

# Women's cancers: do variations in patterns of care explain the worldwide inequalities in survival and avoidable premature deaths? The VENUSCANCER project

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VENUSCANCER is a European Research Council (ERC)-funded worldwide study designed to explain the global inequalities in survival from breast, cervical and ovarian cancers, the three most common cancers in women. The goal is to provide levers for health policy to reduce or eliminate avoidable differences in survival from these cancers.

Opening the World Cancer Congress in Paris (2016), the French President, François Hollande, insisted that women should be at the heart of cancer control, “because they are victims of inequality in access to prevention, treatment and screening in every country in the world”.

Cancers of the breast, ovary and cervix are a major public health problem worldwide. Every year, approximately 2.5 million women are diagnosed with one of these cancers, and they account for over 900,000 deaths (1). Many of these deaths are avoidable, even in low- and middle-income countries (LMICs), where cancers in women represent a major economic burden, both to families that lose a mother, but also to the national economy (2).

Reducing the numbers of cancer deaths in women will require improvements in prevention, but also more effective health systems, to improve the survival of women who do develop one of these cancers (3). Yet access to safe surgery varies widely between the richest and poorest countries (4), and in more than 30 of the poorest countries, radiotherapy services are not available at all (5,6).

Differences in survival from these three cancers between high- and low-income countries are striking (7). Inequalities in survival also exist between high-income countries (8), and even between regions within those countries. The problem has been succinctly summarised: “political toleration of unfairness in access to affordable cancer treatment is unacceptable” (9).

In 2015, the CONCORD programme established worldwide surveillance of trends in 5-year survival over the 15-year

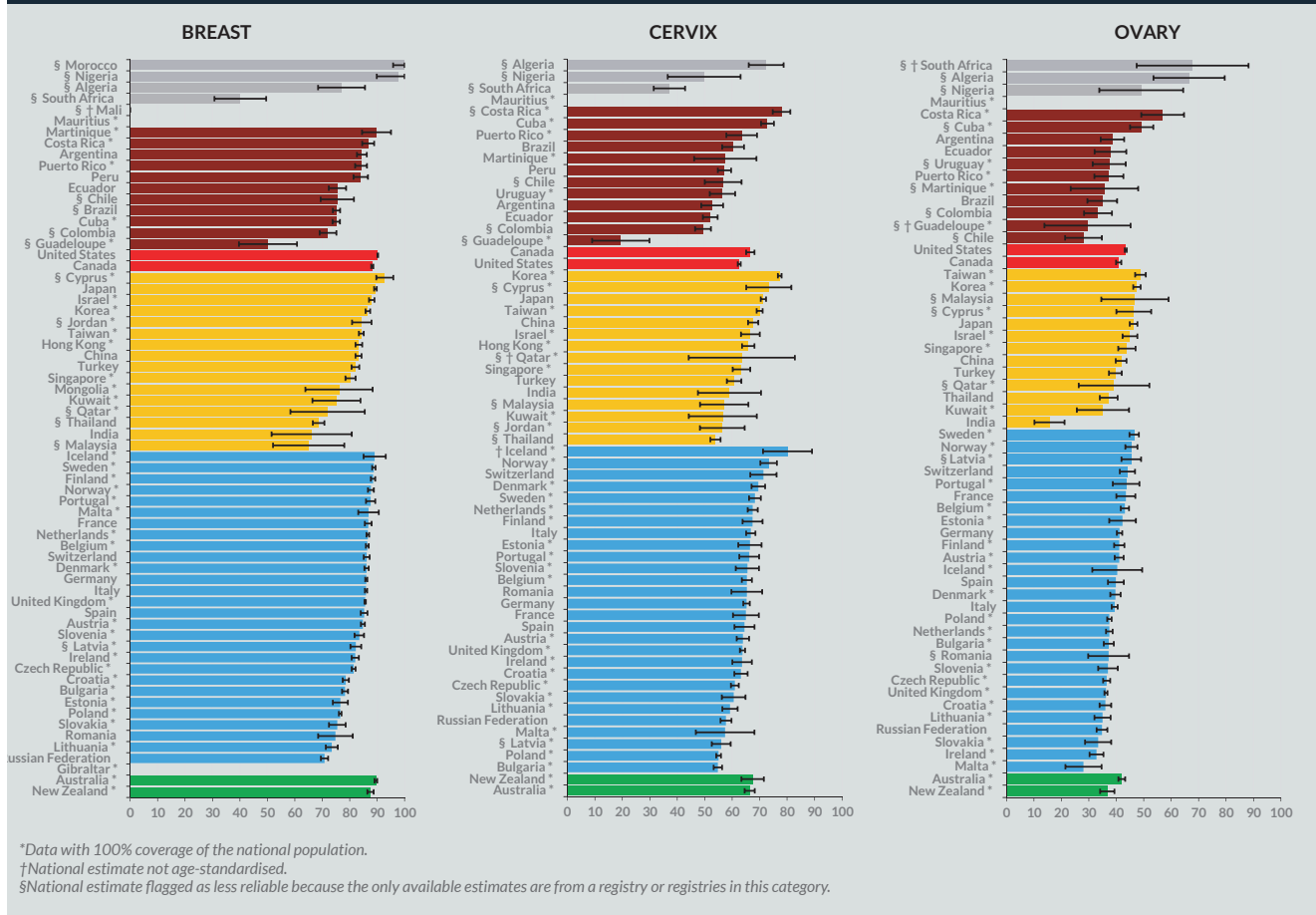
period 1995–2009 (10). It documented for the first time the very wide global differences in survival trends for most of the common cancers, including breast, cervical and ovarian cancers. In 2018, the third cycle of the CONCORD programme updated worldwide trends in survival for patients diagnosed up to 2014. In 2010–2014, age-standardized 5-year net survival for breast cancer varied from 66% in India to 91% in the United States; from 52% in Ecuador to 77% in Korea for cervical cancer, and from 16% in India to 57% in Costa Rica for ovarian cancer (Figure 1) (7).

