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One Health: the need to move from theory to practice in a Public Health perspective

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The term One Health identifies a holistic vision that recognizes how human health, animal health and environmental health are closely interconnected and interdependent, to the extent that they influence and shape each other [1]. Although this idea may seem banal and almost obvious, only in recent years have its prominence and scope significantly influenced the way we think about science, research, and the entire healthcare system, both locally and internationally. Indeed, the One Health vision has been strongly integrated into the agendas of many countries and major international organizations over the past five years, being officially recognized as a major and therefore fundamental strategy. It was as recently as May 2021 that the World Health Organization (WHO), the Food and Agriculture Organization of the United Nations (FAO), the World Organization for Animal Health (OIE), and the United Nations Environment Program (UNEP) established an interdisciplinary group of high-level experts to strengthen cross-sectoral collaboration and first to conceptualize and define the One Health vision, and then to lay the groundwork for its practical implementation [2].

It becomes clear that to move from theory to action and thus apply and implement such a model, it is first necessary to be aware of the historical period we are going through.

Public Health faces challenges such as climate change and the recent COVID-19 pandemic, wars, and an economic crisis that continuously exacerbates inequality, which we cannot expect to address by locking ourselves in our silos of knowledge [3].

As Public Health professionals, how can we stop the burden caused by antimicrobial resistance without considering the vital input that can come from other fields such as veterinary, biology, as well as law and economics? Or again, how can we reduce the number of deaths during heat waves, which will be increasingly frequent, without engaging with meteorologists and climatologists to identify the most dangerous days, as well as with architects and engineers to design greener, tree-lined cities to prevent risks?

So, while from a theoretical point of view we are now able to define One Health, understood as an approach that aims to sustainably balance and optimize the health of people, animals, and ecosystems, it is clearly more complex to apply and implement models that take this vision into account. According to the One Health vision, when designing strategies to address a single problem, the involvement of a variety of sectors and disciplines, as well as the involvement of civil society and policymakers, should be considered. What then should we focus on? Fostering a new way of thinking not only about science but about our lives in general is the first step in translating the holistic One Health vision into reality. In this sense, supporting a change in the broadest conception of the term, as much in the way we produce evidence and implement projects as in the way we conceive of our place within the Planet, is an indispensable step, which is based on at least four key points: awareness, collaboration, sharing, and education and training.

To achieve the same goal, in fact, professionals should be aware both need to adopt this approach to respond to the challenges of the Century and of the importance of recognizing other disciplines as crucial. Transdisciplinarity and multi-sector collaboration provide that broad and representative range of perspectives and knowledge, which is indispensable. We must ensure that these terms are not merely empty words, but that they truly represent a new vision that guides the way we produce evidence and implement policies, projects and activities. Awareness, in its broadest sense, naturally leads us to another key point: collaboration. In this context, numerous projects have been promoted to foster the creation of consortia with different backgrounds and many funds are allocated in many countries, with numerous initiatives especially in the European Union [4]. Such initiatives, extremely complex and challenging in implementation, will increasingly have to become the standard in the process of producing evidence and implementing basic and applied research projects. In this sense, the main challenge is involving professionals whose

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skills and expertise may differ significantly in terms of study and training, yet are closely connected when addressing common problems. Communication, sharing knowledge and experience, admitting the relevance of other disciplines and, when necessary, our own limitations, will allow us not only to achieve our goal, which is the protection and promotion of the health of the population, but also to enrich ourselves personally. Therefore, collaboration should be an opportunity and not a reason for competition or the presumed superiority of one discipline over others.

Awareness, willingness to collaborate, and knowledge sharing then leads to the last key concept that will help us move from theory to practice: education and training. In this context, Public Health plays a key role in proposing a new way of thinking about our place on the Planet and the related relationships that bind us to all its components, which presupposes an immense education and training effort at all levels. Offering a new vision is as complex as it can be, especially in healthcare systems. However, change, not only of the individual behavior but of the entire organization and, more broadly, the entire system, is the only truly effective and lasting tool we have to embrace the One Health vision. Funding and, consequently, transdisciplinary collaboration may cease; professionals and teams may change over time, just as awareness and knowledge are not inherently present. What really remains and endures is education, training, knowledge acquisition, development of critical thinking and reasoning skills. This effort, made even more difficult by the need to transmit knowledge from different disciplines and sectors, must be our priority. The complexity is even greater when we consider that our target is not limited to professionals, but also to policymakers and citizens, the real actors of change. Again, however, it becomes clear how, to meet the challenge of education and training, we cannot rely on our own strengths alone. How could we, as Public Health professionals, educate about the circular economy or new models of urban greenery and sustainable cities to citizens and professionals alike? Such contamination of knowledge is the real force that will enable us to move from theory to practice, without which we will remain in our silos without ever being able to apply the One Health approach. That is why Public Health must strive to be a promoter of this change, bringing together the different stakeholders and proposing innovative models of education and training, both of professionals and citizens.

It becomes clear that change requires awareness, collaboration, sharing and education, concepts that are linked, inseparable and interdependent, to be considered in a circular vision in which one prescinds from the other and at the same time nurtures it. Only by truly committing to, investing in, and believing in these concepts can we translate the holistic One Health vision into practice and ultimately seek to assure ourselves and future generations a future that allows us to live in balance and with respect for the Planet.

AUTHOR CONTRIBUTIONS

LV and WR conceived the research hypothesis. The manuscript was written by LV and WR. All authors read and approved the final version of the manuscript.

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CONFLICT OF INTERESTS

The authors declare no conflicts of interest.

DATA AVAILABILITY

NA

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All-cause and Cause-Specific Excess Deaths during the COVID-19 Pandemic

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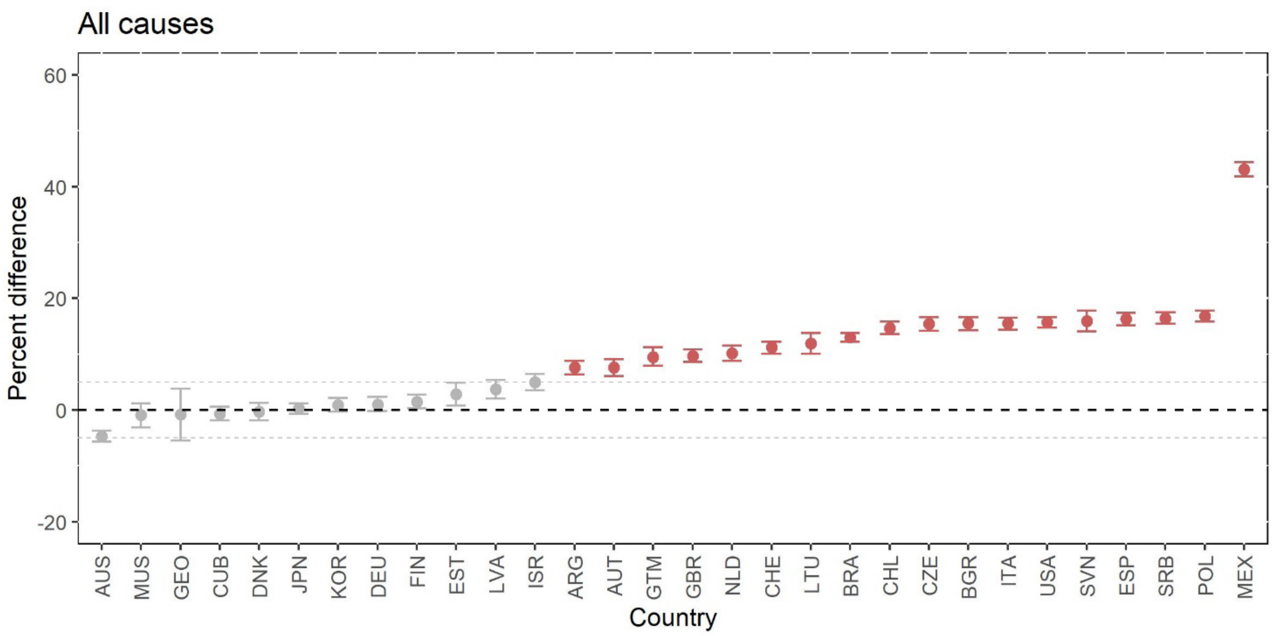
SUMMARY

We estimated the excess mortality during the COVID-19 pandemic (2020-2023) in selected countries worldwide. In Europe, half a million excess deaths occurred annually during the first three years of the pandemic, while a 2.1% excess was observed in 2023 (108,629 deaths). Significant excess mortality was recorded worldwide for all-cause mortality, cardiovascular disease, and diabetes, with peaks in COVID-19 cases closely aligning with these excess deaths. No increase in cancer-related mortality was observed. Gross domestic product per capita, national health expenditure, and vaccination rates were inversely associated with excess mortality. These findings provide insights into the public health impact of COVID-19 and inform future policy decisions.

Keywords: COVID-19; SARS-CoV-2; pandemic; excess mortality; cause-specific mortality; diabetes.

GRAPHICAL ABSTRACT



Percent differences in the number of deaths from any cause registered in 2020 relative to the expected deaths and corresponding confidence intervals by country.

Country abbreviations (ISO 3166 - Country code): ARG (Argentina), AUS (Australia), AUT (Austria), BGR (Bulgaria), BRA (Brazil), CHE (Switzerland),

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CHL (Chile), CUB (Cuba), CZE (Czech Republic), DEU (Germany), DNK (Denmark), ESP (Spain), EST (Estonia), FIN (Finland), GBR (United Kingdom), GEO (Georgia), GTM (Guatemala), ISR (Israel), ITA (Italy), JPN (Japan), KOR (The Republic of Korea), LTU (Lithuania), LVA (Latvia), MEX (Mexico), MUS (Mauritius), NLD (Netherlands), POL (Poland), SRB (Serbia), SVN (Slovenia), USA (United States).

BACKGROUND

The COVID-19 pandemic emerged as a health crisis, leading to seven million deaths officially attributed to SARS-CoV-2 globally. However, certified death counts do not fully capture the pandemic's true impact, as they exclude both deaths not officially attributed to COVID-19 and the indirect consequences of disrupted healthcare systems [1]. To address this gap, researchers have focused on excess mortality, defined as the difference between observed and expected deaths based on historical data [2]. This report, which includes three studies conducted by our research group, analyzes excess mortality across various countries from all causes and specific causes between 2020 and 2023, focusing on demographic and healthcare-related differences.

METHODS

Study 1 investigated total excess mortality and geographic disparities in Europe from 2020 to 2023, using weekly death counts from the Short-term Mortality Fluctuations data series [3]. Study 2 examined all-cause and cause-specific excess deaths across 30 countries worldwide in 2020, using data from the World Health Organization (WHO) [4]. Study 3 explored the association between COVID-19 cases and monthly cause-specific mortality in 16 countries, using monthly cause-specific death data retrieved directly from national statistics offices [5]. Excess deaths were calculated as the difference between observed deaths and expected deaths. Expected deaths were estimated through quasi-Poisson regression models, including demographic and temporal variables along with population size as an offset. Excess deaths were presented in both absolute and relative terms, with 95% confidence intervals derived from Monte Carlo simulations. To assess the robustness of the estimates, we applied the main model to estimate expected deaths for pre-pandemic years using historical mortality data from prior periods, and for pandemic years using varying baseline periods. Additionally, in Study 1, we considered the association between excess mortality and selected socioeconomic indicators, and in Study 3 we calculated Spearman's correlation coefficient (r_s) to assess the relationship between monthly cause-specific excess mortality from 2020 to 2021 and registered COVID-19 cases.

RESULTS

In Study 1, from 2020 to 2023, 22,254,542 deaths were registered across 29 European countries, with an estimated 1,642,586 excess deaths (+8.0%). The highest excess mortality occurred in 2021 (+11.2%), followed by 2020 (+10%), 2022 (+8.6%), and 2023 (+2.1%). Central and Eastern Europe experienced a higher overall increase at +13.2%. The proportion of the population living below the poverty line and the Gini index were directly associated with increased excess death rates, while gross domestic product per capita, health expenditure, and the percentage of people fully vaccinated by the end of 2021 and 2022 were inversely associated. In Study 2, we estimated about 1.4 million excess deaths from all causes across 30 worldwide countries in 2020 (12.2%). Significant excess deaths from ischemic heart disease and cerebrovascular diseases were observed in a third of the countries, from diabetes in 19 countries and from ill-defined causes in 20 countries. In Study 3, a positive correlation was found between COVID-19 cases and monthly excess mortality from all causes in all 16 countries (r_s ranging from 0.61 to 0.91), from cardiovascular disease (CVD) in 11 countries (r_s from 0.45 to 0.85), and for diabetes in 13 countries (r_s from 0.42 to 0.79). Excess mortality was estimated for all causes in 14 countries for both 2020 and 2021, for CVD in seven countries for 2020 and in nine countries for 2021, and for diabetes in 11 countries for 2020 and 12 countries for 2021. No excess mortality was estimated for cancer in any of the countries considered. Overall, estimates based on different combinations of baseline periods were similar in most countries, and estimates for excess deaths in 2019 were near zero.

CONCLUSION

Half a million excess deaths occurred annually in Europe during each of the first three years of the pandemic, with only a modest excess observed in 2023. Globally, substantial excess mortality was recorded for all-cause deaths, CVD, and diabetes, with peaks in COVID-19 cases closely aligning with these excess deaths, while no increase was observed for cancer-related mortality. The response to COVID-19 highlighted major inequalities in health outcomes, influenced by public health policies, demographic structures, socioeconomic factors, and health infrastructure. This research contributes to a deeper understanding of the public health impact of COVID-19, providing insights to inform future policy decisions and ultimately improve preparedness for similar health emergencies.

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The Burden of Diseases and Injury through The Lens of Standard Expected Years of Life Lost: The Lost Productivity and The Distribution of Health Attainment in Countries of Different Health Systems

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SUMMARY

Background: The productivity loss attributable to the burden of diseases in different country contexts reflect the effectiveness of the context specific measures for population health development. So, this study provides insights into the productivity loss from the burden of diseases.
Methods: Using country specific subnational level data, we have quantified the burden of diseases and the consequential lost productivity in two lower middle-income countries i.e., India and Kyrgyzstan; three upper middle-income countries i.e., Belarus, Kazakhstan and the Russian Federation; and one high income country, France. We have computed standard expected years of life lost (SEYLL) as the measure of disease burden, and quantified the present value of lost earnings (PVLE) using our 3P approach (population, participation and productivity).
Results: Our subnational level analysis finds an overall declining trend of SEYLL across regions in each country except in Belarus from 2017 onwards, and in France. We also find that the cumulative percentage loss of PVLE per SEYLL mostly exceeds cumulative GDP per capita growth of the country during the study years.
Conclusion: We have captured the value of earnings and quantified the avoidable loss for the society/country in different contexts and thus, this study demonstrates the potential contribution of population health development to the poverty alleviation programme in low – and middle -income countries.

Keywords: 3P approach; lost earnings; lost life; person years lived; poverty alleviation.

INTRODUCTION

Macroeconomic research on productivity has established the importance of human capital. Like physical capital, human capital in the form of education and health is durable, and accumulates overtime [1, 2]. The linkage between population health and economic productivity is a major policy concern. A 10-percentage-point increase in adult survival rates raises productivity by 6.7 to 13.4 percent, depending on the microeconomic estimates used for calibration [3]. Evidence suggests that older workers in high income countries (HICs) are no less productive than their younger counterparts [4].

Whilst the burden of disease may be a function of poverty, a high disease burden is also likely to adversely affect a nation's productivity, growth and, ultimately, economic development. Between 21 and 47.5 percent of Gross Domestic Product (GDP) growth per working-age population over the time horizon of

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25 to 30 years can be explained by improvements in the health of populations at the country level [5–8]. Bloom et al. [9] also found that each extra year of life expectancy is estimated to increase a country's GDP by 4 percent.

Health is difficult to quantify. Life expectancy at birth is considered to be a positive and an important determinant of economic growth rates. It has been widely acknowledged that a 10% increase in life expectancy is associated with a rise in annual economic growth of 0.3%-0.4% [10]. Summary Measures of Population Health (SMPH) combine mortality and morbidity information of a definite population [11, 12]. Disability Adjusted Life Year (DALY) is one such SMPH. A DALY is the sum of standard expected years of life lost (SEYLL) and years of life lived with disability. Studies have concluded that the SEYLL [12] is a more comprehensive measure of the impact of premature death on health state of the population. The measure of SEYLL puts a relatively higher weight affecting younger population [13, 14].

For realising the health policy goals, it is a necessity to have insights of productivity loss attributable to the burden of diseases in the context of the respective health system. An array of studies have estimated lost productivity caused by cancer [15–17]. Studies have also estimated economic burden of chronic diseases [18, 19]. Rumisha et al. [20] have assessed productivity lost from cancer, chronic disease, infectious disease and injury in a lower-middle income economy and one study of a HIC has also reported productivity lost from hepatitis C [21]. In addition, the COVID – 19 outbreak has triggered to compute economic value per human life lost from such a pandemic [22].

There are three broad approaches that are used for estimating the economic burden of a disease - (1) the "cost-of-illness" [23] that includes the direct costs of the illness for a particular population in a specific period, and the indirect costs of the illness as well. These indirect costs emerge from the human capital approach, which focuses on the years of labour lost due to the disease in a country; (2) the "economic growth model" [18, 24] where the impact of chronic diseases on the GDP of a country is assessed through changes in the model's inputs (e.g., savings rate, labour supply, skills); and (3) the full-income approach [25], which estimates the societal value of welfare losses or gains associated with poor health, early death, or increases in life expectancy valued in monetary terms.

Following the human capital model [26], the average earnings of a worker are considered to be a reasonable measure of labour productivity. Therefore, wages are used for estimating labour productivity losses associated with leaving the labour market prematurely as a result of an illness [21].

GDP per capita minus current health expenditure per person is also used as a measure of value per human life lost [22]. The willingness to pay for an additional year of life is also used to have average value of life lost from illness [27].

Although GDP per capita is widely used [28] as a measure of productivity, it does not capture differences in the earning patterns. Years of life lost (YLL), a measure of premature mortality [29] that considers both the frequency of deaths and the age at which death occurs is the dominant approach to estimate cost of mortality, so, YLL is used to estimate the number of discounted years of productive life lost. YLL for the population is calculated by multiplying the number of deaths by the expected life years remaining for an individual. SEYLL addresses the issue of arbitrary age threshold selection [30] that is practised for computing YLL. The SEYLL compares the age of death to the standard life expectancy of an individual at each age and incorporates time discounting and age weighting. The present value of future lost productivity are calculated using age and gender-specific mortality, wages, and employment rates [31] and so, a discount rate is applied for estimating the present value of the productivity forgone.

In "human capital approach" [32–34] economic value is imputed in YLL due to premature death by assigning average age-specific and gender-specific earnings to those lost years. The value of earnings over a person's lifetime is the most important component of wealth globally and is the central driver of sustainable growth and poverty reduction [35]. So, this study takes an approach that includes, population, participation and productivity, thus, the 3P approach, and estimates the present value of lifetime earnings forgone.

Although the use of YLL for computing lost productivity cost is well documented, we have used disease specific SEYLL for determining allocation decision at the sub national level in six different country contexts. We address policy relevant empirical questions that are (1) burden (SEYLL) and trend of non-communicable diseases, infectious diseases and injury with illustrations from countries with different levels of development and public policy space, (2) mortality pattern that prevails across all age groups, and (3) productivity lost per SEYLL.

The use of subnational data has unfolded in-country differences in population health development (health attainment) and so, we have also considered the productivity dimension of health disaggregated into subnational level for different economies.

METHODS

Data used in this study comes from Belarus, France, India, Kazakhstan, Kyrgyzstan, and Russia. The choice of six countries was guided by the motivation to include countries with (1) different levels of development, (2) population exposed to different health systems and (3) differential participation of genders in the labour force. Thus, following the World Bank classification of countries, 2022, this study has included two lower middle income countries (LMICs), three upper middle income countries (UMICs) and one high income country (HIC).

The sources of subnational level data from the statistical office / public domain of the respective country were

1. Belarus: https://belstat.gov.by/ and http://dataportal.belstat.gov.by/
2. France: http://www.ecosante.fr/ and https://www.scoresante.org/
3. India: https://data.gov.in/resources/ and https://censusindia.gov.in/
4. Kazakhstan: https://stat.gov.kz/ and https://taldau.stat.gov.kz/
5. Kyrgyzstan: http://www.stat.kg/
6. The Russian Federation: https://rosstat.gov.ru/ ; https://minzdrav.gov.ru/ ; https://mednet.ru/ and http://demogr.nes.ru/index.php/ru/demogr_indicat/data

This study has also used the data from Global Health Observatory of WHO, https://platform.who.int/mortality/themes/theme-details/MDB/all-causes; https://www.who.int/data/gho/data/themes/mortality-and-global-health-estimates/ghe-leading-causes-of-death and https://www.healthdata.org/research-analysis/gbd

Information about labour force participation rate and average per capita income comes from International Labour Organization https://ilostat.ilo.org/data/. The average per capita income is an extrapolated information derived from monthly gross minimum wage in PPP (purchasing power parity constant at 2017 USD) of the country multiplied by 12.

The regions in France had been reorganised in 2014 and so, our data of 2017 and of 2011–2014 (in consideration of the merged regions) is from 6 regions in France; in Kazakhstan, the number of regions between 2013–2017 was 16, in 2018 South Kazakhstan oblast had been split into Turkestan oblast and the city of republican significance Shymkent, thus, number of regions in 2018 and 2019 was 17. Similarly, the number of states in India was 28 until 2013, Telengana has been curved out as a separate state from Andhra Pradesh in 2014; however, the data was available from 19 states and the capital city, Delhi til 2013, and from 2014 onwards the data was from 21 states of India and Delhi.

Acknowledging the differences of the disease burden in the study countries, we have studied the effect of a mix of noncommunicable diseases, infectious diseases and injuries. Countries were different and so the data for the diseases / disorders by the countries was often not the same, and also the data points were not similar (Table 1).

Our measure, SEYLL [36, 37] quantified and compared the impact of different diseases and injuries. ILO Convention No. 138 has established the minimum

Table 1. Disease / disorders and Injury in the study countries with the respective data points

Problems/ Disorders	Belarus (UMIC) 2013-2018	France (HIC) 2011-2014 and2017	India (LMIC) 2013-2019	Kazakhstan (UMIC) 2013-2019	Kyrgyzstan (LMIC) 2013-2019	The Russian Federation (UMIC) 2013-2019
Cardiovascular diseases			√			
Circulatory diseases	√	√		√	√	√
Diabetes and Kidney diseases			√			
Digestive diseases	√	√	√	√	√	√
Endocrine system					√	
Genitourinary system					√	
Heart disease		√				
Infectious diseases	√			√	√	
Injuries	√		√	√	√	
Liver		√				
Mental and behavioural			√		√	
Musculoskeletal			√		√	
Neoplasms	√		√	√	√	√
Neurological diseases			√		√	

(continued)

Table 1. Disease / disorders and Injury in the study countries with the respective data points (continued)

Problems/ Disorders	Belarus (UMIC) 2013-2018	France (HIC) 2011-2014 and2017	India (LMIC) 2013-2019	Kazakhstan (UMIC) 2013-2019	Kyrgyzstan (LMIC) 2013-2019	The Russian Federation (UMIC) 2013-2019
Other diseases	√	√	√	√	√	√
Other non-communicable diseases			√			
Skin and subcutaneous diseases			√			
Substance use			√			
Respiratory diseases	√	√	√	√	√	√

age for admission to employment at 15. ILO – 134th Session, 2022, judgment no. 4527 has further set the mandatory age of separation from any active employment at 65 years.

For our analysis, we used the number of deaths, the population, and the mortality for different age groups, gender, and year (the year of data availability) of these 6 countries to construct the life tables at the national and the subnational (regional) levels. From these life tables, we estimated the remaining life expectancy for a defined age range and thus, standard expected years of life lost (SEYLL) was computed. In the next step, SEYLL was used to estimate the productivity losses due to early death. Our approach has also enabled us to present the number of person-years lived after exact age x.

Estimation methods

A. Standard Expected Years of Life Lost (SEYLL) $SEYLL = \sum_{x=1}^{X} d_x e_x$, where x is the age groups at 5-year interval when the person died at being in age X i.e., during the last period at the age interval of 5-years, d_x indicates the number of deaths of people at the age range x, e_x is the number of expected years of life that remain to be lived by a person at the age range x. In addition, dividing SEYLL by the total number of deaths, we estimated the number of years of life lost per death as

$$SEYLL_d = \frac{\sum_{x=1}^{X} d_x e_x}{\sum_{x=1}^{X} d_x}$$

B. With our 3P approach, we computed the present value of lost earnings (i.e., lost productivity) attributable to the SEYLL for population of different working age groups. Present value of lost earnings (PVLE) $PVLE = \sum_{i=1}^{I} \frac{SEYLL_i \times Annual\,wage \times l_i}{(1+r)^t}$, where i = 1, 2, 3, …, I are the age groups at a definite intervals for working age population (15years-64years), l_i denotes labour force participation rate for age groups (15–24, 25–54, 55–64) distributed by gender, r represents the discount rate [38], and t is the average number of years left for attaining the retirement age. Here, we assumed that the mean age of death was at the middle for the age group.

C. We calculated PVLE per SEYLL distributed by gender for each of the six countries.

D. We also presented the mortality pattern that prevailed across all age groups in terms of person years lived above age x (T_x). Thus, total time lived beyond age x i.e., $T_x = \sum_{i=x}^{X} L_{x_i} L_{x_{i+1}} \ldots . l_{x_X}$, where L_x is the cumulative years lived through age x, l_x denotes number of people alive at the beginning of the respective age interval.

RESULTS

Disease specific SEYLL decreased in countries except in France (+6%), Kazakhstan (+23%) and the Russian Federation (+7%) for both the genders, although such a trend was not consistent over the years. SEYLL decreased by almost 7% in Belarus and 11% for female in Kyrgyzstan during the study period (Table 2). SEYLL from digestive diseases, infectious and injuries reduced in Belarus but SEYLL from neoplasms increased in males. The substantially high increase in SEYLL of Kazakhstan was from other diseases (+51% in males and +46% in females) followed by respiratory diseases (+32% in males and +17% in females). Although, declining trend in SEYLL of Kyrgyzstan was found across all diseases and disorders in the population, the top three were infectious diseases, mental and behavioural diseases, and musculoskeletal diseases for both the genders. In the Russian Federation, the substantial reduction (+32% in males and +82% in females) in SEYLL from respiratory diseases was offset

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Table 2. Disease specific SEYLLs for each country

	2013			2014			2015			2016			2017			2018		
	Both	**Male**	**Female**	**Both**	**Male**	**Female**	**Both**	**Male**	**Female**	**Both**	**Male**	**Female**	**Both**	**Male**	**Female**	**Both**	**Male**	**Female**
Circulatory disease	1137637.0	539238.9	598398.1	1191089.8	621940.5	569149.3	1083358.2	536637.9	546720.3	1054237.2	520748.2	533489.0	1039984.9	511322.1	528662.7	1068488.7	505062.4	563426.2
Digestive disease	71332.5	40430.0	30902.4	69465.1	42546.5	26918.6	59173.9	34265.0	24909.0	56496.6	33141.7	23354.9	53689.0	29599.6	24089.3	54910.7	29237.3	25673.4
Infectious disease	16310.6	11969.4	4341.2	16377.2	12583.1	3794.1	12983.9	9625.9	3358.0	12507.6	8926.5	3581.1	11667.3	8112.1	3555.2	11801.8	8012.8	3788.9
Injuries	176286.5	136418.1	39868.4	178726.6	144448.7	34277.8	146054.0	116068.6	29985.4	134974.7	105967.8	29006.8	126577.0	99760.0	26817.0	127119.1	98538.7	28580.4
Neoplasms	295973.4	165842.9	130130.5	310608.4	193334.4	117274.0	290989.2	176880.9	114108.3	288330.1	174404.7	113925.4	294997.1	177002.3	117994.8	300589.3	174835.4	125753.8
Other diseases	417519.4	124814.4	292704.9	350574.5	122404.5	228170.0	334985.2	109448.7	225536.5	334113.2	108006.3	226106.9	316815.7	103413.6	213402.0	375443.3	111082.6	264360.7
Respiratory disease	36014.5	28377.5	7637.0	34545.3	28707.0	5838.4	31197.1	25584.7	5612.4	29391.1	23754.8	5636.3	30188.0	24610.0	5577.9	30253.5	24308.8	5944.7
Total	**2151074**	**1047091.4**	**1103982.6**	**2151386.9**	**1165964.7**	**985422.2**	**1958741.6**	**1008511.8**	**950229.8**	**1910050.6**	**974950.1**	**935100.5**	**1873918.9**	**953819.9**	**920099**	**1968606.2**	**951078**	**1017528.2**

France	2017			2014			2013			2012			2011		
	Both	**Male**	**Female**	**Both**	**Male**	**Female**	**Both**	**Male**	**Female**	**Both**	**Male**	**Female**	**Both**	**Male**	**Female**
Circulatory disease	1438697.4	789176.4	649521.0												
Digestive disease	195361.9	97892.8	97469.0			Paucity of the needed data...									
Heart disease	386467.7	246333.2	140134.5												
Liver disease	117270.6	84037.4	33233.2												
Other diseases	9025191.0	4916091.3	4109099.7												
Respiratory disease	246399.0	243990.2	2408.8												
Total	**11409387.5**	**6377521.4**	**5031866.2**	**11279965.3**	**6350321.1**	**4929644.2**	**11095560.6**	**6258958.8**	**4836601.8**	**10918649**	**6157294.9**	**4761354.1**	**10744003.6**	**6061412.6**	**4682590.9**

India	2013			2014			2015			2016			2017			2018			2019		
	Both	**Male**	**Female**	**Both**	**Male**	**Female**	**Both**	**Male**	**Female**	**Both**	**Male**	**Female**	**Both**	**Male**	**Female**	**Both**	**Male**	**Female**	**Both**	**Male**	**Female**
Total	**252276899**	**133860566.8**	**117385806.5**	**235821208**	**123459696.4**	**111679335**	**236178788.5**	**123953262.9**	**111478212.3**	**228059498.5**	**124353744.4**	**103369728.6**	**226035298.3**	**124915635.5**	**100654332.5**	**218971239.5**	**121773685.1**	**96731674.6**	**213837177.8**	**100473480.1**	**113223506**

(*continued*)

Table 2. Disease specific SEYLLs for each country (continued)

Kazakhstan	2013			2014			2015			2016			2017			2018			2019		
	Both	**Male**	**Female**	**Both**	**Male**	**Female**	**Both**	**Male**	**Female**	**Both**	**Male**	**Female**	**Both**	**Male**	**Female**	**Both**	**Male**	**Female**	**Both**	**Male**	**Female**
Circulatory disease	749268.2	395164.4	354103.7	659233.7	350380.5	308853.2	684718.2	365823.0	318895.3	638383.4	356698.3	281685.2	639520.2	355462.5	284057.7	673941.7	384001.0	289940.6	675055.9	392208.8	282847.2
Digestive disease	245016.0	137114.7	107901.2	250009.2	139563.9	110445.2	259899.4	147871.4	112028.0	253151.7	143970.6	109181.1	235021.4	128451.6	106569.8	252819.1	142358.1	110460.9	265257.2	150017.4	115239.8
Infectious disease	32287.7	21770.8	10516.9	29633.4	19467.6	10165.8	30642.5	20060.2	10582.3	27751.4	18186.8	9564.6	28614.6	18677.6	9937.1	29252.0	18979.6	10272.4	30463.9	19176.8	11287.1
Injuries	295874.5	228782.2	67092.2	280083.8	219107.3	60976.5	288995.7	225682.5	63313.2	267789.4	208436.6	59352.8	254287.1	197220.0	57067.1	268293.7	207916.1	60377.7	270397.9	211436.9	58960.9
Neoplasms	311353.1	168197.9	143155.2	300397.0	161697.1	138699.9	330943.5	175803.1	155140.4	321848.6	172323.6	149524.9	313909.4	166334.1	147575.3	333961.9	179612.0	154349.9	335572.3	180950.7	154621.6
Other diseases	1707938.8	976039.0	731899.7	1841115.3	1044038.0	797077.3	2019395.7	1146239.1	873156.6	2108407.8	1216984.4	891423.4	2211622.3	1265730.4	945891.9	2472552.3	1432339.7	1040212.6	2537533.4	1471252.9	1066280.6
Respiratory disease	290337.4	161384.4	128952.9	306849.5	168884.9	137964.6	368152.3	202108.2	166044.0	364378.0	206892.6	157485.4	337352.7	194502.5	142850.2	350164.0	202030.4	148133.6	363689.4	212286.2	151403.1
Total	**3632075.5**	**2088453.6**	**1543621.9**	**3667322**	**2103139.3**	**1564182.6**	**3982747.3**	**2283587.5**	**1699159.9**	**3981710.4**	**2323493**	**1658217.4**	**4020327.7**	**2326378.7**	**1693949**	**4380984.6**	**2567236.9**	**1813747.7**	**4477970**	**2637329.6**	**1840640.3**

Kyrgyzstan	2013			2014			2015			2016			2017			2018			2019		
	Both	**Male**	**Female**	**Both**	**Male**	**Female**	**Both**	**Male**	**Female**	**Both**	**Male**	**Female**	**Both**	**Male**	**Female**	**Both**	**Male**	**Female**	**Both**	**Male**	**Female**
Circulatory disease	628858.3	323177.7	305680.6	640585.0	324245.6	316339.4	635425.8	323234.8	312191.0	626232.0	307084.4	319147.5	610183.0	309219.9	300963.1	588507.9	301492.5	287015.4	605447.7	309974.6	295473.1
Digestive disease	87159.3	57520.7	29638.6	82862.2	54155.3	28707.0	81650.5	51824.3	29826.2	77655.1	49671.6	27983.6	74378.7	48804.5	25574.2	72831.3	47948.3	24883.1	71179.3	45744.0	25435.3
Diseases of genitourinary system	18341.0	10859.0	7482.0	18063.1	9799.2	8264.0	17380.6	10367.1	7013.5	16845.5	9699.0	7146.6	15347.2	9104.7	6242.5	14482.8	8371.5	6111.3	12272.0	7692.4	4579.5
Endocrinal disease	15391.1	6209.9	9181.1	16000.8	7214.0	8786.8	14285.5	6139.3	8146.1	16751.9	6641.0	10110.8	16043.9	7156.8	8887.1	17045.6	7349.4	9696.1	17021.4	7711.8	9309.5
Infectious disease	36012.2	24667.3	11345.0	32694.3	21781.1	10913.1	31909.3	21179.6	10729.7	28705.9	18652.6	10053.3	28363.0	18108.8	10254.1	25974.3	17465.6	8508.6	22798.3	14081.2	8717.0
Injuries	110423.5	85151.6	25271.9	107282.9	82264.7	25018.2	109565.9	83154.9	26411.0	98320.8	74225.2	24095.6	98394.6	75025.9	23368.7	87792.3	68324.6	19467.7	87419.1	69689.8	17729.3
Mental and behavioral disease	2128.9	1395.7	733.2	1806.0	1132.7	673.3	1552.8	883.1	669.7	1512.3	959.2	553.1	1672.3	1068.8	603.5	1632.4	848.8	783.6	667.1	423.9	243.2
Musculoskeletal disease	3963.2	1154.6	2808.6	3236.3	843.4	2392.9	2926.6	923.7	2002.9	2674.4	940.7	1733.7	2661.2	778.6	1882.6	2154.2	774.6	1379.6	2443.4	592.8	1850.6
Neoplasms	124219.6	64074.5	60145.1	133663.6	69574.6	64089.0	138106.9	70951.0	67155.9	143478.2	74376.4	69101.8	137232.9	71183.9	66049.0	145404.3	73772.2	71632.1	144966.6	74028.4	70938.3
Neurological disease	18321.0	11605.3	6715.7	19751.1	11631.2	8119.9	18260.3	11431.0	6829.3	19048.2	11435.9	7612.3	16803.1	10701.4	6101.7	16207.6	10060.2	6147.4	16126.8	10299.2	5827.6
Other diseases	585270.2	317302.3	267967.9	606535.8	326356.0	280179.8	599091.6	328305.3	270786.3	545767.0	307504.0	238263.0	538565.7	308257.0	230308.7	488966.5	281878.0	207088.5	496621.6	284543.5	212078.1
Respiratory disease	76566.2	44963.4	31602.9	78421.5	44881.9	33539.5	65325.4	37073.5	28251.8	71935.9	39481.2	32454.7	67161.8	38307.3	28854.5	60953.6	35971.2	24982.4	64535.3	37876.1	26659.2
Total	**1706654.5**	**948081.9**	**758572.6**	**1740902.6**	**953879.7**	**787022.8**	**1715481.2**	**945467.7**	**770013.5**	**1648927.3**	**900671.3**	**748256.1**	**1606807.3**	**897717.7**	**709089.6**	**1521952.7**	**854256.9**	**667695.8**	**1541498.7**	**862657.8**	**678840.9**

(continued)

Table 2. Disease specific SEYLLs for each country (continued)

The Russian Federation	2013			2014			2015			2016			2017			2018			2019		
	Both	**Male**	**Female**	**Both**	**Male**	**Female**	**Both**	**Male**	**Female**	**Both**	**Male**	**Female**	**Both**	**Male**	**Female**	**Both**	**Male**	**Female**	**Both**	**Male**	**Female**
Circulatory disease	13729788.4	6888841.3	6840947.1	13578375.9	6782012.9	6796363.0	14004204.8	7127141.8	6877063.0	14655093.2	7625787.6	7029305.6	13504392.4	7021029.5	6483362.9	15109757.8	8014791.8	7094965.9	13551852.2	6966126.4	6585725.8
Digestive disease	705163.1	488443.3	216719.8	1418640.3	845872.7	572767.5	1574274.4	943649.0	630625.4	1621839.4	978761.1	643078.3	1481256.9	881798.1	599458.8	1660931.1	1007255.2	653676.0	803055.8	559891.3	243164.5
Neoplasms	3484718.8	2311745.8	1172973.1	4193417.0	2404842.2	1788574.8	4563379.4	2656955.4	1906424.0	4871459.0	2886631.1	1984827.9	4624511.3	2721301.8	1903209.4	5181641.0	3104278.4	2077362.6	3769639.4	2623243.2	1146396.2
Other diseases	7334796.1	4312437.0	3022359.1	6765618.2	4089717.9	2675900.2	7638889.3	4505216.3	3133673.0	7806870.3	4483804.2	3323066.1	7369678.2	4107421.9	3262256.3	8252922.2	4683160.5	3569761.7	9648877.3	5112147.3	4536730.0
Respiratory disease	1069333.8	428566.9	640766.9	1171241.4	830763.1	340478.3	1206927.7	862211.2	344716.5	1193356.7	862416.3	330940.4	1018564.2	735008.0	283556.2	1145773.9	838083.8	307690.1	409514.0	292037.2	117476.9
Total	**26323800.3**	**14430034.3**	**11893765.9**	**27127292.8**	**14953208.9**	**12174083.9**	**28987675.6**	**16095173.7**	**12892501.8**	**30148618.6**	**16837400.4**	**13311218.2**	**27998402.9**	**15466559.3**	**12531843.6**	**31351026.1**	**17647569.7**	**13703456.4**	**28182938.8**	**15553445.3**	**12629493.5**

by the increase in digestive diseases, neoplasms and other diseases in the population (Table 2).

