THE WORLD OVARIAN CANCER COALITION ATLAS

GLOBAL TRENDS IN INCIDENCE, MORTALITY AND SURVIVAL

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This report has been produced and funded by the World Ovarian Cancer Coalition

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EXECUTIVE SUMMARY

The mission of the World Ovarian Cancer Coalition is to ensure the best possible chance of survival, and the best possible quality of life for every woman with ovarian cancer, wherever she lives.

The World Ovarian Cancer Coalition's Every Woman Study aims to bring together an authoritative evidence base that speaks to the views of women with ovarian cancer across the globe: evidence that will enable us to formally highlight gaps, challenges, opportunities and good practice in order to set out what needs to be done to make our mission a reality. The study will also be informed and strengthened by contributions from the wider ovarian cancer community including patient advocacy organisations as well as world leaders in ovarian cancer research and clinical practice and will provide strong call to actions.

As part of the World Ovarian Cancer Coalition's Every Woman Study, this report presents the results of desk research exploring the latest global ovarian cancer statistics, their potential purpose, accuracy and validity, and trends over time. Reasons for variations between countries as far as they are understood are explored, implications for the Every Woman Study are discussed, and a number of calls to action made.

KEY FINDINGS

- It was estimated that in 2012 there were 239,000 cases, and 152,000 deaths worldwide from ovarian cancer, with some 600,000 women living within five years of a diagnosis.
- It is estimated that by 2035, incidence will increase to 371,000 a year (55%) and deaths will increase by 67% to 254,000.
- In terms of gynecological cancers, the greatest burdens are cervical cancer (less developed countries) and endometrial cancer (more developed countries), but the overall poor survival rates for ovarian cancer, which are considerably worse than those for cervical or endometrial cancers, provide a consistent imperative to seek improvements globally.
- There are major challenges in dealing with global cancer statistics, mainly due to huge variations in registration of cancer incidence and mortality. A country is considered to have high quality data when it records more than 50% of cases. For a considerable number of countries, statistics are estimated rather than based on fact. It is thought this may lead to underestimation of cases and an overestimation of survival rates.
- Although the risk of developing and dying from ovarian cancer is almost twice as high in developed countries when compared to less developed countries, the actual burden (number of cases) is much higher in less developed countries, due to population sizes. For example, China has the largest

number of diagnoses per year (34,575), followed by India (26,834), then the USA (20,874).

- Risk of developing ovarian cancer rises as a country becomes more developed, and as areas become more urbanised. This means the three drivers of cancer burden (increasing populations, increased longevity, and increases in risk because of environmental factors) will mean ovarian cancer becomes even more of an issue in developed, and less developed countries.

- There are also many other variants affecting risk and mortality rates, including ethnicity, tumour types, and age profiles.

- There have been improvements in the mortality rates in recent years but vary according to country. One major factor has been the use of the oral contraceptive pill. The largest declines were in the USA and parts of Europe where early and widespread uptake of the oral contraceptive occurred, possibly also where there has been a reduction on hormone therapy use for middle-aged women. Increasing obesity amongst populations though is seen as having a negative effect.

- Ovarian cancer survival rates vary widely. Different studies can vary in what types of ovarian cancer are included, the level of cancer registration, and background mortality calculations, so comparisons between studies are not advised. The latest five-year survival rates largely fall between 30% and 50% and in general have begun to improve over the last 20 years. There are in depth studies looking at higher income countries to determine why these variances exist, including stage at diagnosis, awareness of symptoms, patient delay seeking help, delays in diagnosis, access to tests, role of family doctors as gatekeepers, and access to treatments. In other countries (often less developed) issues are more fundamental including attitudes to cancer, lack of general physicians let alone those trained in oncology, lack of equipment and access to tests. For example, in Uganda, excluding breast cancer cases, the overall five-year survival rate for cancer was just 13%. This compares to the overall five-year survival rate in Australia, for all cancers, of 68%.[1]

- In recent years a focus on specialist care (in particular surgery) is seen as a way to improve survival.

- Developments in understanding genetic mutations (germline and somatic) offer new hope in terms of targeted treatments, and primary prevention.

- There is a need for good data to drive research and understanding for different communities and tumour types.

- There is a paucity of patient experience data, and certainly none on a global level, and almost none at a national level. Where academic research has been done it tends to focus on the psychological impact of a diagnosis, or on symptoms leading to diagnosis. Charities and pharmaceutical companies have undertaken some of their own research.

RECOMMENDATIONS TO THE WORLD OVARIAN CANCER COALITION

- The World Ovarian Cancer Coalition has an important role to play in providing a call to action to address globally low survival rates.
- The opportunity to provide patient experience insight on a global level would strongly support the call to global action.
- The World Ovarian Cancer Coalition should seek to support global initiatives to improve cancer registration and efforts to develop and sustain infrastructure (training, retention of staff, appropriate equipment).
- The World Ovarian Cancer Coalition should look to work with other global cancer projects such as the Union for International Cancer Control (UICC), the International Agency for Research on Cancer (IARC) and initiatives within the World Health Organisation (WHO) where goals correspond. For example, supporting the following targets for 2025 from the UICC's World Cancer Declaration (2013)[2].
    - Target 2: Population-based cancer registries and surveillance systems will be established in all countries to measure the global cancer burden and the impact of national cancer control programmes.
    - Target 5: Stigma associated with cancer will be reduced and damaging myths and misconceptions about the disease dispelled.
    - Target 6: Population based screening and early detection programmes will be universally implemented, and levels of public and professional awareness about important cancer warning signs and symptoms will have improved.
    - Target 7: Access to accurate cancer diagnosis, quality multimodal treatment, rehabilitation, supportive and palliative care services, including the availability of affordable essential medicines and technologies will have improved.
    - Target 9: Innovative education and training opportunities for healthcare professionals in all disciplines of cancer control will have improved significantly, particularly in low and middle-income countries.
- The World Ovarian Cancer Coalition should look to other site-specific global coalitions to share information and find common action points.
- The World Ovarian Cancer Coalition should continue its efforts to balance the focus between more and less developed nations.
- The World Ovarian Cancer Coalition should periodically review this report and update when required.

GLOBAL CANCER STATISTICS (ALL CANCERS)

According to estimates from the World Health Organisation (WHO) in 2015[3], deaths from cancer along with deaths from coronary heart disease and deaths from stroke are the leading causes of mortality worldwide. It is projected that the number of new cases of cancer each year will increase by 70% between 2012 and 2030[4], rising from 14 million new cancer cases to over 22 million, with an ever-increasing burden on low and middle-income countries[5].

Michel Coleman describes the three engines of escalating cancer burden as being on the move: rapid population growth, ageing populations and an increase in cancer risk (lifestyle/environment) at each age[6]. With the associated strain on economies, timely and accurate statistics are imperative to provide evidence and impetus for identifying and developing cancer control strategies at a national level.

Within this report, the following terms are used:

- Incidence – the number of cases of the disease.
- The incidence rate is the percentage of the population who will develop the disease within given boundaries, for example 7 women per 100,000 female population might develop the disease each year.
- Mortality – the number of deaths from the disease. The mortality rate is the percentage of the population who will die from the disease within given boundaries, for example 3 per 100,000 female population might die from the disease each year.
- 5-year prevalence is the number of people living with 5 years of a diagnosis.
- Survival rates – the percentage of those affected by the disease who are alive at a certain time point beyond diagnosis, for example, 5-year survival rate is the percentage of women alive 5 years after their diagnosis.

Commonly reported cancer statistics include incidence and mortality, however only 34/194 WHO member states report high quality national mortality data, and 68/134 reporting high quality incidence data. In some countries, such as Norway, cancer reporting is a legal requirement, and data is then linked with the cause of death registry. For 2001-2005 data, Norway's cancer data was 98.8% complete, with 93.8% verified by biopsy samples under a microscope[7].

Incidence data derives from population-based cancer registries (PBCR). Although PBCRs may cover national populations, more often they cover smaller, subnational areas, and particularly in countries undergoing development, only selected urban areas. In 2006, about 21% of the world population was covered by PBCR, with sparse registration in Asia (8% of the total population) and in Africa (11%)[8]. In these instances where there is a paucity of cancer data, national incidence and mortality data is often estimated from datasets of regional registries, or neighbouring countries.