## VENUSCANCER

VENUSCANCER, embedded in the CONCORD programme, aims to examine in much greater depth why these enormous differences in survival up to five years after diagnosis still persist for women diagnosed in the most recent years for which data are available in cancer registries. Results from this project will enable us to see how much of the differences in survival between high- and low-income countries can be explained, whether by the biological characteristics of the cancers, or by the health care women receive, or by broader aspects of society, such as women's socio-economic status or level of education. This is the first aim of VENUSCANCER.

The second aim is to examine trends in *avoidable premature deaths*, in relation with each country's gross domestic product and total national expenditure on health. In this context, avoidable premature deaths are defined as deaths that occur within five years of a cancer diagnosis in a given country that

Figure 1: Global distribution by continent and country of age-standardised 5-year net survival for women (15–99 years) diagnosed during 2010–14 with breast, cervical or ovarian cancer



would not be expected to occur if survival from that cancer in that country were as high as in another country, typically in the same world region.

The overall aim of VENUSCANCER is to provide actionable evidence for health policies to reduce the burden of women's cancers worldwide.

**Protocol**

The protocol for data collection has been developed in collaboration with over 300 cancer registries worldwide. This has been a major undertaking in its own right.

Three VENUSCANCER Working Group meetings to discuss the protocol were held during major international conferences in Arequipa, Peru (12 November 2018) at the International Association of Cancer Registries (IACR) conference; in Vancouver, Canada (12 June 2019), during the North American Association of Central Cancer Registries (NAACCR), and in Moscow, Russian Federation, during the Second International Forum of Oncology and Radiology (23 September 2019). The discussion focused on the first aim of the project, to collect detailed demographic, biological and clinical data for women diagnosed with breast, ovarian or cervical cancer during the

most recent year for which data are available, and in as many countries as possible.