The subnational level data revealed a declining trend in Year-on-Year SEYLL across all regions in Belarus till 2017 but this was not so in most of the regions in France, SEYLL of Centre region in France increased noticeably in 2017 compared to the earlier years. Most of India registered a declining trend in SEYLL consistely albeit with an wide variations across Indian states. In Kyrgyzstan, Jalal-Abad oblast and Issyk-Kul oblast registered an increased SEYLL in the population from 2018 onwards (Table 3).

SEYLL per single death for the agegroup 35 years to 64 years was the highest in France (in 2017) for both the genders followed by India for male and in The Russian Federation for female in 2019. The lowest SEYLL per single death for the agegroup 35 years to 64 years was registered in Kazakhstan in 2013 but in 2019, although Kazakhstan stll had the same glory for the men, it was India for the women (Table 4).

When considered all the years, SEYLL per single death for the agegroup 15 years to 64 years was the highest in India for male, and in France for female. The lowest SEYLL per single death for the agegroup 15 years to 64 years was registered in Kazakhstan and remained so throughout this study period (Table 5). Keeping aside France, PVLE per SEYLL was the highest in Belarus for both the agegroups in 2018 and this was the lowest consistently for Kyrgyzstan (Table 4 and Table 5).

Overall total person-years of life lived after attaining age x for all agegroups (T_x) was positive across regions in Belarus except in Mogilev region (≅ –2%). The pattern did register almost uniform across states in India except in Chhattisgarh and Tamil Nadu where T_x was strikingly positive, and negative in Kerala in 2019 compared to the earlier years (Appendix: Table 1).

In 2019, the T_x for female in India did have a quantum positve leaps in Chhattisgarh (+4.7%), Jammu & Kashmir (+9%) and in Tamil Nadu (+3.17%), but negative T_x for male was the highest in Kerala (–2.57%) compared to the earlier years. The year-on-year T_x was consistently positve with some minor fluctuations across all regions in France and in Kyrgyzstan. Pays de la Loire region of France had the highest T_x (+6.50) in 2017 compared to the earlier years. The year-on-year T_x was consistently positve across all regions in the Russian Federation over the years except in Siberian federal district where it registered "negative" in 2019 (Appendix: Table 1).

Graph 1 presents that the countries followed consistently the similar trend over the years where SEYLL of working age was led by India followed by Russia, France and Kazakhstan in that order. SEYLL of working age in Belarus always remained low throughout over the years when SEYLL started increasing after the age of 44 years in France and such an increase became consistently higher from the age of 50 years for the remaining years of the working age. Graph 1 also confirmed that the pattern of SEYLL for different age groups remained consistent over the years in all the countries except in the Russian Federation.

In-country distribution of SEYLL was not static except for the agegroup 60 and 64 years in all the countries, and for all agegroups in Kazakhstan and also in France (Graph 2). SEYLL of agegroup 20–24 years increased consistently while that of agegroup 25–29 years decreased over the years in Belarus. SEYLL of 55 years and above, and that of agegroup 20–24 years together contributed maximum to the total SEYLL in India for all the years. SEYLL of agegroups 20–24 years and that of 50–59 years were having an upward trend in Kyrgyzstan. SEYLL of 55 years and below was increasing from 2017 onwards in the Russian Federation (Graph 2).

Graph 3 presents distribution of diseases and health disordes in the study countries. Belarus, Kyrgyzstan and The Russian Federation were having a relatively higher proportion of circulatory diseases, India and Kazakhstan were having relatively higher prevalence of respiratory diseases. Neoplasms were of concern in all the countries except in France. More than 30% of total diseases was not captured with an appropriate diagnosis in France, Kazakhstan, The Russian Federation and in Kyrgyzstan. Injuries were of significant proportion in Belarus, India, Kazakhstan and Kyrgyzstan (Graph 3).

The trend of the person years lived above age *x* registered an incremental upward trend in Kazakhstan and a consistent downward trend, in France. The position of the female in regard to the person years lived above age *x* was higher than the total in all the countries. T_x for all agegroups was highest in France for both the genders, T_x of male population for the agegroup 35–64 years was highest in India amongst the study countries.

DISCUSSION

This investigation of interwined relationship between the population health and the development unfolded three important insights.

First, the burden measured as SEYLL with the consequential trend of such burden was not aligned with the level of economic development of the country. We found that the disease specific SEYLL increased in France, Kazakhstan and the Russian Federation, on the contrary SEYLL decreased in Belarus and Kyrgyzstan during the study period. Furthermore, reduction of subnational level SEYLL was not uniform across all the regions in France. Moreover, more than 30% of total diseases were captured as "other diseases" without any appropriate diagnosis in the country statistics of France, Kazakhstan, The Russian Federation and in Kyrgyzstan indicating the absence of targeted allocation of health resources and so, the intervention for the population health development with sufficiency apparently remained unmeasured. This revealation also unfolded more of an apparent governance deficit where the health system was decentralised rather than the reasons attribuatbes to the constrained resources. Our findings from the Russian Federations supported the importance of primary healthcare approach where the gain in SEYLL was offset by increasing digestive diseases, neoplasms and other diseases.

Our measure of the total time lived beyond age *x* for each age group had assessed the mortality pattern that prevailed across all age groups. Thus, we captured effectiveness of the measures for population health development at the subnationation level for each country. Our finding of a negatve T_x in 2019 compared to the earlier years in one of the states in India, Kerala suggested that an overall better health indices could not ensure more person years of life beyond age *x*. Here, the evidence from Pays de la Loire and Provence-Alpes Côte d'Azur regions of France, Jammu & Kashmir states of India, and Siberian federal district of the Russian Federation further supported that the positive influence of living environment and individual behaviour add years to life [39]. Olejnik and Żółtaszek [40] argued that after crossing the health economic threshold of around 20 thousand euros per capita, the trend changes by stabilising or reversing. So, a consistent downward trend in T_x of France was in alignment with the notion of mortality rising with prosperity. Here, this empirics from France and India further confirm that higher T_x is associated with higher income of the country, and also with labour force participation of the population. Moreover, our computation of T_x provided a practical approach of establishing the relationship between life expectancy and economic growth [41, 42].

Second, our measure of SEYLL captured the obvious gap between the appropriateness of healthcare service provision and other objectives of the national health systems like acceesibility and affordability. Although the typology of the health systems was diverse, the acceesibility and the affordability principles were at the core of every health system in the study countries. SEYLL per single death was highest for all the years in France compared to other countries in the study. India, a country with a mixed health system and a high out-of-pocket health expenditure demonstrated a widespread reduction of SEYLL albeit differences existed across Indian states in recent years.

Our third empirical finding was that the cumulative percentage loss of PVLE per SEYLL mostly exceeded cumulative GDP per capita growth of the corresponding years. Between 2013 and 2018, the cumulative PVLE per SEYLL for the population of agegroup 35–64 years increased by 55.6% in Belarus; between 2011 and 2017, 53.1% in France, 8.5% in India, 40.5% in Kazakhstan, 157.5% in Kyrgyzstan; and between 2013 and 2019, 77.9% in the Russian Federation while the cumulative GDP per capita growth during the same period was 0.9% in Belarus, 4% in France, 38.4% in India, 11% in Kazakhstan, 13.5% in Kyrgyzstan, and 3.5% in the Russian Federation (World Bank, 2022). The

Table 3. Region specific SEYLLs (male, female and total) for each country with year-on-year change in percentage

Belarus		**SEYLL**			**Year-on-Year (%) change**		
Region	**Year**	**Male**	**Female**	**Both**	**Male**	**Female**	**Both**
Brest Region	2013	151043.8	155351.6	306395.4	-	-	-
	2014	147449.8	152441.2	299891.1	–2.38	–1.87	–2.12
	2015	139440.4	150512.6	289953	–5.43	–1.27	–3.31
	2016	138462	144900	283362.1	–0.7	–3.73	–2.27
	2017	136058.2	144576	280634.2	–1.74	–0.22	–0.96
	2018	137979.6	146024.1	284003.6	1.41	1	1.20
Vitebsk region	2013	143021.3	157023.4	300044.7	–	–	–
	2014	139768.6	151295.3	291063.9	–2.27	–3.65	–2.99
	2015	133167.7	147083.8	280251.6	–4.72	–2.78	–3.71
	2016	128489.2	144664.6	273153.8	–3.51	–1.64	–2.53
	2017	125143.8	140847	265990.9	–2.6	–2.64	–2.62
	2018	126749	140216.7	266965.7	1.28	–0.45	0.37
Gomel region	2013	162430.8	172405.4	334836.2	–	–	–
	2014	157450.8	166921.4	324372.3	–3.07	–3.18	–3.13
	2015	153240.7	161858	315098.7	–2.67	–3.03	–2.86
	2016	145840.6	157952.9	303793.5	–4.83	–2.41	–3.59
	2017	144288	154380.3	298668.4	–1.06	–2.26	–1.69
	2018	145082.1	153611.2	298693.3	0.55	–0.5	0.01
Grodno region	2013	121538.4	131895.8	253434.2	–	–	–
	2014	115118.9	126734	241852.9	–5.28	–3.91	–4.57
	2015	113084.5	121744.9	234829.4	–1.77	–3.94	–2.9
	2016	107776.8	122708.4	230485.1	–4.69	0.79	–1.85
	2017	105248.4	118869.7	224118	–2.35	–3.13	–2.76
	2018	109169.9	118523.8	227693.7	3.73	–0.29	1.6
Minsk city	2013	170178.6	178937.1	349115.7	–	–	–
	2014	170313	180911.3	351224.3	0.08	1.10	0.6
	2015	161278.4	173673.8	334952.1	–5.3	–4	–4.63
	2016	161623	164997.2	326620.3	0.21	–5	–2.49
	2017	154693.4	173084.1	327777.5	–4.29	4.9	0.35
	2018	157624.3	176132.4	333756.7	1.89	1.76	1.82
Minsk region	2013	173691	178482.9	352173.9	–	–	–
	2014	170809	174578	345387	–1.66	–2.19	–1.93
	2015	160806.7	168431.3	329238	–5.86	–3.52	–4.68
	2016	161623	164997.2	326620.3	0.51	–2.04	–0.80
	2017	157398.8	164282.5	321681.3	–2.61	–0.43	–1.51
	2018	160899.2	166018.2	326917.4	2.22	1.06	1.63
Mogilev region	2013	125187.4	129886.4	255073.8	–	–	–
	2014	120021.2	125110.7	245131.9	–4.13	–3.68	–3.9
	2015	114865.8	119028.2	233894	–4.3	–4.86	–4.58
	2016	111485.4	118047.6	229533	–2.94	–0.82	–1.86
	2017	109022.1	117086.8	226108.9	–2.21	–0.81	–1.49
	2018	113574	117001.8	230575.8	4.18	–0.07	1.98

(*continued*)

Table 3. Region specific SEYLLs (male, female and total) for each country with year-on-year change in percentage (continued)

France		SEYLL			Year-on-Year (%) change		
	Region	Year	Male	Female	Both	Male	Female
Ile-de-France	2011	995675.4	799498.4	1795173.9	–	–	–
	2012	997502.9	791361.1	1788864	0.18	–1.02	–0.35
	2013	994030.7	794918.6	1788949.4	–0.35	0.45	0
	2014	988709.7	794789.7	1783499.4	–0.54	–0.02	–0.3
	2017	945564.5	797415.8	1742980.2	–1.45	0.11	–0.76
Centre	2011	267395.8	205064.2	472460	–	–	–
	2012	266322.9	201829.6	468152.4	–0.4	–1.58	–0.91
	2013	264348	203514.9	467863	–0.74	0.84	–0.06
	2014	267366.4	204675.8	472042.2	1.14	0.57	0.89
	2017	346933.8	255544	602477.8	9.92	8.28	9.21
Pays de la Loire	2011	345511.5	251504.9	597016.4	–	–	–
	2012	345710.1	255544.7	601254.8	0.06	1.61	0.71
	2013	346898.9	256974.3	603873.1	0.34	0.56	0.44
	2014	350124.4	260330.9	610455.3	0.93	1.31	1.09
	2017	362993.5	271947	634940.5	1.23	1.49	1.34
Bretagne	2011	342728	249952.4	592680.4	–	–	–
	2012	344834	251214.9	596048.9	0.61	0.51	0.57
	2013	346898.9	256974.3	603873.1	0.6	2.29	1.31
	2014	348366.8	254019	602385.7	0.42	–1.15	–0.25
	2017	355694.1	269415.3	625109.4	0.7	2.02	1.26
Provence-Alpes-Côte d'Azur	2011	484279.2	392738.2	877017.5	–	–	–
	2012	485503.3	392206.2	877709.5	0.25	–0.14	0.08
	2013	486129.3	392757.4	878886.7	0.13	0.14	0.13
	2014	487307.2	393327.2	880634.3	0.24	0.15	0.2
	2017	504782	413215.7	917997.7	1.2	1.69	1.41
Corse	2011	33853.1	25341.2	59194.3	–	–	–
	2012	33395.2	25069.9	58465	–1.35	–1.07	–1.23
	2013	34103	24830	58933	2.12	–0.96	0.8
	2014	33704.4	25091.7	58796.2	–1.17	1.05	–0.23
	2017	36973.1	25203.6	62176.8	3.23	0.15	1.92

India		SEYLL			Year-on-Year (%) change		
State	Year	Male	Female	Both	Male	Female	Both
Andrah Pradesh	2013	9647195.5	7662377	17388954.3	–	–	–
	2014	8586020.1	7551766.4	16177190	–11	–1.44	–6.97
	2015	9056171.2	7890587.2	16990941.4	5.48	4.49	5.03
	2016	9090856.3	7422166.3	16543158.6	0.38	–5.94	–2.64
	2017	9579235.1	7097271.9	16711472.2	5.37	–4.38	1.02
	2018	9160844.9	7337457.8	16558633.9	–4.37	3.38	–0.91
	2019	8657522.2	6907446.5	15638526.8	–5.49	–5.86	–5.56

(continued)

Table 3. Region specific SEYLLs (male, female and total) for each country with year-on-year change in percentage (continued)

India		SEYLL			Year-on-Year (%) change		
State	Year	Male	Female	Both	Male	Female	Both
Assam	2013	4113177.1	3740149.5	7852847.6	–	–	–
	2014	3900670.3	3510946.4	7424580.9	–5.17	–6.13	–5.45
	2015	3871331.3	3152664.1	7032145.8	–0.75	–10.2	–5.29
	2016	3781886.8	3329588.7	7114352.6	–2.31	5.61	1.17
	2017	3699998.8	3161777.3	6868838.2	–2.17	–5.04	–3.45
	2018	3350442.3	3025196.4	6366121.2	–9.45	–4.32	–7.32
	2019	3173160.6	2944864.6	6114838.3	–5.29	–2.66	–3.95
Bihar	2013	11668846.5	10746694.9	22415541.4	–	–	–
	2014	11383768.6	9800361.9	21184130.5	–2.44	–8.81	–5.49
	2015	11064435.4	10237011.4	21301446.7	–2.81	4.46	0.55
	2016	9205402.6	9139507.5	18344910.1	–16.8	–10.72	–13.88
	2017	9697548.2	8354508.7	18052057	5.35	–8.59	–1.6
	2018	9011614.8	8201736.8	17213351.6	–7.07	–1.83	–4.65
	2019	8359695.3	8081957.1	16441652.4	–7.23	–1.46	–4.48
Chhattisgarh	2013	2917877.4	3019471.4	5937348.8	–	–	–
	2014	2707280.1	2319953.7	5001131.9	–7.22	–23.17	–15.77
	2015	2712592.3	2596032.7	5308624.9	0.2	11.9	6.15
	2016	2934064.9	2707123.8	5641188.7	8.16	4.28	6.26
	2017	3064634.1	2593018.9	5657653.1	4.45	–4.21	0.29
	2018	2975684.8	2542776.9	5518461.7	–2.9	–1.94	–2.46
	2019	2996849.8	2382353	5379202.8	0.71%	–6.31	–2.52
Delhi	2013	1274937.7	977976.8	2252914.5	–	–	–
	2014	1269704.7	830434.4	2100139.1	–0.41	–15.09	–6.78
	2015	1017526.4	825925.7	1843452.1	–19.86	–0.54	–12.22
	2016	1185832.1	825861.3	2011693.4	16.54	–0.01	9.13
	2017	1073393.7	908131.2	1981524.9	–9.48	9.96	–1.5
	2018	1022090.3	768126.2	1790216.5	–4.78	–15.42	–9.65
	2019	911567.7	726028.1	1637595.8	–10.81	–5.48	–8.53
Gujarat	2013	6792808.5	5185393.3	11978201.8	–	–	–
	2014	6068714.4	5119077.1	11187791.5	–10.66	–1.28	–6.6
	2015	6192094.3	5146233.5	11338327.8	2.03	0.53	1.35
	2016	5917648.7	4728460.7	10646109.4	–4.43	–8.12	–6.11
	2017	5989225.9	4495293	10484518.9	1.21	–4.93	–1.52
	2018	5918697.5	4441468.6	10360166	–1.18	–1.2	–1.19
	2019	5389407.9	4440003.8	9829411.7	–8.94	–0.03	–5.12
Haryana	2013	2933474.1	2190240.8	5123714.9	–	–	–
	2014	2520524.3	1978907.3	4499431.7	–14.08	–9.65	–12.18
	2015	2736181.3	2070355.6	4806536.9	8.56	4.62	6.83
	2016	2693441.7	2147863.4	4841305.1	–1.56	3.74	0.72
	2017	2744666.5	1938650.2	4683316.7	1.9	–9.74	–3.26
	2018	2821468.3	1970448	4791916.3	2.8	1.64	2.32
	2019	2558316.8	1777529.2	4335846	–9.33	––9.79	–9.52

(continued)

Table 3. Region specific SEYLLs (male, female and total) for each country with year-on-year change in percentage (continued)

India		SEYLL			Year-on-Year (%) change		
State	**Year**	**Male**	**Female**	**Both**	**Male**	**Female**	**Both**
Himachal Pradesh	2013	665286.1	602475.3	1267761.3	–	–	–
	2014	748496.6	504490.6	1252987.2	12.51	–16.26	–1.17
	2015	779015.9	469428.7	1248444.6	4.08	–6.95	–0.36
	2016	658162.1	516893.5	1175055.6	–15.51	10.11	–5.88
	2017	614685.8	405511.7	1020197.6	–6.61	–21.55	–13.18
	2018	637489.6	437606.8	1075096.4	3.71	7.91	5.38
	2019	676534.7	438523.5	1115058.2	6.12	0.21	3.72
Jammu & Kashmir	2013	1174685.5	972277.3	2146962.7	–	–	–
	2014	1199276.5	966328.4	2165604.9	2.09	–0.61	0.87
	2015	1097888.8	863218.4	1961107.2	–8.45	–10.67	–9.44
	2016	1117865.2	923058.2	2040923.4	1.82	6.93	4.07
	2017	1214953.2	829052.2	2044005.4	8.69	–10.18	0.15
	2018	1153997.6	827517.8	1981515.4	–5.02	–0.19	–3.06
	2019	1130893.1	939259.6	2070152.7	–2	13.5	4.47
Jharkhand	2013	3346762.8	3292720.2	6639483	–	–	–
	2014	3322389.2	3225748.7	6548138	–0.73	–2.03	–1.38
	2015	3032832.2	2802318.6	5835150.8	–8.72	–13.13	–10.89
	2016	2842862.8	2892179.8	5735042.6	–6.26	3.21	–1.72
	2017	2739836.3	2649777.4	5389613.7	–3.62	–8.38	–6.02
	2018	2684190	2669799.5	5353989.5	–2.03	0.76	–0.66
	2019	2692781	2488808.6	5181589.6	0.32	–6.78	–3.22
Karnataka	2013	6001477.7	5154909.4	11156387.1	–	–	–
	2014	5480796.3	4777686.3	10258482.6	–8.68	–7.32	–8.05
	2015	5525719.4	4739172.3	10264891.8	0.82	–0.81	0.06
	2016	5848363.3	4608079.1	10456442.4	5.84	–2.77	1.87
	2017	6107255.7	4417226.8	10524482.5	4.43	–4.14	0.65
	2018	5691168	4424928.9	10116097	–6.81	0.17	–3.88
	2019	5493033	4327879.6	9820912.6	–3.48	–2.19	–2.92
Kerala	2013	2495065.1	1875337.5	4370402.6	–	–	–
	2014	2361179.4	2383963.7	4745143.1	–5.37	27.12	8.57
	2015	2435127.3	2222337.7	4657465	3.13	–6.78	–1.85
	2016	2426340.9	1958275.6	4384616.4	–0.36	–11.88	–5.86
	2017	2315136.4	1728622.6	4043759	–4.58	–11.73	–7.77
	2018	2319914.2	1842651.8	4162566	0.21	6.6	2.94
	2019	2541272.3	2119085.3	4660357.7	9.54	15	11.96
Madhya Pradesh	2013	10344856.1	9003313.4	19348169.5	–	–	–
	2014	9706767.5	8985873.1	18692640.6	–6.17	–0.19	–3.39
	2015	9583740.4	8324821.8	17908562.2	–1.27	–7.36	–4.19
	2016	9756233.8	7175373.7	16931607.5	1.8	–13.81	–5.46
	2017	9751972.4	7236050.4	16988022.7	–0.04	0.85	0.33
	2018	9500957.7	6908276	16409233.6	–2.57	–4.53	–3.41
	2019	9196668.1	6932284.5	16128952.7	–3.2	0.35	–1.71

(*continued*)

Table 3. Region specific SEYLLs (male, female and total) for each country with year-on-year change in percentage (continued)

India		SEYLL			Year-on-Year (%) change		
State	**Year**	**Male**	**Female**	**Both**	**Male**	**Female**	**Both**
Maharashtra	2013	9715847.8	7329654.8	17045502.6	–	–	–
	2014	9979797	7666835.5	17646632.5	2.72	4.6	3.53
	2015	10042200.9	7780388	17822588.9	0.63	1.48	1
	2016	9538337.3	7345259.2	16883596.5	–5.02	–5.59	–5.27
	2017	9043802.6	6735928.1	15779730.7	–5.18	–8.3	–6.54
	2018	9757863.2	6878231.2	16636094.4	7.9	2.11	5.43
	2019	9593292.1	7077425.8	16670717.9	–1.69	2.9	0.21
Odisha	2013	5342276.2	4961907.6	10304183.9	–	–	–
	2014	5144443	4689273.5	9833716.5	–3.7	–5.49	–4.57
	2015	5091702.8	4470563.9	9562266.6	–1.03	–4.66	–2.76
	2016	4932993	4189238.2	9122231.1	–3.12	–6.29	–4.6
	2017	5102825.4	4249589.5	9352415	3.44	1.44	2.52
	2018	5116801.6	4060684.3	9177485.9	0.27	–4.45	–1.87
	2019	5020499.5	4193078.2	9213577.7	–1.88	3.26	0.39
Punjab	2013	2535636.6	1993915.9	4529552.4	–	–	–
	2014	2602343.3	2283958.6	4886301.9	2.63	14.55	7.88
	2015	2867021.6	2181841.7	5048863.3	10.17	–4.47	3.33
	2016	2866771.9	2195972.1	5062744.1	–0.01	0.65	0.27
	2017	3196995.7	2158423.7	5355419.4	11.52	–1.71	5.78
	2018	3031813.5	2005565.2	5037378.8	–5.17	–7.08	–5.94
	2019	2891845.5	1997439.7	4889285.1	–4.62	–0.41	–2.94
Rajasthan	2013	7984832.8	7192180.6	15177013.4	–	–	–
	2014	7949321.6	6501305.9	14450627.5	–0.44	–9.61	–4.79
	2015	7346575.6	6491631	13838206.7	–7.58	–0.15	–4.24
	2016	7416322.1	6072308.5	13488630.6	0.95	–6.46	–2.53
	2017	7259910.9	5821962.1	13081872.9	–2.11	–4.12	–3.02
	2018	7178684.9	5837994.8	13016679.7	–1.12	0.28	–0.5
	2019	6816587.9	5935366.9	12751954.8	–5.04	1.67	–2.03
Tamil Nadu	2013	6897526.8	5408471.9	12305998.8	–	–	–
	2014	5831293.5	4965058	10796351.4	–15.46	–8.2	–12.27
	2015	6248949	5188153.6	11437102.6	7.16	4.49	5.93
	2016	6251447.4	4848595.4	11100042.8	0.04	–6.54	–2.95
	2017	6953777.8	4845094.4	11798872.1	11.23	–0.07	6.3
	2018	7229494.9	4897889.5	12127384.4	3.96	1.09	2.78
	2019	7030066.1	4685984.8	11716050.9	–2.76	–4.33	–3.39
Telengana	2014	3299576.3	2781720	6081296.2	–	–	–
	2015	3225247.7	2842340.7	6067588.4	–2.25	2.18	–0.23
	2016	3531005.6	2780146.7	6311152.3	9.48	–2.19	4.01
	2017	3495546.2	2579881.9	6075428.1	–1	–7.2	–3.74
	2018	3470043.3	2645299.8	6115343.1	–0.73	2.54	0.66
	2019	3230579.1	2579943.9	5810523	–6.9	–2.47	–4.98

(continued)

Table 3. Region specific SEYLLs (male, female and total) for each country with year-on-year change in percentage (continued)

India		SEYLL			Year-on-Year (%) change		
State	**Year**	**Male**	**Female**	**Both**	**Male**	**Female**	**Both**
Uttar Pradesh	2013	26290753.8	24622375.7	50913129.5	–	–	–
	2014	23438412.7	22319158.5	45757571.2	–10.85	–9.35	–10.13
	2015	23205163.4	21824006.7	45029170	–1	–2.22	–1.59
	2016	23438760.2	20637863.9	44076624.1	1.01	–5.44	–2.12
	2017	23217601.4	21947180	45164781.3	–0.94	6.34	2.47
	2018	22452016.5	19697869.1	42149885.6	–3.3	–10.25	–6.68
	2019	21881326.7	19968442.3	41849769	–2.54	1.37	–0.71
Uttarakhand	2014	96016.8	88534.1	184550.9	–	–	–
	2015	109178	88169.4	197347.4	13.71	–0.41	6.93
	2016	116498.4	85202.5	201701	6.71	–3.36	2.21
	2017	114155	83410.8	197565.8	–2.01	–2.1	–2.05
	2018	106613.8	83482.3	190096.1	–6.61	0.09	–3.78
	2019	100942.8	79316.9	180259.7	–5.32	–4.99	–5.17
West Bengal	2013	7519628.3	6369617.6	13889245.9	–	–	–
	2014	7320959.5	6393660.9	13714620.4	–2.64	0.38	–1.26
	2015	7656556.1	6649618.3	14306174.4	4.58	4	4.31
	2016	7620128.5	6115381	13735509.5	–0.48	–8.03	–3.99
	2017	7557451.5	6355476.6	13912928.1	–0.82	3.93	1.29
	2018	7541341	5666258	13207599	–0.21	–10.84	–5.07
	2019	7576412.2	5602380.5	13178792.7	0.47	–1.13	–0.22

Kyrgyzstan	SEYLL				Year-on-Year (%) change		
Region	**Year**	**Male**	**Female**	**Both**	**Male**	**Female**	**Both**
Batken oblast	2013	77556.3	71827.6	149383.8	–	–	–
	2014	76685.2	64910.5	141595.7	–1.12	–9.63	–5.21
	2015	74959.5	67271.7	142231.3	–2.25	3.64	0.45
	2016	73439.4	62190.5	135629.9	–2.03	–7.55	–4.64
	2017	73432.9	63455.1	136888	–0.01	2.03	0.93
	2018	65113.2	53167.8	118281	–11.33	–16.21	–13.59
	2019	72048	62474.5	134522.4	–1.89	–1.55	13.73
Bishkek city	2013	146650.1	113130.9	259781	–	–	–
	2014	159668.6	139981.4	299649.9	8.88	23.73	15.35
	2015	154946.7	141397.4	296344.1	–2.96	1.01	–1.1
	2016	161163.3	132192.2	293355.5	4.01	–6.51	–1.01
	2017	168558.6	135765.9	304324.5	4.59	2.7	3.74
	2018	161940.8	132635.9	294576.8	–3.93	–2.31	–3.2
	2019	151029.1	125724.9	276754	–10.4	–7.4	–6.05
Chuy oblast	2013	142179.5	111869.4	254049	–	–	–
	2014	135056.3	109834.2	244890.5	–5.01	–1.82	–3.61
	2015	138078.3	101559.5	239637.8	2.24	–7.53	–2.14
	2016	129244	108581.3	237825.3	–6.4	6.91	–0.76
	2017	119429.9	98755.9	218185.9	–7.59	–9.05	–8.26
	2018	120305.6	94946.3	215252	0.73	–3.86	–1.34
	2019	123937.9	95373.4	219311.3	3.77	–3.43	1.89

(*continued*)

Table 3. Region specific SEYLLs (male, female and total) for each country with year-on-year change in percentage (continued)