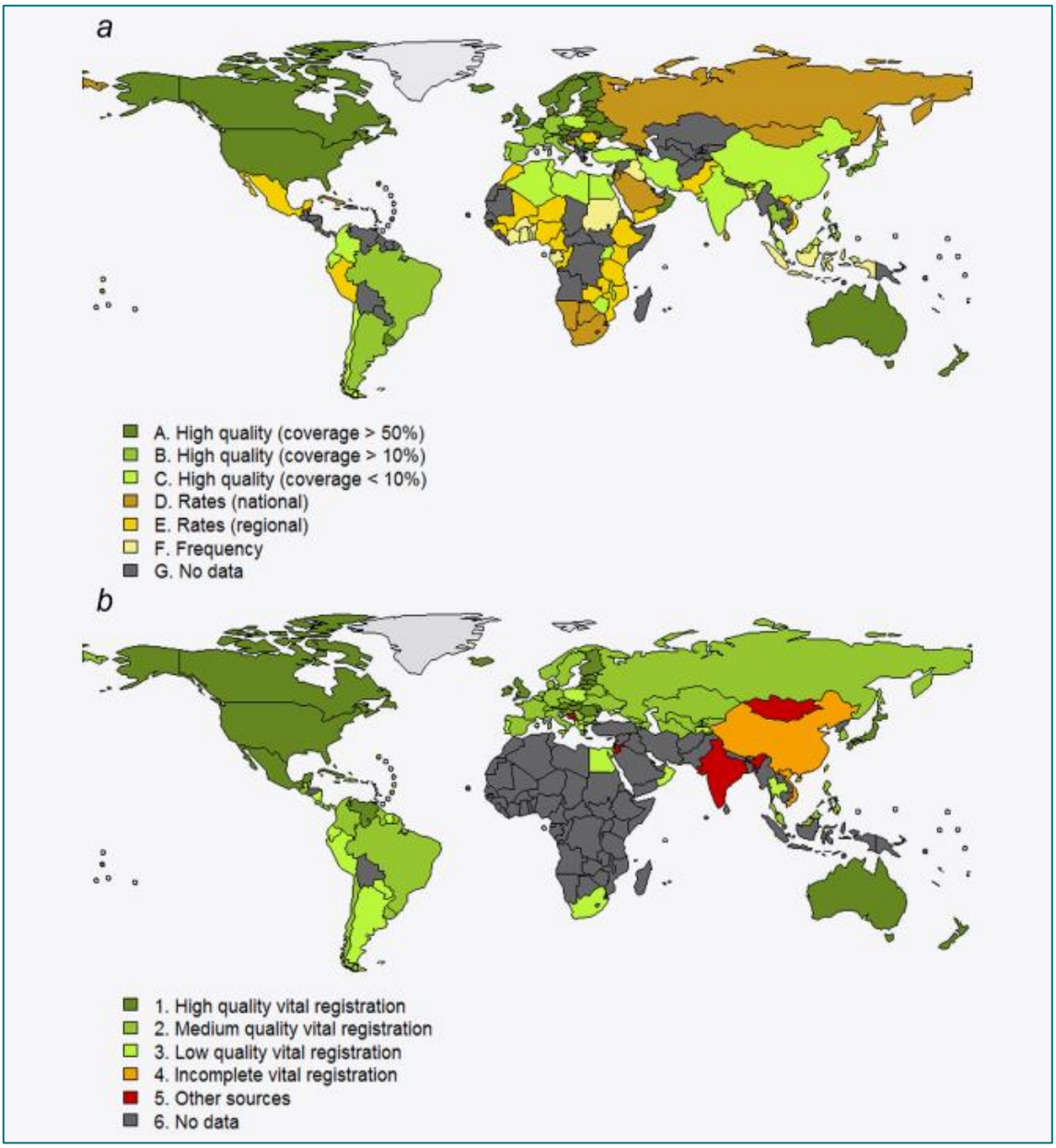
For the purposes of this report, figures will largely relate to those produced by the **Globocan** project.[9]The aim of the project is to provide contemporary estimates of the incidence, mortality and prevalence for major types of cancer, at a national level in 184 countries. The latest figures are the estimates for 2012.

Because methodology has been adapted between different publications of Globocan it is not possible to highlight trends. In an assessment of the Globocan methods by Antoni et al[10] they highlight that the lack of high-quality data could undermine the estimates, and that efforts should be made on an on-going basis to develop and improve the methods used; in addition, support should be given to the Global Initiative for Cancer Registry Development (GICRD)[11]. GICRD say that only one in five low and middle-income countries currently have the necessary data to drive policy and reduce the burden and suffering due to cancer. By 2035 they estimate that 70% of the cancer burden will fall on under-resourced regions least equipped to provide patient care from basic treatment to palliation.

Charts from the Globocan 2012 report show the quality of the data available for cancer incidence (Chart 1a) and mortality (Chart 1b). The Cancer Today website (http://gco.iarc.fr/today/data-sources-methods) indicates resources used for the calculations by country and pulls together the Globocan data.

As an example, in Africa, the countries with the best registration for incidence (high-quality but less than 10% coverage) are Algeria, Libya, Tunisia, Egypt, Uganda, Zimbabwe and Malawi. Large sections of central Africa have no data whatsoever. In terms of mortality data, South Africa and Egypt have low-quality vital registration, but the rest of Africa has no data. In the Globocan study for example, mortality is estimated from incidence data and modelled survival rates.

QUALITY OF GLOBAL CANCER DATA ON 1a) INCIDENCE, and 1b MORTALITY[12]



OVARIAN CANCER GLOBAL STATISTICS

Ovarian cancer is the 7th most common cancer, and 8th most common cause of death from cancer in women in the world.

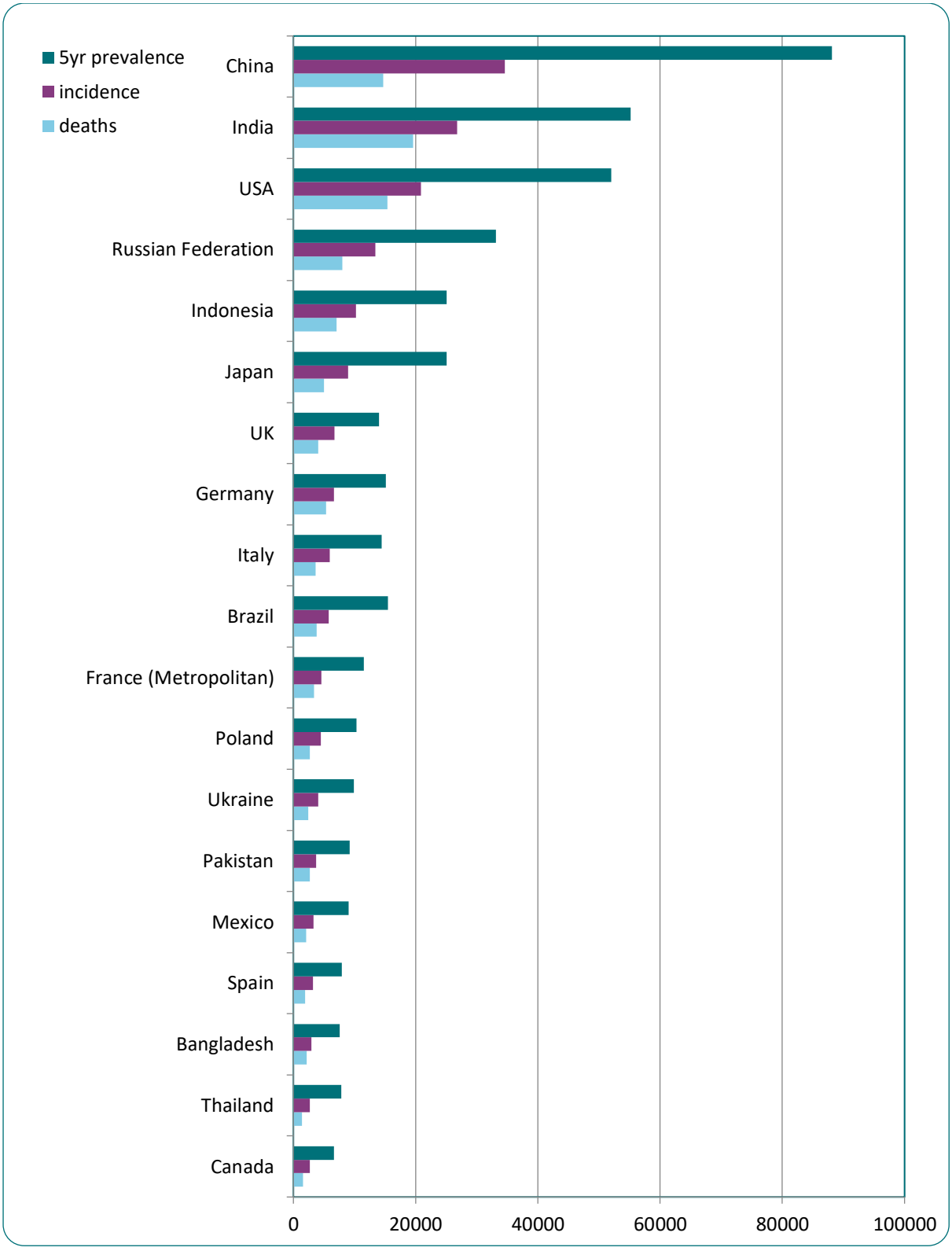
In 2012 the Globocan study estimated there were 239,000 cases, and 152,000 deaths (representing 3.6% of cancer cases, and 4.3% of cancer deaths). Worldwide there are almost 600,000 women living within five years of an ovarian cancer diagnosis (5-year prevalence).

The Globocan study predicts that by 2035 there will be a worldwide increase of 55% in incidence to 371,000, and an increase in deaths of 67% to 254,000[13]. These figures were calculated using UN World Population Prospects (2012 revision) and applying Age Standardised Rates in the corresponding populations.

In terms of numbers affected by continent, the figures are as follows for 2012.

OVARIAN CANCER	INCIDENCE 2012	MORTALITY 2012	5-YEAR PREVALENCE
ASIA	111,887	66,215	276,073
EUROPE	65,584	42,749	157,198
NORTH AMERICA	23,529	16,995	58,702
LATIN AMERICA AND CARIBBEAN	17,921	11,471	48,439
AFRICA	17,755	13,085	41,052
OCEANIA	2,043	1,402	5,160

On the next page is a list of countries with the highest number of cases, together with the number of deaths, and five-year prevalence (women living within five years of diagnosis).