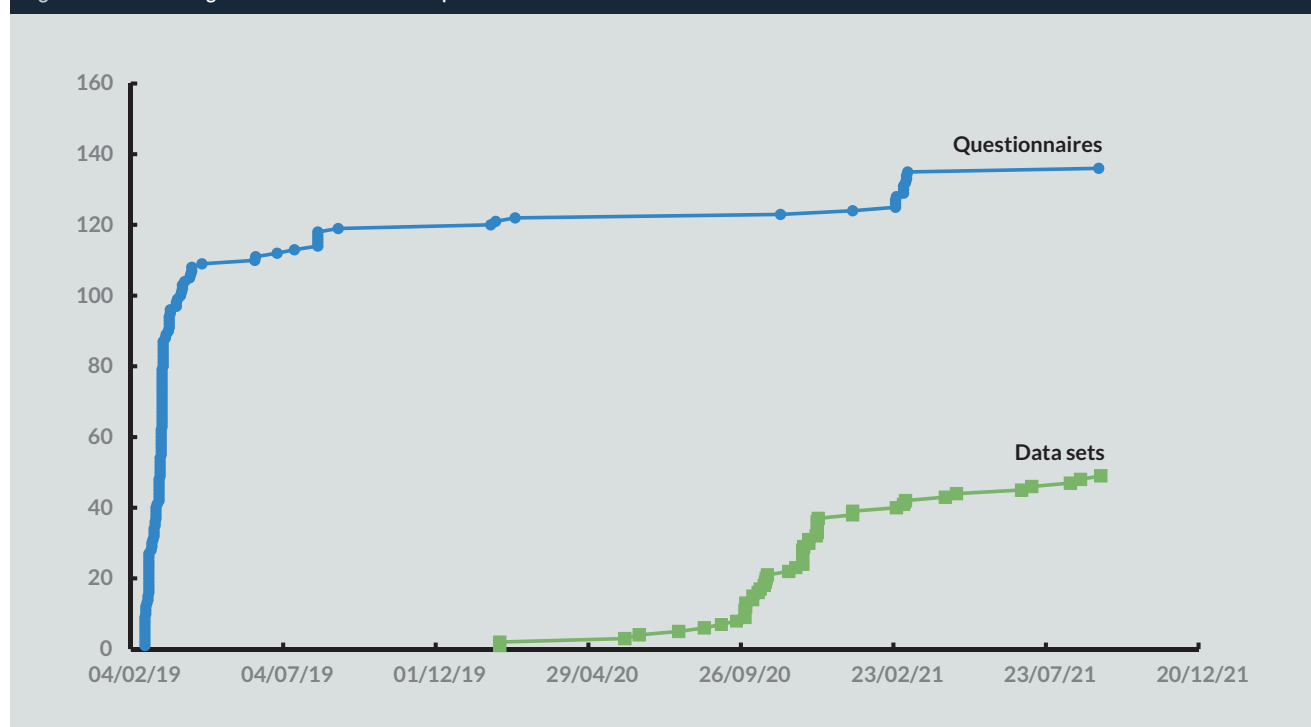
The ERC Consolidator grant enabled support to be provided for visa, travel, accommodation and conference fees for six colleagues from LMICs (Brazil, Cuba, Nigeria, Russian Federation, South Africa, and Thailand), who would not otherwise have been able to participate in these meetings.

Three questionnaires were developed to help refine the protocol for data collection. The questionnaires were designed:

- To identify cancer registries that are willing to contribute to this challenging part of the VENUSCANCER project.
- To identify which registries have data at the required level of completeness.
- To identify which registries are willing to increase the completeness of their data.
- To select cancer registries in LMICs that would be eligible for financial support for data collection.

The questionnaires were presented during the VENUSCANCER Working Group meetings. My research team helped our colleagues to complete the questionnaires, and we discussed which variables were more likely to be collected and

Figure 2: Number of registries that have submitted questionnaires or data



complete in their registry.

In February 2019, over 300 cancer registries were invited to complete online questionnaires to identify those which have data at the required level of completeness, or were willing to improve their data. Analyses of the questionnaires were presented in Lisbon, Portugal (May 2019), in Vancouver, Canada (June 2019) and in Moscow, Russian Federation (September 2019). By September 2019, 123 cancer registries in 42 countries (4 lower-middle-income, 14 upper-middle-income, 24 high-income) had submitted at least one questionnaire, but most registries (80%) submitted all three.

Cancer registries have continued to submit questionnaires to be considered for participation. By mid-September 2021, we had received 374 questionnaires from 136 cancer registries (Figure 2). The impact of the COVID-19 pandemic is visible.

For most of the data items that we wish to examine, the answer as to whether they are collected routinely was categorised as “Yes”, “No” or “Unknown” and, if “Yes”, the expected level of completeness was categorised as less than 25%, 25%–49%, 50%–74%, 75%–100%, or unknown. Several questions invited free-text replies.

The questionnaire on breast cancer included 71 questions, which produced more than 300 separate data items (variables). The questionnaire on cervical cancer included 62 questions (300 variables), while the questionnaire on ovarian cancer included 54 questions (over 250 variables).

We will include cancer registries with the highest availability and completeness of the required data. Following analysis of the questionnaires for each cancer, the data collection

protocol was finalised in November 2019. The protocol enables cancer registries to start their own database for the study, but following rigorous agreed rules.