Kyrgyzstan	SEYLL				Year-on-Year (%) change		
Region	Year	Male	Female	Both	Male	Female	Both
Issyk–Kul oblast	2013	74871.1	58444.9	133316.1	–	–	–
	2014	73422.7	49506.7	122929.4	–1.93	–15.29	–7.79
	2015	74415.1	57232.2	131647.3	1.35	15.6	7.09
	2016	57346.4	57430.1	114776.5	–22.94	0.35	–12.82
	2017	69621.5	46469	116090.5	21.41	–19.09	1.14
	2018	67364.6	47627	114991.6	–3.24	2.49	–0.95
	2019	75596.6	55015.5	130612.1	8.58	18.39	13.58
Jalal–Abad oblast	2013	160080.7	141510.5	301591.2	–	–	–
	2014	172819.3	147377	320196.3	7.96	4.15	6.17
	2015	173019.1	143323.4	316342.6	0.12	–2.75	–1.2
	2016	168429.5	141265	309694.6	–2.65	–1.44	–2.1
	2017	160810	125450.2	286260.2	–4.52	–11.2	–7.57
	2018	145528.7	124028	269556.7	–9.5	–1.13	–5.84
	2019	147641.3	128830.8	276472.1	–8.19	2.69	2.57
Naryn oblast	2013	49748.5	33650.3	83398.8	–	–	–
	2014	47439	41720.8	89159.8	–4.64	23.98	6.91
	2015	47503	27730.6	75233.6	0.13	–33.53	–15.62
	2016	44277.4	31590.7	75868.2	–6.79	13.92	0.84
	2017	44061.5	32904.8	76966.3	–0.49	4.16	1.45
	2018	39492.2	29008	68500.2	–10.37	–11.84	–11
	2019	36143.8	26704.6	62848.4	–17.97	–7.94	–8.25
Osh city	2013	81728.2	63464.9	145193.1	–	–	–
	2014	84117.5	76541.4	160658.9	2.92	20.6	10.65
	2015	84712.9	82841.7	167554.5	0.71	8.23	4.29
	2016	84225.1	66567.5	150792.6	–0.58	–19.64	–10
	2017	82870.2	62145.2	145015.4	–1.61	–6.64	–3.83
	2018	66143.2	51074.6	117217.7	–20.18	–17.81	–19.17
	2019	72058.7	54343.4	126402.1	–13.05	6.4	7.84
Osh oblast	2013	163058.7	129561.1	292619.8	–	–	–
	2014	156200.4	122988.6	279189	–4.21	–5.07	–4.59
	2015	154542.5	124883.7	279426.2	–1.06	1.54	0.08
	2016	143017.2	115451.2	258468.3	–7.46	–7.55	–7.5
	2017	143134.2	114580	257714.1	0.08	–0.75	–0.29
	2018	142163.3	103524.8	245688.1	–0.68	–9.65	–4.67
	2019	143839.5	97881.1	241720.6	0.49	–5.45	–1.61
Talas oblast	2013	52208.8	35112.9	87321.7	–	–	–
	2014	48470.7	34162.3	82633	–7.16	–2.71	–5.37
	2015	43290.6	23773.2	67063.8	–10.69	–30.41	–18.84
	2016	39528.9	32987.5	72516.4	–8.69	38.76	8.13
	2017	35798.8	29563.5	65362.3	–9.44	–10.38	–9.87
	2018	46205.3	31683.4	77888.7	29.07	7.17	19.16
	2019	40362.9	32492.7	72855.6	–12.64	2.55	–6.46

(continued)

Table 3. Region specific SEYLLs (male, female and total) for each country with year-on-year change in percentage (continued)

The Russian Federation		SEYLL			Year-on-Year (%) change		
Region	**Year**	**Male**	**Female**	**Both**	**Male**	**Female**	**Both**
Central Federal District	2013	4639607.9	3729004	8368611.5	–	–	–
	2014	4679760.1	3721784	8401543.9	0.87	–0.19	0.39
	2015	4500201.1	3695434	8195635.5	–3.84	–0.71	–2.45
	2016	4431723.1	3678614	8110337.5	–1.52	–0.46	–1.04
	2017	4288077.9	3593321	7881399.1	–3.24	–2.32	–2.82
	2018	4337293.8	3601275	7938568.8	1.15	0.22	0.73
	2019	4312731.2	3559796	7872527	0.57	–0.93	–0.11
Far Eastern Federal District	2013	820547.5	585538.7	1406086.2	–	–	–
	2014	805215	582787.5	1388002.5	–1.87	–0.47	–1.29
	2015	772926.3	574215.6	1347141.9	–4.01	–1.47	–2.94
	2016	758291.5	559594.8	1317886.3	–1.89	–2.55	–2.17
	2017	720247.8	539152.2	1259400	–5.02	–3.65	–4.44
	2018	707440.4	548780.5	1256220.9	–1.78	1.79	–0.25
	2019	711759.9	547430.4	1259190.3	–1.18	1.54	–0.02
North Caucasian Federal District	2013	788356.7	588795.5	1377152.2	–	–	–
	2014	799646.1	587681.7	1387327.8	1.43	–0.19	0.74
	2015	779189.5	574286.2	1353475.7	–2.56	–2.28	–2.44
	2016	761016.4	571327.2	1332343.6	–2.33	–0.52	–1.56
	2017	729640.9	555522	1285162.8	–4.12	–2.77	–3.54
	2018	730546.4	546377.1	1276923.5	0.12	–1.65	–0.64
	2019	723301.5	552346.7	1275648.2	–0.87	–0.57	–0.74
Northwestern Federal District	2013	1626256.6	1353970	2980226.5	–	–	–
	2014	1644594.3	1363964	3008558.1	1.13	0.74	0.95
	2015	1621803.2	1364189	2985992	–1.39	0.02	–0.75
	2016	1590903.4	1349673	2940576	–1.91	–1.06	–1.52
	2017	1532389	1305069	2837457.7	–3.68	–3.3	–3.51
	2018	1534703	1304842	2839544.9	0.15	–0.02	0.07
	2019	1520187	1302697	2822884	–0.8	–0.18	–0.51
Siberian federal district	2013	2298602.3	1737131	4035733.3	–	–	–
	2014	2302938.9	1752662	4055600.6	0.19	0.89	0.49
	2015	2281186	1741553	4022739.1	–0.94	–0.63	–0.81
	2016	2232454	1723807	3956261.3	–2.14	–1.02	–1.65
	2017	2108719.7	1644951	3753670.8	–5.54	–4.57	–5.12
	2018	2066546.8	1646517	3713063.8	–2	0.1	–1.08
	2019	2192386.3	1798531	3990917.4	3.97	9.34	6.32
Southern Federal District	2013	1589816.3	1260857	2850672.9	–	–	–
	2014	1613044.3	1267774	2880818.4	1.46	0.55	1.06
	2015	1581225.9	1268017	2849242.5	–1.97	0.02	–1.1
	2016	1559811.1	1257046	2816856.8	–1.35	–0.87	–1.14
	2017	1502097	1214283	2716379.5	–3.7	–3.4	–3.57
	2018	1483341.1	1209627	2692968.1	–1.25	–0.38	–0.86
	2019	1496343	1197567	2693909.6	–0.38	–1.38	–0.83

(continued)

Table 3. Region specific SEYLLs (male, female and total) for each country with year-on-year change in percentage (continued)

The Russian Federation		**SEYLL**			**Year-on-Year (%) change**		
Region	**Year**	**Male**	**Female**	**Both**	**Male**	**Female**	**Both**
Ural federal district	2013	1462337.1	1103712	2566049.1	–	–	–
	2014	1468853.5	1115459	2584312.3	0.45	1.06	0.71
	2015	1458661.5	1110094	2568755.6	–0.69	–0.48	–0.6
	2016	1430729.2	1101194	2531922.8	–1.91	–0.8	–1.43
	2017	1354693.9	1053013	2407707.3	–5.31	–4.38	–4.91
	2018	1331973.5	1056214	2388187.8	–1.68	0.3	–0.81
	2019	1309386.7	1031217	2340603.6	–3.34	–2.07	–2.79
Volga Federal District	2013	3710287.3	2882399	6592686.1	–	–	–
	2014	3707978.2	2891838	6599815.7	–0.06	0.33	0.11
	2015	3588095.2	2832192	6420287	–3.23	–2.06	–2.72
	2016	3463560.8	2770993	6234553.9	–3.47	–2.16	–2.89
	2017	3283715.3	2677954	5961669.6	–5.19	–3.36	–4.38
	2018	3258697.8	2666487	5925185	–0.76	–0.43	–0.61
	2019	3210629.4	2610712	5821341.4	–2.23	–2.51	–2.35

Table 4. $SEYLL_d$ (male, female and total) for the age range 35 years to 64 years and the present value of lost earnings (PVLE) for each country over the years

					Productivity losses					
		$SEYLL_d$			**PVLE (million USD PPP 2017)**			**PVLE/SEYLL (USD per SEYLL)**		
Country	**Year**	**Male**	**Female**	**Both**	**Male**	**Female**	**Both**	**Male**	**Female**	**Both**
Belarus	2013	20.99	28.43	23.04	1431.8	580.82	2012.62	2616.03	2060.76	3677.25
	2014	21.11	28.79	23.22	1367.98	562	1929.98	2591.62	2062.74	4654.36
	2015	21.15	28.33	23.08	1357.12	530.84	1887.97	2679.22	2123.84	4803.06
	2016	21.06	28.36	23.06	1302.38	530.69	1833.07	2679.13	2138.70	4817.83
	2017	20.91	28.09	22.87	1344.55	524.81	1869.36	2810.98	2182.73	4993.71
	2018	20.94	28.11	22.89	1589.87	610.9	2200.77	3232.72	2488.57	5721.28
France	2011	29.4	35.54	31.36	31484.82	15874.43	47359.25	9788.10	8735.17	14723.19
	2012	29.22	35.36	31.17	33582.45	16854.92	50437.37	10357.33	9234.74	19592.07
	2013	29.09	35.23	31.04	34853.37	17673.45	52526.82	10744.92	9666.42	20411.34
	2014	29.01	35.17	30.97	35456.36	18214.69	53671.05	10889.38	9909.76	20799.14
	2017	29.61	35.47	31.51	38081.64	19905.68	57987.33	11800.97	10742.60	22543.57
India	2013	24.79	26.58	25.47	60705.11	13323.23	74028.34	1469.09	489.79	1958.88
	2014	24.88	26.29	25.47	53536.72	12969.95	66506.66	1398.23	452.65	1850.89
	2015	30.74	34.19	32.15	64119.13	15308.88	79428.01	1583.38	493.97	2077.36
	2016	24.64	26.39	25.31	65175.81	13642.24	78818.05	1522.54	479.31	2001.85
	2017	25.01	26.55	25.59	68982.29	12926.17	81908.46	1595.20	463.79	2059
	2018	24.57	26.09	25.16	65347.34	12131.19	77478.54	1571.89	437.76	2009.65
	2019	26.21	24.59	25.25	45758.79	20106.94	65865.74	1611.97	512.94	2124.90

(*continued*)

Table 4. $SEYLL_d$ (male, female and total) for the age range 35 years to 64 years and the present value of lost earnings (PVLE) for each country over the years (continued)

					Productivity losses					
		$SEYLL_d$			PVLE (million USD PPP 2017)			PVLE/SEYLL (USD per SEYLL)		
Country	Year	Male	Female	Both	Male	Female	Both	Male	Female	Both
Kazakhstan	2013	16.57	20.3	18.43	1072.27	1095.28	2167.56	1410.21	1175.40	2850.67
	2014	17.13	20.97	19.05	1103.89	1118.51	2222.4	1403.76	1162.19	2565.95
	2015	18.95	22.94	20.95	1197.63	1189.73	2387.36	1376.89	1129.72	2506.61
	2016	19.3	23.21	21.26	1184.16	1173.82	2357.98	1336.90	1101.59	2438.48
	2017	19.7	23.58	21.64	1205.47	1194.31	2399.78	1333.12	1103.57	2436.69
	2018	21.49	25.62	23.56	1475.02	1460.22	2935.24	1495.12	1241.81	2736.94
	2019	21.78	26.01	23.9	2182.25	2177.24	4359.49	2182.48	1823.87	4006.35
Kyrgyzstan	2013	24.16	28.36	25.52	58.55	20.46	79	295.06	183.91	398.16
	2014	23.57	27.77	24.91	58.08	20.81	78.89	300.52	193.39	493.91
	2015	27.64	32.26	29.13	60.9	22.32	83.23	316.02	202.26	518.28
	2016	24.22	28.1	25.51	66.78	24.21	90.98	360.52	225.82	586.34
	2017	24.36	28.74	25.79	78.9	27.48	106.38	412.23	251.13	663.37
	2018	24.82	28.81	26.11	111.07	38.02	149.09	570.16	351.77	921.93
	2019	24.58	28.83	25.96	121.96	43.32	165.28	627.37	398	1025.38
The Russian Federation	2013	21.47	28.08	23.44	12168.25	5422.31	17590.56	1504.59	1211.69	2716.28
	2014	22.05	28.41	23.94	12693.72	5557.32	18251.04	1531.66	1229.48	2761.14
	2015	25.79	33.1	27.83	13264.92	5721.6	18986.52	1482.19	1191.27	2673.46
	2016	22.28	28.43	24.1	17139.78	7323.92	24463.7	1844.58	1484.05	3328.64
	2017	22.57	28.56	24.34	18361.68	7747.66	26109.34	1916.01	1536.93	3452.94
	2018	22.8	28.65	24.52	26760.39	11235.28	37995.67	2779.43	2235.06	5014.48
	2019	23.05	29.19	24.89	23025.33	10109.44	33134.77	2674.30	2158.47	4832.77

Table 5. $SEYLL_d$ (male, female and total) for the age range 15 years to 64 years and the present value of lost earnings (PVLE) for each country over the years

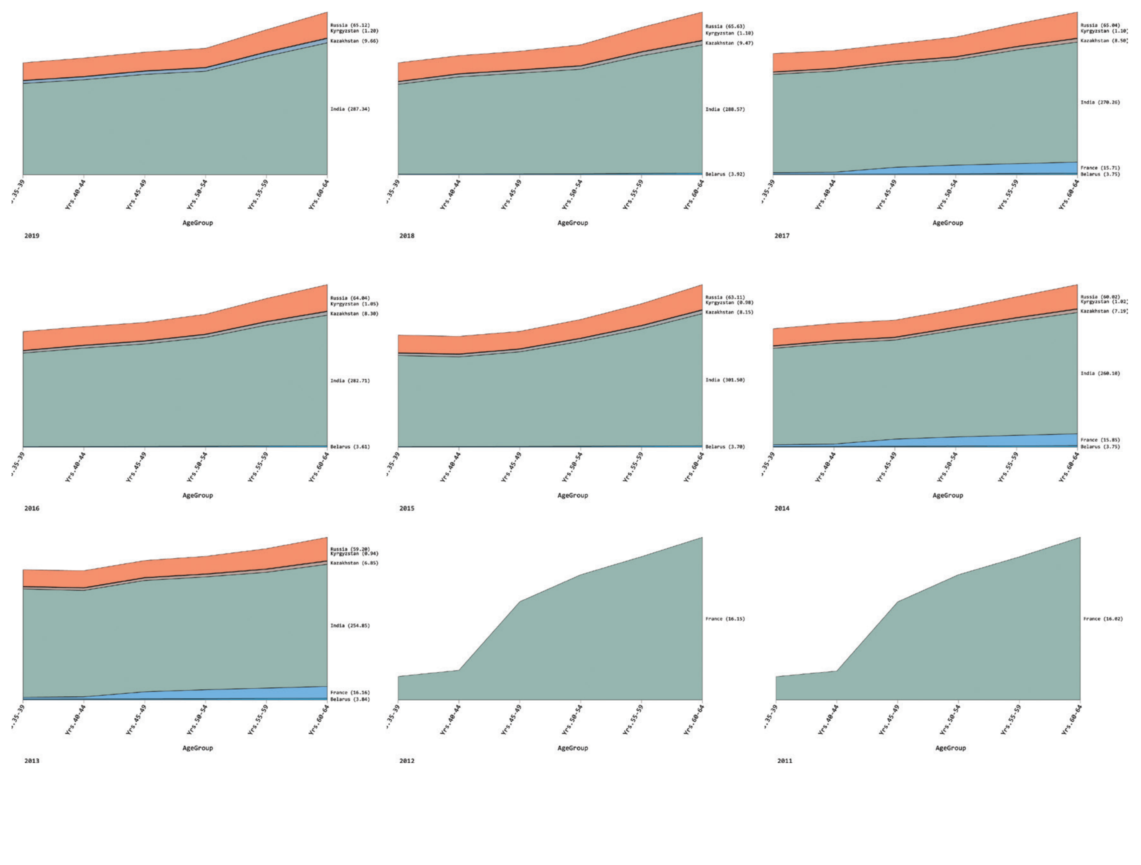
					Productivity losses					
		$SEYLL_d$			PVLE (million USD PPP 2017)			PVLE/SEYLL (USD per SEYLL)		
Country	Year	Male	Female	Both	Male	Female	Both	Male	Female	Both
Belarus	2013	22.97	30.25	24.95	1583.02	635.05	2218.07	2400.96	1965.68	4366.64
	2014	23.09	30.47	25.08	1509.95	611.54	2121.49	2380.20	1977.45	4357.65
	2015	23.09	30.47	25.08	1480.39	577.03	2057.42	2489.98	2038.46	4528.44
	2016	22.72	29.96	24.7	1413.68	574.93	1988.62	2495.56	2053.63	4549.18
	2017	22.41	29.55	24.34	1491.19	574.2	2065.38	2718.78	2141.51	4860.29
	2018	22.37	29.47	24.28	1707.05	655.3	2362.35	3044.05	2409.83	5453.88
France	2011	30.4	36.41	32.3	32640.28	16325.33	48965.61	9387.56	8458.31	17845.87
	2012	30.26	36.25	32.15	34827.81	17341.99	52169.8	9907.05	8925.10	18832.15
	2013	30.18	36.15	32.06	36193.93	18191.21	54385.14	10252.85	9331.27	19584.12
	2014	30.12	36.11	32.01	36839.7	18755.04	55594.74	10371.95	9554.60	19926.55
	2017	30.54	36.28	32.39	39312.35	20404.68	59717.03	11333.95	10402.58	21736.53
India	2013	29.5	32.8	30.79	73309.51	16645.26	89954.77	1180.04	374.81	1554.85
	2014	29.77	31.79	30.61	64468.09	15707.6	80175.7	1116.23	356.30	1472.53
	2015	29.01	30.39	29.59	75825.53	18033.23	93858.75	1289.61	398.25	1687.86
	2016	28.75	31.43	29.79	76598.5	16261.89	92860.39	1260.19	384.94	1645.12
	2017	29.41	32.11	30.45	81700.95	15791.7	97492.65	1302.87	365.27	1668.14
	2018	29.02	30.88	29.73	77614.04	14332.73	91946.78	1283.26	356.03	1639.29
	2019	31.16	28.86	29.8	54093.97	23715.11	77809.08	1298.52	422.78	1721.30

(continued)

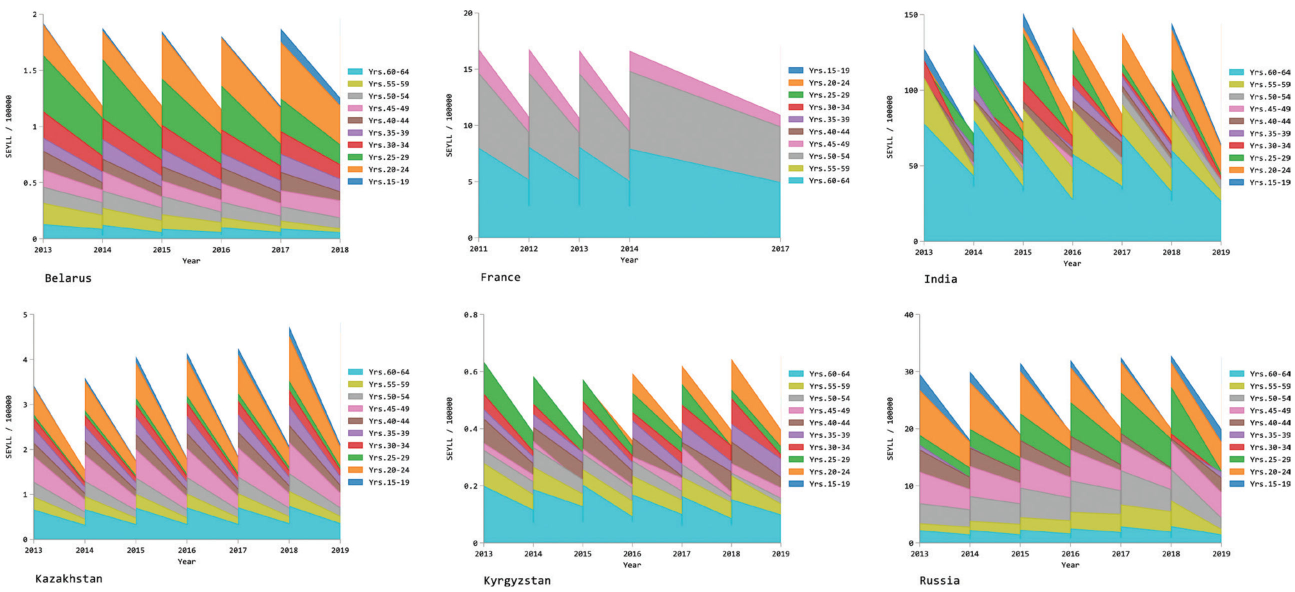
Table 5. SEYLL$_d$ (male, female and total) for the age range 15 years to 64 years and the present value of lost earnings (PVLE) for each country over the years (continued)

					Productivity losses					
		SEYLL$_d$			**PVLE (million USD PPP 2017)**			**PVLE/SEYLL (USD per SEYLL)**		
Country	**Year**	**Male**	**Female**	**Both**	**Male**	**Female**	**Both**	**Male**	**Female**	**Both**
Kazakh-stan	2013	19.01	22.7	20.85	1218.03	1248.3	2466.33	1233.08	1058.18	2291.26
	2014	19.57	23.36	21.46	1253.43	1276.33	2529.76	1232.64	1051.49	2284.13
	2015	21.43	25.38	23.4	1355.5	1356.86	2712.37	1217.25	1028.76	2246.01
	2016	21.77	25.65	23.71	1337.33	1335.79	2673.13	1181.78	1002.02	2183.80
	2017	22.18	26.01	24.09	1358.24	1355.85	2714.09	1178.52	1002.92	2181.44
	2018	24.01	28.09	26.05	1654.56	1650.59	3305.15	1326.02	1130.51	2456.53
	2019	24.3	28.48	26.39	2444.75	2456.19	4900.94	1935.98	1659.50	3595.48
Kyrgyzstan	2013	27.84	32.23	29.24	69.63	23.98	93.6	251.70	160.02	411.72
	2014	27.2	31.93	28.72	68.77	24.74	93.51	256.37	166.74	423.11
	2015	28.04	32.06	29.35	71.56	25.96	97.51	267.99	175.47	443.46
	2016	27.65	31.97	29.08	77.58	27.9	105.48	310.37	194.79	505.16
	2017	27.82	32.4	29.3	91.59	31.47	123.06	354.31	218.29	572.60
	2018	27.87	32.58	29.41	125.84	43.08	168.91	498.21	301.58	799.78
	2019	27.74	32.25	29.19	138.22	48.39	186.61	544.24	345.37	889.61
The Russian Federation	2013	23.5	30.07	25.43	13625.28	5989.83	19615.11	1384.65	1144.99	2529.64
	2014	24.27	30.52	26.1	14350.51	6181.98	20532.48	1400.03	1158.96	2558.99
	2015	24.33	30.6	26.15	15073.97	6403.83	21477.8	1348.86	1118.35	2467.21
	2016	24.72	30.8	26.48	19649.77	8235.52	27885.29	1664.71	1385.57	3050.28
	2017	25.25	31.08	26.93	21308.33	8774.41	30082.74	1707.62	1427.36	3134.99
	2018	25.55	31.25	27.19	31039.07	12729.09	43768.16	2462.44	2066.35	4528.79
	2019	24.98	31.03	26.77	25492.52	11045.47	36537.99	2468.27	2044.19	4512.46

Graph 1. SEYLL/100,000 over the years for age group between 35 years and 64 years



Graph 2. SEYLL/100,000 between 15 years and 64 years for each country



observed low cumulative percentage loss of PVLE per SEYLL while high cumulative GDP per capita growth could be attributed to extremely low labour force participation rate in India combined with the relatively low wage rate. So, we found that PVLE for the population of age group 35–64 years (Table 5) accounted an enormous amount ranging from 4.33% (reference: size of Kyrgyzstan economy, 9.37 billions USD in 2019) to 19.55% (reference: size of Belarus economy, 60 billions USD in 2018), in other countries this avoidable loss was around 10% of the size of the respective economy in the corresponding last year of this study. India was an outlier for this computation for the reasons explained earlier. Thus, this empirical study contributes to the contestation over population health development with the consent for balancing sustainability of the economy and alleviation of the poverty.

The uniqueness of this study is in the demonstration of the use of SEYLL for allocation decisions and computing productivity loss. Our 3P approach is relatively more robust than considering GDP per capita while computing productivity of the citizen because GDP per capita does not include standard (cost) of living at the individual level and also ignores income inequality.

Our computation of PVLE in million USD PPP constant at 2017 provided an important insight that can be incorporated into the poverty alleviation programme in low – and middle – income countries.

Further, using SEYLL with gender responsiveness was also consistent with the intergenerational actions for populational health development when the mandate of public health is not only for prolonging life but also promoting good health. Here, we nuanced gender disaggregation to extract value from SEYLL for decision making.

Despite the age of the data, the use of the subnational data introduced an approach to capture the differential effects of the determinants on population health development. The subnational level data availability constrained this study for the limited number of years and that was also not uniform across the study countries. The most thwarting limitations of this study were (1) short-term horizon with gaps in data points and (2) paucity of disease specific data availability with consistency across study countries. Since we presented here PVLE per SEYLL only for the population during peak working age, such findings were to be inferred with the contextual approach in consideration. However, not with standing these limitations, this study updated and expanded the use of SEYLL for a prudent health policy planning with an efficient allocation of available resources where the sufficiency component of healthcare service provision ought to be embedded with the equity in oucome.

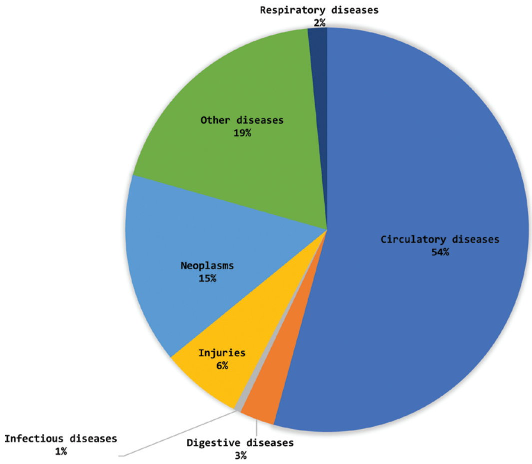
CONCLUSIONS

Our approach demonstrates relevance and usability of the data for health policy while addressing navigational problem of the information overload, generates also evidence for the legislation and provides solution for handling of the uncertainty. Such an approach further contributes to build consensus for the policy making.

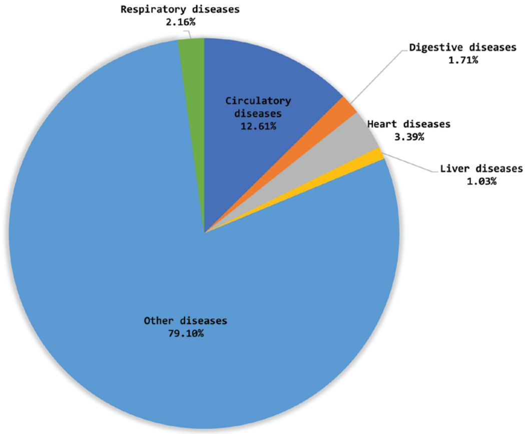
We have captured the value of earnings and quantified the avoidable loss for the society / country in different contexts and thus, this study circumvents the paradoxes and the pifalls of valuing investment for population health development with no "one size – fits all" construct.

We conclude with the note that this study has established the need to strengthen data (inputs for health policy) at the country level to adjust the effects from the determinants and the contexts through (1) establishing the synergies among the interventions and (2) demonstrating the actions that balance the trade-offs and address the negative spill-over effects.

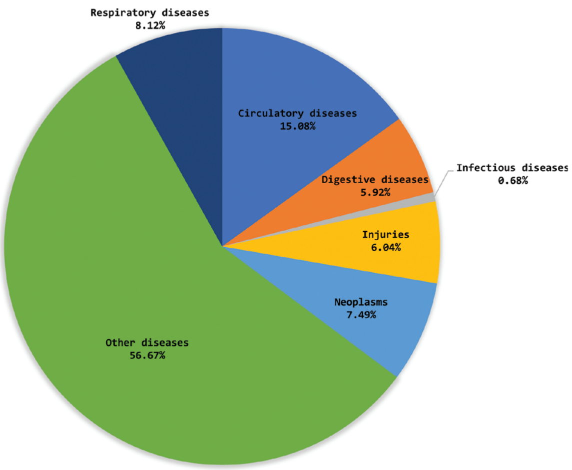
Graph 3. Distribution of SEYLL by diseases / disorders in the latest year



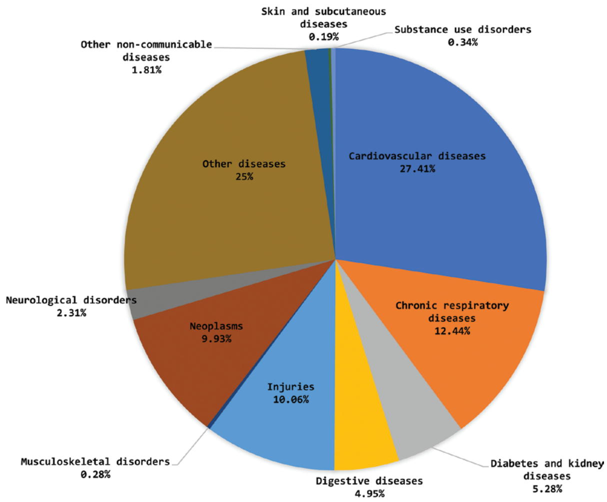
Belarus – 2018



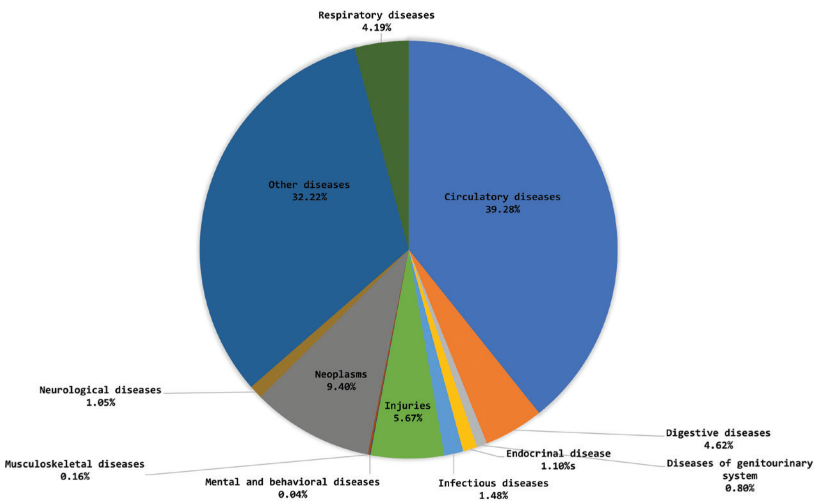
France – 2017



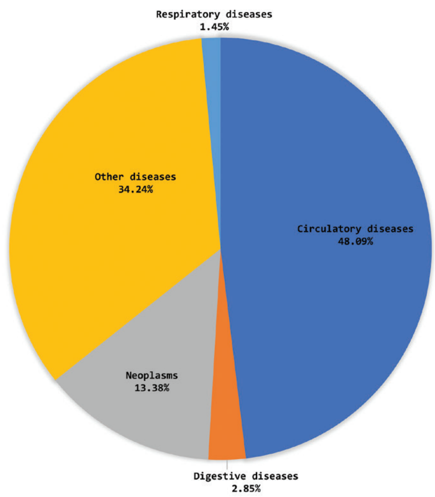
India – 2019



Kazakhstan – 2019

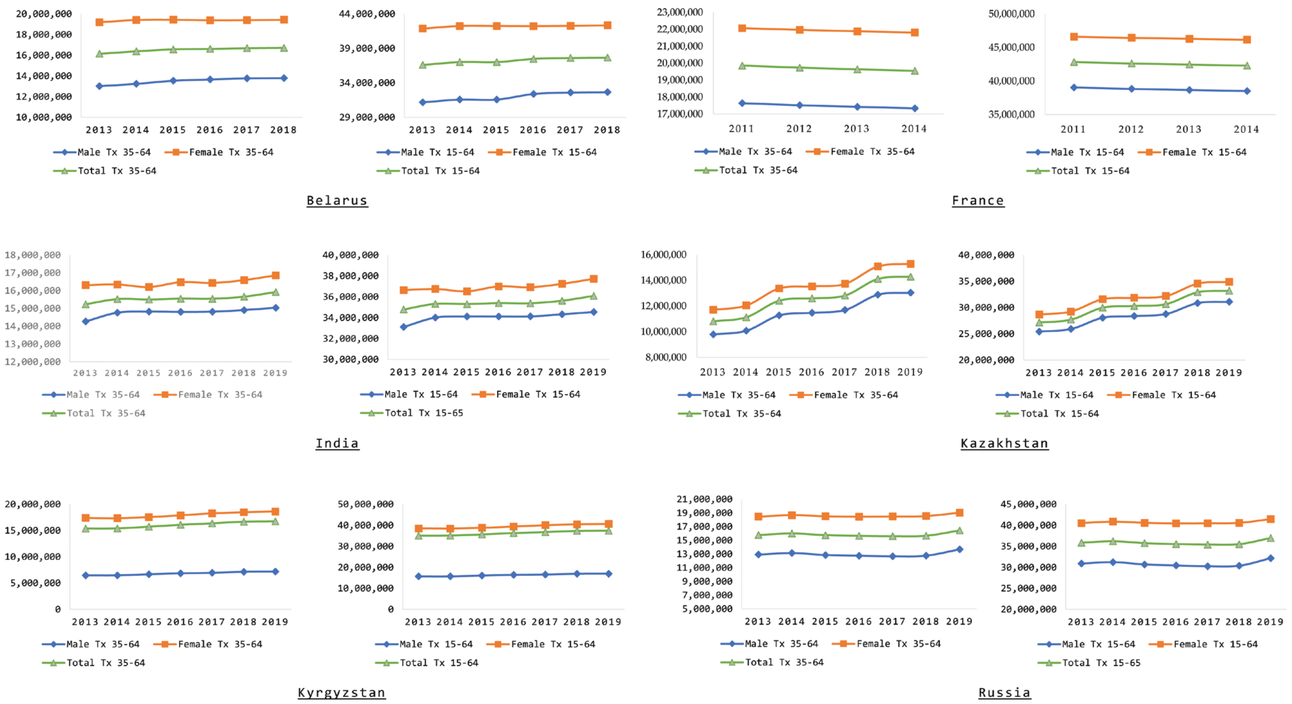


Kyrgyzstan – 2019



Russia – 2019

Graph 4. Distribution of person years lived above age x (T_x) for different years



AUTHORS CONTRIBUTIONS

Both the authors contributed to conceptualisation, methodology, formal analysis and interpretation, data curation and writing the manuscript.

COMPETING INTERESTS

The authors declare no competing interests.