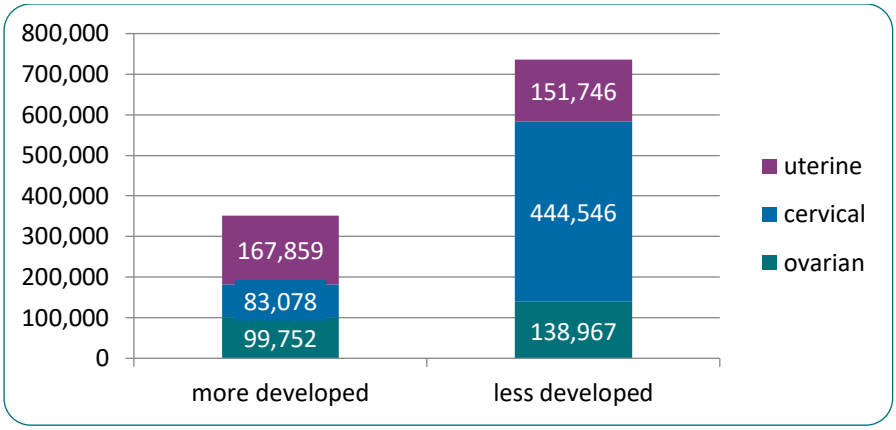
COUNTRIES WITH THE LARGEST NUMBER OF WOMEN WITH OVARIAN CANCER
(source Globocan)

OVARIAN CANCER AS A PRIORITY IN TERMS OF WOMEN'S CANCER

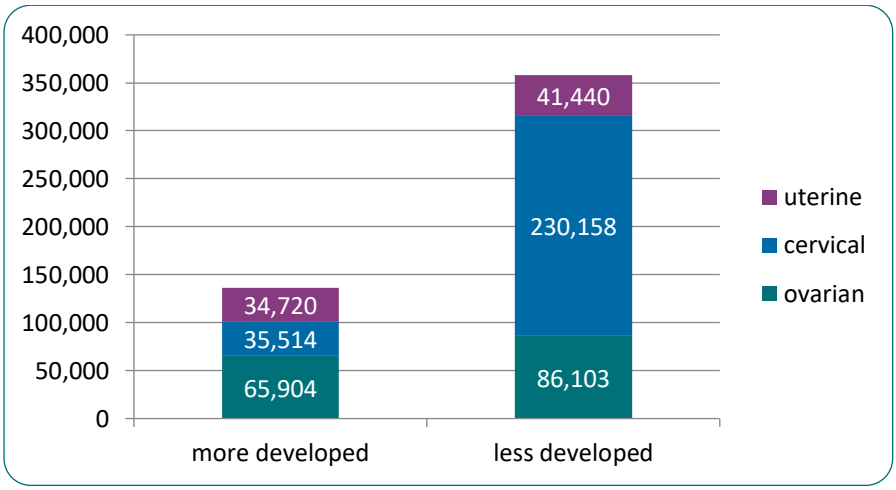
By far the most common 'women's cancer' is breast cancer. In 2012, there were estimated to be 1,671,149 cases, and 521,907 deaths. There were thought to be 6.2 million women living within five years of a diagnosis. All figures are taken from Globocan.

When considering the most common gynecological cancers, the burden is affected by the development status of a country but differs according to the cancer site. Cervical cancer is a much greater issue in less developed parts of the world, largely due to lack of screening, vaccination and poor sexual health. Uterine cancer is strongly linked to body mass index and has seen a steep rise in incidence in more developed parts of the world in recent years. As such, different countries will place differing priorities in terms of gynecological and more generally women's cancer control.

GYNECOLOGICAL CANCER INCIDENCE (2012)



GYNECOLOGICAL CANCER MORTALITY (2012)



OVARIAN CANCER – VARIABLE FACTORS

The term 'ovarian cancer' is not a singular diagnosis, rather it is an umbrella term for a multitude of different types of cancer that affect the ovaries, fallopian tubes, and the primary peritoneal cavity. It is estimated that there are more than 30 different types of ovarian cancer, and there is a very wide variation in terms of incidence of the different types, and outlook for women diagnosed with differing forms.

As the following section outlines, there are certain factors that increase a woman's risk of developing ovarian cancer:

- Age.
- Family history.
- Where she lives in the world.
- Hormonal and reproductive factors.

Where a woman lives, her ethnicity, and whether or not she has a family history not only has a bearing on her overall risk but can affect the type of ovarian cancer she may develop, and the age at which it starts.

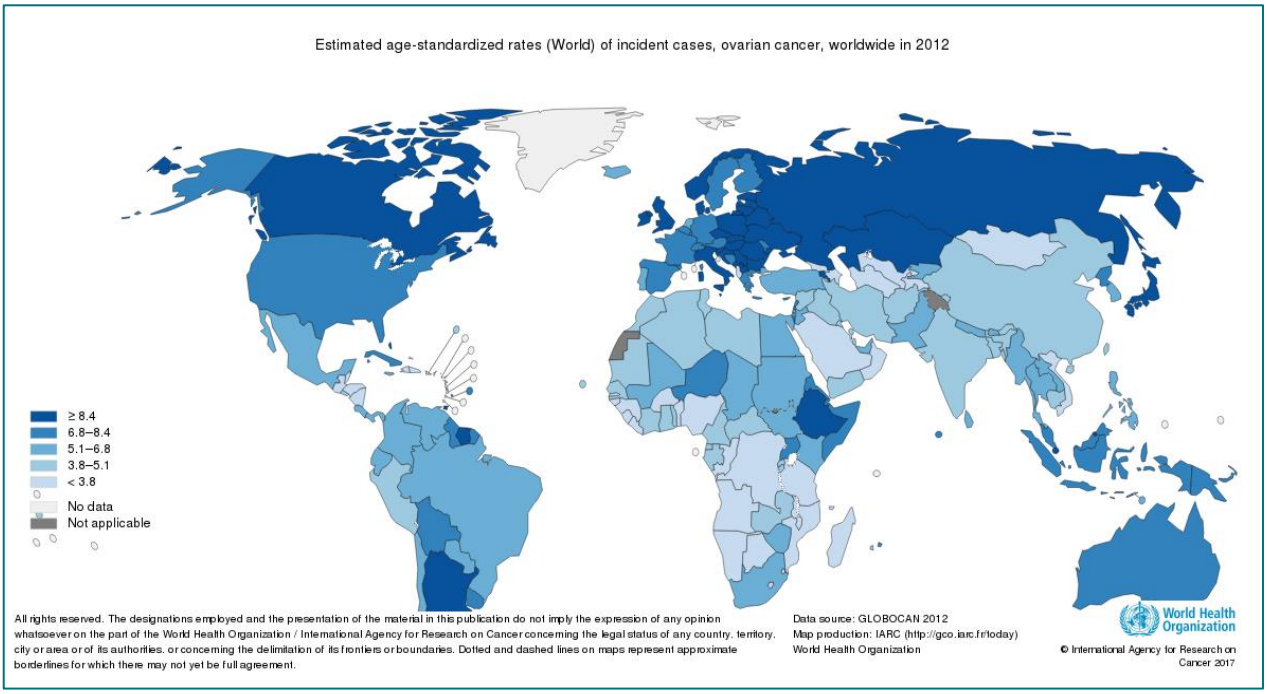
VARIATIONS IN INCIDENCE AND MORTALITY RATES, AND BURDEN OF DISEASE

Age standardised incidence rates (ASR) from 2012 are highest in more developed regions, with rates in these areas exceeding 7.5 per 100,000, and lowest in Sub-Saharan Africa with rates below 5 per 100,000. For explanations of the terminology see Appendix 1. The average risk of dying from ovarian cancer before the age of 75 is twice as high in more, rather than less developed regions, with deaths from the disease ranking as the 5th most common among women in more developed regions[14].

	INCIDENCE (ASR) PER 100,000	MORTALITY (ASR) PER 100,000
LESS DEVELOPED	5.0	3.1
MORE DEVELOPED	9.2	5.0
WORLD AVERAGE	6.1	3.7

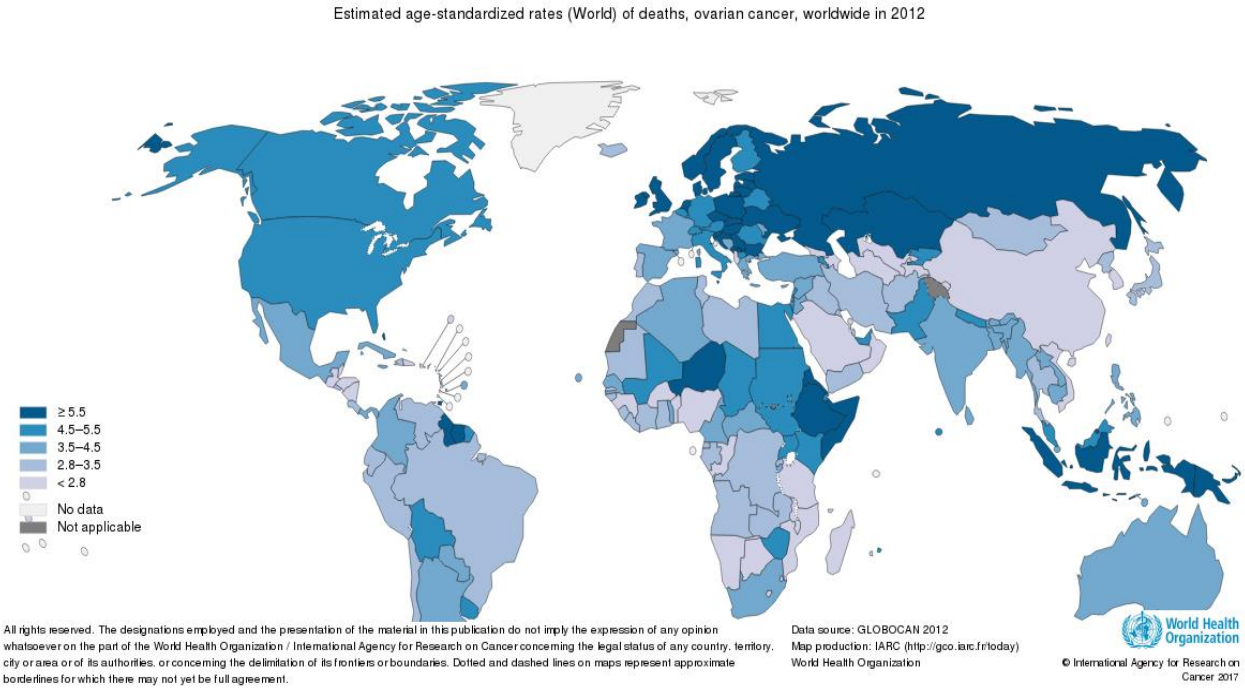
However, as can be seen from the following chart, in terms of actual numbers of women affected by ovarian cancer, the majority live and die in less developed parts of the world because of population sizes.