We defined “basic information” as demographic data (e.g., age) and tumour data (e.g., the anatomic site and microscopic appearance of the tumour). We evaluated three criteria for the inclusion of cancer registries in VENUSCANCER:

- Basic information, plus data on stage at diagnosis and treatment: for all three cancers, slightly more than 50% of cancer registries collected these data with adequate completeness.
- Basic information, plus data on stage at diagnosis, treatment and molecular biomarkers: for all cancers, around 30% of cancer registries collected these data with adequate completeness.
- Basic information plus data on stage at diagnosis, molecular biomarkers, treatment *and* socioeconomic status: for all cancers, only 5% of cancer registries collected these data with adequate completeness.

However, after considering the willingness of colleagues to collect additional data for individual women from clinical records, these percentages rose to 76%–79%, 44%–51%, and 9%–14%, respectively.

If we include only registries that can provide all the variables we want to analyse at the required level of completeness (option 3), the worldwide scope of the project would be severely constrained. Therefore, we selected the criteria that will enable us to conduct a study on patterns of care with the

widest possible geographic scope (option 1). Nevertheless, we will also perform parallel analyses by tumour sub-type for those registries that can provide data on biomarkers (option 2), and analyses by socioeconomic status for the small proportion of registries that aim to submit this information (option 3).

Over 100 registries submitted questionnaires for each cancer; incidence for 2015–2017 was complete in over 90 of these registries. Data completeness was high for stage, staging procedures and treatment, only moderate for molecular biomarkers, and low for comorbidities and socioeconomic status.

Most cancer registries were willing to improve their data completeness before submitting their data to VENUSCANCER. Results for breast cancer are shown in Figures 3–5. Similar results are available for cervical and ovarian cancers (data not shown).

The call for data was issued on 21 December 2019. The original deadline for data submission was 30 June 2020. Due to the COVID-19 pandemic, this deadline was postponed to September 2020. Since the pandemic has been affecting the various areas of the world at different times, data collection is still ongoing. By mid-September 2021, we had received data sets from 49 cancer registries: 44 data sets for breast cancer, 42 for cervical cancer and 27 for ovarian cancer (Figure 2). We expect to receive more data sets in the coming months.

## Expected results

Health policymakers need good evidence on the reasons for international disparities in cancer survival, in order to focus

their policy initiatives.

Such evidence can come from “high-resolution” studies, in which detailed clinical data that are not systematically captured at cancer registration are obtained directly from the medical records, such as the stage of disease at diagnosis, the investigations carried out to identify the stage of disease, and the types of treatment provided for each patient. Analysis of these data can show the extent to which international differences in survival are likely to be due to differences in stage at diagnosis or, for example, to under-treatment in the elderly.

High-resolution studies can thus identify the key drivers of inequalities in cancer survival.

VENUSCANCER will be a particularly important high-resolution study, because it is both population-based and worldwide. It will provide details of the biological and molecular characteristics of tumours in all women diagnosed with cancer of the breast, ovary or cervix in a given country or region, and on patterns of care, as well as short- and medium-term survival, in over 40 countries.

Analysis of the VENUSCANCER data will highlight the strengths and weaknesses of the health system in providing care for all women diagnosed with one of these three common cancers in each country.

Trends over time in the number of avoidable premature deaths among cancer patients will offer a powerful contrast with outcomes in better-performing health systems in neighbouring countries. They stimulate policymakers to plan more appropriate cancer control strategies. Avoidable

premature deaths are a powerful way to express inequalities in survival as a single number that is suitable for policymakers: “Politicians do not like to do things that are too difficult. Simple, clear messages are important” (Baroness Delyth Morgan, Breast Cancer Now).

Even in the twenty-first century, safe and effective surgery is not yet available in many countries in the world. In some countries, radiotherapy may be considered a luxury, or may simply be unavailable (4). Examination of recent trends in cancer survival, and in the number of avoidable premature deaths, in the light of the distribution of patterns of care, will contribute key evidence for



Figure 4: Breast cancer – availability and completeness of treatment data 2012-2017 (from questionnaires)