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APPENDIX

Table 1. Person-years lived above age x across age groups

Belarus		T_x			Year-on-Year (%) change		
Region	**Year**	**Male**	**Female**	**Both**	**Male**	**Female**	**Both**
Brest Region	2013	51830078.4	66752113.5	59364113.4	–	–	–
	2014	52587814.4	67439772.9	60130577.4	1.46	1.03	1.29
	2015	53126615.7	66986400	60236205.4	1.02	–0.67	0.18
	2016	53589032.1	67106120.1	60545360.3	0.87	0.18	0.51
	2017	53090016.1	66927122.3	60159682.6	–0.93	–0.27	–0.64
	2018	53660750.1	67087942.1	60568739.4	1.08	0.24	0.68
Vitebsk region	2013	49748190.1	64811400.1	57346889.4	–	–	–
	2014	50483871.7	65622235.4	58169469.4	1.48	1.25	1.43
	2015	51070312.6	65584216.8	58492724.2	1.16	–0.06	0.56
	2016	51479629.9	65387065.3	58647036.4	0.8	–0.3	0.26
	2017	51988368.9	65820463.1	59137816.4	0.99	0.66	0.84
	2018	52156479.7	65935305.9	59255931.6	0.32	0.17	0.2
Gomel region	2013	50044560.5	65746838.6	57945370	–	–	–
	2014	50274512.1	66010724.8	58193169	0.46	0.4	0.43
	2015	51352591.6	66004257.3	58845553.4	2.14	–0.01	1.12
	2016	51721836.4	65894803.4	59015250.6	0.72	–0.17	0.29
	2017	52125611.3	66276533.1	59417283.8	0.78	0.58	0.68
	2018	52018084.7	66558711.8	59464066.7	–0.21	0.43	0.08
Grodno region	2013	50146045.9	66024674.9	58074780.4	–	–	–
	2014	51653046	67001364.3	59437706.1	3.01	1.48	2.35
	2015	51994884.6	67029368.5	59630999.9	0.66	0.04	0.33
	2016	52134914.3	66378175.9	59428337.8	0.27	–0.97	–0.34
	2017	52466053	66777707.6	59781789.7	0.64	0.6	0.59
	2018	52356899.3	66507618.6	59578246.9	–0.21	–0.40	–0.34
Minsk city	2013	55656908.9	71141869.4	63870928.5	–	–	–
	2014	55691017.3	71294106	63980702.3	0.06	0.21	0.17
	2015	56581263.4	71817838	64753847.8	1.6	0.73	1.21
	2016	56888676	71602649.5	64846078.6	0.54	–0.3	0.14
	2017	57356209.8	71633449.1	65124242.3	0.82	0.04	0.43
	2018	57582094.6	71688992	65273543.6	0.39	0.08	0.23
Minsk region	2013	49251327.4	65169781.3	57095783.4	–	–	–
	2014	49839665	66151427.4	57881145.4	1.19	1.51	1.38
	2015	51111549.9	65746621.4	58451432.3	2.55	–0.61	0.99
	2016	51276881.8	66079646.1	58686293.8	0.32	0.51	0.4
	2017	51605433.7	65889401.9	58793573.5	0.64	–0.29	0.18
	2018	51952458.7	65828961.4	58940065.9	0.67	–0.09	0.25

(*continued*)

Table 1. Person-years lived above age x across age groups (continued)

Belarus		T_x			Year-on-Year (%) change		
Region	Year	Male	Female	Both	Male	Female	Both
Mogilev region	2013	49869071.4	65087166.1	57473192.1	–	–	–
	2014	50465226.6	65272683.6	57921939.8	1.2	0.29	0.78
	2015	51252571.5	66057257.6	58744908.3	1.56	1.2	1.42
	2016	51623136.6	65514309.9	58722327.4	0.72	–0.82	–0.04
	2017	52123170.5	64849387.3	58708893.6	0.97	–1.01	–0.02
	2018	51312865.7	65359077	58440306.9	–1.55	0.79	–0.46

France		T_x			Year-on-Year (%) change		
Region	Year	Male	Female	Both	Male	Female	Both
Ile-de-France	2011	65942893.3	76950954.6	71622393.5	–	–	–
	2012	66139614	77227228.8	71851788.4	0.3	0.36	0.32
	2013	66565690.2	77590579.4	72242454.5	0.64	0.47	0.54
	2014	67088201.4	78019485.4	72725345	0.78	0.55	0.67
	2017	67432164.6	77918715.4	72813147.5	0.17	–0.04	0.04
Centre	2011	63053812.1	75676672.3	69245161.8	–	–	–
	2012	63600034	76410521.7	69878746.1	0.87	0.97	0.91
	2013	64091960.7	76658206.4	70262279.7	0.77	0.32	0.55
	2014	64270270.9	76970481.9	70494707.7	0.28	0.41	0.33
	2017	64279192.1	76365589.7	70209766.8	0	–0.26	–0.13
Pays de la Loire	2011	64046180	77346815.1	70617123.8	–	–	–
	2012	64472714.4	77535492.7	70936871.3	0.67	0.24	0.45
	2013	64741896.3	77723048.6	71164300.1	0.42	0.24	0.32
	2014	65049037.7	77968075.6	71439912.2	0.47	0.32	0.39
	2017	77730601.6	77730601.6	71227424.9	6.5	–0.1	–0.1
Bretagne	2011	61924679.8	75595110.8	68654946.5	–	–	–
	2012	62108872.6	75728578.2	68789658.9	0.3	0.18%	0.2
	2013	62246666.2	75921059.8	69281075.9	0.22	0.25%	0.71
	2014	62739433.2	76105661.8	69292251.3	0.79	0.24%	0.02
	2017	63241962.4	76143194.8	69564611.9	0.27%	0.02%	0.13
Provence-Alpes-Côte d'Azur	2011	64614675.1	76687018.7	70722946.1	–	–	–
	2012	64850170.6	76835797.6	70905844.8	0.36	0.19	0.26
	2013	65247663.4	77069722.2	71220787.9	0.61	0.3	0.44
	2014	65756541.2	77240402.1	71568030.4	0.78	0.22	0.49
	2017	77256392.5	77256392.5	71553025.3	5.83	0.01	–0.01
Corse	2011	64576435.2	75326612.9	69847083.5	–	–	–
	2012	65163900.8	75705537.4	70347786.8	0.91	0.5	0.72
	2013	64795867	76505767.6	70510744.4	–0.56	1.06	0.23
	2014	65265995.4	76889773.9	70960934.5	0.73	0.5	0.64
	2017	66506196.2	77769475.6	72091479.6	0.63	0.38	0.53

(*continued*)

Table 1. Person-years lived above age x across age groups (continued)

	India		T_x		Year-on-Year (%) change		
State	**Year**	**Male**	**Female**	**Both**	**Male**	**Female**	**Both**
Andrah Pradesh	2013	55077775	61127053	57933937	–	–	–
	2014	56154220	59597678	57856655	1.95	–2.5	–0.13
	2015	56657275	60257716	58449907	0.9	1.11	1.03
	2016	57762724	60888793	59239458	1.95	1.05	1.35
	2017	55654608	59334944	57362871	–3.65	–2.55	–3.17
	2018	57638113	61547140	59523692	3.56	3.73	3.77
	2019	58551889	61720999	60197058	1.59	0.28	1.13
Assam	2013	50889510	54586152	52525444	–	–	–
	2014	52840708	56576243	54601181	3.83	3.65	3.95
	2015	53594743	56671224	55036546	1.43	0.17	0.8
	2016	54133152	58730483	56114899	1	3.63	1.96
	2017	54738845	58244274	56325831	1.12	–0.83	0.38
	2018	54910230	57850681	56107171	0.31	–0.68	–0.39
	2019	54926030	57391216	55998606	0.03	–0.79	–0.19
Bihar	2013	56190611	57011695	56603567	–	–	–
	2014	58088458	57831509	57957473	3.38	1.44	2.39
	2015	58466068	55816045	57147987	0.65	–3.49	–1.4
	2016	56900449	57346652	57100843	–2.68	2.74	–0.08
	2017	56898202	57018342	56855887	0	–0.57	–0.43
	2018	56731641	56043252	56460718	–0.29	–1.71	–0.7
	2019	57233500	56859265	57092443	0.88	1.46	1.12
Chhattisgarh	2013	50144109	54700459	52451223	–	–	–
	2014	50219727	52892802	50980848	0.15	–3.3	–2.8
	2015	50658817	55405542	52959408	0.87	4.75	3.88
	2016	50985363	55770432	53320595	0.64	0.66	0.68
	2017	50039998	55286184	52527962	–1.85	–0.87	–1.49
	2018	49447521	52997954	51264779	–1.18	–4.14	–2.4
	2019	50430680	55505073	52907072	1.99	4.73	3.2
Delhi	2013	61052633	63830459	62277901	–	–	–
	2014	62622138	68065852	64948097	2.57	6.64	4.29
	2015	62207305	68148170	64921185	–0.66	0.12	–0.04
	2016	59339859	67319354	62378481	–4.61	–1.22	–3.92
	2017	60361416	70390765	64126514	1.72	4.56	2.8
	2018	61893084	70013588	65076718	2.54	–0.54	1.48
	2019	61551923	70835013	64968791	–0.55	1.17	–0.17
Gujarat	2013	55428280	63002380	58935236	–	–	–
	2014	56538164	63781520	59729399	2	1.24	1.35
	2015	56549932	63417813	59703440	0.02	–0.57	–0.04
	2016	56301503	63488415	59508681	–0.44	0.11	–0.33
	2017	55276037	62493484	58544274	–1.82	–1.57	–1.62
	2018	55698273	64926083	59687297	0.76	3.89	1.95
	2019	56547257	64684017	60226034	1.52	–0.37	0.9

(*continued*)

Table 1. Person-years lived above age x across age groups (continued)

	India		T_x		Year-on-Year (%) change		
State	Year	Male	Female	Both	Male	Female	Both
Haryana	2013	54758499	62556184	58431763	–	–	–
	2014	55114343	61720779	58151504	0.65	–1.34	–0.48
	2015	55640781	62644355	58934998	0.96	1.5	1.35
	2016	56296524	63927259	59815746	1.18	2.05	1.49
	2017	55533676	63505695	59115779	–1.36	–0.66	–1.17
	2018	54034225	64534715	58661793	–2.7	1.62	–0.77
	2019	53664242	63280183	58054606	–0.68	–1.94	–1.04
Himachal Pradesh	2013	59297859	66454408	62637374	–	–	–
	2014	58597284	70277828	63474056	–1.18	5.75	1.34
	2015	58811579	69272216	63528684	0.37	–1.43	0.09
	2016	57490139	67274394	61799869	–2.25	–2.88	–2.72
	2017	58938995	67201663	62596612	2.52	–0.11	1.29
	2018	57206988	66627723	61313023	–2.94	–0.85	–2.05
	2019	57531687	65986416	61447422	0.57	–0.96	0.22
Jammu & Kashmir	2013	61474358	72532991	65520163	–	–	–
	2014	62179704	73659788	66212723	1.15	1.55	1.06
	2015	63025455	72366503	66901582	1.36	–1.76	1.04
	2016	63421992	73988046	67597474	0.63	2.24	1.04
	2017	65293704	71168360	67807303	2.95	–3.81	0.31
	2018	63962641	71798895	67199630	–2.04	0.89	–0.9
	2019	65131721	78249323	70092201	1.83	8.98	4.3
Jharkhand	2013	52857876	55802784	54332692	–	–	–
	2014	56927191	56926553	57043443	7.7	2.01	4.99
	2015	56370225	56584508	56417168	–0.98	–0.6	–1.1
	2016	58448190	56599069	57544753	3.69	0.03	2
	2017	58263027	56107361	57194023	–0.32	–0.87	–0.61
	2018	57874840	56039513	56932851	–0.67	–0.12	–0.46
	2019	57499461	56451370	56894243	–0.65	0.73	–0.07
Karnataka	2013	54185256.7	60174566.6	57142889.5	–	–	–
	2014	55314036.8	59447387.8	57352233.6	2.08	–1.21	0.37
	2015	55118265.7	58777928.1	56925165.8	–0.35	–1.13	–0.74
	2016	54146566.5	58765257.9	56350150.1	–1.76	–0.02	–1.01
	2017	54476663.1	59210689.8	56706578.2	0.61	0.76	0.63
	2018	55031813	59812745.9	57291665.7	1.02	1.02	1.03
	2019	54440961.5	61041493.7	57549749.1	–1.07	2.05	0.45
Kerala	2013	59220034.3	68039071.1	63611565.3	–	–	–
	2014	59840593.5	68452669.1	64054800.8	1.05	0.61	0.7
	2015	59580537.1	68601242.5	64075935.5	–0.43	0.22	0.03
	2016	57840116.7	66083009.7	61885784.3	–2.92	–3.67	–3.42
	2017	59378433.6	67709181.5	63435081	2.66	2.46	2.5
	2018	58944047.9	67576344.7	63115335.5	–0.73	–0.2	–0.5
	2019	57429342	67352705.8	62215869.5	–2.57	–0.33	–1.43

(continued)

Table 1. Person-years lived above age x across age groups (continued)

	India		T_x		Year-on-Year (%) change		
State	**Year**	**Male**	**Female**	**Both**	**Male**	**Female**	**Both**
Madhya Pradesh	2013	50859113	57409683	53924473	–	–	–
	2014	51604200	57463810	54322108	1.47	0.09	0.74
	2015	52371936	57237244	54666054	1.49	–0.39	0.63
	2016	53131770	58661398	55667161	1.45	2.49	1.83
	2017	53930511	59233506	56324922	1.5	0.98	1.18
	2018	54409778	59206215	56668986	0.89	–0.05	0.61
	2019	54502043	59102352	56733956	0.17	–0.18	0.11
Maharashtra	2013	57769653	63722075	60567132	–	–	–
	2014	58226832	63628993	60737597	0.79	–0.15	0.28
	2015	59655703	62771098	61167127	2.45	–1.35	0.71
	2016	58759202	62693555	60578794	–1.5	–0.12	–0.96
	2017	59382290	62418499	60804122	1.06	–0.44	0.37
	2018	59091884	64294375	61476598	–0.49	3.01	1.11
	2019	59398931	64790749	61872986	0.52	0.77	0.64
Odisha	2013	53358534	56699896	54931998	–	–	–
	2014	55127245	60392753	57498021	3.31	6.51	4.67
	2015	55293122	60411274	57632977	0.3	0.03	0.23
	2016	55998665	59901579	57719171	1.28	–0.84	0.15
	2017	56853389	60436779	58493569	1.53	0.89	1.34
	2018	58120589	61176135	59541786	2.23	1.22	1.79
	2019	58649846	62008447	60262147	0.91	1.36	1.21
Punjab	2013	59191542	64916753	61857455	–	–	–
	2014	59550439	65857998	62424923	0.61	1.45	0.92
	2015	60899811	65844665	63262599	2.27	–0.02	1.34
	2016	61550061	68108143	64520285	1.07	3.44	1.99
	2017	57071241	63567865	59940529	–7.28	–6.67	–7.1
	2018	57751153	64708777	60881562	1.19	1.79	1.57
	2019	58099121	63614113	60712063	0.6	–1.69	–0.28
Rajasthan	2013	54119805	62344742	58035707	–	–	–
	2014	53683468	61831097	57528438	–0.81	–0.82	–0.87
	2015	53842296	61678045	57275321	0.3	–0.25	–0.44
	2016	54301340	62818928	58088618	0.85	1.85	1.42
	2017	54181636	63040461	58047784	–0.22	0.35	–0.07
	2018	54520382	62507478	58117797	0.63	–0.85	0.12
	2019	54932776	63203652	58725880	0.76	1.11	1.05
Tamil Nadu	2013	55538141	62032273	58623936	–	–	–
	2014	56792465	61808812	59146198	2.26	–0.36	0.89
	2015	56718621	62396360	59339254	–0.13	0.95	0.33
	2016	57523396	63655551	60470285	1.42	2.02	1.91
	2017	57685914	63054668	60198645	0.28	–0.94	–0.45
	2018	59011322	64907690	61662600	2.3	2.94	2.43
	2019	60271825	66966585	63490141	2.14	3.17	2.96

(*continued*)

Table 1. Person-years lived above age x across age groups (continued)

	India		T_x		Year-on-Year (%) change		
State	**Year**	**Male**	**Female**	**Both**	**Male**	**Female**	**Both**
Telengana	2014	55930526	59180866	57425343	–	–	–
	2015	55725040	59471317	57209040	–0.37	0.49	–0.38
	2016	56623978	61663593	58698840	1.61	3.69	2.6
	2017	55061179	58563338	56668564	–2.76	–5.03	–3.46
	2018	55399776	59768906	57307184	0.61	2.06	1.13
	2019	55839829	60274677	57828233	0.79	0.85	0.91
Uttar Pradesh	2013	51374061	56533362	53690189	–	–	–
	2014	53082428	55830775	54427470	3.33	–1.24	1.37
	2015	52955624	55348825	54084165	–0.24	–0.86	–0.63
	2016	53218310	56238722	54621754	0.5	1.61	0.99
	2017	53170848	56880378	54887740	–0.09	1.14	0.49
	2018	53712560	56739087	55128471	1.02	–0.25	0.44
	2019	54186292	57663990	55859446	0.88	1.63	1.33
Uttarakhand	2014	55949762	66852592	60815227	–	–	–
	2015	54469847	62968333	58493493	–2.65	–5.81	–3.82
	2016	52710322	63270161	57485245	–3.23	0.48	–1.72
	2017	52544844	61903148	56647159	–0.31	–2.16	–1.46
	2018	54640248	63020572	58314509	3.99	1.81	2.94
	2019	53787936	62747868	58123209	–1.56	–0.43	–0.33
West Bengal	2013	56045846	59698923	57716818	–	–	–
	2014	57398962	60830836	58949472	2.41	1.9	2.14
	2015	58798361	61703681	60169887	2.44	1.43	2.07
	2016	59170220	61732767	60349742	0.63	0.05	0.3
	2017	59017904	61210811	60077811	–0.26	–0.85	–0.45
	2018	58212971	62928110	60333345	–1.36	2.81	0.43
	2019	59309752	64457226	61643025	1.88	2.43	2.17

Kyrgyzstan			T_x		Year-on-Year (%) change		
Region	**Year**	**Male**	**Female**	**Both**	**Male**	**Female**	**Both**
Batken oblast	2013	58770926.6	63001765	58682333.2	–	–	–
	2014	58693278.3	62167040.2	60425867.6	–0.13	–1.32	2.97
	2015	58885498.1	63022643	60968320.3	0.33	1.38	0.9
	2016	55382128.6	62839141.7	59003725.2	–5.95	–0.29	–3.22
	2017	56380447	65398242.7	60742765.8	1.8	4.07	2.95
	2018	57348443.2	65554233.8	61310171.5	1.72	0.24	0.93
	2019	58000148.3	66443446.6	62087002.1	2.87	1.6	1.27
Bishkek city	2013	55554061.9	67594061.1	62140007.1	–	–	–
	2014	55607787	67252656.5	61987770.7	0.1	–0.51	–0.24
	2015	57555521.2	67990270.2	63386326	3.5	1.1	2.26
	2016	59590227.1	69343862.6	65032205.7	3.54	1.99	2.6
	2017	59715690	70090466.6	65473100.4	0.21	1.08	0.68
	2018	61063275.3	70918572.4	66333309.8	2.26	1.18	1.31
	2019	60955153.6	71352975.4	66690932.1	2.08	1.8	0.54

(continued)

Table 1. Person-years lived above age x across age groups (continued)

Kyrgyzstan		T_x			Year-on-Year (%) change		
Region	**Year**	**Male**	**Female**	**Both**	**Male**	**Female**	**Both**
Chuy oblast	2013	48810477.5	61550368.7	55010018.3	–	–	–
	2014	49322979.3	61281669	55226158.4	1.05	–0.44	0.39
	2015	51177910.6	62725050.3	56967290.9	3.76	2.36	3.15
	2016	51599677.2	63508875.8	57530100.7	0.82	1.25	0.99
	2017	52341659.2	64146256	58251075.6	1.44	1	1.25
	2018	53074606.8	64162419.5	58590761.5	1.4	0.03	0.58
	2019	53917178.7	65463764.2	59689468	3.01	2.05	1.88
Issyk-Kul oblast	2013	47165797.2	60903469.5	53732768.5	–	–	–
	2014	48193791.8	62265784.4	54898348.5	2.18	2.24	2.17
	2015	48789166.6	61816040.3	55083652	1.24	–0.72	0.34
	2016	51081778.7	63384414.6	57167345.6	4.7	2.54	3.78
	2017	50455704.3	65316251	57610813.3	–1.23	3.05	0.78
	2018	51304904.3	65187179.2	58201987	1.68	–0.2	1.03
	2019	51882550	65009341.1	58326225	2.83	–0.47	0.21
Jalal-Abad oblast	2013	53241605	62111931.9	57609234.1	–	–	–
	2014	52714594.5	61637813.3	57113089.3	–0.99	–0.76	–0.86
	2015	52988592.4	61832844.3	57296639.5	0.52	0.32	0.32
	2016	54428072.1	62983145.6	58681395.5	2.72	1.86	2.42
	2017	55068520.7	64049552.1	59524440.1	1.18	1.69	1.44
	2018	56642994.5	64450807.7	60587085.4	2.86	0.63	1.79
	2019	56311067.3	64202749	60247503.3	2.26	0.24	–0.56
Naryn oblast	2013	47476648.8	61630919.8	53924216.5	–	–	–
	2014	47789581.7	61975817.1	54248265.5	0.66	0.56	0.6
	2015	48507603.1	61596632.7	54531069.3	1.5	–0.61	0.52
	2016	49840854.5	62833485.9	55857765.7	2.75	2.01	2.43
	2017	51624627.6	63471786.3	57211169.8	3.58	1.02	2.42
	2018	50723855.8	64528515.6	58196799.3	–1.74	1.66	1.72
	2019	50724351.1	64085917.2	56932127.9	–1.74	0.97	–2.17
Osh city	2013	50940947.4	58924476.7	54996516.2	–	–	–
	2014	51487423.8	58361856.5	55103978.6	1.07	–0.95	0.2
	2015	51962081.8	60602612.7	56373753.5	0.92	3.84	2.3
	2016	52499334.3	61026635.4	56916144.4	1.03	0.7	0.96
	2017	54947257.4	61186019.1	58200437.6	4.66	0.26	2.26
	2018	55588287.7	63319839.4	59714098.6	1.17	3.49	2.6
	2019	56081561.6	64450494.5	60520011.8	2.06	5.34	1.35
Osh oblast	2013	54275884.8	62579367.7	58316897.1	–	–	–
	2014	53709828.3	62332103.6	57946770.3	–1.04	–0.4	–0.63
	2015	54803899.2	62289003.3	58476827.5	2.04	–0.07	0.91
	2016	56202608.9	63496818.5	59830999.7	2.55	1.94	2.32
	2017	56225908.6	64542107.6	60326900.2	0.04	1.65	0.83
	2018	56912544.3	65491480.7	61394302.7	1.22	1.47	1.77
	2019	56750815.1	65770742.1	61196283.8	0.93	1.9	–0.32

(*continued*)

Table 1. Person-years lived above age x across age groups (continued)

Kyrgyzstan		T_x			Year-on-Year (%) change		
Region	**Year**	**Male**	**Female**	**Both**	**Male**	**Female**	**Both**
Talas oblast	2013	51313173.2	61963857.4	56381415.3	–	–	–
	2014	49483847.9	62961911.9	55752194.3	–3.57	1.61	–1.12
	2015	51528019.3	64163767.6	57528902.1	4.13	1.91	3.19
	2016	52713757	63493375.6	57875353.1	2.3	–1.04	0.6
	2017	53675406.9	64667194.4	59015833.1	1.82	1.85	1.97
	2018	55636800.7	65428692	60460220.9	3.65	1.18	2.45
	2019	54406938.2	65408912.5	59716333	1.36	1.15	–1.23

The Russian Federation		T_x			Year-on-Year (%) change		
Region	**Year**	**Male**	**Female**	**Both**	**Male**	**Female**	**Both**
Central Federal District	2013	51432430	66673841	59243019	–	–	–
	2014	51521199	66878784	59375701	0.17	0.31	0.22
	2015	52571876	67149927	60091731	2.04	0.41	1.21
	2016	53529324	67607213	60818863	1.82	0.68	1.21
	2017	54621885	68415646	61801304	2.04	1.2	1.62
	2018	54794002	68501047	61904983	0.32	0.12	0.17
	2019	55624789	69063301	62593576	1.84	0.95	1.28
Far Eastern Federal District	2013	46004818	61815417	53703150	–	–	–
	2014	46391829	62110250	54072309	0.84	0.48	0.69
	2015	46926469	62368667	54504742	1.15	0.42	0.8
	2016	47846622	63186267	55397595	1.96	1.31	1.64
	2017	48767095	63932733	56288976	1.92	1.18	1.61
	2018	49158326	63893817	56516892	0.8	–0.06	0.4
	2019	49164600	63973139	56522626	0.82	0.06	0.42
North Caucasian Federal District	2013	56258972	67979979	62363944	–	–	–
	2014	56426418	68106740	62490044	0.3	0.19	0.2
	2015	57121614	68732948	63167456	1.23	0.92	1.08
	2016	58239869	69419617	64088016	1.96	1	1.46
	2017	59122625	70104801	64881564	1.52	0.99	1.24
	2018	59553382	70595272	65340229	0.73	0.7	0.71
	2019	60456078	70707644	65832788	2.26	0.86	1.47
Northwestern Federal District	2013	50094443	65643234	58132865	–	–	–
	2014	50367184	65865597	58365529	0.54	0.34	0.4
	2015	50815976	65920321	58639887	0.89	0.08	0.47
	2016	51787642	66613229	59501442	1.91	1.05	1.47
	2017	52801970	67378423	60422683	1.96	1.15	1.55
	2018	53196025	67839151	60865147	0.75	0.68	0.73
	2019	54000720	68231237	61473529	2.27	1.27	1.74
Siberian federal district	2013	48300163	64841711	56647097	–	–	–
	2014	48378762	64862170	56701570	0.16	0.03	0.1
	2015	48609230	64914575	56843188	0.48	0.08	0.25
	2016	49583482	65705856	57771750	2	1.22	1.63
	2017	50849920	66563334	58911714	2.55	1.31	1.97
	2018	51034612	66424465	58940495	0.36	–0.21	0.05
	2019	49822709	65024628	57576185	–2.02	–2.31	–2.27

(*continued*)

Table 1. Person-years lived above age x across age groups (continued)

The Russian Federation		T_x			Year-on-Year (%) change		
Region	**Year**	**Male**	**Female**	**Both**	**Male**	**Female**	**Both**
Southern Federal District	2013	51526775	65987275	58885011	–	–	–
	2014	51356751	65844464	58710880	–0.33	–0.22	–0.3
	2015	51884614	66099930	59136427	1.03	0.39	0.72
	2016	52770697	66712226	59908185	1.71	0.93	1.31
	2017	53831810	67375027	60803448	2.01	0.99	1.49
	2018	54429067	67646397	61245976	1.11	0.4	0.73
	2019	54429344	67909625	61355785	1.11	0.79	0.91
Ural federal district	2013	48300163	64841711	56647097	–	–	–
	2014	48378762	64862170	56701570	0.16	0.03	0.1
	2015	48609230	64914575	56843188	0.48	0.08	0.25
	2016	49583482	65705856	57771750	2	1.22	1.63
	2017	50849920	66563334	58911714	2.55	1.31	1.97
	2018	51034612	66424465	58940495	0.36	–0.21	0.05
	2019	51709869	66943724	59557519	1.69	0.57	1.1
Volga Federal District	2013	48079060	65025852	56568232	–	–	–
	2014	48182663	65230848	56722405	0.22	0.32	0.27
	2015	48865028	65434029	57212574	1.42	0.31	0.86
	2016	50247743	66274859	58399830	2.83	1.29	2.08
	2017	51374899	66949339	59370358	2.24	1.02	1.66
	2018	51479339	66973697	59426541	0.2	0.04	0.09
	2019	52186371	67671274	60153010	1.58	1.08	1.32

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The Obstetric Panorama in the Metropolitan Region of Baixada Santista – Brazil: Prevalence and Profile of Parturients

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SUMMARY

Background: The birth of a child is a significant milestone for mothers and families. However, concerns regarding the type and safety of delivery persist. Evidence shows that vaginal delivery provides immunological and respiratory benefits for the baby and offers protective factors for the mother. Despite this, cesarean sections remain prevalent, particularly in developing regions. Objective: This study aimed to analyze delivery data from the Região Metropolitana da Baixada Santista (RMBS) between 2019 and 2022, identifying the predominant delivery method and examining the socioeconomic and cultural profiles of mothers. Methods: Data was obtained from the TABNET/DATASUS database in the Live Birth Information System (SISNAC). Results: Between 2019 and 2022, 86,198 deliveries were recorded, with 53% being cesarean sections and 47% vaginal deliveries, exceeding the 15% cesarean rate recommended by the WHO. Vaginal delivery was more common among mothers aged 10–24 years, while cesarean sections predominated among those aged 25–54 years. Women with 1–11 years of education favored vaginal delivery, while those with ≥12 years of education had cesarean rates more than double vaginal deliveries. Cesarean sections were more prevalent among white and yellow ethnicities. Single mothers predominantly chose vaginal delivery, whereas married, widowed, separated, or cohabiting women favored cesarean sections. Conclusion: The high prevalence of cesarean deliveries in RMBS appears to be associated with maternal age, education level, socioeconomic status, marital status, and prenatal care access. These findings highlight the need for targeted interventions to promote evidence-based delivery practices.

Keywords: cesarean delivery, vaginal delivery, natural delivery, live birth, prenatal, epidemiology.

INTRODUCTION

The birth of a child is a remarkable moment in the life of a woman in labor, defined as a pregnant woman experiencing active labor and delivery, and her family. However, it is worth noting that there are several questions related to both the type and safety of the delivery that the pregnant woman will undergo [1]. It has been scientifically proven that vaginal birth can bring immunological and respiratory benefits to the baby, in addition to providing a protective factor for the mother. Even with the positive scientific evidence regarding vaginal birth, the number of cesarean sections is still predominant, especially in developing countries [2].

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Research indicates that vaginal birth is not associated with a higher risk of postpartum hemorrhage, nor with the need for the woman in labor to be admitted to an Intensive Care Unit (ICU). These are some of the benefits of vaginal birth compared to cesarean section. In addition, vaginal birth has a lower probability of uterine rupture and problems related to placental implantation. These benefits also extend to the newborn, as vaginal birth is less associated with the need for ventilatory support and complications for the baby's health [3].

During vaginal birth, there is a high production of oxytocin, which facilitates lactation and promotes uterine involution, reducing the chances of hemorrhages and hematomas, which contributes to a faster recovery for the woman. This process also facilitates initial contact with the baby after birth, strengthening the bond between mother and child. For the newborn, the benefits include better respiratory adaptation and cardiac stabilization, as well as a lower propensity for allergies, such as asthma, due to contact with the mother's vaginal bacterial flora, which favors colonization from birth. There is also a lower chance of infections for both. Therefore, it is essential that pregnant women are informed about the advantages of vaginal birth during prenatal care, as it continues to be the safest form of birth, offering significant benefits for both the mother and the baby [4].

Aiming to strengthen and improve women's health, the Brazilian Ministry of Health created a set of actions and guidelines, the Comprehensive Women's Health Care Program (PAISM), created in 1983 and implemented in 1984. This health policy was created to ensure women's right to safe childbirth and to meet their emotional, social, family and reproductive health needs. It trained health professionals and provided the necessary structures for care [5].

Considering the high rate of cesarean sections, the Ministry of Health has implemented initiatives to humanize care during labor and birth. These actions are based on guidelines from the World Health Organization (WHO) and on the disadvantages associated with cesarean sections when compared to vaginal birth, particularly in relation to perinatal and maternal mortality. In addition, recent studies in the field of humanization of medical care have highlighted the benefits of vaginal birth compared to cesarean sections, both for maternal and newborn health. These studies emphasize the importance of raising awareness and demystifying the widespread belief that a cesarean section is the best option for the baby [6].

Due to the great diversity of the Brazilian population, it does not fit into a single social and educational pattern, and since there are large differences in the standards of each region in relation to health care, it is not possible to generalize the type of obstetric care provided by the various institutions. Depending on the region, there are different characteristics linked to demographic, cultural, and socioeconomic aspects that determine specific patterns of behavior of the female population [7,8].

The Metropolitan Region of Baixada Santista (MRBS) was established by State Complementary Law No. 815 of 1996. In addition to the city of Santos, the MRBS is a region made up of the following municipalities: Bertioga, Cubatão, Guarujá, Itanhaém, Mongaguá, Peruíbe, Praia Grande, and São Vicente [9]. The city of Santos was considered in the last Census as the most feminine city in the country, with the highest proportion of women among its inhabitants. Out of the 418,908 residents of Santos, 228,800 are female. While the national average is of 51.5% women, in Santos, this percentage rises to 54.68%, which represents 82.9 men for every 100 women in the municipality. Data regarding the female population in the municipalities of the MRBS show that it has a predominance of the female population with the exception of the municipality of Mongaguá [10].

The term Women of Childbearing Age (WCA) in Brazil corresponds to the age group from 10 to 49 years old. It is a broad range that includes adolescent and adult women, who find themselves in different life situations and inserted in cultural, family and social contexts that are constantly evolving [11,12]. According to the last census, the total number of women in Brazil represents 51.5% of the population, which is equivalent to 104,548,325 women; WCA represent 60,945,468, which is equivalent to 58.3% of the total number of women. In MRBS, the total number of women of childbearing age is 55% [10].

Thus, the present study aims to analyze data on births performed in the Unified Health System (SUS) of Baixada Santista in the period from 2019 to 2022; identify the most common type of birth and analyze the socioeconomic and cultural profile of parturients.

METHODS

This study is a descriptive, cross-sectional, retrospective, and quantitative epidemiological analysis based on secondary data. The data were collected from the TABNET/DATASUS database in the Live Birth Information System (SISNAC). The study followed these steps: Access to information >> Health information (TABNET) >> Vital statistics >> Live births >> São Paulo. The study focused on the Baixada Santista Health Macroregion, which includes the municipalities of Bertioga, Guarujá, Santos, São Vicente, Cubatão, Praia Grande, Mongaguá, Itanhaém, and Peruíbe. The data analyzed covered births by the mother's place of residence for the period from 2019 to 2022, the most recent year with available data.

The variables considered in this study included type of delivery, maternal age, education level, race, and marital status. Since all data were obtained from a public database and did not include any personally identifiable information, the study was exempted from evaluation by the Research Ethics Committee, following Resolution No. 510/2016 of the National Health Council (CNS).

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The data were described, subjected to a descriptive statistical analysis, and are presented through graphs that express the absolute and/or percentage distribution of the variables analyzed.

RESULTS

Number of Births

During the studied period (2019 to 2022), 86,198 births were performed by the SUS throughout the MRBS. In 2019, the municipality with the highest number of births was Santos, with 4,364 births; in 2020 to 2022, the city of Praia Grande had 4,371, 4,215, and 4,214 births, respectively. 2019 was also the year with the highest number of births in the period analyzed, with 22,499. The municipality of Praia Grande had the highest number of births in the period from 2019 to 2022, 17,045, even though it was the fifth municipality in terms of the percentage of Women of Childbearing Age (WCA).

Types of Births

In Figure 1, we can see the distribution of types of births by municipality, where we can see that out of the 86,198 births performed in the MRBS during the period evaluated, 53% were cesarean sections and 47% were vaginal births.