	INCIDENCE 2012	MORTALITY 2012	5 YEAR PREVALENCE
LESS DEVELOPED	138,967	86,013	341,206
MORE DEVELOPED	99,752	65,904	245,418
TOTAL	**238,719**	**151,917**	**586,624**



To view the global map of Age Standardised Incidence Rates for ovarian cancer go to https://gco.iarc.fr/today/online-analysis-map then select heatmap, incidence, global, ASR, ovary (from drop down menu).

To view the global map of Age Standardised Mortality Rates for ovarian cancer follow the link above but select Mort. etc.



Rates of incidence and mortality, as already shown, are higher in more developed countries. As countries undergo development, ovarian cancer rates appear to rise, particularly in urban areas. This has been demonstrated in studies in China and Egypt, where incidence rates are almost twice as high in urban areas as opposed to rural areas[15]. In China, incidence and mortality is rising to the extent that authors have called for it to be recognised as a significant public health problem in Chinese women. An Asian wide study found a significant positive correlation between the Human Development Index (which measures the socio-economic status of people living in different countries) and the standardised incidence rate of ovarian cancer[16]. The paper also points out the impact of a falling birth rate and better life expectancy resulting in increasingly older populations will mean that non-communicable diseases such as cancer will increasingly place a significant burden in the future, particularly in developing countries. The authors point to genetic and environmental factors, such as socioeconomic conditions, and lifestyle affecting risk.

VARIATION BY TYPES OF TUMOUR

Limited evidence suggests that there is a difference in the balance of types of ovarian cancer, depending on the level of development in a country. In developed countries, 90% of ovarian cancer cases are epithelial in origin, with germ cell tumours accounting for 2-3% of cases, and sex cord stromal tumours accounting for 5-6%. However in Africa and Asia, it appears that germ cell tumours account for between 10 and 15% of cases[17]. These tumours are more treatable and occur in younger women.

VARIATION BY RACE

Variations have been described between different races in other studies[18]. Morris et al.[19] reported that ovarian cancer incidence was higher in White (12.8/100,000) than Black (9.8/100,000) women. Yet, when compared with White women, the African-American women were more likely to have higher mortality, the authors say potentially due to the lack of sufficient diagnostics and sophisticated treatments, meaning women presented with later stage disease and had shorter disease-free survival. Additionally a study in California over 10 years, showed that among patients with advanced-stage ovarian cancer, African American race, low social economic status, and treatment by low volume providers are significant and independent predictors of receiving no surgery, no debulking surgery, no chemotherapy and non-standard treatment sequences[20]. It is clear that optimum cancer diagnosis and care is not accessible to all.

A study in the US showed that the median age for diagnosis for Asian women was 56, vs. 64 for white women[21]. Asian women were more likely to undergo primary surgery, have an earlier stage of disease, have a diagnosis of a non-serous histology and have lower grade tumours. 5-year disease specific survival was higher compared to whites (59.1% vs 47.3% $p<0.001$). There were also differences within the Asian women studied, between those who were born in the US and those who were immigrants, with the immigrants presenting at a younger age, and having better survival. A subset analysis of the different ethnicities showed differences in survival: 5-year disease specific survival: Vietnamese 62.1%, Filipino 61.5%, Chinese 61.0%, Korean 59%, Japanese 54.6% and Asian Indian/Pakistani 48.2% $p<0.015$.

The opportunities offered by developments in genomics have been identified as a way to drive improvements for people with cancer in different population groups, and by one study in particular for women with cancer in India. It calls for much more widespread collection of data to enable development and use of type appropriate treatments for populations that are more diverse than previously studied [22].

VARIATION IN AGE PROFILE

It is commonly reported that the risk of ovarian cancer is strongly related to age, highest in older females. However, comparing ages for peak incidence and mortality around the world, it appears to vary according to country, and not always associated to that country's average life expectancy. Possible explanations might include co-morbidities, variations in tumour type, and/or exposure to risk factors. As the paper mentioned above, there are significant differences in median age of diagnosis amongst women of different races.

For example, in the United Kingdom, according to figures from Cancer Research UK, over half (53%) of cases are diagnosed in women aged 65 and over. Age specific incidence rates peak in the UK for women aged 75-79, then drop sharply. Average life expectancy for women in the UK is 83. For the same period (2012-14) the peak rate of ovarian cancer deaths occurred in the 85-89 age group. In the Unites States, according to the U.S. Cancer Statistics Working Group in 2010, the peak ovarian cancer incidence rate is found among women aged 80-84 in the United States (U.S.Cancer Statistics Working Group, 2010). In contrast, however, one study on

gynecological cancers in a Ghanaian teaching hospital[23], showed the mean age seen for women with ovarian cancer was 46 years old, but there was little or no commentary or comparative data. Here, average life expectancy is 63.9 for women. In the Jiangsu province of China, age specific incidence peak appears to peak aged 60-64, with age specific mortality highest in the 65-69 age group (average life expectancy is 77.6 for women).

FAMILY HISTORY

For generations, it has been clear that in some families, ovarian cancer is more prevalent than in the general population. A major breakthrough came in 1994 when it was discovered that faults in the BRCA1 and 2 genes could increase a woman's risk of developing breast or ovarian cancer. Tests were developed afterwards to identify germline mutations (i.e. those passed on from generation to generation) that could then identify women at risk. With a mutated BRCA1 gene, a woman has a risk of 44% of developing ovarian cancer by the age of 80, and a 17% risk with a mutated BRCA2 gene[24]. Mutations in other genes such as TP53 and RAD51c can also play a role in raising the risk of ovarian cancer, but the impact is nowhere near as significant as the BRCA genes.

Germline (inherited) BRCA mutation is associated in ovarian cancer with distinct clinical behaviour: earlier age of diagnosis, improved survival, visceral distribution of liver disease, higher response rates to platinum and non-platinum agents, and sensitivity to PARP inhibitors. It is increasingly apparent that a proportion of sporadic ovarian cancers also share the pathological and clinical traits of BRCA mutation, but in the absence of a germline mutation. This has been called 'BRCAness'– homologous recombination (HRD) DNA repair defect is present in the absence of a germline mutation, a term first used by the team at the Institute of Cancer Research in London but now being redefined as understanding increases [25]. A study by the Cancer Genome Atlas Research Network has shown 9% BRCA1, 8% BRCA2, 3% somatic (i.e. acquired) mutation of the BRCA genes. HRD is present mostly (but not exclusively) in high grade serous ovarian cancers[26]. The study authors conclude that the benefits of new PARP treatments go beyond germline mutations, therefore access to BRCA Somatic Mutational Analysis in routine clinical practise is needed, either by archived specimen or new biopsy.

Up until recently, tests were only carried out on women who had several close blood relations affected by ovarian and/or breast cancer. However, the now recognised risk of ovarian cancer patients, even those with no known family history, harbouring a mutation in BRCA1/2, together with the first poly adenosine diphosphate ribose polymerase inhibitors (PARPi; Olaparib [Lynparza]; Niraparib; Rucaparib) being licenced for the treatment of BRCA-mutated ovarian cancer has led to reconsideration of referral criteria for ovarian cancer patients[27].

The potential to test more women with ovarian cancer will help in two important areas:

- To determine the most appropriate individualised treatments
- To find those at increased risk (beyond those with a clear family history). If managed correctly with appropriate support and counselling for those undergoing testing, the prospect of increased primary prevention is a significant one, potentially reducing the impact of this deadly disease in future years.

There is still much more work to be done, in different populations, to identify where mutations occur within the BRCA1 and 2 genes. For example, in women of Ashkenazi Jewish descent, founder mutations occur mainly in three sites[28], whereas in different populations mutations can occur at many different points. A recent study by Rebbeck et al has shown that the risks may vary by type and location of BRCA mutation[29].

TRENDS IN MORTALITY RATES

A recent paper by Malvezzi et al[30] in 2016 examines the trends in mortality rates. Their findings are laid out below:

While ovarian cancer incidence rates continue to rise, age adjusted ovarian cancer mortality rates have levelled or even declined over the last 2 decades. However, the authors highlight there are persisting and substantial differences in ovarian cancer patterns and trends:

- In the EU, age-adjusted ovarian cancer mortality rates decreased 10% between 2002 and 2012, to 5.2 per 100,000. The decline was 16% in the USA, to 4.9 per 100,000 in 2012. Latin American countries had lower rates, and declines were observed in Argentina and Chile. Likewise, modest declines (2.1%) were observed in Japan, whose rate remained low (3.2 per 100,000 in 2012). Australia had a rate of 4.3 per 100,000 in 2012, and a 12% decline.
- The falls were larger in young women, rather than in middle or old age. Recent rates at age 20–49 were higher in Japan than in the EU and the USA. Predictions to 2020 indicate a further 15% decline in the USA and 10% in the EU and Japan. The authors attribute some of the progress to the long-term protective effect of the Oral Contraceptive Pill (OCP) (decreasing risk), particularly in countries of Northern Europe and the USA where uptake of the OCP was early and more widespread.
- These authors say a recent decrease in menopause hormone use may also partly explain the fall in rates for middle aged and elderly women in countries like Germany, the UK or the USA, where the use of menopausal hormones was more common. Part of the falls in these countries may be due to the fact that they had the highest ovarian cancer rates in the past.
- They argue that delays in the adoption of recent advancements in diagnosis and management may have unfavourably affected mortality in central and eastern European countries in ovarian as other cancers, and say

improvements in ovarian cancer management are however likely limited, apart from advancements in the treatment of ovarian germ cell tumours, which account for less than 10% of all ovarian cancers. The authors say it is difficult to explain the persisting high rates in central and Eastern Europe. They suggest fertility has been relatively low in that area over the last decades, and multiple parity and breastfeeding reduce ovarian cancer risk. However, they say the substantial differences are unlikely to be explainable by differences in fertility alone. Other environmental factors, including obesity and diet, have been related to ovarian cancer risk. The quantification of their effect on national mortality rates remains undefined.

