemala and Honduras. PATH. Seattle, WA. January 2019.
30. Unger-Saldaña K, Ventosa-Santaulària D, Miranda A, Verduzco-Bustos G. Barriers and explanatory mechanisms of delays in the patient and diagnosis intervals of care for breast cancer in Mexico. *Oncologist*. 2018;23(4):440–453. doi:10.1634/theoncologist.2017-0431
31. Ilaboya D, Gibson L, Musoke D. Perceived barriers to early detection of breast cancer in Wakiso District, Uganda using a socioecological approach. *Glob Health*. 2018;14(1):9. doi:10.1186/s12992-018-0326-0
32. Olasehinde O, Boutin-Foster C, Alatisse OI, et al. Developing a breast cancer screening program in Nigeria: evaluating current practices, perceptions, and possible barriers. *J Glob Oncol*. 2017;3(5):490–496. doi:10.1200/JGO.2016.007641
33. Islam RM, Billah B, Hossain MN, Oldroyd J. Barriers to cervical cancer and breast cancer screening uptake in low-income and middle-income countries: a systematic review. *Asian Pac J Cancer Prev*. 2017;18(7):1751–1763. doi:10.22034/APJCP.2017.18.7.1751
34. Moodley J, Constant D, Botha MH, van der Merwe FH, Edwards A, Momberg M. Exploring the feasibility of using mobile phones to improve the management of clients with cervical cancer precursor lesions. *BMC Womens Health*. 2019;19(1):2. doi:10.1186/s12905-018-0702-1
35. Linde DS, Andersen MS, Mwaiselage JD, Manongi R, Kjaer SK, Rasch V. Text messages to increase attendance to follow-up cervical cancer screening appointments among HPV-positive Tanzanian women (Connected2Care): study protocol for a randomised controlled trial. *Trials*. 2017;18(1). doi:10.1186/s13063-017-2215-x
36. Gurol-Urganci I, de Jongh T, Vodopivec-Jamsek V, Atun R, Car J; Cochrane Consumers and Communication Group, ed. Mobile phone messaging reminders for attendance at healthcare appointments. *Cochrane Database Syst Rev*. 2013. doi:10.1002/14651858.CD007458.pub3
37. Bukowski A, Chávarri-Guerra Y, Goss PE. The potential role of patient navigation in low- and middle-income countries for patients with cancer. *JAMA Oncol*. 2016;2(8):994–995. doi:10.1001/jamaoncol.2016.0766
38. Bittencourt L, Scarinci IC. Training community health workers to promote breast cancer screening in Brazil. *Health Promot Int*. 2017. doi:10.1093/heapro/dax058
39. Seidman G, Atun R. Does task shifting yield cost savings and improve efficiency for health systems? A systematic review of evidence from low-income and middle-income countries. *Hum Resour Health*. 2017;15(1). doi:10.1186/s12960-017-0200-9



## International Journal of Women's Health

Dovepress

### Publish your work in this journal

The International Journal of Women's Health is an international, peer-reviewed open-access journal publishing original research, reports, editorials, reviews and commentaries on all aspects of women's healthcare including gynecology, obstetrics, and breast cancer. The

manuscript management system is completely online and includes a very quick and fair peer-review system, which is all easy to use. Visit <http://www.dovepress.com/testimonials.php> to read real quotes from published authors.

Submit your manuscript here: <https://www.dovepress.com/international-journal-of-womens-health-journal>