Prenatal Consultations

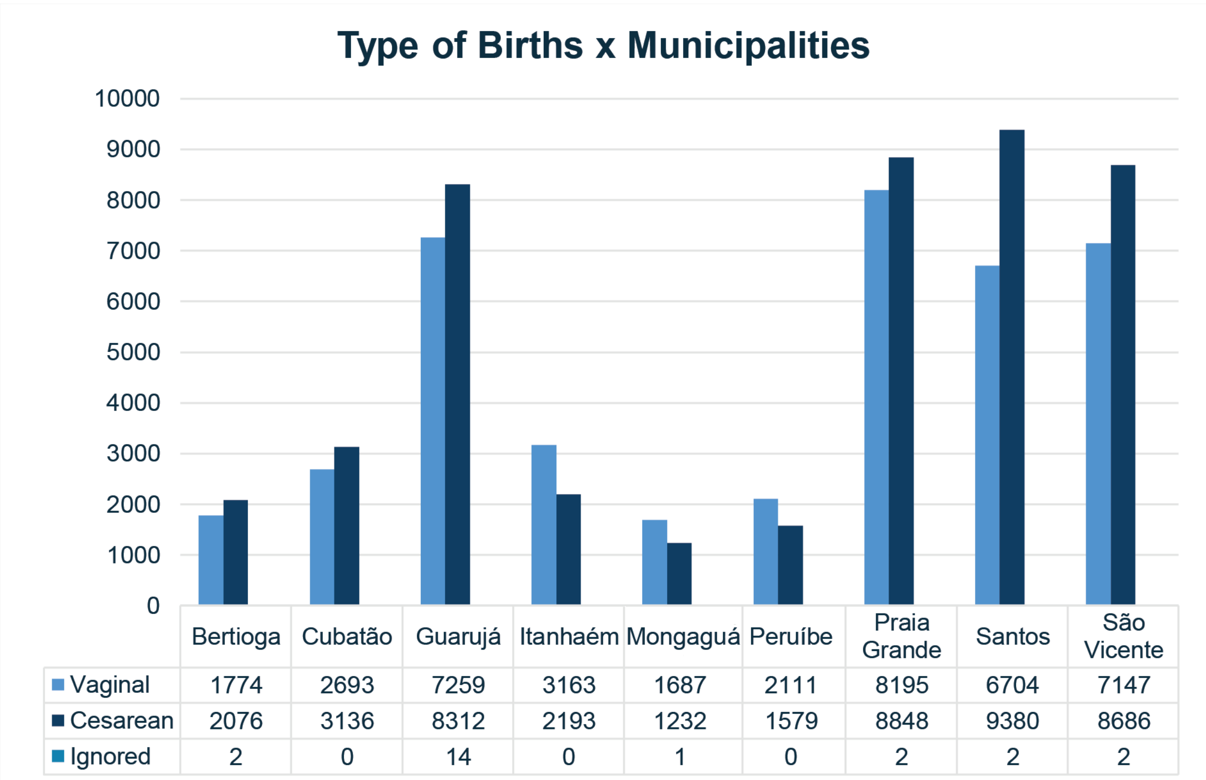
It was found that most women attended more than six prenatal consultations, as recommended by the Ministry of Health. Women who opted for a cesarean section received more adequate prenatal care compared to women who had a vaginal birth, with 54% of the former attending 7 or more consultations.

Age of the Parturient

In Figure 2, we can observe the type of delivery in relation to the mother's age and we can see that in the age group of 10 to 24 years, vaginal delivery is predominant and that from the age of 25 to 54 years, cesarean delivery is predominant. The highest percentage of vaginal births is in the age group of 10 to 19 years and of cesarean delivery in the age group of 50 to 54 years.

Analyzing the data, we found that the municipality of Guarujá has the highest number of births in the age group of 10 to 14 years (80); São Vicente in the age groups of 15-19 years (1,772) and 20 to 24 years (4,101); Praia Grande in the age group of 25 to 29 years (4,205) and the city of Santos has the highest number of births in the age group of 30 to 54 years. The highest number of births is concentrated in the age group of 20 to 34 years, which represents 69% of the births performed in the period.

Figure 1. Type of births performed during the period from 2019 to 2022 distributed by the Municipalities of the MRBS



	Bertioga	Cubatão	Guarujá	Itanhaém	Mongaguá	Peruíbe	Praia Grande	Santos	São Vicente
Vaginal	1774	2693	7259	3163	1687	2111	8195	6704	7147
Cesarean	2076	3136	8312	2193	1232	1579	8848	9380	8686
Ignored	2	0	14	0	1	0	2	2	2

Figure 2. Type of delivery performed in relation to the maternal age during the period from 2019 to 2022 in the MRBS

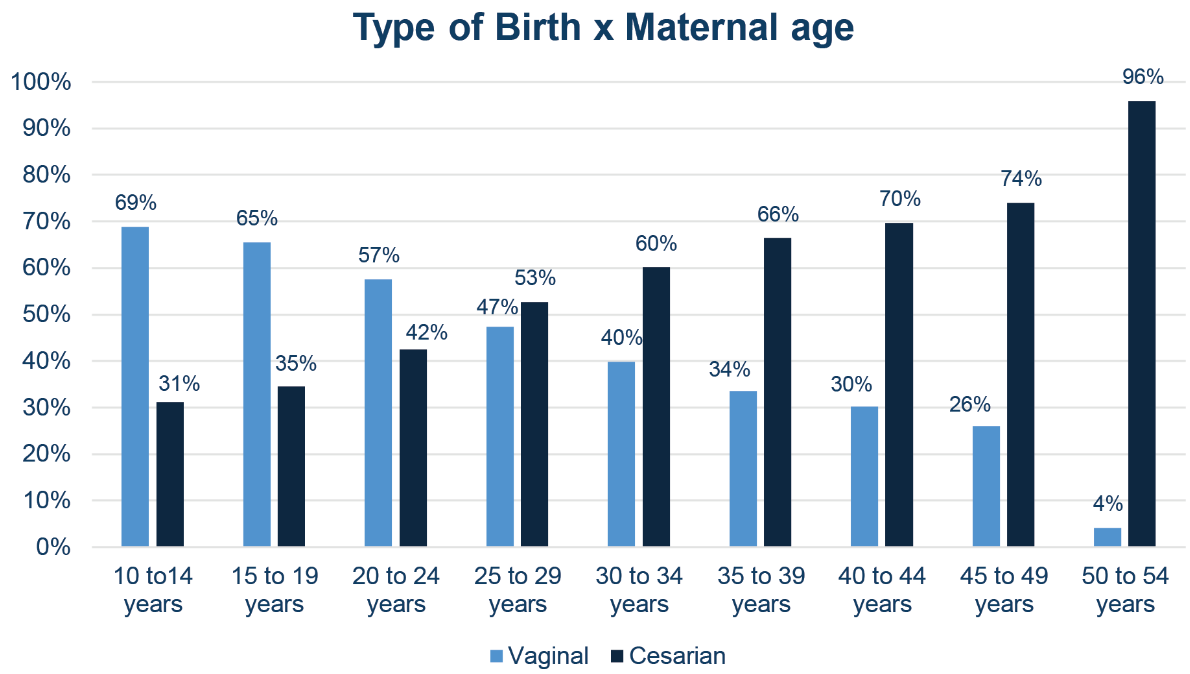
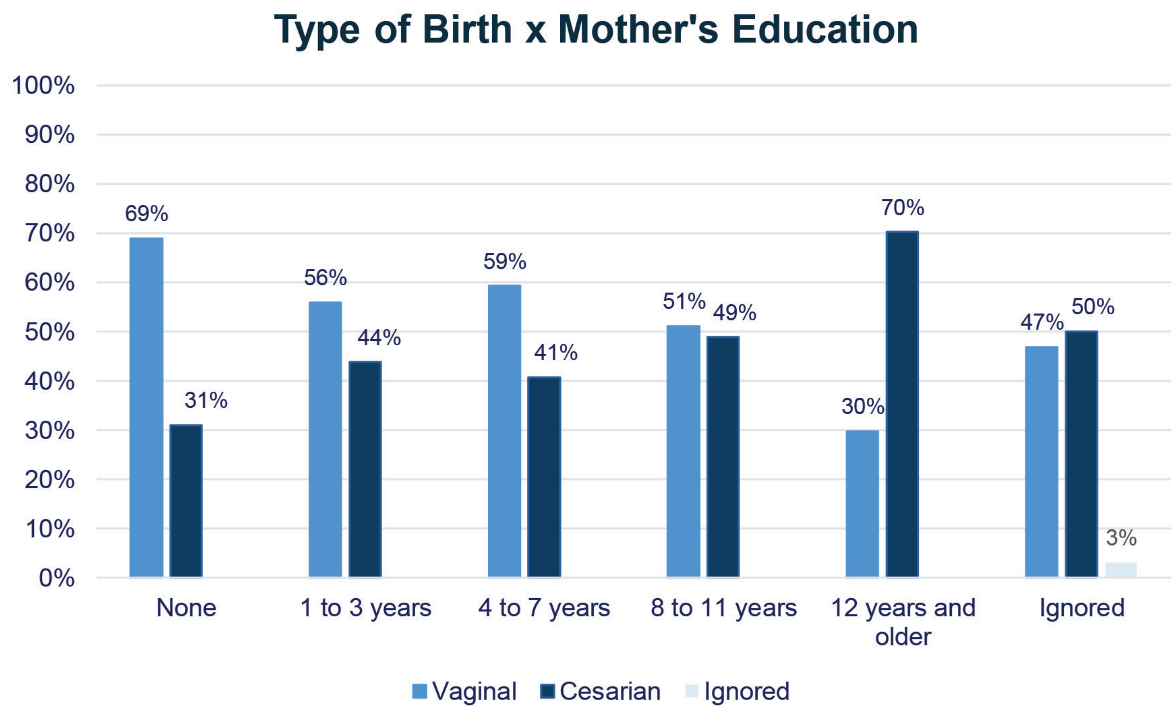


Figure 3. Type of births performed in relation to the mother's education in years during the period from 2019 to 2022 in the MRBS



Education of the Parturient

The study also assessed the mother's education (in years) regarding the type of delivery (Figure 3). We can see that from 1 to 11 years of education, there is a higher number of vaginal deliveries compared to cesarean sections, but when mothers have 12 years of education or more, there is more than twice as many cesarean deliveries compared to vaginal deliveries. This leads us to reflect that the higher the mother's education, the greater the choice for cesarean section.

Race of the Parturient

Based on the data in Figure 4, we found that among the Asian race (60%) and the White race (59%), cesarean section is more common than vaginal delivery compared to other races. In this study, it was found

Figure 4. Type of delivery performed in relation to the race of the parturient in the period from 2019 to 2022 in the MRBS

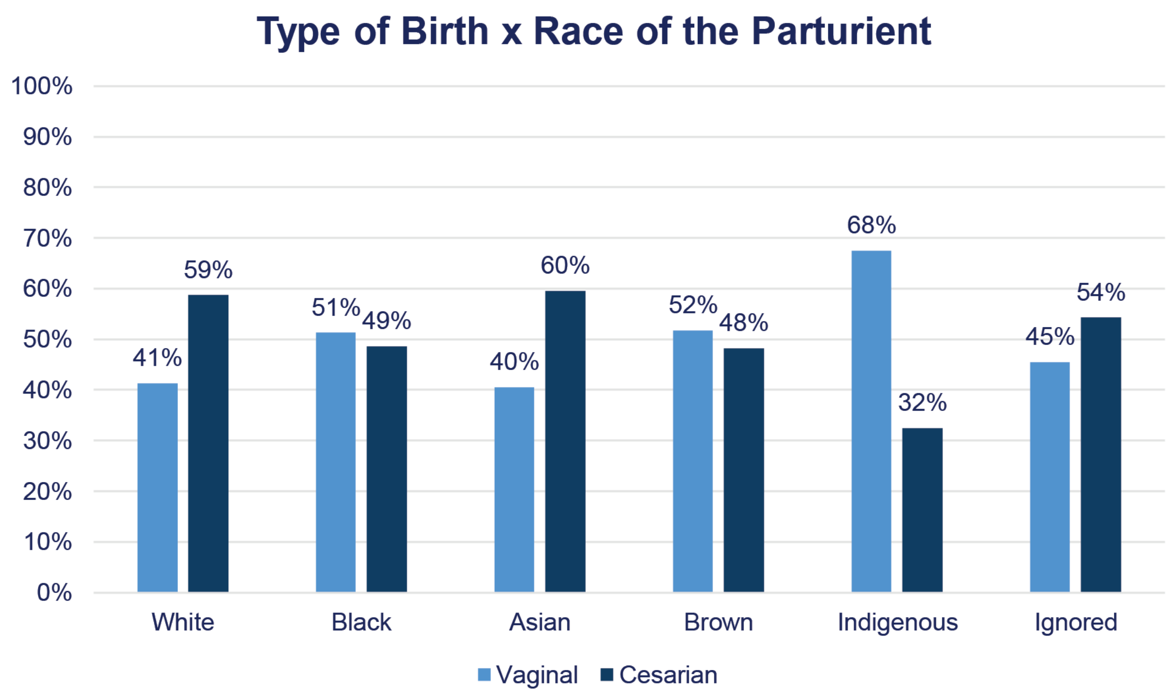
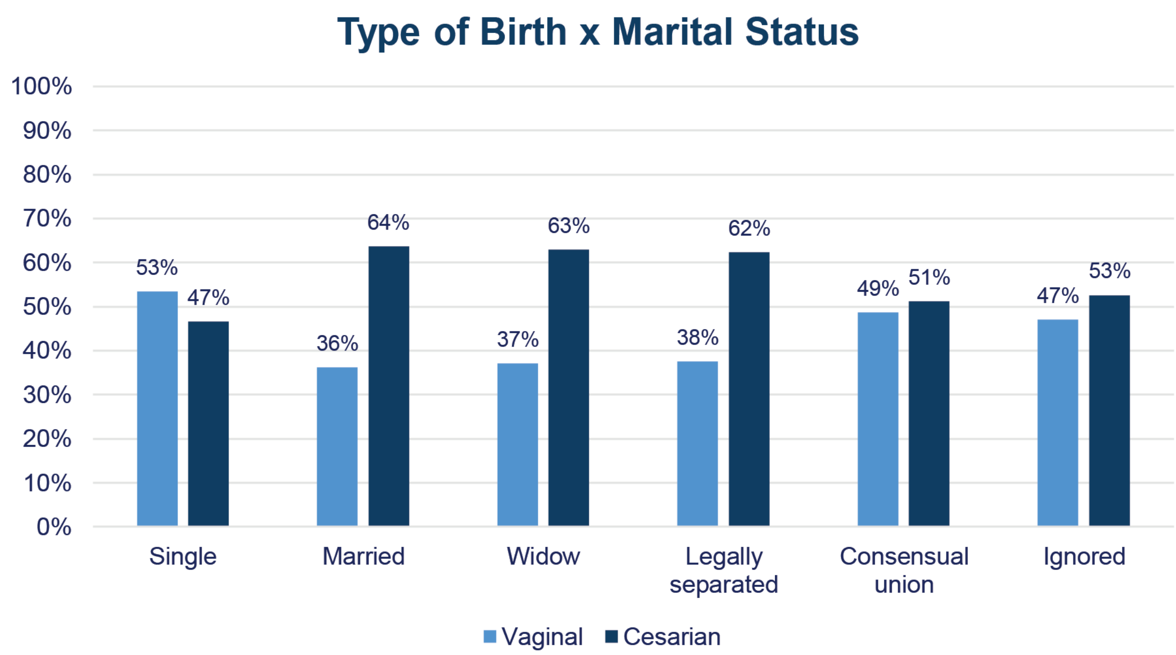


Figure 5. Type of delivery performed in relation to the Marital Status of the Parturient in the period from 2019 to 2022 in the MRBS



that black, brown and indigenous women performed most of their deliveries vaginally, which may suggest a lower propensity for interventionist practices.

Marital Status of the Parturient

We can see in Figure 5 that women with single marital status opt for vaginal birth, while married women, widows, legally separated women and women living in a consensual union choose cesarean section.

DISCUSSION

This study analyzed data from Tabnet/Datasus and found that, from 2019 to 2022, 86,198 births were performed in the MRBS. The municipality of Praia Grande had the highest number of births in this period, 17,045. Overall, the number of births decreased in all municipalities in the MRBS in the period analyzed, which is in line with data from the IBGE Civil Registry Statistics [13], where in 2022 Brazil recorded the lowest number of births since 1977, being the fourth consecutive decline in the total number of births in the country.

Of the 86,198 births performed in the MRBS in the period evaluated, 53% were cesarean sections and 47% were vaginal births, which shows that the number of cesarean sections is well above the 15% recommended by the World Health Organization (WHO) [14]. When we analyze the distribution of births by municipality during this period, we found that in the municipality of Santos, 58% of births were cesarean sections, and in the municipality of Itanhaém, 59% were vaginal births.

According to the study by Betran *et al.* (2021), Brazil is among the five countries with the highest cesarean section rates in the world, ranking second with 56%. The country is followed by the Dominican Republic (58%), Cyprus (55%), Egypt (52%) and Turkey (51%) [15]. Due to the high incidence of cesarean sections in Brazil, several agencies responsible for maternal and neonatal health have implemented measures and prepared documents with the aim of promoting cesarean sections only when clinically necessary and discouraging those performed by choice. An example of these documents is the "Guidelines for Care for Pregnant Women: Cesarean Sections", approved by the Ministry of Health (MS) in 2016. The main purpose of these guidelines was to establish parameters for performing cesarean sections [16].

The impact of women's integration into the labor market, which imposes increasing demands, cannot be overlooked as a factor contributing to the increasing prevalence of cesarean sections. Although cesarean sections are a less time-consuming procedure, offering the mother and the doctor flexibility in choosing the date and time of the surgery, the benefits presented are predominantly non-clinical. The authors reveal that disadvantages such as prolonged postpartum recovery, delays in lactation, lack of active participation in the birth process, and the general risks associated with a surgical procedure are often overlooked [17].

As a result of the transition from vaginal births to cesarean sections, scientific research that addresses morbidity and mortality rates, both perinatal and maternal, associated with the method of delivery, as well as topics related to the humanization of health and the cultural demystification of cesarean birth, have been the subject of discussion on a global scale [18].

According to the recommendation of the World Health Organization (WHO) [14], the appropriate number of prenatal consultations would be equal to or greater than six; and this is what we observed in the data collected in the MRBS. 54% of women who opted for a cesarean section attended 7 or more consultations. However, this monitoring does not happen in the same way throughout the country. In 2019 in Brazil, there were 339,379 thousand births whose pregnant women had 4 to 6 prenatal consultations, 113,696 thousand in the entire Northeast region and 15,858 thousand in the state of Pernambuco. The number of births of pregnant women who did not have any monitoring was 25,064, 9,284 and 1,150, respectively [19].

Regarding the type of delivery and the mother's age, we found that in the age group of 10 to 24 years, vaginal delivery predominates and from 25 to 54 years, cesarean delivery predominates, which is in agreement with the results found in the literature. The study carried out by Santos *et al.* (2009) found that as maternal age increases, the number of vaginal deliveries decreases [20]. Ximenes and Oliveira (2004) also found a greater number of vaginal deliveries in adolescents between 10 and 19 years of age (70.2%) and in parturients over 35 years of age, a slightly higher percentage (51.4%) in surgical deliveries20. In the study by Nomura *et al.* (2004), it was also found that patients aged 35 years or older had a higher proportion of cesarean deliveries [21].

When we analyze the mother's level of education in relation to the type of delivery, we find that when mothers have 1 to 11 years of education, we have a higher number of vaginal deliveries compared to cesarean deliveries, but when they have 12 years of education or more, we have more than twice as many cesarean deliveries as vaginal deliveries. This data is in accordance with the literature, where in the study by Mauadié *et al.* (2024), the variable education, in the category greater than or equal to 12 years, corresponds to 77% of cesarean deliveries and only 23% of vaginal deliveries [22]. This leads us to reflect that the higher the mother's education, the greater the choice for cesarean delivery. This demonstrates that the level of education, insertion in the job market and the growing demands faced by women in contemporary society are factors that can intensify the preference for cesarean delivery. This is due to the ability to choose dates, locations and times, allowing greater control by the woman or doctor over the birth process [6].

Education is a relevant variable in the health area and impacts several aspects of human life. There is a direct relationship between educational level and type of birth: women with a higher level of education are less likely to have a vaginal birth [23] The level of education is strongly associated with the type of birth, as mothers with a higher level of education are up to six times more likely to opt for a cesarean section. This phenomenon can be explained by both maternal convenience and medical reasons, in addition to the higher economic cost associated with cesarean sections. Women with a higher level of education generally have better financial conditions to bear these costs in the private sector [24]. This reinforces that the choice of type of birth is linked not only to clinical factors, but also to access to the resources available to each woman.

When we analyze the data regarding the type of birth performed in relation to the race of the parturient, we find that in the Asian race (60%) and the White race (59%) cesarean section is superior to vaginal birth compared to other races. The studies by Santos et al. (2022) and Schiller (2015) observed, with regard to the variable color/race, that women of light ethnicity, who self-declared as white or yellow, had a higher incidence of cesarean sections compared to vaginal births. This behavior differs from the group of women of dark ethnicities, such as brown, black and indigenous women, which is in agreement with the findings of the present study [23,25]. These results are highly significant, as they suggest that access to cesarean sections is not limited only to financial factors, but also involves racial issues, making the procedure less accessible to minorities.

Regarding the marital status of the parturient and the choice of delivery method, we found that single women opt for vaginal birth, while married women, widows, legally separated women and women living in consensual unions choose cesarean sections. Schiller (2015) analyzed the profile of parturients and the types of birth in Brazil and found that the highest percentages of cesarean sections are found among married and separated parturients in the five macro-regions. However, it is in the South, Central-West, and Southeast regions that the percentages of cesarean sections exceed the percentages of vaginal births in all marital statuses of the parturients [25]. Santos *et al.* (2022) investigated the relationship between marital status and type of birth, finding that single women had a higher prevalence of vaginal births. In contrast, among married women, the rate of cesarean sections was significantly higher, confirming the results of our study [23]. Marital status is a relevant factor, since the presence of a father figure can provide greater economic stability to the family, influencing the choice of cesarean section due to better financial conditions to afford the procedure. Single mothers, on the other hand, generally face economic limitations that make this option difficult [26].

The high number of cesarean sections in Brazil, also observed in the MRBS, appears to be related not only to biological factors, but mainly to social and cultural aspects. This context, although challenging because it is a complex sociocultural construction, can be changed through educational actions. It is essential to provide information to pregnant women about the different delivery methods, the procedures involved, and the consequences for the health of the mother and baby. This guidance can be offered during prenatal care, through lectures and informative materials, such as booklets and pamphlets. In addition, conducting more comprehensive studies on the subject is crucial, not only to increase society's knowledge, but also to raise awareness among public authorities, encouraging the adoption of measures that reduce the occurrence of unnecessary cesarean sections in the country.

This study found that the prevalence of cesarean deliveries in the MRBS appears to be associated with the mother's age, socioeconomic profile, number of prenatal consultations, education level and marital security. As in many regions of Brazil, in the MRBS there is an urgent need to expand and improve the information provided to women about the real risks associated with birth methods, broadening the understanding of the naturalness of birth, as well as promoting the humanization of this process so that the number of cesarean deliveries gradually decreases and can reach the ideal rate recommended by the WHO, which would be between 10% and 15% of all births performed.

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DATA AVAILABILITY STATEMENT

The datasets used in this study are from public domain, available from DATASUS, a Brazilian government website. Available from https://datasus.saude.gov.br/.

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Multiple Imputation Approaches for Missing Time-to-Event Outcomes with Informative Censoring: Practical Considerations from a Simulation Study Based on Real Data

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SUMMARY

Missing outcomes data represent a common threat to the validity and robustness of clinical trials with time-to-event outcomes. Recent extensions of multiple imputations (MI), namely controlled-MI, have been introduced as a viable approach for sensitivity analysis in the presence of informative censoring, yet they lack validation based on real data. In this study we used data from a randomized trial to generate realistic scenarios of censoring mechanisms and compare several imputation approaches for missing outcome data. Our results confirm the relevance of multiple imputations especially in studies with long follow-up and higher proportion of potentially informative censoring.

Keywords: missing data; multiple imputations; survival analysis; informative censoring.

Missing outcomes data represent a common threat to the validity and robustness of clinical trials and prospective epidemiologic studies with time-to-event outcomes. The most common reason for outcome missingness in these contexts is censoring, which generally occurs when patients are lost to follow-up or withdraw consent from an ongoing clinical study. Several studies have outlined the importance of critically evaluating missing outcome data in clinical studies, as well as the relevance of multiple imputations (MI) in this context, and researchers are expected to justify their handling of missing data [1-4]. Statistical approaches commonly used to report primary results in prospective studies, such as the non-parametric Kaplan-Meier estimator or the Cox regression model, generally provide valid estimates of the effect of interest under the assumption that censoring mechanisms are unrelated to either exposure or outcome. This assumption, commonly referred to as non-informative censoring, corresponds to an assumption of missingness at random for missing outcome data. There are several settings, however, where this assumption might not be met. In a clinical trial, for example, occurrence of adverse or safety events could lead to drug discontinuation and potential study withdrawal. If the occurrence of a given adverse event is more likely to occur for a specific treatment regime, this would lead to a higher risk of censoring in a specific study arm (i.e. informative censoring). Recent MI extensions, namely controlled-MI, have been introduced as a viable alternative for sensitivity analysis in the presence of informative censoring [5]. In particular, γ-imputation provides a flexible tool that allows incorporating existing knowledge on the potential censoring mechanisms to evaluate how the treatment effect would change under different scenarios [6]. In brief, γ-imputation relaxes the non-informative censoring assumption of the Cox model by including a γ term, corresponding to the log-HR comparing censored and uncensored individuals, and then uses MI to impute censored observations based on this modified Cox model [7].

Existing literature and recommendations for missing outcome data are largely based on theoretical considerations and simulation studies alone. Simulations

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are often conducted based on general assumptions for the censoring distributions and study population, and limited information from real data is available for clinical researchers and epidemiologists. To such end, in this study we used data from the DECLARE-TIMI 58 trial [8], a randomized, double-blind, multinational, placebo-controlled, phase 3 trial, to generate realistic scenarios of potential censoring mechanisms based on real data. This large clinical study (n=17,160) experienced very limited censoring due to withdraw consent or loss to follow-up (<2%), and we therefore evaluated it as the real target population. The detailed information on the occurrence of safety events and drug discontinuation collected was used to generate fictitious alternative settings of censoring that are likely to occur in real settings. First, we evaluated a potential scenario where all adverse events that led to drug discontinuation (affecting ~7.5% of participants) also led to trial follow-up discontinuation and therefore censoring. As several of these adverse events are associated with treatment, such censoring would be informative. Next, under the same censoring mechanisms and trial characteristics, we generated additional fictitious trials gradually increasing the proportion of censored individuals, the length of follow-up, and the proportion of trial participants experiencing the primary event. We then applied MI and γ-based controlled-MI to impute censored observations under all settings, comparing bootstrapped HRs from imputed data to the HRs from the complete data reported in the study. When using controlled-MI, γ values are provided by the user. In our example we used reported information on adverse events to define individual-specific γ values as the inverse of the log(HR) reported in the trial safety results. In practice, when the effect of the main exposure (e.g. treatment) on censoring is unknown, it is recommended to evaluate a range of potential γ values based on clinical background and a-priori hypothesis.

Table 1 summarizes results from the different evaluated settings. Results indicate that both standard

Table 1. Estimates of treatment effects (dapagliflozin vs placebo) for primary endpoints of DECLARE-TIMI 58 using multiple imputations and controlled multiple imputations, under different replications of the trial data summarizing settings with informative censoring

			MACE			HHF/CVD	
Original trial DATA[a]			0.93 (0.85, 1.03)			0.83 (0.73, 0.95)	
			MI	**Controlled-MI[c]**		**MI**	**Controlled-MI**
Modified trial DATA[b]			0.924 (0.834, 1.023)	0.937 (0.853, 1.030)		0.833 (0.719, 0.964)	0.824 (0.710, 0.955)
Simulated trial DATA[d]		**Real HR**			**Real HR**		
A: Trial data with higher censoring proportion	~15%	0.931	0.932 (0.842, 1.033)	0.928 (0.839, 1.027)	0.826	0.821 (0.739, 0.912)	0.817 (0.736, 0.908)
	~30%	0.962	0.970 (0.872, 1.08)	0.956 (0.859, 1.065)	0.829	0.832 (0.745, 0.93)	0.823 (0.738, 0.917)
B: Trial data with longer follow-up	5y	0.936	0.932 (0.851, 1.022)	0.931 (0.849, 1.02)	0.826	0.821 (0.739, 0.912)	0.817 (0.736, 0.908)
	10y	0.936	0.947 (0.882, 1.016)	0.939 (0.876, 1.006)	0.847	0.866 (0.772, 0.972)	0.852 (0.755, 0.96)
C: Trial data with higher events proportion	~20%	0.925	0.926 (0.837, 1.024)	0.924 (0.836, 1.022)	0.841	0.845 (0.761, 0.937)	0.844 (0.761, 0.936)
	~50%	0.917	0.913 (0.826, 1.01)	0.911 (0.823, 1.007)	0.824	0.827 (0.745, 0.917)	0.825 (0.744, 0.915)

MACE=Major Adverse Cardiovascular Events; HHF/CVD= hospitalization for heart failure or cardiovascular death

[a] *Original data without imputations*

[b] *All participants experiencing drug discontinuation due to adverse event (~7.5 %) are censored on the day of the adverse event*

[c] *For individuals experience adverse events associated with treatment (potential informative censoring), gamma values are defined as the inverse of the log(HR) for that adverse event. For all other censored individuals, gamma=0 (i.e. non-informative censoring)*

[d] *Results based on 10 replications of the trial data under the different detailed setting. The table shows the average real HRs from the 10 replications and the average HRs estimated from MI and controlled-MI*

MI and controlled-MI provide robust inference under all evaluated scenarios, with slightly improved performances of controlled-MI only with heavy censoring (~30%) and longer follow-up (10 years). These results confirm the relevance of multiple imputations approaches for missing outcome data in prospective studies. We join previous researchers in recommending their inclusion as sensitivity analyses in study protocols and statistical analysis plans, especially in studies with long follow-up and higher proportion of potentially informative censoring. Controlled-MI, and in particular γ-imputation, can be used to assess the extent to which potential informative censoring would affect primary trial results, thus providing a powerful tool for sensitivity analysis for prospective studies in the presence of missing outcome data and censoring for which reasons are unknown.

To our knowledge, this is the first study comparing MI and controlled-MI approaches for missing outcome data using extensive simulated scenarios that are based on real data and censoring mechanisms occurring in applied clinical and epidemiologic research. By generating fictitious replications of a complete clinical study and using observed information on adverse events mechanisms to generate censoring, this study can help practitioners appreciate the advantages of different imputation approaches under realistic settings in prospective studies in clinical epidemiology.

DISCLAIMER

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Emergency Department Departures: Untangling the Complexities of Early Exits in a Large Italian region

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SUMMARY

Leaving Emergency Departments (ED) early is an important failure of these structures, constituting a risk for the health of the people who renounce the benefits of such healthcare, and a cost to the countries that finance healthcare service for their citizens. In order to implement actions to reduce the extent of this failure, an understanding of the characteristics of patients who leave EDs early is needed. This research scrutinizes the determinants of early ED departure in the hospitals of the region of Campania, Italy, where around a tenth of the Italian population lives. We adopt a quantitative framework, utilizing a novel robust dataset of about 1,000,000 observations, employing both Probit and Logit estimators. Our analysis reveals that factors including being a woman, having Italian citizenship, arriving by ambulance, severity of condition, and reporting a trauma, are associated with decreased probability of premature ED departure, while residing in high-income municipalities and being under 65 correlates with an increased likelihood of early leaving. The value of this information for policymakers and healthcare providers is discussed.

Keywords: Emergency Department; Early Emergency Department Departure; Healthcare Access; Patient Decision-making; Emergency Department Efficiency

BACKGROUND

Premature departure (i.e. before the conclusion of visit procedures) from the Emergency Department (ED) of a hospital is an important problem that poses health risks for individuals who forego the benefits of available healthcare. Moreover, it is a waste of the limited resources of EDs [1], and a public cost for countries that provide healthcare to their citizens. Indeed, as is well known, various governments around the world offer health services to their citizens without requiring the final user to (directly) pay for these. An extensive scientific debate discusses the economic efficiency of these situations, which is largely unrelated to the medical nature of the specific service, and which can more generally be referred to the nature of common goods, an approach that goes back to Hardin's seminal article [2]. Indeed, given the well-known and widely studied incentives for consumers to consume more than needed when they do not pay for a good, an ample scientific debate deals with the issue. Usually, when it comes to health, economists try to find the optimal balance in a difficult trade-off between economic efficiency and giving equal opportunities to citizens from different backgrounds.

Countries with largely publicly funded healthcare, although the extent to which it is free at the point of use varies, such as the United Kingdom (where the National Health Service provides healthcare that is free at the point of use for residents, funded through taxation), Sweden (where patients usually pay small fees for visits, while some services, like child healthcare, are free), Norway (where patients pay co-payments until they reach an annual limit, after which further care is free), Spain (where the public healthcare system offers universal coverage, and most services are free for residents, with some groups, like unemployed citizens, receiving completely free care), and Italy (where the National Health Service provides free healthcare for residents, covering services like doctor visits, emergency care, and hospitalization, while some specialist services may require co-payments), differ

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significantly in their political institutions and social structures. These differences have been analysed in detail in the comparative healthcare literature [3,4].

Among these countries, of particular interest is the case of Italy, a nation where the vast majority of health services are provided to citizens by the public healthcare system, which is paid for mostly with taxpayers' money, with no, or with very limited, direct charges to users [5].

The literature suggests that when a government provides health services without asking for a payment from the final user, there is an increase in their utilization, particularly among the unemployed and less educated [6], and that this leads to a reduction of household health expenditure [7,8]. On the other hand, while the implementation of user fees has been suggested to have economic benefits as well [9] – although issues of equal access need to be addressed – the point has also been raised that individual fees inevitably elevate the financial burden borne by individuals and alleviate the redistribution of wealth from affluent and healthy individuals to those who are economically disadvantaged and unwell [10]. It has also been suggested that there is a risk that free government health services may primarily benefit the better-off, suggesting the need for targeting measures and alternative financing mechanisms [11].

While of general importance, optimizing the delivery of health services to users is even more important when these services are offered for free, since some market-created incentives that would improve efficiency in a scenario where the final user directly pays are not in place in the case of healthcare funded by the taxpayer. Among these services, we believe the case of EDs to be of special interest, for at least three reasons. First, reducing the number of unnecessary visitors to EDs is a crucial means of preventing their congestion and keeping these departments operating smoothly, which is important given the fundamental role they play in safeguarding people's health, and the fact that by their very nature these departments work with emergencies. Second, a patient who leaves an ED prematurely signifies the inadequacy of an emergency care delivery system in achieving its objectives of delivering assistance to individuals requiring urgent medical attention [12]. Notably, it has already been suggested that patients who leave EDs before the doctor's visit are a useful indicator of the quality of emergency care [13]. Hence, it seems important to understand who leaves early and why, in order to suggest policies that may improve the efficacy of these departments. Third, financing EDs involves considerable cost to public expenditure, and hence optimizing the process is an important way to avoid unnecessary public spending and a waste of public resources.