- Finally, the authors say it is also difficult to explain the low rates in Japan and Korea. Diet and leanness in the past may partly account for them, but parity and OC use were relatively low in those countries. Thus, hormonal and reproductive features cannot account for their low rates. Recent trends in these countries have not been declining appreciably, suggesting a future global levelling of ovarian cancer mortality, as confirmed by the recent rates higher in young Japanese women compared with western countries.

SUMMARY

In summary the following complex factors have been shown to be, or potentially linked to the risk for an individual woman of developing ovarian cancer and the chance of her dying from the disease:

RISK FACTOR	OUTLINE	NOTES
AGE	In general increased age increases risk of developing ovarian cancer	
GEOGRAPHIC LOCATION/SOCIO-ECONOMIC STATUS	Increased risk in more developed countries, and more developed parts of countries	Risk can be altered by moving
RACE/ETHNICITY	Risk varies according to race/ethnicity	Affects age profile, and types of tumour
FAMILY HISTORY	Increases risk	Affects age profile and types of tumour
HORMONAL OR REPRODUCTIVE FACTORS	Use of oral contraceptive pill, number of pregnancies and duration of breastfeeding affect risk (positively)	Applies around the world, but cultural factors determine effect

SURVIVAL RATES FOR OVARIAN CANCER

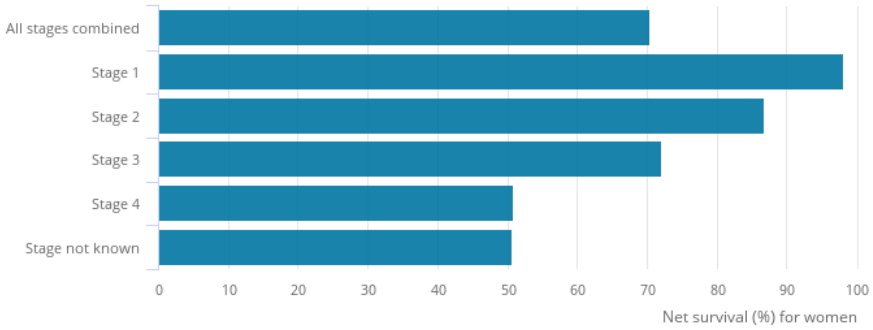
Comparing survival rates between countries, and between cancer types is a near impossible task, as they are measured in many different ways, using different criteria, and including or excluding certain data. The figures contained in this section should only be used within the context that they are cited and not taken as applicable in other situations. Usually they are cited in terms of one or five-year survival and indicate the proportion of women diagnosed with ovarian cancer, who are likely to be alive at one year, and five years post diagnosis. For an individual woman, of course it is impossible to estimate this likelihood with any certainty. However, for many women (but certainly not all) they would like to know what the possibilities are.

For the purpose of comparing ovarian cancer survival statistics with those of breast, cervical or endometrial cancer, these figures have been extracted from a study looking at 10, 5 and 1-year survival amongst common types of cancer in people diagnosed in England and Wales over a period of 40 years[31] up until 2011.

	BREAST	ENDOMETRIAL	CERVICAL	OVARIAN
5-YEAR SURVIVAL	87%	79%	67%	46%

STAGE OF DIAGNOSIS

It is accepted that both one- and five-year survival rates for ovarian cancer are very much determined by the stage at which it is diagnosed, i.e. the extent to which it has spread. The chart below is taken from the Office for National Statistics Statistical Bulletin: Cancer survival by stage at diagnosis for England: Age-standardised 1-year net survival (%) for women (aged 15 to 99 years) diagnosed with ovarian cancer in 2015, followed up to 2016,[32]



Figures from the National Cancer Institute SEER Database, for patients diagnosed between 2004 and 2010 in the United States gave the following 5-year survival rate for epithelial ovarian cancer[33]:

FIGO STAGE AT DIAGNOSIS	5 YEAR RELATIVE SURVIVAL (EPITHELIAL OVARIAN CANCER) – U.S
I	90%
II	70%
III	39%
IV	17%

SHORT-TERM MORTALITY AND EMERGENCY PRESENTATION

A report by the National Cancer Registration and Analysis Service (NCRAS) in England highlighted short-term ovarian cancer mortality as a particular issue, with 15% of women with ovarian cancer dying within 2 months of their diagnosis[34]. Three risk factors were identified for death within a year of diagnosis:

- Emergency presentation (56% died in first year).
- Advanced age - 43% of those aged 70-79 died in first year, and 70% of over 80s.
- Tumour morphology – those who had 'unclassified epithelial ovarian cancer' or 'miscellaneous or unspecified 'morphology.

Women who had more than one of these risk factors had an even higher chance of dying quickly.

A study in the US concluded for a sample of over 9,000 women with either stage III or IV disease that 43% died within the first year, 26% of the cohort within the first 90 days. Older age, increased co-morbidity, stage IV disease, lack of a visit to a gynecologic oncologist and surgery were all associated with an increase in 90-day mortality[35].

It is clear that there is a very significant proportion of women with ovarian cancer, for whom their diagnosis comes too late, where their performance status is such they cannot receive treatment, or that emergency presentation means an increased risk of non-assessment by a multi-disciplinary team and surgery by a non-specialist where surgery is required as a matter of urgency.

TUMOUR DEVELOPMENT

With ovarian cancer it is becoming apparent that there can be fundamental differences between early and later stage tumours, with suggestions there may not always be a linear and predictable connection (ie start at FIGO stage I and progress through II, III, IV). Lengyel in 2010 described ovarian tumours as developing in any of 3 potential sites (the surface of the ovary, the fallopian tube, or the mesothelium lined peritoneal cavity)[36]. He then says there is either a stepwise mutation from slow growing borderline tumour to well differentiated carcinoma (type 1), or there evolves a genetically unstable high-grade serous carcinoma that spreads rapidly (type 2). In particular, this type may be very hard to detect at an early point.

LOCAL VARIATIONS - DIAGNOSIS

This uncertainty however should not delay attempts to improve the speed and stage of diagnosis for women with ovarian cancer. The imperative is not just moral, but financial too. Analysis of costs in England showed potential for significant savings, if all Clinical Commissioning Groups (CCGs) who organise health services in a particular area were able to achieve the levels of early diagnosis of the best performing CCGs for ovarian cancer, then £16m per annum could potentially be saved, and 1,400 patients would benefit[37]. To put this figure into context, the National Cancer Research Institute partners (U.K) spent a total of £8.5m on ovarian cancer research in 2015-6[38]. On those figures, if the money saved was diverted, the ovarian cancer research spend in the UK could be almost trebled.

LOCAL AND NATIONAL VARIATIONS IN SPECIALIST SURGERY

Following the Calman-Hine report in the UK (1995), national guidance was introduced on commissioning cancer services. “Improving outcomes in gynecological cancers – The Manual 1999” provided a focus for the creation of specialist cancer centres, where women were treated by subspecialty trained surgeons and received multidisciplinary team care[39]. However, progress towards centralisation and specialistion of care was slow. A study published in 2015 showed that by 2009 many women were still not receiving specialist surgery, and the majority were not being operated on by General Medical Council accredited gynecologic oncologists, and there was considerable regional variation[40]. Anecdotal evidence in the UK more recently is that the situation has improved, but it is included here to demonstrate that shifting towards surgery in specialist centres is not necessarily straightforward or timely. The focus on specialist surgery has been of interest around the world.

In 2009 Bristow et al showed that after controlling for other factors, ovarian cancer surgery performed by a high-volume surgeon was associated with a 69% reduction in the risk of in-hospital death, while high-volume care was associated with increased likelihood of cytoreduction, shorter length of stay and lower hospital related costs of care[41]. Another study in California in 2014 led by Bristow, showed that among patients with advanced stage ovarian cancer, the provider combination of high-volume hospital and high-volume physician is an independent predictor of improved disease specific survival. However, it highlighted that access to high-volume ovarian cancer providers is limited, and the barriers are more pronounced for patients with low socioeconomic status, Medicaid insurance and racial minorities[42].

An observation study in Tokyo, Japan, led by Shinichi Tate and Makio Shozu tracked the implementation of an aggressive surgery protocol for 5 years. They studied 106 patients. They underwent training for 9 months prior to beginning the service. They confirmed that implementing such a regime did not cause a significant increase in mortality, and they saw increases in median progression free survival (from 14.6 to 25 months), and overall survival (38 months to 68 months)[43].

VARIATION IN SURVIVAL RATES BETWEEN COUNTRIES

Although it is often hard to provide direct comparisons between survival rates, a number of studies discuss variation between different countries. It is inadvisable to take the results from one study and compare them to another study's results.

The CONCORD Studies

The CONCORD-2 study published in 2015 aimed to initiate a worldwide surveillance of cancer survival as a metric of the effectiveness of health systems[44]. Previous studies (ICBP, Eurocare, and SurvCan) all adopted different methods, and so results cannot be brought together. Their most recent study (CONCORD-3) which was published in 2018 is discussed below[45]. Reasons for differences may include:

- Time lag in collection of data from around the world means comparative data is often older than that currently being used in a specific country.
- Differences may occur in which morphology codes are or are not included.
- Researchers construct life tables to estimate background mortality in a given country or region. Variations in the type of data used to construct these tables will result in variations in the resulting survival rates[46].