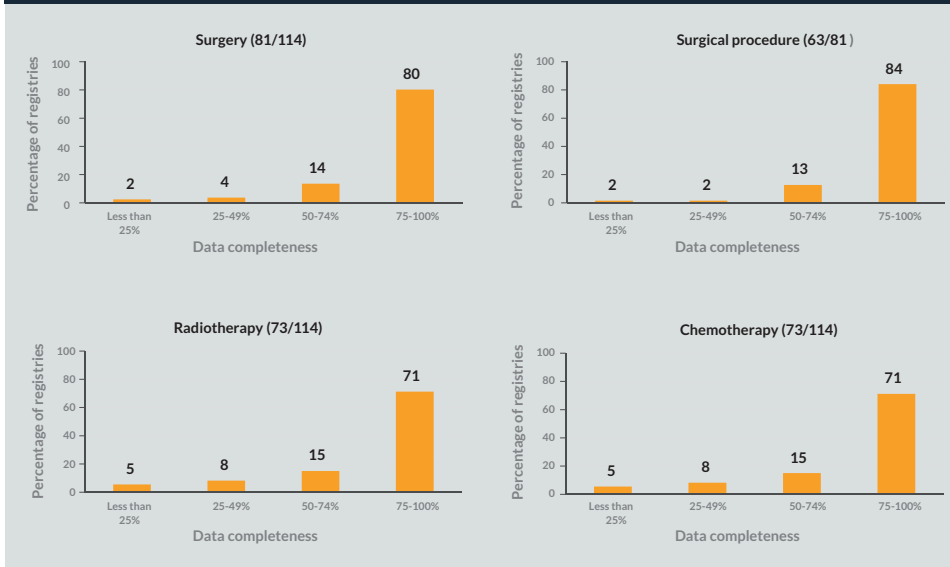


Figure 5: Breast cancer – availability and completeness of data on molecular biomarkers 2012-2017 (from questionnaires)



planning appropriate cancer control strategies to guarantee equal access to cancer prevention, screening and treatment to women in every country in the world.

The evidence from this research will help drive policy to reduce inequalities in survival from the most common cancers in women. This work will involve targeted dissemination of the findings to scientists, policymakers, cancer patients and the general public. Results from VENUSCANCER will also be used by the Organisation for Economic Co-operation and Development (OECD) in its *Health at a Glance* series, and for the WHO Global Breast Cancer Initiative.

### COVID-19 pandemic: ethical, legal and administrative issues

The COVID-19 pandemic of 2020–2021 has changed many aspects of our lives, including research. Many technical and

administrative problems have arisen, both at the London School of Hygiene and Tropical Medicine (LSHTM) and among cancer registries around the world.

One of the most important features of this ERC consolidator grant, offering financial support to cancer registries in LMICs, has turned out to be more difficult than we expected, due to the need to set up legal contracts between LSHTM and each registry or its host institution. Other difficulties have arisen because English is not the mother tongue for most of our colleagues in LMICs, and because it has proved impossible for some cancer registries even to open a bank account, or if that is achieved, to receive financial support from another country, in this case the United Kingdom.

The United Kingdom's exit from the European Union (EU) also did not help. In many European countries, where the General Data Protection Regulation (GDPR) was already mis-interpreted or over-interpreted by administrators,

it has become much more difficult to obtain essential data for research, e.g., full dates of birth, diagnosis or last known vital status. Similar regulations have created problems in releasing detailed data in North America.

Despite the difficulties posed by the COVID-19 pandemic and by Brexit, we have finalised the legal contracts to permit the transfer of funds for data collection to selected cancer registries in LMICs, and data-sharing agreements with cancer registries in the 27 EU Member States to enable transmission of sensitive personal data in compliance with the EU GDPR. Nevertheless, this was an extremely time-consuming exercise.

Unless cancer control policies are to be based on statistical projections from data that are scanty or of average quality, or even, where data are non-existent, modelled on the basis of untestable assumptions from data collected in other countries, action is urgently required to create population-based cancer

registries that can provide a continuous stream of high-quality data in most countries. This would imply availability of adequate resources to register all patients with cancer in a timely fashion, the right to access up-to-date national or regional death records to establish their vital status, the legislative stability to operate efficiently over the long term, and the autonomy to deploy all their data for research. ■

#### Acknowledgements

*I would like to thank Pamela Minicozzi and Veronica Di Carlo for their help in analysing the questionnaires and preparing the figures.*

*Professor Claudia Allemani is Professor of Global Public Health at LSHTM. Her main interests are in international comparisons of cancer survival, "high-resolution" studies on patterns of care, as well as the estimation of avoidable premature deaths, with a focus on their impact on cancer policy. She has 20 years' experience in this domain. She is co-Principal Investigator of the CONCORD programme for the global surveillance of cancer survival and Principal Investigator of VENUSCANCER.*

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