Among all the challenges involved in running an ED, avoiding having patients who abandon the ED before their visit procedures have concluded is crucial, if this investment of public money is to be optimized. Abandoning an ED before the conclusion of visit procedures incurs a considerable public cost for countries that offer this service to their citizens, such as Italy. It happens frequently; in 2019 and in the first two months of 2020 (i.e. before the COVID-19 emergency erupted in Italy, imposing lockdowns and creating incentives to avoid hospitals), there were 214,757 of these events in hospitals in Campania (a region of Italy) alone. Of these over a quarter, 54,722 patients, left before even seeing a physician. The cost for a white code, i.e. a visit to the ED that is not considered an emergency by the doctors, and hence is not supported by public spending (a provision created to prevent citizens from visiting the ED as a way of avoiding the lengthier non-emergency route to access to healthcare), was established in Italy by law 296/2006 as being €25, for patients who did not benefit from any supplementary exam or visit by a specialist. Using this very conservative estimate as the baseline cost imputed to those early leavers (and please note that this is the bare minimum to be considered), to compute the waste of resources one should also add the cost of an ambulance bringing the patient there (9,914 of the aforementioned cases who left hospital before their treatment had concluded were brought to the hospital by an ambulance).

Hence, if we estimate an ambulance call at having an average cost of €150 (a cost which depends, obviously, on the distance, though for relative short rides €150 is usually the minimum price requested by private ambulances), the total cost of these events was €5,368,925 for curtailed visits, plus €1,487,100 for ambulance rides, giving a total of €6,856,025 for the fourteen months considered. Assuming that this waste that occurred in Campania is representative of the rest of Italy, given that the region hosts around a tenth of the Italian population (5.802 million out of a population of 59.11 million), the national cost of this early leaving would be about €4,897,160 per month. Considering the very conservative attitude adopted in this estimation the real expenditure would appear to be considerable, and this could be avoided, or at the very least reduced, by knowing more about the characteristics of patients that abandon EDs before the conclusion of their treatment. This would allow hospitals and policymakers to implement policies designed specifically to address these subjects and reduce this inefficiency.

Previous scientific literature suggests that patients leave the ED for a variety of reasons, including long waiting times, spontaneous resolution of symptoms, and dissatisfaction with staff or facilities. These findings emerge across different national contexts: Carmel et al. analyzed patients in Israel, which operates a universal health insurance model with public and non-profit health plans [14]; Fernandes et al. examined the Canadian system, which offers universal, publicly funded healthcare at the provincial level [15]; Fry et al. investigated this behavior in Australia, which also has a universal healthcare system supported by Medicare [16]; Hsia et al. studied the phenomenon in the United

States, where access to care is often contingent on private insurance coverage[12]; Lee et al. reported on Hong Kong, which provides a predominantly public healthcare system funded through taxation [17]; and Lerner addressed the issue within the U.S. system [18], like Weiss et al., which focuses on dissatisfaction with staff communication [19]. More recent work by Rowe et al., which focuses on symptom improvement [20], and Mohsin et al., both in Australia, a system with universal healthcare [21], and Mahmoudian-Dehkordi et al. in Iran, a mixed public-private system, confirms similar motives in different contexts [22].

Low acuity ratings are particularly associated with early departure, as shown in studies from Canada [15,23], and again in the U.S. [24]. The study by Hsia et al. underscores that patients with limited insurance coverage, a uniquely U.S. concern, are more likely to leave without being seen [12]. Demographically, those who leave early are often younger, single men with less severe conditions, as observed by Carmel et al. in Israel [14].

Nonetheless, it is important to highlight that most of these previous findings are obtained in countries with very different healthcare systems and cultures (the previous cited articles use data from countries including Australia, Canada, Hong Kong, Israel, Taiwan, and the US). This heterogeneity may easily create distinct sets of incentives for the patients to decide to stay or leave, leading to limited external validity for these results. For instance, consider the relevance of having health insurance to such a decision for patients in the US, where ED visits must often be paid for, as compared to Italy.

To the best of our knowledge, there are a few retrospective studies focusing on the consequences of leaving ED early, but there is no contribution that specifically examines the characteristics of patients that do so in Italy. In Italy, ED departments are usually open 24/7, and patients may arrive via ambulance services or independently. Following the initial diagnosis, the triage process commences, determining whether patients should be admitted, and with what level of priority, or discharged. A colour code is assigned to the patient, according to the severity of his/her condition, and hence according to the urgency of receiving treatment. EDs contend with heightened service demand, leading to elevated costs. Additionally, EDs typically function within the constraints of limited human resources and budgetary allocations [1]. One study has highlighted that this lack of available literature makes it critical to identify the determinants that could be associated with visits to the ED [25], and that this acquiring knowledge is essential for directing interventions at the hospital level to enhance the accessibility of emergency medical services [12]. This seems especially important, since as of now efficiency measurements assessing performance in the emergency department lack uniformity and standardization [26]. Moreover, a retrospective cohort study of Lazio's EDs suggests that patients that leave before being visited by a doctor have a greater risk of ED re-admission compared to discharged patients, even though the effects on hospitalization and mortality are more controversial [13].

In the present study, we aim to fill this gap in the literature by identifying the characteristics of both the patients that left the ED before being visited by a physician, and those that left before the closure of their medical record (i.e. the conclusion of the procedure). We do so by means of a quantitative analysis that exploits data about all the patients that visited EDs in Campania, Italy, between 1 January 2019 and 28 February 2020 (a cut-off point chosen in order to prevent the COVID-19 emergency from affecting our findings).

Our results, obtained through regression analysis with both Probit and Logit estimators, suggest that distance from the ED does not affect the decision to leave early, while being a woman, being an Italian citizen, living in a municipality with higher education levels, arriving at the ED by ambulance, having a more serious condition, and being in the ED because of trauma, are all characteristics correlated with a lower probability of leaving the ED early. Moreover, being under 65 years old (for all the sub-categories of age considered), and residing in a municipality with higher income per capita are characteristics correlated with a higher probability of leaving early.

METHODS

To identify the characteristics correlated with leaving the ED early within a quantitative framework, we require data about ED patients, their socio-demographic characteristics, and information about the specific context of their experience. For our main source of data we relied on the STAR-EMUR Regione Campania's dataset on ED admissions in each hospital of the region. This source offers micro-level data about every patient in every ED of all of Campania's hospitals, and it is the only official one for Italy. It is compiled for the Italian Superior Institute of Health (Istituto Superiore di Sanità) by each hospital and offers micro-level data about each and any patient in all the hospital EDs in the Campania region. Data contains anonymised individual-level data for each ED admission, including the patient's age, gender, municipality of residence, and nationality (Italian or not). It also reports how the patient arrived at the ED (e.g., ambulance or other means), the exact time of check-in and of the medical consultation (if any), and the primary reason for seeking emergency care, as recorded in the triage assessment. No personal identifiers or clinical history are included, in full compliance with privacy regulations.

We gathered these data from 2019 to the end of February 2020, to avoid the inclusion of data from the COVID-19 emergency and the related restrictions on movement, which are likely to affect both the dynamic of going to the ED and of leaving it early.

Unfortunately, no information is provided in this dataset about education or income level of the patient, which may affect the decision to leave early.

To enrich the set of data on which we perform our analysis, we attached to the aforementioned dataset the following data:

- Data about the geographical location of the hospitals in Campania, in order to be able to calculate the distance between the residence of the patient, as gathered in the previous dataset, and the ER.
- The distance, expressed in time (minutes), that is required to travel between the patient's municipality of residence and the hospital (data taken from the Italian National Statistic Agency – ISTAT);
- The per capita taxable income from work in the patient's municipality of residence (data taken from the Italian Revenue Agency);
- The share of population over 9 years old in the municipality that in 2021 (last available census data) had a secondary education (high school) diploma (both data about the education level and the population are taken from ISTAT) to obtain a measure of education.

In this way, we managed to impute to each observation information that are unfortunately not available at the individual level. Given both the size of the sample (we included 980,579 observations for the regression that has as dependent variable the patients that left before the closure of the medical record, and 806,194 for those that left before being seen by a doctor, i.e. all those who survived the listwise deletion process), and the small size of many municipalities (the average population of the municipalities present in the sample is just 15,429.51 inhabitants), we believe that this strategy is empirically reliable, since the municipality average is representative enough of the observations to which it is imputed.

With these operations, we built a dataset with information about patients that left the ED early, both before being seen by a physician (labelled "Leaves before Being Visited") and before the closure of the medical record (labelled "Leaves before MR closure") which are our dependent variables, augmented with four matrixes of independent variables.

The first, labelled *Demographic*, controls for the characteristics of the patient, and is composed of six dichotomous dummy variables to distinguish between the ages of the patients (following Agovino et al., [27]), we included dummies to control for patients under 15 years old, those between 15 and 24, 25–34, 35–44, 45–54, and 55–64, with the omitted, and hence reference, modality being patients over 65 years old), and two dichotomous dummy variables: a first signalling whether the patient is female, and a second signalling whether she or he is Italian citizen. The second matrix, labelled *Municipality*, controls for the characteristics of the municipality of residence of the patient, and is composed of the logarithm of the per capita income of the municipality, to control for an income effect; the distance in time from the municipality to the hospital, to control for the investment made to reach the hospital, and the share of municipal population that in 2021 had a high-school diploma, as a measure of education. The third matrix, labelled *Incident*, controls for the characteristic of the emergency that led to the ED, and is composed of four dichotomous dummies: the first two are equal to one if the patient was coded as yellow or red upon admittance; the third control for whether she or he arrived in an ambulance; and, finally, one controls for whether the patient reports a trauma as her or his main problem. Finally, the last matrix includes hospital-level fixed effects, to prevent any local specificity from affecting our results. Descriptive statistics about the variables are presented in Table 1, while Table 2 reports the distribution of

Table 1. Descriptive Statistics

Label	Variable	Obs	Mean	Std. dev.	Min	Max
Leaves before Being Visited	Dichotomous dummy variable, equal to 1 if the patient abandoned the ED before being visited by a physician	980,579	0.0399081	0.1957433	0	1
Leaves before MR closure	Dichotomous dummy variable, equal to 1 if the patient abandoned the ED before the closure of the Medical Record	980,579	0.0734066	0.2608029	0	1
Under 15 y.o.	Dichotomous dummy variable, equal to 1 if the patient is between 0 and 15 years old	980,579	0.1355515	0.3423119	0	1
15–24 y.o.	Dichotomous dummy variable, equal to 1 if the patient is between 16 and 24 years old	980,579	0.1096046	0.3123965	0	1

(*Continued*)

Table 1. Descriptive Statistics (Continued)

Label	Variable	Obs	Mean	Std. dev.	Min	Max
25–34 y.o.	Dichotomous dummy variable, equal to 1 if the patient is between 25 and 34 years old	980,579	0.1314723	0.3379164	0	1
35–44 y.o.	Dichotomous dummy variable, equal to 1 if the patient is between 35 and 44 years old	980,579	0.1272993	0.3333081	0	1
45–54 y.o.	Dichotomous dummy variable, equal to 1 if the patient is between 45 and 54 years old	980,579	0.1353333	0.3420794	0	1
55–64 y.o.	Dichotomous dummy variable, equal to 1 if the patient is between 55 and 64 years old	980,579	0.1240012	0.3295831	0	1
Women	Dichotomous dummy variable, equal to 1 if the patient is a woman	980,579	0.4882738	0.4998627	0	1
Ita.Citizen	Dichotomous dummy variable, equal to 1 if the patient is an Italian citizen	980,579	0.988931	0.1046253	0	1
Log Income pc	Logarithm of the taxable income from work per capita of the municipality of residence of the patient	980,579	9.775822	0.1677096	9.129075	10.21894
Eff.Dist.in time	Distance in minutes between the municipality of residence of the patient and the hospital	980,579	16.95452	28.37142	0	762
Secondary Education pc	Share of the municipality population aged 9+ in 2021 that has at least a secondary education diploma	980,579	0.3393009	0.0267932	0.1693936	0.4693042
Yellow code	Dichotomous dummy variable, equal to 1 if the patient has been coded as yellow in the triage	980,579	0.226611	0.418639	0	1
Red code	Dichotomous dummy variable, equal to 1 if the patient has been coded as red in the triage	980,579	0.013799	0.1166559	0	1
Arr.Ambulance	Dichotomous dummy variable, equal to 1 if the patient has arrived at the ED in an ambulance	980,579	0.1035031	0.3046151	0	1
Trauma main probl.	Dichotomous dummy variable, equal to 1 if the patient has reported trauma as the main problem	980,579	0.2194887	0.4139004	0	1

key patient characteristics across those who left the ED before being seen by a physician and those who completed the process.

Statistically significant differences are observed for all variables considered. Women were slightly less likely to leave early compared to men (3.85% vs. 4.13%, $p < 0.001$), while Italian citizens exhibited a higher early departure rate (4.02%) than non-citizens (1.62%, $p < 0.001$). Patients arriving by ambulance were markedly less likely to leave (1.15%) than those who arrived independently (4.32%, $p < 0.001$), consistent with the assumption of more severe conditions. Similarly, those presenting with trauma were less likely to leave early (2.84%) than non-trauma patients (4.31%, $p < 0.001$).

After these preliminary operations to build the dataset, we ran a regression to estimate the correlations between certain characteristics of the patient and their decision to leave the ED early. We opt to use both Probit and

Table 2. Distribution of observed characteristics in patients that leave before the visit and patients who do not

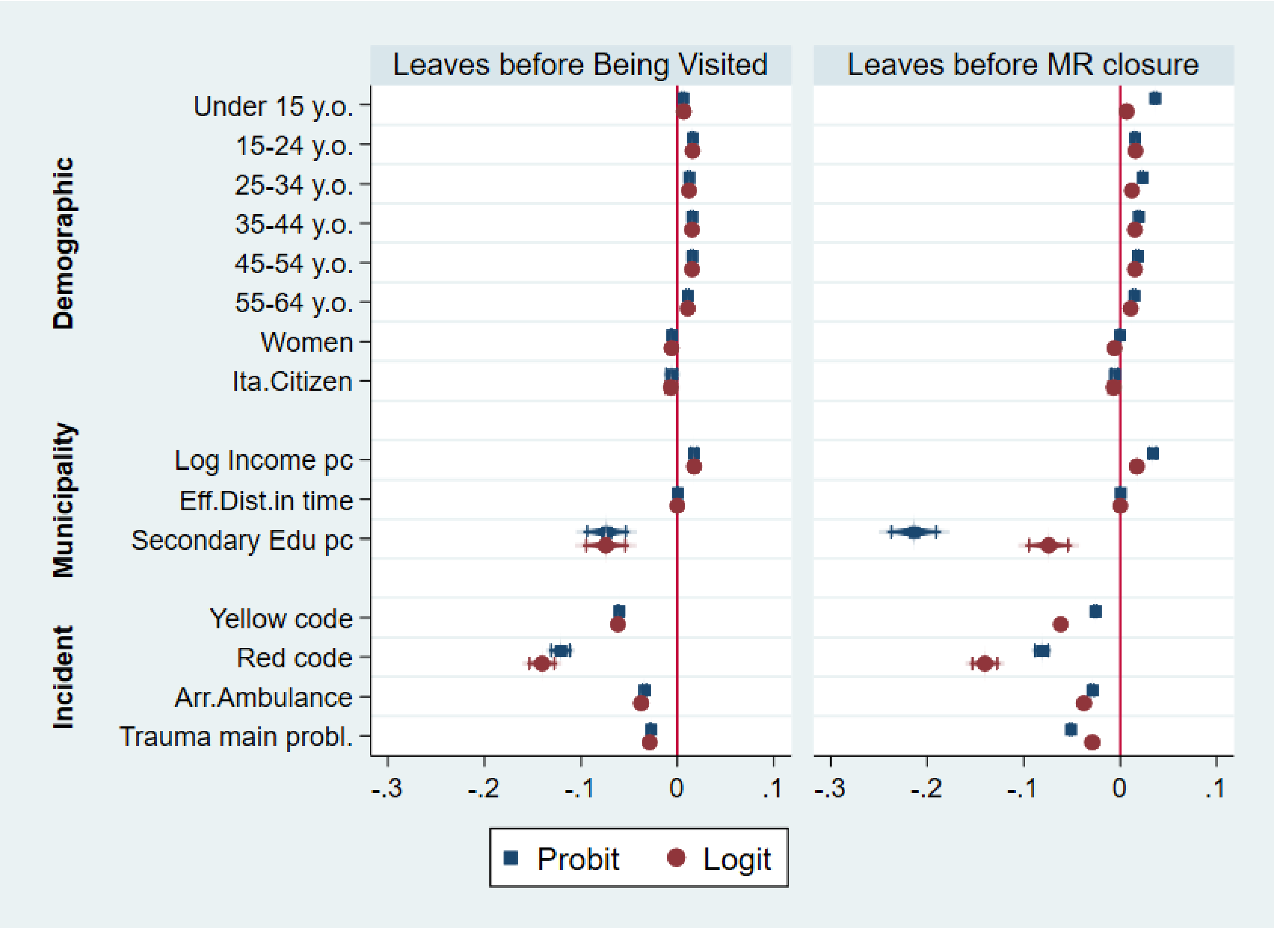
	Leaves before being visited		
Gender	**No**	**Yes**	**Total**
M	481,068	20,705	501,773
	95.87%	4.13%	100.00%
F	460,365	18,426	478,791
	96.15%	3.85%	100.00%
NR	13	2	15
	86.67%	13.33%	100.00%
Total	941,446	39,133	980,579
	96.01%	3.99%	100.00%
Pearson chi^2 (2)	52.8092	Pr=0.000	
Italian Citizen			
No	10,678	176	10,854
	98.38%	1.62%	100.00%
Yes	930,768	38,957	969,725
	95.98%	4.02%	100.00%
Total	941,446	39,133	980,579
	96.01%	3.99%	100.00%
Pearson chi^2 (1)	160.7994	Pr=0.000	
Arrived in Ambulance			
No	841,120	37,966	879,086
	95.68%	4.32%	100.00%
Yes	100,326	1,167	101,493
	98.85%	1.15%	100.00%
Total	941,446	39,133	980,579
	96.01%	3.99%	100.00%
Pearson chi^2 (1)	2.4e+03	Pr=0.000	
Trauma main problem			
No	732,332	33,021	765,353
	95.69%	4.31%	100.00%
Yes	209,114	6,112	215,226
	97.16%	2.84%	100.00%
Total	941,446	39,133	980,579
	96.01%	3.99%	100.00%
Pearson chi^2(2)	953.4385	Pr=0.000	

Logit estimators, which are the natural choice given the dichotomous nature of our dependent variable [28–31]. More details about the estimations, and some robustness checks, are provided in Appendix 1.

RESULTS

Results of the marginal effects of the estimation are presented in Figure 1, for both Probit (whose values

Figure 1. Regression results (Marginal Effects)



are represented by blue squares) and Logit (whose values are represented by red circles) regressions, run with robust standard errors.

On the left-hand side of the figure are the marginal effects computed in a regression where the dependent variable discriminates for patients that leave the ED before being seen by a physician. On the right-hand side, meanwhile, are the results when the dependent variable discriminates for patients who left before closure of their medical record, i.e. the conclusion of the procedure. The solid and blurred lines after the square and the circle represent confidence intervals of 95% and 90%, respectively, which are quite small, possibly because of the size of the sample.

An initial result is that the marginal effects for both the estimators are very similar, suggesting some robustness in our findings and indicating that these are not dependent on the chosen estimator. Moreover, we can also see that for the two different dependent variables the results also follow very similar patterns. This suggests that the determinants of leaving the ED early are similar in both cases.

Not all the variables report a statistically significant marginal effect: the distance (expressed in minutes) between the municipality of residence of the patient and the ED is not, suggesting that this variable does not affect the decision to leave the ED. On the other hand, notably, women, Italian citizens, those residing in more educated municipalities, patients that arrived by ambulance, individuals with severe health conditions (i.e. red or yellow codes), and those that reported a trauma, exhibit a reduced likelihood of premature ED departure. On the other hand, residing in municipalities with higher income per capita, and being younger than 65, are factors associated with an increased probability of early departure. These multivariate patterns align with the univariate findings suggested by Table 2, reinforcing the profile of early leavers as generally less acute and more autonomous patients.

DISCUSSION

This research, conducted on observational data from Campania, Italy, from January 2019 to February 2020, discerned several factors influencing early departure from ED. Our findings, and our observation of increase premature departure among patients from higher-income municipalities, does not align with prior research indicating low-income, uninsured patients' increased likelihood of early ED departure [23,24]. This suggests that in Italy the people leaving early are possibly those that have alternative, better options, possibly because of the fact that the health system is mostly public funded. Additionally, akin to research on lower acuity ratings predicting early departure [17,18], our study also suggests a negative correlation between severity (red or yellow codes) and early departure, with a lower probability of leaving correlated to the most severe code (red). Moreover, all the variables controlling for the age of the patients have positive coefficients, suggesting that patients younger than 65 are more likely to leave early than patients older than 65 (the omitted, and hence reference, modality).

Intriguingly, though it confirms previous results, our study also diverges from some findings in the literature, as our sample reveals that women are less likely to leave the ED prematurely compared to men, contrary to suggestions of single men being more inclined to early departure, a result derived over twenty years ago from an analysis in Israel [14]. This warrants further exploration of underlying factors, especially in light of the well-known differences in risk-aversion between genders, which suggests that women should leave early less frequently [32].

Furthermore, the lack of significance regarding the distance (in minutes) between the municipality where the patient resides and the ED can be seen as indicating the unimportance of this factor in determining early departure from ED. This is quite interesting, since the finding can be seen as meaning that the investment (in terms of time) made to reach the ED in Campania apparently does not play a role in deciding whether or not to leave the ED. This may be interpreted as suggesting that this cost is not too high, and hence that there is a good distribution of EDs across Campania. On the other hand, it is also important to highlight that our analysis, as with any analysis of a big, heterogeneous sample, reports mean values as the result. Hence, we cannot exclude that the distribution of access to each ED creates disparities in the opportunity to access some of the EDs, which, though statistically not significant, are of course an important policy issue for people who live in municipalities that are not served by a hospital, or one with an ED.

It is also interesting to highlight the role played by education in our setting. Our results suggest that people who live in more educated municipalities are less likely to leave the ED early: this is a finding that implies interesting consequences. First, it highlights the importance of education in this setting too, and indicates a further return on investments in education. Second, assuming that education is correlated to health literacy, as a part of the literature does, this underlines the importance to public health of raising the levels of health literacy (and in Italy its levels are unfortunately very low [33–35]. By implying further benefits to public spending from having a more educated population, this result has important consequences in terms of budget allocation. For all these reasons, more research into the relationship is needed.

The findings of this study have several implications for healthcare providers and policymakers. By understanding the factors that contribute to earfigure 1ly ED departure, healthcare providers can develop targeted interventions to reduce the occurrence of this phenomenon. Policymakers can also consider implementing policies that address the underlying factors that drive early ED departure, such as socioeconomic and education disparities in the population.

Providers, armed with insights into the determinants of early ED departure, can strategically design multifaceted interventions. Improving communication strategies within the ED setting, tailoring patient education initiatives to highlight the potential consequences of premature departure, and actively addressing healthcare access barriers are pivotal steps for mitigating this phenomenon. Furthermore, healthcare providers may explore collaborative efforts with local emergency services to optimize ambulance protocols, ensuring timely and appropriate patient care upon arrival at the ED.

Simultaneously, policymakers bear the responsibility for formulating comprehensive strategies to address the societal underpinnings of premature ED departure. Recognizing the role of education and income disparities, policymakers should prioritize the expansion of affordable healthcare initiatives, thereby bolstering equitable access to medical services. Crafting policies that specifically target hospital serving areas with lower income per capita and lower education levels, as well as fostering community-based healthcare initiatives, are critical measures for promoting patient retention within emergency healthcare systems.

In tandem, fostering cross-sectoral collaborations between healthcare providers and policymakers becomes imperative. By integrating efforts, stakeholders can collectively develop and implement interventions that not only address immediate concerns within the ED but also contribute to broader systemic improvements in healthcare accessibility and equity.

CONCLUSIONS

In summary, this study has investigated the determinants of early ED departure in Campania, Italy, leveraging a dataset of around 1,000,000 observations and employing Probit and Logit estimators with robust standard errors. Within this quantitative framework, significant association emerged, revealing that factors such as being a woman, having Italian citizenship, having a higher level of education, arriving at the ED by ambulance, having a more severe condition, and whether or not the health issue is traumatic, are all characteristics associated with a decreased likelihood of premature ED departure. Conversely, residing in municipalities with lower income per capita and being younger than 65 are factors linked to an increased probability of early leaving.

While providing interesting new results on the characteristics of early ED leavers in Campania, Italy, which to the best of our knowledge have not been discussed by previous literature, this research is not exempt from limitations, which must be acknowledged. The observational nature of the data poses constraints on establishing causal relationships, and the focus on a specific geographic region may limit external validity and hence generalizability to broader contexts. Additionally, despite the extensive dataset with micro-level data, there may be unaccounted confounding variables that could influence the observed associations. These limitations underscore the need for caution in extrapolating findings beyond the study's specific context.

Looking ahead, future research could explore the nuanced dynamics of patient-physician communication within the ED setting, investigating how effective communication strategies may influence the likelihood of ED early departure. While the focus of this study is on demographic and clinical characteristics associated with patients who leave the ED early, it is important to highlight that is crucial to delve into the underlying reasons behind their decisions. Future research could incorporate qualitative methods, such as patient interviews or surveys, to directly capture these motivations. By understanding the "why" behind premature departures, healthcare providers can develop more targeted and effective interventions to address these specific concerns. Moreover, our study as an underlying assumption that all premature departures from the ED are undesirable. This may not hold universally. Authors suggested that some patients who leave ED without being seen or against medical advice tend to have positive outcomes, particularly if their initial assessment suggests low acuity. Hence, it is essential to differentiate between cases where early departure poses a significant health risk and those where patients may reasonably manage their conditions through alternative healthcare settings, even although it is unfortunately very hard to have data that allow for such a distinction. Nonetheless, recognizing it can help refine our interpretation of the data and avoid biases that might skew the study's conclusions.

Furthermore, examining the impact of socio-cultural factors on patient decision-making processes during ED visits could provide valuable insights into the intricate interplay between individual characteristics and healthcare outcomes. Exploring the temporal trends in early ED departure rates and their correlation with evolving healthcare policies would also contribute to a more comprehensive understanding of this phenomenon. These potential avenues of research aim to enrich our understanding of early ED departure dynamics, offering valuable insights for refining interventions and policies in emergency healthcare.

These findings not only contribute to the academic understanding of early ED departure but also hold practical implications. The insights gleaned from this research serve as a foundation for targeted interventions aimed at mitigating premature departures, thereby bolstering the overall efficiency of ED systems. By incorporating these findings into healthcare practices, providers can refine patient care strategies, optimize resource allocation, and potentially enhance patient outcomes. As the healthcare landscape evolves, these research outcomes provide a timely and valuable resource for informing evidence-based interventions and policies to address the complex dynamics surrounding early ED departure in the Italian context.

In conclusion, our investigation provides valuable insights into the characteristics of patients who leave the ED early in Italy. These findings can inform interventions aimed at reducing the occurrence of early ED departure, enhancing the overall efficiency of ED systems, and improving patient outcomes.

JEL codes I11; I12; I18

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DECLARATIONS OF INTEREST

No author perceives any conflict of interest

DATA AVAILABILITY

The data that support the findings of this study are not openly available due to reasons of sensitivity and are available from the corresponding author upon reasonable request.

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APPENDIX 1 – DETAILS OF THE EMPIRICAL ANALYSIS

To study the determinants of early departure from ED and answer our research question, we model the early leaving from ED, both before being seen by a physician and before the closure of the medical record, as a function of four matrixes: demographic, municipality, incident, and hospital. In more formal terms, we estimate equation (1):

$$EL = \alpha + \beta_1 \, Demo + \beta_2 Muni + \beta_3 Incident + \beta_4 Hospital + \varepsilon \quad (1)$$

where EL (early leaving) is a dichotomous dummy variable operationalized in two different ways: in different regressions it may either assume the value of 1 if the patient left before being seen by a physician, or if she or he left before the closure of the medical record, which is when the procedure is concluded and the patient is discharged. This variable is expressed as the function of four matrixes:

- *Demo*, a matrix composed of eight variables, describing the demographic characteristics of the patient: *Under 15 years old*, *15–24 y.o.*, *25–34 y.o.*, *35–44 y.o.*, *45–54 y.o.*, and *55–64 y.o.*, *Women*, and *Italian citizenship*. All these variables are dichotomous dummy variables built from data gathered from Regione Campania's dataset on ED admissions;
- *Municipality*, a matrix composed of three variables, describing the characteristics of the municipality where the patient lives. Given the lack of better information, these allow us to attach more data to each patient. These three variables are *Log Income pc*, the logarithm of the per capita income of the municipality; *Eff.Dist.in time*, the effective distance (in minutes) between the municipality and the hospital; and *Secondary Edu. Pc.*, the share of population aged 9+ living in the municipality that has a secondary education diploma in 2021. This latter variable is our operationalization of education and, by extension, of health literacy;
- *Incident*, a matrix composed of four dichotomous dummy variables, describing the characteristics of the reasons for which the patient went to the ED. These are *Yellow* and *Red code*, variables equal to 1 if the patient was coded at admittance by this level of urgency; *Arr.Ambulance*, a variable discriminating for patients that arrived by ambulance, and *Trauma main probl.*, a variable equal to 1 if the main problem of the patient has been reported as a trauma;
- *Hospital*, a matrix of hospital-level fixed effects, to prevent any specificity of the ED or the area in which it is located from affecting the results.

Equation (1) has been estimated through Probit and Logit estimators, with robust standard errors, always including the hospital-level fixed effects, and adding the matrixes with the most relevant determinants one at a time, to see what happens to the coefficients when the covariates are added. The results of the computation of both the coefficients and the marginal effects, for both the operationalizations of the dependent variable, are reported respectively in tables A1, A2, A3 and A4, for the Probit estimator, and A5, A6, A7 and A8 for the Logit estimator.