The CONCORD-3 analysis of data from 71 countries in 18 cancer types, revealed very wide differences in survival that are likely to be attributable to differences in access to early diagnosis and optimum treatment. Results for ovarian cancer were based on data from over 865,000 women in 61 countries diagnosed 2010-2014, and overall was of a higher quality (i.e. more complete) than CONCORD-2 which the authors note may be driving any improvements or worsening of figures.

The data was collected for ovarian cancer and included fallopian tube, uterine ligaments, and adnexa, as well as the peritoneum and retroperitoneum where high grade serous carcinomas are often detected.

The results by country are included in the Appendix.

For women diagnosed during 2010–14, 5-year survival was in the range 40–49% in 24 countries: in Canada and the USA; seven countries in Asia (Singapore [south Asia]; China, Korea, Japan, and Taiwan [east Asia]; and Israel and Turkey [west Asia]); 14 European countries (Denmark, Estonia, Finland, Iceland, Latvia, Norway, and Sweden [northern Europe]; Portugal and Spain [southern Europe]; and Austria, Belgium, France, Germany, and Switzerland [western Europe]); and Australia.

Survival was in the range 30–39% in 19 countries: four in Central and South America (Argentina, Brazil, Ecuador, and Puerto Rico); Kuwait and Thailand; 12 European countries (Ireland, Lithuania, and the UK [northern Europe]; Croatia, Italy, and Slovenia [southern Europe]; Bulgaria, the Czech Republic, Poland, Russia, and Slovakia [eastern Europe]; and the Netherlands [western Europe]); and New Zealand.

Survival was less than 30% in Malta and less than 20% in India (Karunagappally; table 7).

Survival trends between 1995–99 and 2010–14 were fairly flat in most countries. However, 5-year survival rose by 5–10% in the USA; Israel, Korea, and Taiwan; 11 European countries (Denmark, Iceland, Ireland, Norway, and Sweden [northern Europe]; Portugal and Spain [southern Europe]; Bulgaria and Poland [eastern Europe]; and France and Switzerland [western Europe]); and Australia. Survival increased by more than 10% in Estonia and Latvia, and by 20% in Japan.

International Cancer Benchmarking Partnership Study

The International Cancer Benchmarking Partnership Study (ICBP) has been working to track and analyse survival rates for breast, bowel, lung and ovarian cancers in high-income countries (or states within). Canada (Alberta, British Columbia, Manitoba, Ontario), Australia (New South Wales, Victoria), the United Kingdom (England, Scotland, Wales, Northern Ireland), Norway, Sweden, and Denmark are the participating countries. They have been considered suitable for comparison due to their level of cancer registration and spend on healthcare. There are five modules looking at:

- Cancer survival.
- Population awareness and beliefs about cancer.
- Attitudes, behaviours and systems in primary care.
- Delays in diagnosis and treatment and the causes thereof.
- Treatments, co-morbidities and other factors.

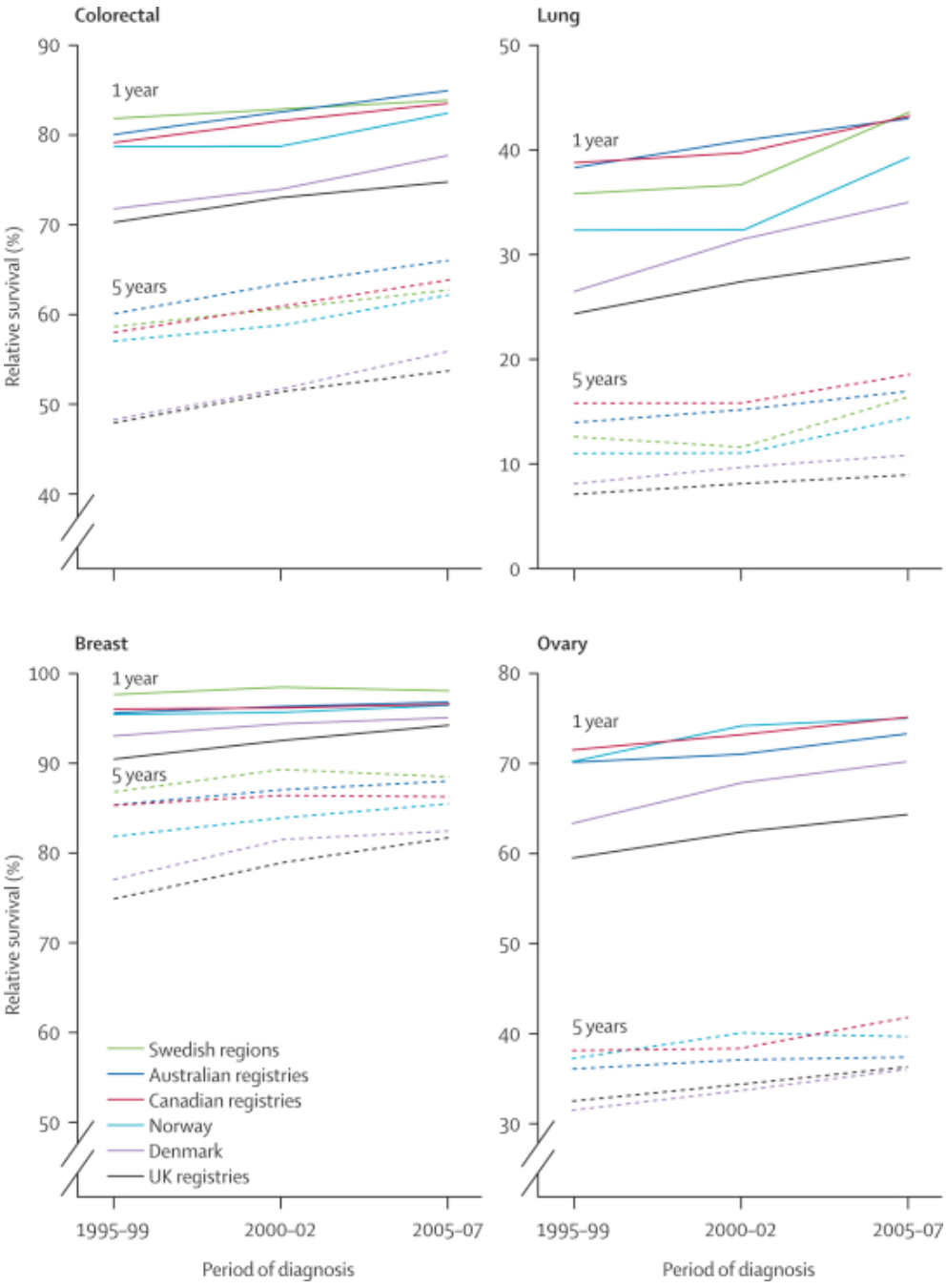
Results to date have shown that variation is quite wide, and they are beginning to inform cancer policy in order to improve cancer survival. Whilst survival for all the cancers studied has improved in the period 1995-2007, the gap between best performing (Australia, Canada, Sweden) and lowest performing (UK and Denmark) has remained largely unchanged other than for breast cancer, where it has narrowed.

In terms of ovarian cancer for Denmark and the UK, it is apparent that poor one-year survival rates drive the overall survival rates, pointing to issues with diagnosis and initial treatment. This is particularly so for the UK, where five-year survival rates for women, if they survive the first year are the second highest. Sweden did not participate in the ovarian module. Norway and Canada had the best results overall.

OVARIAN CANCER SURVIVAL – INTERNATIONAL CANCER BENCHMARKING PARTNERSHIP STUDY (ICBP)

DIAGNOSED 2005-2007	AUSTRALIA %	CANADA %	DENMARK %	NORWAY %	UK %
1 YR SURVIVAL	73.5	75.6	70.6	75.2	65.0
5 YR	37.5	41.9	36.1	39.7	36.4
5 YR SURVIVAL IF SURVIVED 1ST YEAR	48.7	54.4	48.8	50.9	53.8

ICBP SURVIVAL TRENDS FOR FOUR CANCERS



For ovarian cancer, different stages of diagnosis account for some but not all variability[47]. The UK and Denmark had the lowest one-year survival. Denmark had the lowest proportion of diagnoses at an early stage, but overall, the UK had a similar proportion to the other countries. However, the UK was worst in terms of recording stage at diagnosis, with 30% of data missing, compared to 10% in Norway. Survival was worse for those whose stage was not recorded. The paper highlights the need for routine recording and transferral of stage data to Cancer Registries and calls for a global consensus to make stage data in Cancer Registries more consistent. In the UK survival for women diagnosed with later stage disease was worse, potentially

implying access to treatment is worse in the UK for this group, or that diagnosis of advanced stage disease is later. There was also some discussion that there may be differences in tumour biology contributing to the differing figures.

Awareness of ovarian cancer symptoms and beliefs about cancer were examined. In the UK, perceived barriers to symptom presentation were highest with 34% of people believing they would be wasting the doctor's time, and people had less knowledge of age and other risk factors. This compared to 9% in Sweden. Knowledge of the symptoms of ovarian cancer (in particular persistent bloating) was consistently low across all participating countries[48].

The ICBP Study has also shown a correlation between primary care physician's willingness to act and cancer survival in that jurisdiction. And while there are differences say in access to advice on whether or not to refer to secondary care, and access to diagnostic tests, no consistent reasons for this variation in willingness have yet been found for the cancers studied as a whole, and further work is being carried out. However, the authors of the study concluded that some jurisdictions might consider lowering the thresholds for primary care physicians to investigate cancer either directly, or by specialist referral to improve outcomes.

The study is on-going, but already in the UK and in Denmark, results are already helping focus efforts to improve cancer survival at a national level, with moves to improve access to diagnostic tests, improve family doctors' knowledge, improve awareness of symptoms, and improve cancer registration. For example, the creation of multi-disciplinary diagnostic centres for patients with vague symptoms ("one-stop shops" has been successfully rolled out in Denmark and is currently being piloted in the UK[49].

Eurocare

The Eurocare 5 study (2015) which looked at cancer survival across Europe for people diagnosed between 2000 and 2007 concluded that despite increases over time, survival for women's cancers remained poor in Eastern Europe, likely due to advanced stages of diagnosis, and or suboptimum access to adequate care. Low survival for women living in the UK/Ireland and Denmark, it suggested was possibly due to late detection and delays in referral. Overall the study highlighted poor survival for ovarian cancer across the continent and over time and suggested the need for major research effort to improve the prognosis for this common cancer[50].

Lower income countries

In lower income countries, the challenges can be starker and more obvious. Developing countries are still coping with huge burdens of communicable disease, poor infrastructure and very limited health budgets. Michel Coleman however describes the three engines of escalating cancer burden as being on the move: rapid population growth, an ageing population and increase in cancer risk at each age[51]. Consequently, these lower income countries will be increasingly challenged coping with the cancer burden.

Sankaranarayan et al evaluated 300,000 cancer deaths in Africa, Asia and Central America between 1990 and 2001 in Lancet Oncology[52]. The project called SurvCan

showed that just 22% of cancer patients in Gambia survived 5 years, and in Uganda (excluding breast cancer patients) the figure was even lower at 13%. The authors concluded that it was not surprising there was a huge stigma surrounding a cancer diagnosis. They highlighted that variations in survival correlated with early detection initiatives and level of development in health services. They also concluded that wide variation in cancer survival between regions emphasises the need for urgent investments in improving awareness, population-based cancer registration, early detection programmes, health-services infrastructure, and human resources.

A position paper produced by the African Organisation for Research and Training in Cancer in 2016, highlighted particular issues[53]:

- Lack of early and accurate diagnosis is a challenge to appropriate care. More than 80% of patients in Africa are diagnosed at advanced stages of cancer. Inadequate pathology leads to wrong diagnosis and patients may receive inappropriate treatment. Scarcity of care providers and researchers is a problem in pathology training, and many countries have less than one pathologist for every million.

- Access to healthcare - cancer is often seen as a disease caused by spiritual curses, and as such cancer cases are often referred to healers or shamans for traditional or spiritual treatment. Health care providers in rural areas lack training on cancer, often misdiagnosing cancer as other illness. Lack of data on cancer prevalence and trends in Africa and historical focus on communicable diseases decrease government efforts on cancer research and treatment.

- Availability of treatment modalities - high quality treatment is difficult due to limited healthcare sources and low affordability. The current number of physicians practicing in Africa (145,000) represents 5% of the European total (2,877,000). Treatment access is also limited: Approximately 22% of the 54 African countries have no access to anti-cancer therapies. Barriers to treatment include significant out-of-pocket expenses. Out-of-pocket health expenditure is estimated to push many people globally into dire poverty when treatment costs are substantially higher than income.

- Finally, there is a constant threat to the clinician pool due to ‘brain drain’. More than half of 168 medical schools surveyed reported losing between 6 to 18% of teaching staff to emigration in the last 5 years. It will be critical to attract African health care personnel to more attractive settings with better salaries, working conditions, career paths and support.

In 2013 a report in Lancet Oncology entitled ‘Status of radiotherapy resources in Africa’ showed a huge variation in accessibility to machines, with South Africa and Egypt having over 60% of the equipment[54].

At the American Society for Clinical Oncology annual meeting in 2015, Dr Gilberto Lopes MD, MBA, FAMS explored reducing the global economic burden of cancer. Having examined data from the Union for International Cancer Control[55] he highlighted that while the economic burden of each cancer case in the US, UK, and

Japan ranged from $183 - $460 per patient every year, in South America, India and China it ranged from a paltry $0.54 to $7.92 per patient. Overall, high-income regions spent 5-10 times more on cancer control on a per capita basis, than low or middle-income countries.

SUMMARY

In summary, the reasons for variations in survival rates between countries are complex, and still to a considerable extent, not yet understood. Whilst the balance of tumour types in any country may differ, and may impact on survival rates, there are many other known and suspected reasons for variation as the table below indicates.

KNOWN OR POTENTIAL FACTORS FOR VARIATION IN SURVIVAL RATES	OUTLINE	NOTES
DELAYS IN DIAGNOSIS	- Low awareness - Delays seeking help - Stigma surrounding cancer preventing women seeking help	
DELAYS IN INITIAL INVESTIGATIONS	- Doctors not realising symptoms may indicate ovarian cancer - Access to tests - Willingness of doctor to investigate - Lack of referral to specialist care	Diagnosis following an emergency presentation is a key driver for early deaths
LACK OF DOCTORS (GENERAL)		In some low-income countries
DIFFERENCES IN STAGE AT DIAGNOSIS	Varies between different countries. Some influence of balance of tumour types and behaviour but may indicate prolonged diagnosis.	In particular, looking at 1 and 5-year survival rates can provide an indicator of whether there are issues with treatment or diagnosis.
LACK OF SPECIALIST STAFF	Trained in gynecologic oncology	Particularly in low-income countries but not exclusively
ABILITY TO RETAIN SPECIALIST STAFF		Issue in lower income countries in particular

ACCESS TO SPECIALIST SERVICES	High-volume centres and surgery performed by high-volume surgeons are important	
ACCESS TO PATHOLOGY/SPECIALIST PATHOLOGY	Getting the diagnosis right can drive accessing the right treatments	In some very low-income settings, even diagnosing as cancer would be progress. Finding out the tumour type will drive more accurate treatments for individuals
ACCESS TO EXISTING AND NEW DRUGS		Not just in low-income countries, applicable in high-income countries too.

DATA ON OVARIAN CANCER PATIENT EXPERIENCE

While there has been much academic discussion about incidence, mortality and survival around the globe, very little academic research has taken place into women's experience of being diagnosed and living with ovarian cancer.

Some studies exist highlighting the psychological impact of such a devastating diagnosis and being subjected to aggressive surgical and medical protocols. They call for screening of women for psychological distress.[56] A systematic review of studies focusing on quality of life for women with ovarian cancer in 2016 concluded that there was a wide range of conditions as a result of treatment that may persist for a long time and impact negatively on a woman's quality of life. It noted that studies proposing interventions and treatments were lacking.[57] In terms of policy development, the National Health Service in England introduced the National Cancer Patient Experience Survey comparing experiences of people with different cancers and different locations within England. Results have been used to monitor national progress on cancer care, and to provide information to drive local quality improvements, and inform the work of various charities and stakeholder groups supporting cancer patients.[58]

In terms of looking at the overall experience of women, from the time when they were or were not aware of symptoms, through treatment and living with the disease, it is mainly the charitable sector or pharmaceutical companies who have highlighted particular issues over the years, in individual countries. Whilst not seeking publication in academic journals, these insights can provide valuable information to clinicians, researchers and policy makers alike, in addition showing women going through the experience that they are not alone in what they face. Recent examples include the Target Ovarian Cancer Pathfinder Study (2009, 2012, 2016) in the United Kingdom, Ovarian Cancer Australia surveys in 2014 and 2015, and 'Our Way Forward' by pharmaceutical company Tesaro, in the USA in 2017.

IN CONCLUSION

The heightened risk of ovarian cancer in developed countries, and the increasing burden of ovarian cancer in developing countries provide compelling reasons to address globally low survival rates.

High quality cancer registration is vital for providing evidence for cancer control strategies and action in different countries. For the developing world resource issues are paramount, including access and retention to suitably trained medical staff, and diagnostic equipment.

Sankaranarayanan and Ferlay provide a useful summary in their chapter on gynecological cancers in The Handbook of Disease Burdens and Quality of Life Measures[59]: The differences in the outcome of cancer treatment across the world are due to vast disparities in health service infrastructures, human resources, service delivery, and accessibility to services. A significant proportion of patients are unable to access and avail or complete preventive, diagnostic, and therapy services in many countries due to inadequate health care services and financing. Formulation and translation of appropriate cancer control policies and investments in raising awareness, human resources development, and healthcare infrastructure are vital to reduce the current burden of gynecological cancer in low- and medium-resource countries. On the other hand, attention should be focused on emerging cost-effective options to sustain and further improve current control prospects in the developed world.

RECOMMENDATIONS

- There is a compelling call to address globally low survival rates.
- The opportunity to provide patient experience on a global level would strongly support the call to global action.
- There is a need to improve data quality and improve the balance between high and low-income countries, race and ethnicity and tumour type, and to have more reliable, representative international comparison data in relation to survival.
- Efforts to support global initiatives to improve cancer registration, and develop and sustain infrastructure (training, retention of staff, appropriate equipment) in many countries, particularly low-income ones are important.
- From improving early detection, to reducing delays, and opening up access to best practise treatments, clinicians and methods, there are many ways that exist today to make a concerted effort to improve survival and quality of life, no matter where a woman lives.
- The World Ovarian Cancer Coalition has an important role to play in providing a call to action to address globally low survival rates.
- The opportunity to provide patient experience insight on a global level would strongly support the call to global action.

- The World Ovarian Cancer Coalition should seek to support global initiatives to improve cancer registration and efforts to develop and sustain infrastructure (training, retention of staff, appropriate equipment).

- The World Ovarian Cancer Coalition should look to work with other global cancer projects such as the Union for International Cancer Control (UICC), the International Agency for Research on Cancer (IARC) and initiatives within the World Health Organisation (WHO) where goals correspond. For example supporting the following targets for 2025 from the UICC's World Cancer Declaration (2013)[60]:

    - Target 2: Population-based cancer registries and surveillance systems will be established in all countries to measure the global cancer burden and the impact of national cancer control programmes.