Table A1. Coefficients – Probit - Det.of abandoning ER before visit

	(A1.1)	(A1.2)	(A1.3)
	Leaves before Being Visited	**Leaves before Being Visited**	**Leaves before Being Visited**
Under 15 y.o.	0.283***	0.285***	0.0653***
	(29.08)	(29.19)	(6.37)
15–24 y.o.	0.339***	0.339***	0.174***
	(36.04)	(36.01)	(17.55)
25–34 y.o.	0.319***	0.320***	0.134***
	(34.89)	(34.94)	(13.93)
35–44 y.o.	0.340***	0.341***	0.170***
	(37.27)	(37.35)	(17.70)
45–54 y.o.	0.312***	0.313***	0.170***
	(34.49)	(34.54)	(18.00)
55–64 y.o.	0.224***	0.224***	0.120***
	(23.41)	(23.46)	(12.08)

(*Continued*)

Table A1. Coefficients – Probit - Det.of abandoning ER before visit (Continued)

	(A1.1)	(A1.2)	(A1.3)
	Leaves before Being Visited	**Leaves before Being Visited**	**Leaves before Being Visited**
Women	–0.0371***	–0.0370***	–0.0667***
	(–7.30)	(–7.27)	(–12.70)
Ita.Citizen	–0.0887**	–0.0901**	–0.0659*
	(–2.34)	(–2.38)	(–1.70)
Log Income pc		0.152***	0.192***
		(7.12)	(8.73)
Eff.Dist.in time		0.0000190	0.0000990
		(0.19)	(1.01)
Secondary Education pc		–0.953***	–0.821***
		(–7.18)	(–5.99)
Yellow code			–0.676***
			(–74.34)
Red code			–1.352***
			(–20.79)
Arr.Ambulance			–0.382***
			(–28.35)
Trauma main probl.			–0.310***
			(–44.66)
Hospital Fixed Effects	YES	YES	YES
Constant	–1.845***	–2.992***	–3.181***
	(–39.89)	(–14.68)	(–15.22)
Observations	806194	806194	806194
Pseudo R^2	0.086	0.087	0.125
Log lik.	–143017.0	–142976.6	–136978.2
Chi-squared	21520.9	21561.7	28727.1

t statistics in parentheses

* $p < 0.1$, ** $p < 0.05$, *** $p < 0.01$

Table A2. Coefficients – Probit - Det.of abandoning ER before medical record closure

	(A2.1)	(A2.2)	(A2.3)
	Leaves before MR closure	**Leaves before MR closure**	**Leaves before MR closure**
Under 15 y.o.	0.379***	0.381***	0.293***
	(50.22)	(50.46)	(36.85)
15–24 y.o.	0.160***	0.161***	0.123***
	(20.98)	(21.09)	(15.44)
25–34 y.o.	0.249***	0.251***	0.187***
	(35.43)	(35.62)	(25.36)
35–44 y.o.	0.214***	0.216***	0.153***
	(29.67)	(29.90)	(20.37)
45–54 y.o.	0.197***	0.198***	0.147***
	(27.49)	(27.72)	(19.82)

(*Continued*)

Table A2. Coefficients – Probit - Det.of abandoning ER before medical record closure (Continued)

	(A2.1)	(A2.2)	(A2.3)
	Leaves before MR closure	**Leaves before MR closure**	**Leaves before MR closure**
55–64 y.o.	0.160***	0.162***	0.117***
	(21.51)	(21.69)	(15.41)
Women	0.0207***	0.0200***	–0.00415
	(5.10)	(4.94)	(–1.01)
Ita.Citizen	–0.0502***	–0.0428**	–0.0479***
	(–3.02)	(–2.57)	(–2.84)
Log Income pc		0.228***	0.275***
		(13.30)	(15.80)
Eff.Dist.in time		0.000360***	0.000452***
		(4.95)	(6.22)
Secondary Education pc		–1.867***	–1.733***
		(–16.45)	(–15.04)
Yellow code			–0.210***
			(–35.44)
Red code			–0.659***
			(–19.25)
Arr.Ambulance			–0.235***
			(–25.60)
Trauma main probl.			–0.415***
			(–69.12)
Hospital fixed effects	YES	YES	YES
Constant	–1.471***	–3.045***	–3.361***
	(–54.66)	(–18.72)	(–20.38)
Observations	980579	980579	980579
Pseudo R^2	0.108	0.109	0.125
Log lik.	–229522.4	–229347.4	–225071.1
Chi-squared	48940.4	48985.3	50337.5

t statistics in parentheses
* $p < 0.1$, ** $p < 0.05$, *** $p < 0.01$

Table A3. Marginal Effects– Probit - Det.of abandoning ER before visit

	(A3.1)	(A3.2)	(A3.3)
	Leaves before Being Visited	**Leaves before Being Visited**	**Leaves before Being Visited**
Under 15 y.o.	0.0264***	0.0265***	0.00585***
	(29.05)	(29.17)	(6.37)
15–24 y.o.	0.0316***	0.0316***	0.0156***
	(35.91)	(35.88)	(17.53)
25–34 y.o.	0.0297***	0.0298***	0.0120***
	(34.78)	(34.82)	(13.92)

(*Continued*)

Table A3. Marginal Effects– Probit - Det.of abandoning ER before visit (Continued)

	(A3.1)	(A3.2)	(A3.3)
	Leaves before Being Visited	**Leaves before Being Visited**	**Leaves before Being Visited**
35–44 y.o.	0.0317*** (37.12)	0.0318*** (37.20)	0.0152*** (17.67)
45–54 y.o.	0.0291*** (34.36)	0.0291*** (34.41)	0.0152*** (17.97)
55–64 y.o.	0.0208*** (23.37)	0.0209*** (23.42)	0.0108*** (12.07)
Women	–0.00345*** (–7.29)	–0.00344*** (–7.27)	–0.00598*** (–12.69)
Ita.Citizen	–0.00826** (–2.34)	–0.00838** (–2.38)	–0.00591* (–1.70)
Log Income pc		0.0142*** (7.11)	0.0172*** (8.73)
Eff.Dist.in time		0.00000177 (0.19)	0.00000887 (1.01)
Stud.in pop.18–26		–0.0886*** (–7.18)	–0.0736*** (–5.99)
Yellow code			–0.0606*** (–72.95)
Red code			–0.121*** (–20.77)
Arr.Ambulance			–0.0342*** (–28.28)
Trauma main probl.			–0.0278*** (–44.47)
Hospital Fixed Effects	YES	YES	YES
Observations	806194	806194	806194

*Marginal effects; t statistics in parentheses (d) for discrete change of dummy variable from 0 to 1   * p < 0.1, ** p < 0.05, *** p < 0.01*

Table A4. Marginal Effects– Probit - Det.of abandoning ER before medical record closure

	(A4.1)	(A4.2)	(A4.3)
	Leaves before MR closure	**Leaves before MR closure**	**Leaves before MR closure**
Under 15 y.o.	0.0476*** (50.45)	0.0478*** (50.69)	0.0362*** (36.94)
15–24 y.o.	0.0201*** (20.99)	0.0202*** (21.11)	0.0152*** (15.45)
25–34 y.o.	0.0312*** (35.50)	0.0314*** (35.70)	0.0231*** (25.38)
35–44 y.o.	0.0268*** (29.68)	0.0271*** (29.92)	0.0189*** (20.37)

(Continued)

Table A4. Marginal Effects– Probit - Det.of abandoning ER before medical record closure (Continued)

	(A4.1)	(A4.2)	(A4.3)
	Leaves before MR closure	Leaves before MR closure	Leaves before MR closure
45–54 y.o.	0.0246*** (27.49)	0.0249*** (27.72)	0.0181*** (19.81)
55–64 y.o.	0.0201*** (21.51)	0.0203*** (21.69)	0.0145*** (15.41)
Women	0.00259*** (5.10)	0.00251*** (4.94)	–0.000512 (–1.01)
Ita.Citizen	–0.00629*** (–3.02)	–0.00536** (–2.57)	–0.00591*** (–2.84)
Log Income pc		0.0286*** (13.30)	0.0339*** (15.80)
Eff.Dist.in time		0.0000451*** (4.95)	0.0000558*** (6.22)
Stud.in pop.18–26		–0.234*** (–16.46)	–0.214*** (–15.05)
Yellow code			–0.0259*** (–35.50)
Red code			–0.0814*** (–19.25)
Arr.Ambulance			–0.0290*** (–25.61)
Trauma main probl.			–0.0513*** (–69.27)
Hospital Fixed Effects	YES	YES	YES
Observations	980579	980579	980579

*Marginal effects; t statistics in parentheses (d) for discrete change of dummy variable from 0 to 1 * p < 0.1, ** p < 0.05, *** p < 0.01*

Table A5. Coefficients – Logit - Det.of abandoning ER before visit

	(A5.1)	(A5.2)	(A5.3)
	Leaves before Being Visited	Leaves before Being Visited	Leaves before Being Visited
Under 15 y.o.	0.647*** (30.26)	0.650*** (30.39)	0.154*** (6.96)
15–24 y.o.	0.738*** (36.99)	0.738*** (36.95)	0.366*** (17.65)
25–34 y.o.	0.698*** (35.70)	0.699*** (35.74)	0.280*** (13.76)
35–44 y.o.	0.738*** (38.04)	0.740*** (38.13)	0.352*** (17.53)
45–54 y.o.	0.676*** (35.04)	0.677*** (35.08)	0.353*** (17.80)
55–64 y.o.	0.489*** (23.82)	0.490*** (23.86)	0.250*** (11.92)

(Continued)

Table A5. Coefficients – Logit - Det.of abandoning ER before visit (Continued)

	(A5.1)	(A5.2)	(A5.3)
	Leaves before Being Visited	**Leaves before Being Visited**	**Leaves before Being Visited**
Women	–0.0727*** (–6.78)	–0.0724*** (–6.76)	–0.140*** (–12.74)
Ita.Citizen	–0.192** (–2.37)	–0.195** (–2.41)	–0.156* (–1.92)
Log Income pc		0.328*** (7.16)	0.401*** (8.64)
Eff.Dist.in time		0.00000902 (0.04)	0.000155 (0.76)
Stud.in pop.18–26		–1.992*** (–7.13)	–1.708*** (–5.99)
Yellow code			–1.418*** (–70.92)
Red code			–3.230*** (–17.76)
Arr.Ambulance			–0.864*** (–27.49)
Trauma main probl.			–0.665*** (–44.60)
Hospital Fixed Effects	YES	YES	YES
Constant	–3.393*** (–34.00)	–5.887*** (–13.45)	–6.149*** (–13.88)
Observations	806194	806194	806194
Pseudo R^2	0.087	0.087	0.125
Log lik.	–142970.7	–142929.2	–136946.7
Chi-squared	20745.7	20811.6	30423.0

t statistics in parentheses ** p < 0.1, ** p < 0.05, *** p < 0.01*

Table A6. Logit-Det.of abandoning ER before medical record closure

	(A6.1)	(A6.2)	(A6.3)
	Leaves before Being Visited	**Leaves before Being Visited**	**Leaves before Being Visited**
Under 15 y.o.	0.647*** (30.26)	0.650*** (30.39)	0.154*** (6.96)
15–24 y.o.	0.738*** (36.99)	0.738*** (36.95)	0.366*** (17.65)
25–34 y.o.	0.698*** (35.70)	0.699*** (35.74)	0.280*** (13.76)
35–44 y.o.	0.738*** (38.04)	0.740*** (38.13)	0.352*** (17.53)
45–54 y.o.	0.676*** (35.04)	0.677*** (35.08)	0.353*** (17.80)
55–64 y.o.	0.489*** (23.82)	0.490*** (23.86)	0.250*** (11.92)
Women	–0.0727*** (–6.78)	–0.0724*** (–6.76)	–0.140*** (–12.74)

(*Continued*)

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Table A5. Coefficients – Logit - Det.of abandoning ER before visit (Continued)

	(A6.1)	(A6.2)	(A6.3)
	Leaves before Being Visited	**Leaves before Being Visited**	**Leaves before Being Visited**
Ita.Citizen	–0.192** (–2.37)	–0.195** (–2.41)	–0.156* (–1.92)
Log Income pc		0.328*** (7.16)	0.401*** (8.64)
Eff.Dist.in time		0.00000902 (0.04)	0.000155 (0.76)
Secondary Edu pc		–1.992*** (–7.13)	–1.708*** (–5.99)
Yellow code			–1.418*** (–70.92)
Red code			–3.230*** (–17.76)
Arr.Ambulance			–0.864*** (–27.49)
Trauma main probl.			–0.665*** (–44.60)
Constant	–3.393*** (–34.00)	–5.887*** (–13.45)	–6.149*** (–13.88)
Observations	806194	806194	806194
Pseudo R^2	0.087	0.087	0.125
Log lik.	–142970.7	–142929.2	–136946.7
Chi-squared	20745.7	20811.6	30423.0

t statistics in parentheses * $p < 0.1$, ** $p < 0.05$, *** $p < 0.01$

Table A7. Marginal Effects-Logit-Det.of abandoning ER before visit

	(A6.1)	(A6.2)	(A6.3)
	Leaves before Being Visited	**Leaves before Being Visited**	**Leaves before Being Visited**
Under 15 y.o.	0.0288*** (30.12)	0.0289*** (30.25)	0.00667*** (6.95)
15–24 y.o.	0.0328*** (36.71)	0.0328*** (36.67)	0.0159*** (17.62)
25–34 y.o.	0.0310*** (35.45)	0.0311*** (35.49)	0.0121*** (13.74)
35–44 y.o.	0.0328*** (37.73)	0.0329*** (37.82)	0.0153*** (17.50)
45–54 y.o.	0.0301*** (34.79)	0.0301*** (34.82)	0.0153*** (17.77)
55–64 y.o.	0.0217*** (23.73)	0.0218*** (23.78)	0.0109*** (11.91)
Women	–0.00323*** (–6.78)	–0.00322*** (–6.76)	–0.00607*** (–12.73)
Ita.Citizen	–0.00854** (–2.37)	–0.00866** (–2.41)	–0.00679* (–1.92)

(*Continued*)

Table A7. Marginal Effects-Logit-Det.of abandoning ER before visit (Continued)

	(A6.1)	(A6.2)	(A6.3)
	Leaves before Being Visited	**Leaves before Being Visited**	**Leaves before Being Visited**
Log Income pc		0.0146*** (7.15)	0.0174*** (8.63)
Eff.Dist.in time		0.000000401 (0.04)	0.00000675 (0.76)
Stud.in pop.18–26		–0.0886*** (–7.13)	–0.0742*** (–5.99)
Yellow code			–0.0616*** (–68.84)
Red code			–0.140*** (–17.72)
Arr.Ambulance			–0.0375*** (–27.36)
Trauma main probl.			–0.0289*** (–44.22)
Hospital Fixed Effects	YES	YES	YES
Observations	806194	806194	806194

t statistics in parentheses* $p < 0.1$, ** $p < 0.05$, *** $p < 0.01$

Table A8. Marginal Effects – Logit - Det.of abandoning ER before MR closure

	(A7.1)	(A7.2)	(A7.3)
	Leaves before Being Visited	**Leaves before Being Visited**	**Leaves before Being Visited**
Under 15 y.o.	0.0288*** (30.12)	0.0289*** (30.25)	0.00667*** (6.95)
15–24 y.o.	0.0328*** (36.71)	0.0328*** (36.67)	0.0159*** (17.62)
25–34 y.o.	0.0310*** (35.45)	0.0311*** (35.49)	0.0121*** (13.74)
35–44 y.o.	0.0328*** (37.73)	0.0329*** (37.82)	0.0153*** (17.50)
45–54 y.o.	0.0301*** (34.79)	0.0301*** (34.82)	0.0153*** (17.77)
55–64 y.o.	0.0217*** (23.73)	0.0218*** (23.78)	0.0109*** (11.91)
Women	–0.00323*** (–6.78)	–0.00322*** (–6.76)	–0.00607*** (–12.73)
Ita.Citizen	–0.00854** (–2.37)	–0.00866** (–2.41)	–0.00679* (–1.92)
Log Income pc		0.0146*** (7.15)	0.0174*** (8.63)
Eff.Dist.in time		0.000000401 (0.04)	0.00000675 (0.76)
Stud.in pop.18–26		–0.0886*** (–7.13)	–0.0742*** (–5.99)

(*Continued*)

Table A8. Marginal Effects – Logit - Det.of abandoning ER before MR closure (Continued)

	(A7.1)	**(A7.2)**	**(A7.3)**
	Leaves before Being Visited	**Leaves before Being Visited**	**Leaves before Being Visited**
Yellow code			–0.0616*** (–68.84)
Red code			–0.140*** (–17.72)
Arr.Ambulance			–0.0375*** (–27.36)
Trauma main probl.			–0.0289*** (–44.22)
Hospital Fixed Effects	YES	YES	YES
Observations	806194	806194	806194

*Marginal effects; t statistics in parentheses (d) for discrete change of dummy variable from 0 to 1 * p < 0.1, ** p < 0.05, *** p < 0.01*

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An Examination of Support for More Diverse Alcohol Warning Labels (AWLs) in Ireland

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SUMMARY

Alcohol poses a significant threat to public health in Ireland. In 2026, Ireland is due to introduce a mandatory alcohol warning label (AWL). Using a convenience sample of students and staff at an Irish Technological University (TU), this research sought to explore support for current and potentially expanded alcohol control measures. Online survey data was collected from 335 participants. Analysis revealed a very high level of support for the forthcoming introduction of Ireland's AWL. Additionally, there was considerable support for a broader range of AWLs. More than half of the respondents supported the introduction of bland packaging on alcohol containers, and over 60% supported the introduction of more explicit tobacco-style graphic warnings on alcohol. Over 40% of respondents reported that AWLs would impact their intention to consume alcohol.

Keywords: Alcohol; Alcohol Control; Alcohol Warning Labels; Bland Packaging; Graphic warnings; Ireland

INTRODUCTION

Alcohol has been identified by the WHO as an important Commercial Determinant of Health (CDoH) [1,2]. Alcohol is responsible for more than 3 million deaths annually and causes more than 5% of the total global burden of disease and injury [3–5]. Research from Ireland confirms that the adverse impact of alcohol is also highly evident there [6–7]. In response to this threat, the Irish Government passed the Public Health (Alcohol) Act, 2018 [8]. Although criticised for its slow implementation and deficits [9–11], this Act has introduced Minimum Unit Pricing (MUP) of alcohol and significant restrictions on alcohol advertising. Importantly, from May 2026 onward, alcohol containers in Ireland must display a prescribed alcohol warning label (AWL) [12]. As can be seen from Figure 1, this label features a warning about the threat posed by alcohol in developing liver disease and cancer. The warning also features a pictograph warning pregnant women not to drink, nutritional information, and a website address for further information [12]. There is growing evidence and support for the introduction of AWLs [13–16].

Figure 1. Ireland's Forthcoming Alcohol Warning Label [17]

This research sought to explore support for the overall introduction of AWLs, as well as its various constituent elements. It also examined approval of more substantive alcohol control measures, such as more explicit tobacco-style graphical warnings, as well

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as the introduction of bland packaging. Support and opposition to a more diverse range of AWLs are also investigated [18].

METHOD

Ethical approval for this study was given by the Queen's University of Belfast and the Technological University of the Shannon. Data was collected via anonymous MS Forms surveys and subsequently examined in SPSS. Data was collected from an opportunistic sample of 335 respondents who were students or employees of a provincial Technological University (TU) in the Republic of Ireland. College participation in Ireland is significantly higher than the EU-27 average [19], and the TU sector in Ireland teaches a broad range of courses from apprenticeships in the Trades to PhDs. As such, it attracts a broader socio-economic base of students than the traditional university sector [20]. Based on a 90% confidence level and a 5% margin of error, the target sample size was 268.

The participants included 90 men (26.9%) and 244 women (73.1%). The participants ranged in age from 18 to 73, with a mean age of 37.4 (SD=15.9). 24.5% (82) of participants lived in rural areas, 15.5% (52) in villages, 23.9% (80) in towns, and 33.7% (113) in a city. Full-time employees comprised 47.5% (159) of the respondents, while students accounted for 20.6% (69) of the respondents. 20.0% (67) of respondents worked part-time, with 12% (40) reporting other status. Of the sample, 40.9% (137) of respondents scored over five on the AUDIT-C, indicating potentially hazardous drinking, i.e. a level at which individuals are at risk of harm or experiencing harm from their alcohol consumption.

RESULTS

Support for Ireland's forthcoming AWLs was 81.1% (272). Table 1 details support for various components of Ireland's proposed AWLs. The risk-to-pregnancy pictogram was the most strongly supported element (80.6%, 270). Almost two-thirds (63.9%; n = 167) of respondents were supportive of more explicit tobacco-style graphic alcohol warnings (AWLs), while more than half (52.3%, 136) supported the introduction of bland packaging for alcohol containers, similar to that currently required in Ireland for tobacco packaging.

Table 1 also examines support for a more diverse range of AWLs as recommended elsewhere [18]. The most substantial level of support was evident for an AWL focussing on the risk of drink-driving (86.3%, 289). Support for all 11 AWLs exceeded 73%. Of the respondents, 56.4% (189) did not feel AWLs would impact their intention to consume alcohol, while 43.3% (145) reported that it would.

Table 1. Degree of Support/Opposition for Proposed & More Diverse Health Warnings/ Interventions

Warning Type	Strongly support	Tend to support	Either support nor oppose	Tend to oppose	Strongly oppose
Elements of forthcoming (May 2026) Alcohol Warning Label					
Ireland's proposed AWL	50.7% (170)	30.4% (102)	10.5% (35)	4.8% (16)	3.6% (12)
Risk to pregnancy	59.7% (200)	20.9% (70)	7.8% (26)	8.4% (28)	3.3% (11)
Risk of liver disease	52.4% (175)	25.1% (84)	10.2% (34)	8.1% (27)	4.2% (14)
Risk of cancer	51.0% (171)	24.8% (83)	11.6% (39)	8.4% (28)	4.2% (14)
Nutritional information	39.7% (133)	32.5% (109)	17.0% (57)	6.3% (21)	4.5% (15)
Enhanced alcohol control measures					
Tobacco-style graphic AWLs	40.0% (134)	22.4% (75)	11.0% (37)	17.6% (59)	9.0% (30)
Plain packaging for alcohol	29.9% (100)	25.7% (86)	16.7% (56)	15.8% (53)	11.9% (40)

(*continued*)

Table 1. Degree of Support/Opposition for Proposed & More Diverse Health Warnings/ Interventions (continued)

Warning Type	Strongly support	Tend to support	Either support nor oppose	Tend to oppose	Strongly oppose
Proposed warning about the risk of alcohol and...					
Foetal Alcohol Syndrome (FAS)	57.3% (192)	19.7% (66)	9.3% (31)	9.3% (31)	4.5% (15)
Drink driving	67.5% (226)	18.8% (63)	6.9% (23)	4.2% (14)	2.7% (9)
Taking medications	53.4% (179)	25.1% (84)	12.5% (42)	6.3% (21)	2.7% (9)
Swimming	48.7% (163)	26.0% (87)	15.5% (52)	6.9% (23)	3.0% (10)
Cardio-vascular disease	50.4% (169)	24.5% (82)	14.6% (49)	6.3% (21)	4.2%% (14)
Operating machinery	54.0% (181)	23.9% (80)	11.6% (39)	6.9% (23)	3.6% (12)
Using ladders & working at heights	46.9% (157)	26.6% (89)	15.5% (52)	6.6% (22)	4.5% (15)
Fertility	48.1% (161)	26.0% (87)	13.4% (45)	7.2% (24)	5.4% (18)
Young People	56.1% (188)	23.0% (77)	10.7% (36)	6.0% (20)	4.2% (14)
Alcohol dependency	57.3% (192)	20.6% (69)	10.7% (36)	6.6% (22)	4.8% (16)
Polydrug use	54.7% (177)	23.2% (75)	11.8% (38)	5.6% (18)	4.6% (15)

DISCUSSION / CONCLUSION

Support for Ireland's forthcoming AWL was notable at over 80% (81.1%), although this is somewhat lower than that reported elsewhere [21]. There was also widespread approval of the introduction of a more diverse range of AWLs. More than half of respondents were also supportive of both plain packaging for alcohol (55.6%) and more explicit tobacco-style graphic warnings for alcohol (62.4%). Over 40% (43.3%) of respondents reported that AWLs would impact their intention to consume alcohol. Future research should explore the public acceptability of other impacts of alcohol including self-harm, suicide, domestic violence, rape, and sexual assault, as well as assault and homicide.

AUTHORS CONTRIBUTIONS

All authors contributed to the conceptualisation of the study and data collection. FH led the formal analysis of the data, as well as interpretation and data curation. All authors contributed to the writing and review of the manuscript.

ETHICAL APPROVAL

This study was approved by the research ethics committees of the Queen's University of Belfast (QUB), and the Technological University of the Shannon (TUS).

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CONFLICTS OF INTEREST

All authors are involved in alcohol control research, policy and advocacy.

DATA AVAILABILITY

Data available on request.

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Role of Covariates in Case Control Studies with Skewed Exposure: Evidence from Monte Carlo Simulations

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SUMMARY

Case-control studies, a widely used observational study design, are essential for investigating the association between exposure and outcomes. In such studies, logistic regression is commonly employed to analyse the relationship between binary outcome and exposure, accounting for covariates, confounders, and effect modifiers. However, skewed exposure distributions, where the exposure is disproportionately distributed among cases and controls, pose significant challenges. In this case, the parameter estimates may be biased, leading to an over- or underestimation of the true effect size, and this can affect the interpretability and reliability of the estimated coefficients.

This study aims to address these challenges by conducting a series of Monte Carlo simulation experiments to assess the impact of skewed exposure on the power of the Wald test and the bias in estimated logistic regression coefficients. The simulations focus on the role of continuous covariates in producing reliable estimates of exposure effects. The study highlights the importance of preliminary knowledge of exposure and covariate effects, as these factors play a crucial role in selecting an appropriate sample size. These simulations, which required significant computational time, highlight the robustness of the estimates with larger sample sizes and a greater number of covariates, eliminating the potential bias introduced by skewed exposure.

Keywords: Case control study; logistic regression; skewed exposure; odds ratio; sample size.

INTRODUCTION

Case-Control study design, is a common observational study that involves researchers observing and measuring both exposure and outcome among participants to examine their association [1]. In this design, individuals with a particular outcome (cases) are compared to those without the outcome (controls), assessing the presence or absence of exposure in both groups to identify potential risk factors. Due to its speed and efficiency, the case-control study is frequently the preferred design for research on the causes of disease [2].

In case-control studies, the odds ratio (OR) is often used as a measure of association between exposure and a binary outcome. Logistic regression is a widely used statistical technique for analyzing case-control data, as it allows researchers to account for the effects of covariates, confounders, and potential effect modifiers [3].

The logistic regression model to study the relationship between the binary outcome (Y) and exposure (X), in the presence of p covariates/confounders/effect modifiers $C_1, C_2, C_3 \ldots C_p$ is given by,

$$\log \frac{p}{1-p} = \alpha + \beta X + \beta_1 C_1 + \beta_2 C_2 + \ldots + \beta_p C_p$$

Where $p = E\left(Y \mid X, C_1, C_2, ..C_p\right)$

By including covariates/confounders/effect modifiers in the logistic regression model, their effects are accounted for, but the researcher is particularly interested in coefficient β. A positive coefficient indicates a positive association between the exposure and the outcome, while a negative coefficient indicates a negative association. The magnitude of the coefficient represents the strength of the association.

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A skewed exposure in case control studies is defined as an exposure which is disproportionately distributed among cases and controls. A binary skewed exposure is defined as a categorical variable with despaired marginal distribution.

Foxman et al. [4] conducted a case-control study of contraceptives and Urinary Tract Infection among college women and the cross tabulation reported clearly indicated that Diaphragm usage as a skewed exposure with majority of the women not using it.

Table 1. Cross tabulation of Diaphragm usage and Urinary Tract Infection, Foxman et al [4]

Diaphragm usage	Urinary Tract Infection	
	Yes	No
Yes	7	0
No	140	290

A skewed exposure may lead to one of two potential issues:

(i) Problem of Separation: This occurs when the maximum likelihood estimates do not converge, leading to what is known as complete or quasi-complete separation. In such cases, standard logistic regression fails to provide finite estimates [5,6,7].

(ii) Biased Estimates with Wide Confidence Intervals: Even if the maximum likelihood estimates do converge, they may be biased, resulting in wide confidence intervals. This leads to underpowered inference regarding the exposure, making it difficult to draw reliable conclusions [8].

The exact logistic regression and Firth's approach are two very well-known methods to handle the problem of separation. The exact logistic regression is regression technique that provides precise parameter estimates by conditioning on sufficient statistics, making it especially suitable for small or sparse datasets. However, it is often criticized for its computational cost and inability to handle large number of covariates and large sample size [9,10,11]. Firth's approach is a bias-reduction method for logistic regression that applies a penalized likelihood function to improve parameter estimation. Also, there are other methods to handle the problem of separation and are discussed in detail by Mansournia et al [12].

But there are instances when the model does converge, the results obtained may be unreliable due to the skewness in the exposure distribution. This aspect is investigated by Alkhalaf and Zumbo (2017) [8] by considering only one covariate and they concluded that estimates are not reliable. However, the specific effects of skewed exposure on case-control studies, considering factors such as the degree of skewness, sample size, and covariate effect size, and number of covariates remain unexplored.

Thus, this paper aimed to conduct a series of Monte Carlo simulations to assess the power of the Wald test and the bias in estimated logistic regression coefficients, demonstrated the role of continuous covariates in producing the reliable estimates of exposure effect.

Simulation Experiments

Six simulation experiments were conducted to evaluate the Wald test in logistic regression. Experiment I focused on the Type I error rate of the Wald test, varying sample sizes and skewness probabilities. Experiment II assessed the power of the Wald test, bias in exposure coefficient estimates, and confidence interval widths with a single covariate, considering different sample sizes, skewness probabilities, and effect sizes. Experiments III through VI extended this by examining the effects of increasing numbers of covariates (two to five) on the Wald test's performance, following similar procedures to those in Experiment II. These simulation experiments help understand how the inclusion of multiple covariates affects the performance of logistic regression models in case of skewed exposure. In R (Version 4.4.0), user defined functions were specially developed to run different simulation experiments.

Simulation Experiment I

This is a 22×10 experimental design where Monte Carlo simulations were conducted, considering a response variable (Y), a skewed binary exposure (X), and a covariate C_1.

The simulations considered two experimental factors: the sample size, denoted as n, the probability of skewness (or prevalence) of exposure, denoted as p_s, and there were 22 values for n ranging from 20 to 500, 10 values for p_s, ranging from 0.05 to 0.5. The simulation is executed for 1000 times for each cell of 22×10 experimental design. The $(i,j)^{th}$ cell of this experimental design represents the simulation corresponding to i^{th} sample size and j^{th} probability of skewness.

The logistic regression model considered is

$$\log \frac{p}{1-p} = \alpha + \beta X + \beta_1 C_1$$

This simulation experiment is carried out to estimate the type I error rate of Wald test used in logistic regression model to detect the impact of the exposure. The null and alternative hypothesis of interest are $H_0 : \beta = 0 \ Vs H_1 : \beta \neq 0$.

The type I error rate is estimated only for skewed exposure as it is of primary interest in most of the epidemiological context.

The simulation procedure for $(i,j)^{th}$ cell of the experimental design is as follows:

- The covariates are generated from a prespecified probability distributions. $X \sim Bernoulli(p_s)$ and $C_1 \sim Normal(22,5)$

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- The regression coefficients are set to zero and the probability p is generated using logistic regression model. The predicted probability serves as the expected value for the Bernoulli distribution from which the data on outcome variable is drawn.
- The logistic regression model is fitted to the simulated data, and the occurrence of type I error is noted down.
- The procedure is repeated for 1000 simulations.

The empirical type I error rate for $(i,j)^{th}$ cell of the experimental design is computed as the number of times the true null hypothesis is rejected at the level of 5% divided by 1000.

The Bradley's rule [13] was used to decide whether the type I error rate meets the criteria. The type I error rate between 0.025 and 0.075 was considered as the meeting the liberal criteria. In simulations if generated datasets fail to yield convergence with the maximum likelihood estimation method, such datasets are excluded.

Simulation Experiment II

This is a $22 \times 10 \times 3 \times 3$ experimental design with four design factors: the sample size, denoted as n, the probability of skewness of exposure, denoted as p_s, and the regression coefficient of X denoted as β_X, the regression coefficient of covariate is β_C. There were 22 values for n ranging from 20 to 500, 10 values for p_s, ranging from 0.05 to 0.5, three distinct values for β_X were considered, namely 0.683 (odds ratio=1.98), 1.1(odds ratio=3), and 1.38 (odds ratio=3.97), corresponding to small, moderate, and large effects of exposure, respectively [14]. There were 3 values for β_C namely 0.683, 1.1 and 1.38 corresponding to small, moderate, and large effects of covariate.

In the $(i,j,k,l)^{th}$ simulation of this experiment, 1000 datasets were generated according to the previously outlined procedure (as in simulation experiment I), considering i^{th} sample size, j^{th} probability of skewness, k^{th} value of β_X and l^{th} value of β_C.

The power of Wald test to detect the effect of exposure is defined as the number of times the false null hypothesis is rejected during $(i,j,k,l)^{th}$ simulation divided by 1000. The bias of $(i,j,k,l)^{th}$ simulation is the difference between estimated regression coefficient and the actual value. The mean bias is the mean of all these differences. The mean squared error for $(i,j,k,l)^{th}$ simulation is the average squared deviation of these differences.

$$Bias = \bar{\beta}_{ijkl} - \beta$$

$$Mean\ Bias = \frac{\sum(\bar{\beta}_{ijkl} - \beta)}{n}$$

$$Mean\ Squared\ Error = \frac{\sum\left(\bar{\beta}_{ijkl} - \beta\right)^2}{n}$$

This simulation experiment was run for 9 scenarios depending on the strength of effects of exposure and covariates. These 9 scenarios are tabulated below:

Table 2. Combinations of exposure and covariate effects

		Covariate effect		
		Small	**Moderate**	**Large**
Exposure effect	**Small**	Scenario 1	Scenario 2	Scenario 3
	Moderate	Scenario 4	Scenario 5	Scenario 6
	Large	Scenario 7	Scenario 8	Scenario 9

For each of these nine scenarios, the mean bias and mean squared error of the regression coefficients are computed for various values of n and p_s. The percentage bias was calculated as $\%bias = \frac{(\bar{\beta}_{ijkl} - \beta)}{\beta} \times 100$ where $\bar{\beta}_{ijkl}$ is the average estimate of β for $(i,j,k,l)^{th}$ simulation.

The estimator is unbiased if the percentage bias is 0%. The percentage bias within ±5% was considered acceptable [15]. The 95% confidence interval for β during $(i,j,k,l)^{th}$ simulation was computed as $[\bar{\beta}_{ijkl} - Z_{1-\frac{\alpha}{2}} SE(\bar{\beta}_{ijkl})\ \bar{\beta}_{ijkl} + Z_{1-\frac{\alpha}{2}} SE(\bar{\beta}_{ijkl})]$ where $SE\left(\bar{\beta}_{ijkl}\right)$ is the square root of mean squared error.

The width of the confidence interval in each simulation was calculated as

$$Width = 2 \times Z_{1-\frac{\alpha}{2}} \times SE(\bar{\beta}_{ijkl})$$

Plots of sample size versus percentage bias for different probabilities of skewness, and plots of sample size versus width of the confidence interval for various probabilities of skewness, are generated. These plots help us understand how percentage bias decreases and the width of the confidence interval narrows as sample size increases. The optimal sample size is identified as the point where the percentage bias is within ±5%, and after which the width of the confidence interval reaches a minimum and then saturates.

Simulation Experiment III-VI

The simulation experiments III, IV, V and VI work similar to experiment II, with number of covariates increased. In all experiments, the values of β_X are fixed at 0.683, 1.1, and 1.38, corresponding to small, moderate, and large effect sizes of the exposure, respectively. The values of β_C correspond to the effect sizes of these covariates on the outcome, with different sets of values used to simulate small, moderate, and large effects. As the number of covariates increases across experiments III to VI, the values of β_C correspond to combinations of effect sizes for each covariate, reflecting various strength levels of their association with the outcome.

Table 3. The Details of Simulation Experiments

Experiment	**III**	**IV**	**V**	**VI**
Design	$22\times10\times3\times3$	$22\times10\times3\times3$	$22\times10\times3\times3$	$22\times10\times3\times3$
Values of β_X	$\begin{bmatrix}0.683\\1.1\\1.38\end{bmatrix}$	$\begin{bmatrix}0.683\\1.1\\1.38\end{bmatrix}$	$\begin{bmatrix}0.683\\1.1\\1.38\end{bmatrix}$	$\begin{bmatrix}0.683\\1.1\\1.38\end{bmatrix}$
β_C	$\begin{bmatrix}0.683 & 0.683\\1.1 & 1.1\\1.38 & 1.38\end{bmatrix}$	$\begin{bmatrix}0.683 & 0.683 & 0.683\\1.1 & 1.1 & 1.1\\1.38 & 1.38 & 1.38\end{bmatrix}$	$\begin{bmatrix}0.683 & 1.1 & 1.38\\0.683 & 1.1 & 1.38\\0.683 & 1.1 & 1.38\\0.683 & 1.1 & 1.38\end{bmatrix}^T$	$\begin{bmatrix}0.683 & 1.1 & 1.38\\0.683 & 1.1 & 1.38\\0.683 & 1.1 & 1.38\\0.683 & 1.1 & 1.38\\0.683 & 1.1 & 1.38\end{bmatrix}^T$
Covariates	$C_1 \sim Normal(22,5)$ $C_2 \sim Normal(35,15)$	$C_1 \sim Normal(22,5)$ $C_2 \sim Normal(35,15)$ $C_3 \sim Gamma(80,15)$	$C_1 \sim Normal(22,5)$ $C_2 \sim Normal(35,15)$ $C_3 \sim Gamma(80,15)$ $C_4 \sim Beta(3,4)$	$C_1 \sim Normal(22,5)$ $C_2 \sim Normal(35,15)$ $C_3 \sim Gamma(80,15)$ $C_4 \sim Beta(3,4)$ $C_5 \sim Normal(5,1)$

In the $(i,j,k,l)^{th}$ simulation of this experiment, 1000 datasets were generated according to the previously outlined procedure (as in simulation experiment I and II), considering i^{th} sample size, j^{th} probability of skewness, k^{th} value of β_X and l^{th} row of β_C. For each scenario the plots of percentage bias and width of confidence interval are generated and the optimal sample size is decided.

RESULTS

The Monte Carlo simulations of this study took approximately 1874 minutes i.e., 31.23 hours of execution time. Even though these experiments were time-consuming, a pattern in percentage bias and the width of the confidence interval emerged, providing the sample size guidelines. The results of this experiment may not be particularly pleasing to researchers who wish to conduct case-control studies with limited small sample sizes. However, preliminary knowledge about exposure and covariate effect would help researchers choose the optimal sample size.