    - Target 5: Stigma associated with cancer will be reduced and damaging myths and misconceptions about the disease will be dispelled.

    - Target 6: Population based screening and early detection programmes will be universally implemented, and levels of public and professional awareness about important cancer warning signs and symptoms will have improved.

    - Target 7: Access to accurate cancer diagnosis, quality multimodal treatment, rehabilitation, supportive and palliative care services, including the availability of affordable essential medicines and technologies will have improved.

    - Target 9: Innovative education and training opportunities for healthcare professionals in all disciplines of cancer control will have improved significantly, particularly in low- and middle-income countries.

- The World Ovarian Cancer Coalition should look to other site-specific global coalitions, e.g. pancreatic cancer, lymphoma, and kidney, and brain, to share information and find common action points.

- The World Ovarian Cancer Coalition should continue its efforts to balance the focus between more and less developed nations.

- The World Ovarian Cancer Coalition should periodically review this report and update when required.

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APPENDIX 1

Glossary of terms - as defined in the Globocan 2012 estimates

Incidence

Incidence is the number of new cases arising in a given period in a specified population. This information is collected routinely by cancer registries. It can be expressed as an absolute number of cases per year or as a rate per 100,000 persons per year (see *Crude rate* and *ASR* below). The rate provides an approximation of the average risk of developing a cancer.

Mortality

Mortality is the number of deaths occurring in a given period in a specified population. It can be expressed as an absolute number of deaths per year or as a rate per 100,000 persons per year.

Prevalence

The prevalence of a particular cancer can be defined as the number of persons in a defined population who have been diagnosed with that type of cancer, and who are still alive at the end of a given year, the survivors. ***Complete*** prevalence represents the number of persons alive at certain point in time who previously had a diagnosis of the disease, regardless of how long ago the diagnosis was, or if the patient is still under treatment or is considered cured. *Partial prevalence* , which limits the number of patients to those diagnosed during a fixed time in the past, is a particularly useful measure of cancer burden.

Prevalence of cancers based on cases diagnosed within one, three and five are presented as they are likely to be of relevance to the different stages of cancer therapy, namely, initial treatment (one year), clinical follow-up (three years) and not yet cured (five years). Patients who are still alive five years after diagnosis are usually considered cured since the death rates of such patients are similar to those in the general population. They would be included in complete prevalence figures. There are exceptions, particularly breast cancer.

Prevalence is presented for the adult population only (ages 15 and over), and is available both as numbers and as proportions per 100,000 persons.

Crude rate

Data on incidence or mortality are often presented as rates. For a specific tumour and population, a crude rate is calculated simply by dividing the number of new cancers or cancer deaths observed during a given time period by the corresponding number of person years in the population at risk. For cancer, the result is usually expressed as an annual rate per 100,000 persons at risk.

ASR (age-standardised rate)

An age-standardised rate (ASR) is a summary measure of the rate that a population would have if it had a standard age structure. Standardization is necessary when comparing several populations that differ with respect to age because age has a powerful influence on the risk of cancer. The ASR is a weighted mean of the age-specific rates; the weights are taken from population distribution of the *standard population*. The most frequently used standard population is the *World Standard Population*. The calculated incidence or mortality rate is then called age-standardised incidence or mortality rate (world). It is also expressed per 100,000. The world standard population used in GLOBOCAN is as proposed by Segi and modified by Doll. The age-standardised rate is calculated using 10 age-groups (0-14;15-39;40-44;45-49;50-54;55-59;60-64;65-69;70-74;75+).

APPENDIX 2

Five- year survival for women with ovarian cancer diagnosed between 2000 and 2014, from 77 countries, taken from the CONCORD-3 study.

*denotes data that is considered unreliable

** denotes the estimate is not age standardised

The initial figure is the estimate. The figures in brackets represent the interval in which the probability of the result is 95% i.e. there is a 95% chance of the actual rate lying within this range. The narrower the interval, the more likely the estimate is to be correct or nearly correct.

REGISTRATION AREA (CASES RECORDED 2000-2014)	SURVIVAL ESTIMATE FOR THOSE DIAGNOSED 2005-2009	SURVIVAL ESTIMATE FOR THOSE DIAGNOSED 2010-2014
Africa (1010 cases analysed)		
Algerian registries (423)	54.3 (44.7-63.8)*	66.5* (53.5-79.5)
Mauritius (244)	79.7 (69.6-89.8)	-
Nigeria (225)	59.4* ** (24.9-93.9)	49.1* (33.8-64.4)
South Africa (Eastern Cape) (118)	81.0* ** (58.8-100)	67.8* ** (47.4-88.2)
America (Central and South) (16,023)		
Argentinian registries (1,688)	43.2 (38.6-47.9)	38.6 (34.3-42.9)
Brazilian registries (1,201)	34.1(29.4-38.9)	34.9 (29.5-40.3)
Chilean registries (698)	29.0 (23.3-34.7)	28.05 (21.3-34.7)
Colombian registries (1,759)	35.4 (30.3-40.6)	33.3* (28.2-38.4)
Costa Rica (1408)	47.1 (40.5-53.7)	56.9 (49.1-64.7)
Cuba (4560)	38.4 (33.1-44.5)	37.9 (32.1-43.7)
Ecuadorian registries (1,732)	38.8 (33.1-44.5)	37.9 (32.1-43.7)
Guadeloupe (110)	24.2* ** (8.9-39.5)	29.5* ** (13.8-45.2)
Martinique (191)	34.0 (24.6-43.4)	35.7* (23.4-48)
Puerto Rico (1,728)	37.2 (33.4-41.1)	37.3 (32.0-42.6)
Uruguay (948)	37.4 (31.9-42.8)	37.4* (31.4-43.4)
America (North) (312,954)		
Canada (31,395)	41.0 (40.0-42.0)	40.9 (39.9-41.8)
US registries (281,559)	42.0(41.7-42.4)	43.4 (43.1-43.8)

Asia (109,998)		
Chinese registries (10,517)	40.6(38.8-42.5)	41.8(39.8-43.7)
Cyprus (553)	46.2* (39.9-52.4)	46.4*(40.0-52.7)
Indian registries - 2 (172)	13.2 (7.7-18.7)	15.6 (10.2-21.1)
Israel (5663)	43.5 (41.1-45.9)	45.0(42.3-47.7)
Japanese registries (31,244)	43.9 (42.8-45.1)	46.3 (44.9-47.7)
Korea (28,076)	44.1(42.7-45.5)	47.5(46.2-48.9)
Kuwait (221)	35.4(25.2-45.6)	35.1(25.6-44.7)
Malaysia (Penang) (805)	36.4*(27.3-45.6)	46.8*(34.5-59.0)
Qatar (214)	62.6* **(47.5-77.6)	39.2*(26.3-52.1)
Singapore (3514)	46.8(42.8-50.7)	43.9(40.7-47.0)
Taiwan (16,872)	47.5(45.5-49.5)	48.8(46.9-50.8)
Thai registries (5,469)	35.8(32.3-39.3)	37.2(34.0-40.5)
Turkish registries (6678)	40.0(37.4-42.6)	39.7(37.3-42.0)
Europe (399,675)		
Austria (11,567)	41.2(39.6-42.7)	41.0(39.4-42.7)
Belgium (10,447)	42.8(41.3—44.3)	43.1(41.6-44.6)
Bulgaria (12,206)	33.9(32.2-35.5)	37.3(35.4-39.1)
Croatia (7,138)	33.4(31.3-35.5)	36.0(33.9-38.2)
Czech Republic (18,875)	35.2(34.0-36.5)	36.5(35.2-37.8)
Denmark (9,024)	37.4(35.7-39.2)	39.7(37.8-41.6)
Estonia (2,122)	37.2(33.8-40.7)	42.3(37.4-47.1)
Finland (8,101)	44.2(42.2-46.2)	41.1(39.2-43.0)
French registries (8,658)	42.1(40.4-43.7)	43.5(40.0-46.9)
German registries (38,064)	40.6(39.6-41.6)	41.2(40.2-42.2)
Iceland (276)	40.9(31.3-50.5)	40.3(31.2-49.4)
Ireland (4,952)	31.2(28.9-33.4)	32.8(30.3-35.3)
Italian registries (31,025)	39.3(38.5-40.1)	39.4(38.3-40.5)
Latvia (3,842)	39.8(36.5-43.1)	45.5(41.9-49.0)
Lithuania (5,452)	31.6(29.5-33.8)	35.0(32.0-37.9)

Malta (547)	27.5(22.0-33.0)	28.0(21.4-34.6)
Netherlands (19,252)	37.2(36.0-38.5)	37.5(36.2-38.7)
Norway (7,207)	42.8(40.7-45.0)	45.5(43.3-47.7)
Poland (53,462)	35.4(34.6-36.2)	37.5(36.7-38.3)
Portugal (6,532)	31.8(39.7-44.0)	43.6(38.7-48.4)
Romania (Cluj) (460)	28.9*(22.3-35.6)	37.2*(29.7-44.6)
Russia Registries (10,628)	33.2(31.3=35.0)	34.8(32.8-36.8)
Slovakia (5,207)	34.5(31.7-37.3)	33.4(28.6-38.2)
Slovenia (2,750)	35.4(32.3-38.4)	37.0(33.4-40.5)
Spanish registries (7,710)	37.9(36.1-39.6)	39.8(36.9-42.7)
Sweden (12,132)	42.9(41.2-44.6)	46.5(44.8-48.2)
Swiss registries (4,964)	42.0(39.5-44.4)	44.1(41.3-46.8)
United Kingdom (97,061)	33.2(32.6-33.7)	36.2(35.7-36.8)
Oceania (25,841)		
Australian registries (21,124)	41.0(39.8-42.2)	42.0(40.8-43.2)
New Zealand (4,717)	33.4(31.0-35.9)	36.7(34.1-39.3)