The results of simulation experiment I is presented in Table 4. The aim of this experiment was to estimate the type I error rate of Wald test used in logistic regression in the presence of skewed exposure. It is observed that as the sample size increases, the type I error rates tend to approach Bradley's criteria more closely. However,

Table 4. Type I Error Rates by Sample Size and Probability of Skewness

		Probability of Skewness									
Sample size		**0.05**	**0.1**	**0.15**	**0.2**	**0.25**	**0.3**	**0.35**	**0.4**	**0.45**	**0.5**
	20	0.006	0.004	0.003	0.011	0.012	0.018	0.016	0.032	0.03	0.021
	50	0.005	0.006	0.015	0.032	0.029	0.052	0.044	0.051	0.047	0.046
	100	0.006	0.034	0.046	0.048	0.048	0.044	0.05	0.054	0.051	0.062
	150	0.006	0.054	0.046	0.034	0.058	0.051	0.052	0.044	0.045	0.044
	200	0.018	0.048	0.038	0.057	0.041	0.059	0.054	0.047	0.047	0.041
	250	0.034	0.045	0.046	0.042	0.052	0.054	0.058	0.038	0.053	0.05
	300	0.033	0.057	0.054	0.047	0.032	0.049	0.057	0.043	0.07	0.04
	350	0.037	0.048	0.054	0.053	0.054	0.046	0.05	0.039	0.047	0.066
	400	0.035	0.043	0.058	0.047	0.051	0.049	0.052	0.042	0.048	0.055
	450	0.048	0.041	0.038	0.05	0.043	0.063	0.046	0.043	0.049	0.055
	500	0.035	0.046	0.04	0.052	0.044	0.045	0.044	0.049	0.043	0.049
	550	0.049	0.04	0.052	0.054	0.047	0.047	0.046	0.062	0.039	0.043
	600	0.035	0.045	0.054	0.05	0.05	0.055	0.043	0.059	0.048	0.047

(continua)

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Table 4. Type I Error Rates by Sample Size and Probability of Skewness (continua)

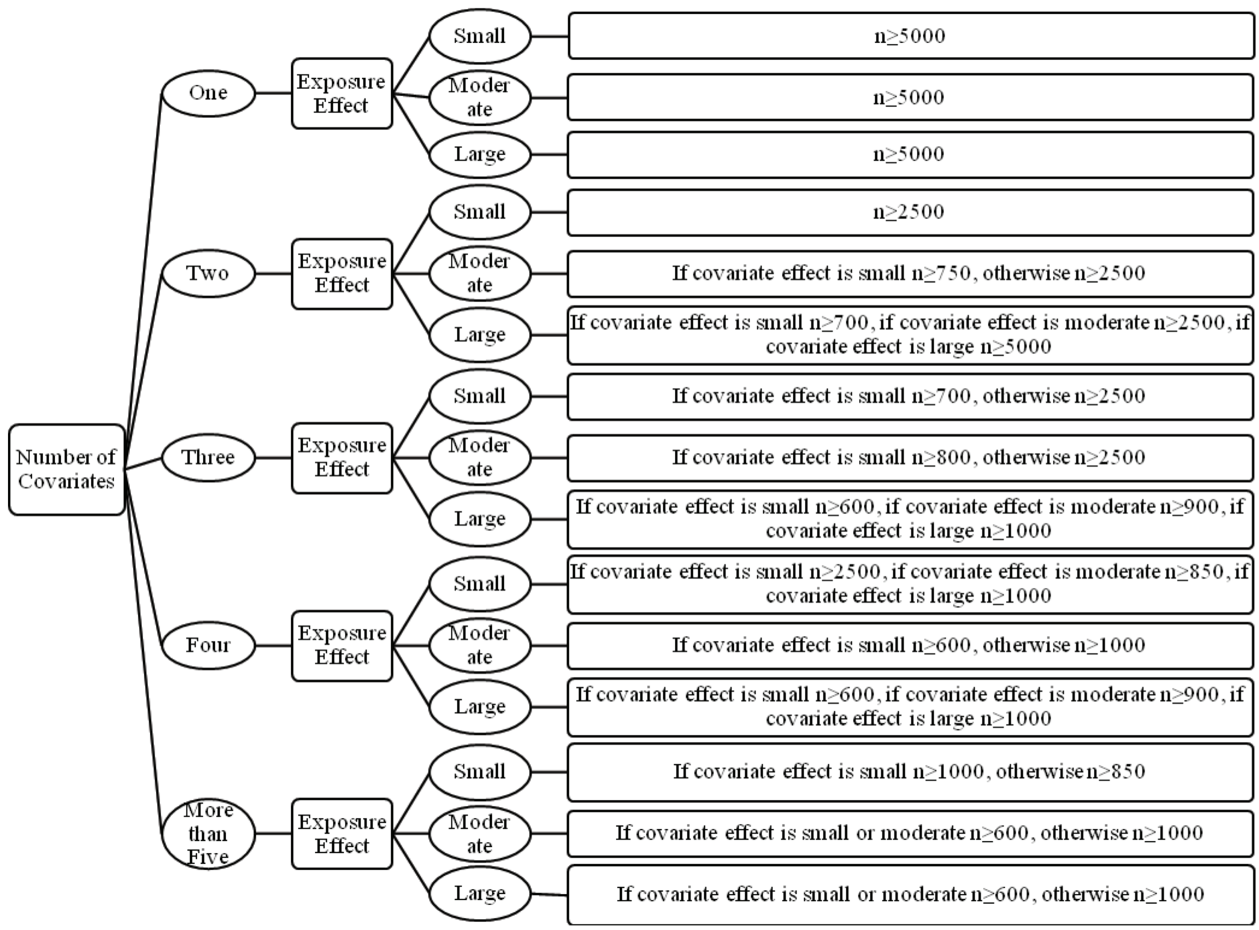
	Probability of Skewness									
	0.05	**0.1**	**0.15**	**0.2**	**0.25**	**0.3**	**0.35**	**0.4**	**0.45**	**0.5**
650	0.045	0.049	0.05	0.037	0.054	0.054	0.049	0.042	0.043	0.039
700	0.035	0.05	0.046	0.041	0.05	0.044	0.057	0.051	0.07	0.045
750	0.037	0.041	0.052	0.039	0.043	0.072	0.053	0.052	0.044	0.045
800	0.044	0.055	0.045	0.042	0.04	0.042	0.062	0.046	0.047	0.052
850	0.05	0.046	0.051	0.043	0.051	0.053	0.064	0.051	0.055	0.059
900	0.045	0.049	0.039	0.049	0.039	0.052	0.041	0.059	0.056	0.058
1000	0.037	0.048	0.045	0.05	0.06	0.075	0.052	0.047	0.062	0.051
2500	0.063	0.055	0.062	0.056	0.039	0.044	0.046	0.05	0.047	0.058
5000	0.063	0.053	0.058	0.054	0.048	0.055	0.05	0.045	0.046	0.048

with smaller sample sizes, particularly when $n = 20$, there is a higher likelihood of deflated type I error rates.

The plots of sample size versus percentage bias and plots of sample size versus width of confidence interval for all nine scenarios of simulation experiments II to VI are provided in the supplementary material.

The figure presents general guidelines for determining sample size, based on percentage bias and the width of the confidence interval. If the percentage bias is within ±5% and the confidence interval is also narrower, that sample size is reported as the optimal one. However, several inputs, such as exposure effect size and covariate effect size, are required. This may seem challenging to researchers, as using these guidelines necessitates a significant amount of prior knowledge. However, this paper offers additional insights. In case-control studies, where numerous covariates are often present, it is safe to assume that there are at least five covariates. If this is the case, and the exposure effect is greater than the covariate effect, a sample size of 600 is sufficient. However, if the sample size is around 1,000, a skewed exposure does not significantly impact the estimates of the odds ratio, the power of the Wald test, or the width of the confidence interval if the number of covariates is at least five. Hence a larger sample size and an increased number of covariates contribute to more stable and reliable estimates, reducing the potential bias that might be introduced by a skewed exposure.

Figure 1. Flowchart of Optimal Sample Size Guidelines



DISCUSSION

There are various approaches in the literature addressing case-control studies where logistic regression fails to provide finite estimates for the odds ratio of exposure. This paper investigates the reliability of these estimates when they are finite.

The patterns in both percentage bias and the width of the confidence interval, lead to the development of sample size guidelines. These guidelines are crucial for researchers, particularly those engaged in case-control studies. The results also emphasize the importance of preliminary knowledge regarding exposure and covariate effects. Such knowledge enables researchers to select an appropriate sample size from a range of options.

The covariates considered in all the simulation experiments are continuous in nature, and hence simulated using continuous probability distributions. Further simulation can be conducted to study the impact of categorical covariates.

As the number of covariates increases, the impact of skewed exposure on the estimates of the exposure effect diminishes, particularly when the sample size is larger. This finding is significant because it suggests that, with sufficient sample size, the skewness of exposure does not substantially affect the exposure effect estimates, in studies with numerous covariates. The larger sample sizes and a greater number of covariates not only enhance the robustness of the estimates but also mitigate the potential bias introduced by skewed exposure.

CONFLICT OF INTEREST

The authors declare that they have no conflict of interest.

FUNDING

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The authors have no relevant financial or non-financial interests to disclose.

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Impact Assessment of Controlled Mechanical Ventilation Systems for Air Quality in School Buildings: A Study Protocol

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SUMMARY

Background: Indoor air is an important public health issue and the COVID-19 pandemic has highlighted even more the importance of indoor air quality in schools. One of the main measures to preserve good indoor air quality is to maintain adequate indoor air exchange, and energy-efficient mechanical ventilation has been shown to be effective in improving indoor air quality and health of the occupants.
Methods: A pre-post study and trend analysis will be carried out. As the project involves the installation of Controlled Mechanical Ventilation (CMV) systems in schools, the primary aim of the study is to assess the perceived indoor air quality in classrooms in a population of primary and secondary school students without (pre-installation) and with (post-installation) CMVs. The secondary aim is the assessment of health outcomes, investigating the prevalence of dermatological, respiratory, ocular and general disorders reported before and after the intervention, and stratifying by sociodemographic variables. The evaluation of the effectiveness of CMV systems on air quality will be evaluated through chemical-physical and microbiological sampling after the installation of CMVs. The perceived air quality and health assessment will be performed through a survey, distributed before and after CMVs installation.
Conclusions: The present study protocol aims to highlight the importance of indoor air quality for students and school personnel, as well as propose new strategies and measures to deal with this raising issue, enacting measures and systems that will be sustainable from an environmental, energetical, and acoustic point of view, while still ensuring the best possible health outcomes.

Keywords: indoor air quality, controlled mechanical ventilation, prevention, public health, school.

INTRODUCTION

Indoor air is an important public health issue, particularly in school buildings where students spend much of their time. Indoor air quality can be affected by multiple factors, such as human activity, humidity and ventilation, having negative long-term health consequences in individuals who are exposed to it. Epidemiological studies have shown that exposure to indoor air pollutants, such as dust mites, moulds, volatile organic compounds (VOCs), and nitrogen oxides, can cause respiratory or cardiovascular diseases, allergies, as well as it can have neurobehavioral effects in children [1–3]. Although the role that indoor air can play in the transmission of airborne pathogens was already known

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[4], the COVID-19 pandemic has made the importance of indoor air quality in schools even more apparent, as the virus is transmitted by air [5]. Italy was greatly affected by the COVID-19 pandemic [6], underlining the importance of emergency preparedness [7] and the need to establish prevention strategies concerning indoor air quality [8].

One of the main measures to preserve good indoor air quality is to maintain adequate indoor air exchange. This process is not always satisfied by simply opening the windows, but requires the use of specifically dedicated systems and strategies, which must at the same time minimize their impact from an energetical, environmental and acoustic point of view, as well as ensure the health and safety of the occupants. In this regard, energy-efficient mechanical ventilation has been shown to be effective in improving indoor air quality [9,10] and occupant health [11].

From an occupational medicine perspective, the health aspects related to air quality are key for safe and healthy working environments. In particular, healthcare professionals and occupational physicians are essential to assess indoor air quality, collaborate to identify sources of pollution, as well as proposed solutions to improve air quality and prevent negative health consequences for indoor occupants [3].

The importance of indoor air quality and wellbeing of occupants can be traced in several national and international policies. At the international level, the World Health Organization (WHO) issued in 2009 and 2010 two guidelines on indoor air quality for dampness and mould [12] and selected pollutants [3]. In the European landscape, the importance of the well-being of occupants of living environments has been emphasized in the document "Towards a strategy for a sustainable urban environment" (COM 2004-60) in which the indoor air quality in buildings is listed as a priority [13].

The "European Environment and Health Strategy" (COM/2003/338), also known as the SCALE (Science, Children, Awareness, Legal Instrument, Evaluation) initiative, is aimed at combating the increase of chronic diseases in childhood through cross-sectoral and multidisciplinary initiatives aimed at reducing risk factors present in indoor living environments and in particular in the home, school, and daycare centers, where children spend most of their time [14].

At a national level, the Italian Ministry of Health has been promoting and developing important initiatives for years in the field of protection and promotion of health in confined spaces. In 2020, the National Plan for the protection and promotion of health in confined environments was issued, and the following year, with the Agreement of 27/02/21 the priority areas of intervention were identified and fed the National Prevention Plan in indoor environments. The plan, in line with the European Commission and the WHO, provided indications for regulatory and technical actions, design and construction of buildings, research and training actions for professionals and health communication and education for citizens. The National Prevention Plan 2010-2012 and 2014-2018 provided strategic guidelines to improve the hygiene requirements of IAQ in schools and other environments frequented by children. In addition to the numerous guidelines and initiatives funded, the Ministry of Health participates in the work of the National Indoor Study Group set up at the National Institute of Health, which has produced reference documents on monitoring strategies for VOCs, Particulate Matter (PM) and its chemical characterization, microbiological pollutants and allergens in indoor environments [15–20].

This protocol is inscribed in the context of the activities of the project "necessARIA: need for efficient air exchange strategies for the health of occupants in school buildings" winner of the call for proposals for the Italian National Plan for Complementary Investments (PNC). The project envisages collaboration, integration of skills and synergistic study of Italian schools through the involvement of four types of expertise: Health Operational Units (OU), Engineering OU, Environment Laboratory OU, as well as three Italian Regional Administrations and one Autonomous Province.

The project pays particular attention to the possible clinical consequences of low-quality indoor air, exploring the role of confounding factors and evaluating the relationships between technical parameters, and chemical, physical and microbiological samplings. The main goal is to promote strategies aimed at the improvement of indoor air quality in schools, which will result in a significant health benefit for students, as well as teaching, technical and administrative staff, as highlighted in the Prime Ministerial Decree of 26 July 2022 [21] .

MATERIALS AND EQUIPMENT

The project involves the installation of Controlled Mechanical Ventilation (CMV) systems in schools. With this system the exhaust air, saturated with humidity, carbon dioxide and harmful substances, is sucked out of the system, enters the exchanger where it transfers its thermal energy to the new air taken from the outside and filtered before arriving at the exchanger. This system allows a reduction in the concentration of indoor pollutants and an improvement in indoor air quality. An impact assessment will be carried out, through the evaluation of the effectiveness of CMV systems on air quality and health outcomes, performing a pre-post and trend analysis. The primary objective of the study is to assess the perceived indoor air quality in classrooms in a population of primary and secondary school students with and without CMV. Health outcomes will be declined in the secondary objective of assessing health status in the selected population, investigating the prevalence of dermatological, respiratory, ocular and general disorders reported before and after the intervention and stratifying by sociodemographic variables.

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METHOD DETAILS

To serve the stated objectives a three-step methodology will be adopted, consisting of: (1) Indoor air quality (IAQ), Indoor Environmental Quality (IEQ) evaluation and survey (pre-intervention); (2) CMV installation; (3) IAQ and IEQ evaluation, and survey (post-intervention).

Population sampling

The population will consist of specific classrooms of primary and secondary schools recruited in the area of competence of the following OU related to the necessARIA project: the Autonomous Province of Bolzano - South Tyrol, the Marche Region, the Abruzzo Region, the Polytechnic University of Marche, the University of Bari Aldo Moro and the G. D'Annunzio University of Chieti-Pescara.

Population will be recruited according to the following two inclusion criteria: being students belonging to primary and secondary schools in the Regions/Autonomous Provinces involved; the parents/legal guardians have accepted the informed consent and to the processing of data, self-declaring that they have read and understood the information.

Failing one or both the aforementioned criteria will lead to exclusion.

Considering the methodology adopted, based predominantly on an exploratory survey, a formal estimate of the sample of subjects to be enrolled is not necessary.

The sample will be represented by the students at the schools recruited within the necessARIA project. Thirty-five classrooms equipped with CMV systems for monitoring indoor air quality will be recruited, in the 4 regions involved (Autonomous Province of Bolzano, Abruzzo, Marche, and Puglia). Considering an average of 15 children per class, providing for the recruitment of 35 classrooms, it is estimated that about 525 children are for the group of those "exposed" to CMV implants. The control group will be represented by the same classes but with CMVs off. The sampling is expected in consecutive days, one day with CMVs off and the next day with CMV on.

IAQ and IEQ evaluation

IAQ and IEQ are related concepts that focus on the quality of the indoor environment, particularly in buildings. These parameters are crucial for the health, comfort, and well-being of occupants. Their evaluation will be performed by experimental measurements and numerical analyses before and after the installation of CMV in the Schools' rooms.

The evaluation of the effectiveness of CMV systems on air quality will be evaluated also through the correlations with numbers of air volume changes per hour (n) and maximum flow rate (m3/h).

IAQ is influenced by various factors, including the concentration of pollutants such as: PM, VOCs, Carbon dioxide (CO2), Radon, formaldehyde, and other indoor pollutants.

In addition to IAQ, IEQ considers factors such as: Thermal Comfort (by measuring air temperature, relative humidity, thermal radiation symmetry), Lighting Quality, Acoustic and Occupant Comfort, and Well-being factors like ergonomic design, aesthetics, and psychological aspects.

Measurements will be carried out in accordance with EN ISO standards (Table1) and the reporting of results will use the interval limits of Ministerial Decree 18/12/75 and EN standards.

These data will be integrated into an operational checklist along with classroom occupancy profile, heating and ventilation system switch-on profile (if present), window opening profile, test start and end date and time, total test duration, data acquisition interval, instrument/sensor name with its technical data sheet and installation data, identification of the instrument/sensor on the floor plan with installation height and distance from perimeter walls.

For the flow rate, it will be calculated on supply and extract air flow rate and air velocity, and

Table 1. Normative references measurement and limits of indoor variables studied

Measure	Measure: Normative reference (ref)	Limits: Normative reference (ref)
Air temperature	EN ISO 7726:2002 [22]	DM 18/12/75 [23] EN 16798-1:2019 [24]
Relative humidity	EN ISO 7726:2002 [22]	DM 18/12/75 [23] EN 16798-1:2019 [24]
CO_2	EN ISO 16000-26:2012 [25]	EN 16798-1:2019 (24]
Radon	ISO 11665 series [26]	D.Lgs n. 101/2020 [27] DM 23/06/2022 n. 256 [28]
Air change rate (ACH)	UNI EN 12599:2012 [29]	DM 18/12/75 [23] UNI EN ISO 10339 [30]
RT, C_{50}, STI, $L_{ic,int}$, $L_{id,int}$	UNI 11532-2:2020 [31]	DPCM 05/12/97 [32] DM 23/06/2022 n. 256 [28]

technical data sheet. Other data will be collected: type of ventilation system (centralised, decentralised, decentralised with ducts, etc.), type and position of filters, number of available ventilation plant speeds, efficiency of heat recovery unit, ventilation plant documentation, date and time of test start and end, total test duration, data acquisition interval, instrument/sensor name with its technical data sheet and installation data.

The assessment of acoustic comfort in building environments pertains to the subjective satisfaction or well-being of individuals in relation to the acoustic conditions of a given space. It gauges how well the sound environment aligns with the expectations and preferences of the occupants.

Specifically, in a school environment, the main indices to be examined include reverberation time (RT), Speech Transmission Index (STI), clarity (C50), sound pressure level from service equipment (i.e. HVAC systems) and outdoor noise.

These parameters are crucial for evaluating the overall acoustic quality and ensuring an environment conducive to effective communication and learning.

Microbiological sampling

Microbiological monitoring of air and classroom surfaces with CMVs will be performed in each school selected for the study. Specifically, sampling will be performed in the same classrooms on different days, with students present and CMVs on, and with students present and CMVs off.

Microbiological sampling of air

The microbial contamination of the classroom air and the effectiveness of the CMVs will be assessed by active sampling.

Active sampling will be performed on solid substrates using the Surface Air System instrument, SAS Super ISO 180 (PBI International, Milan, Italy) and on liquid substrates using the Coriolis®μ instrument (Bertin Technologies, Montigny le Bretonneux, France). For each sampling, 200 L of air is aspirated through the SAS and the Coriolis®μ. The devices should be positioned at a height of approximately 1 metre from the floor and in the centre of the classroom. For each point a double sampling by SAS will be performed both to evaluate the total bacterial load and the total mycotic charge. The number of colony-forming units will be expressed in colony-forming units per cubic meter (CFU/m3).

For SAS, the Total Bacterial Count (TBC) will be determined on 55 mm and 90 mm plates containing Plate Count Agar (PCA; Becton-Dickinson, Heidelberg, Germany), while for Total Fungal Count (TFC) / Total bacterial count (TBC), plates containing Sabouraud gentamicin-chloramphenicol agar (Liofilchem, Roseto degli Abruzzo, Italy) and DG18 respectively will be used. According to UNI EN ISO 4833-1:2013 [33], PCA plates will be incubated at 30 ± 1 °C for 72 hours for research of bacteria. For fungi, according to NF V08-059:2002 (34) Sabouraud plates will be incubated at 25 ± 2 °C for 5 days. The results will be expressed as the mean of two plates in colony-forming units. The air bacterial and fungal load (AFL) will be defined as the number of captured CFU/m3 of air, respectively.

A cone containing 15 mL of liquid substrate (0.005% Triton X-100) will be used for Coriolis®μ analysis, as recommended by the manufacturer. This medium will be used to evaluate the presence of the microbial community present in the air using Next Generation Sequencing (NGS) technologies.

Microbiological sampling of surfaces

Microbiological analyses of surfaces will be carried out on desks, chairs and door handles. Sampling will be performed using contact plates containing Plate Count Agar + Neutralizing (Liofilchem, Roseto degli Abruzzo, Italy), to find bacteria, and contact plates containing Sabouraud CAF Agar + Neutralizing (Liofilchem, Roseto degli Abruzzo, Italy) to find fungi. After sampling, the plates will be transported to the laboratory in containers refrigerated at 4°C and the PCA plates will be incubated at 30 ± 1 °C and monitored daily for 72 ± 3 hours [33], while the Sabouraud plates at 25 ± 2 °C and monitored for 5 days [34]. After incubation, the presence of colonies will be expressed as colony forming units for cm^2 (CFU/cm^2).

The identification of suspicious colonies will be performed by matrix-assisted laser desorption/ ionization time-of-flight mass spectrometry (MALDI-TOF MS, Biomèrieux, Marcy l'Etoile, France). The filamentous fungi no identifiable by MALDI-TOF MS, will be identified based on their macroscopic and microscopic morphological features, in accordance with the methods described by de Hoog et al [35]. The macroscopic examination will be based on visual observation of morphological characteristics and color of aerial mycelium, while the microscopic analysis will be performed by preparation of lactophenol cotton blue-stained slides. The slides will be prepared with tape that adhered to aerial mycelium and placed on the lactophenol cotton blue-stained slides.

CMV characterization

Smoke test

The smoke test will be carried out using a particle counter and a smoke generator. The objective is to evaluate the decay time of the particles generated using the ventilation system. A checklist will be adopted to collect: test start and end date and time, total test duration, data acquisition interval, air volume used for each measurement, start and stop time of smoke generator, ventilation system speed used during the test, sensor/instrument name and data sheet, identification of the sensor/instrumentation on the floor plan, specifying the installation height of the particle counter and distance from perimeter walls. The test procedure will involve the following steps:

1. during the first phase, the particle counter will be positioned outside the classroom to evaluate the external environmental condition. A data acquisition at 1 minute intervals will be used and an air sample equal to 1 litre will be taken for measurement. This step will be carried out until a stationary condition of the measured particles is reached;
2. during the second phase, the particle counter will be moved inside the classroom, centrally positioned on top of a desk, to evaluate the internal stationary condition;
3. during the third phase, before turning on the smoke generator, all the windows, doors and any existing shielding (e.g. roller shutters) in the classroom will be closed in order to evaluate only the influence of the ventilation system. Once all the openings will be closed, the smoke generator will be turn on until the classroom is completely saturated, then it will be turn off. The measurement continues until the stationary conditions obtained before turning on the smoke generator are reached.

The test can be repeated for each available speed of the ventilation system. Since the time available in schools is usually not enough to carry out multiple tests, at least one test will be carried out at the speed that is normally used during teaching activities or at the speed that guarantees the flow rate required by the regulations. Moreover, since this test is the most demanding from a temporal point of view, it will be always carried out at first and, at the end of all the tests, the equipment used inside the classroom will be collected.

Blower door test

The blower door test is conducted to assess the air permeability of the classroom envelope according to UNI EN ISO 9972:2015. The test consists in generating a pressure difference equal to 50 Pascal between inside and outside, using a fan temporarily mounted on the door through an adaptable frame and a sheet that seals the door itself. The air flow generated by the set pressure difference defines the infiltration air flow rate at 50 Pa (q_{50}). By calculating the ratio between the q_{50} value and the internal room volume, the number of air changes at 50 Pa (n_{50}) will be obtained. The data related to flow rates at different pressure differences, will be integrated into a checklist along with test start and end date and time, total test duration, sensor/instrument name and data sheet, identification of the sensor/instrumentation on the floor plan. In particular, the test procedure will involve the following steps:

1. the frame is installed in the door compartment and the sheet positioned, avoiding infiltration points;
2. the fan is inserted into the sheet and fixed to the frame horizontal bar;
3. the tubes are screwed onto the sheet and onto the pressure gauge depending on the test type to be carried out (pressure or depression, depending on the direction of the air flow generated by the fan). In the case of classrooms with a false ceiling, the test will be carried out only in depression;
4. to start the test the fan will be turn on. To obtain the value of n_{50}, various flow-pressure points must be defined to construct a straight line and obtain the flow rate at 50 Pa (q_{50}). At least 5 points will be always considered, in a pressure difference range between 20 Pa and 60 Pa;
5. once the straight line will be constructed, the value of q_{50} will be obtained. The value of n_{50} will be obtained calculating the ratio between q_{50} and the room volume.

Indoor Fluid-Dynamics (IDF)

IFD will include three different tests: the measurement of the flow rate provided by the ventilation system, the smoke test to assess the efficiency of the system and the blower door test to evaluate the permeability of the room (standard references in Table 1).

In addition to the experimental campaign, Computational Fluid-Dynamics (CFD) simulations will be performed for better understanding and optimising the thermal conditions within educational facilities. Specifically, COMSOL Multiphysics (version 6.2) [36] will be employed for the analyses due to its capability to integrate various physics modules, including fluid dynamics, heat transfer, and environmental conditions. This enables the creation of comprehensive models for evaluating complex systems like indoor environments.

The fluid dynamics simulations for indoor thermal comfort will consider several parameters and variables, such as classroom layout, geometry, material properties, outdoor weather conditions, occupancy patterns, and the presence or absence of mechanical ventilation systems. By inputting these factors into COMSOL Multiphysics, different ventilation scenarios can be modelled, and direct comparisons conducted, aiming to identify more efficient mechanical ventilation systems compared to traditional natural ventilation mechanisms.

EXPECTED OUTCOME

For the evaluation of health aspects, a questionnaire will be developed and administrated, concerning health problems arising in students belonging to the recruited classrooms, and will be answered by the children through the help of their parents/ legal guardian. In addition, the questionnaire will investigate the perceived air quality during school hours. Data collection of perceived air quality and state of health (respiratory, dermatological, ocular and general disorders) will take place through the multiple administration of the questionnaire, repeated every six months for two years. In total, the questionnaire will be administered 5 times: at time 0, at 6 months, at 12 months, at 18 months, at 24 months.

The questionnaire administered will consist of three sections, described below:

a. General questions about the child. This section consists of 7 questions (from A1 to A7) and analyses the socio-demographic characteristics of the population in question (date of compilation, region of birth, municipality of residence, school and class data, age, gender);
b. Questions about the child's school environment. This section consists of 17 questions (from B1 to B17) with a 5-point Likert scale, to be filled in by the students belonging to the recruited classrooms. To make it easier for primary school students to fill them in, the answers are represented with a visual scale. This section investigates the conditions of the school environment, in terms of lighting, noise, and microclimatic parameters.
c. Questions about the child's health status and home. This section consists of 21 multiple-choice questions (C1 to C21). This section is expected to be completed by the child's parents. It investigates the state of health of the pupils included in the study with regard to problems related to indoor air quality. The investigated health problems are:
   - Respiratory disorders (9 questions);
   - Skin disorders (1 question);
   - Eye disorders (1 question);
   - Other health issues (4 questions).

   Questions C16 to C21 explore the home environment and the extracurricular environment, assessing the presence of family members who smoke, ventilation and heating systems in the home, heavy traffic conditions near the home and the habit of physical activity.

The questionnaire consists of a total of 45 questions, with an average completion time of about 20 minutes.

The questionnaire, developed in collaboration with the OUs involved and validated through focus groups of experts (engineers, public health physicians, occupational medicine physicians, biologists), will be further validated through a pilot study on two classes (one with CMV and one without CMV), evaluating the internal validity of the questionnaire through the calculation of Cronbach's alpha.

The questionnaire, built and validated in Italian, will be translated and adapted to the English and German versions according to a forward/backward translation process and then to a pre-test ("cognitive debriefing"), to facilitate its compilation in the Autonomous Province of Bolzano - South Tyrol.

The questionnaire will be distributed in paper form, through agreements with the administrative staff of the schools recruited by the OUs related to the project. An online version will also be developed, through Microsoft Forms, generating a QR code to facilitate dissemination. In this case, the questionnaire will be sent to the children's parents/legal guardians, also using the digital class register tools.

Responses will be made pseudo-anonymous, through progressive coding, to avoid multiple completion by the same person at each deadline. However, adjustments will be made during statistical analysis to control the bias.

The questionnaire will be accompanied by a factsheet describing the objectives of the project and of the present study, the impact of air quality on the health of school building occupants, and the intended use of the data collected. The questionnaire compilation requires the signing of the informed consent by a parent/legal guardian of the enrolled student.

The paper-form completed questionnaires will be collected and archived for ten years at the Università Cattolica del Sacro Cuore after computerization of the data on a spreadsheet (Microsoft Excel).

QUANTIFICATIONS AND STATISTICAL ANALYSIS

The sample will be described in its clinical and demographic characteristics by means of the appropriate descriptive statistical indexes. In detail, qualitative data will be expressed as absolute frequency and relative percentage, while quantitative variables such as mean and standard deviation (SD) or median and interquartile range (IQR), as appropriate. To verify the Gaussian distribution of quantitative variables, the Shapiro-Wilk test will be applied.

To compare data between exposed and unexposed subjects, Student's t-test for independent samples or Mann Withney's U-test, depending on their distribution, will be used in case of comparisons between quantitative data. Qualitative data will be compared using the Chi-Square test or the exact Fisher-Freeman-Halton test, as appropriate.

The incidence over time in respiratory, dermatological, ocular and general disorders will be analyzed in terms of incidence rates and compared between exposed and unexposed through the incidence rate ratio. ANOVA test will be deployed to analize the variance across the 5 time-points. Appropriate graphs will also be drawn to evaluate the trend in the 5 time-points. Poisson regression models can be fitted to assess the influence of children's age, in relation to the classes involved, gender, geographical location and housing data.

Statistical significance is set for values of $p < 0.05$. Suggestive P values ($0.05 \leq P < 0.10$) will also be reported. The entire set of analyses will be conducted with STATA 18 software [37].

For the evaluation of the comfort of the occupants of indoor school environments, COMSOL Multiphysics software [36] will be used for numerical simulation of air quality by modelling thermo-hygrometric parameters, acoustic and HVAC (heating, ventilation and air conditioning) systems. To run simulations related to rooms or indoor environments using COMSOL Multiphysics, it is necessary to create geometric modelling, define initial and parameter conditions, choose physical models, define materials, configure a mesh, and, finally, run the numerical simulation. The results will be used to prepare reports for school leaders and project partners to make engineering or management decisions to optimize indoor air quality, energy efficiency, and room acoustics.

The data collected will be processed in compliance with the European Regulation 2016/679 on privacy (so-called GDPR), Legislative Decree 196/2003 ("Personal Data Protection Code" and subsequent additions) and Legislative Decree 101/2018. The data collected will be recorded on a single computerized database accessible by password only by researchers and kept according to current legislation. The data will only be kept for as long as is strictly necessary for the investigation and then deleted.

LIMITATIONS

The present study has some limitations. Some limitations concern the use of surveys, such as the lack of precise description of the population and the presence of bias among respondents. Among these, the risk of "self-selection bias" prevails, as participation implies the respondent's willingness to take an active part in the study and this willingness could be influenced by interest in the topic treated. A further limitation to consider is the possibility of "social desirability bias", according to which the respondent may tend to select the most socially acceptable answer rather than the most truthful. In addition, the low response rate could be an important limitation, as well as the willingness of the individuals interviewed to pay full attention to the questions asked for more than a certain amount of time (e.g., 5-10 minutes). Another limitation concerns sampling. A larger sample could provide an assessment of heterogeneity among respondents in more detail and provide coefficients with more precise estimates. Finally, a methodological limitation inherent in the use of surveys could be the reluctance of the students/family to fill in the questionnaire motivated by doubts relating to the processing of data despite the explicit guarantee of the anonymity of the survey itself.

TROUBLESHOOTING

The present study protocol aims to be a foundation for all future studies in the necessARIA project.

This project aims to assess efficacy and effectiveness of new measures to tackle the indoor air quality issue, by performing chemical-physical and microbiological assessment of indoor air quality post intervention (CMVs installation).

At the same time, this project aims to highlight the importance of perceived indoor air quality for students and school personnel from a health perspective, assessing the respiratory, dermatological, ocular, neurobehavioral and general health outcomes in this population.

Finally, necessARIA aims to propose new strategies and measures to deal with the raising issue of sustainability in indoor air quality improvement, enacting measures and systems that will be sustainable from an environmental, energetical, and acoustic point of view, while still ensuring the best possible health outcomes.

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AUTHOR CONTRIBUTIONS

Conceptualization: L.V., U.M.; Data curation: M.F.R., F.B., C.P., C.D.P., S.M., G.C.; Funding acquisition: U.M.; Methodology: M.F.R., F.B., C.P., C.D.P., S.M., G.C.; Writing – original draft: M.F.R., F.B., R.L., C.P., C.D.P., S.M., G.C.; Writing – review & editing: R.L., U.M, necessARIA working group.

DECLARATION OF INTEREST

The authors report no conflicts of interest.

ETHICS AND CONSENT

The study protocol received ethical approval from IRB of Università Cattolica del Sacro Cuore in Rome (ID: 5859).

SCOPE STATEMENT

This study focuses on the possible clinical consequences of low-quality indoor air and it promotes strategies to improve indoor air quality in schools by installing controlled mechanical ventilation systems. The aim of this research project is improving health outcomes related to indoor air quality in students, teachers, technical and administrative staff. It also includes considerations related to topics such as prevention in the workplace and energy sustainability.

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Smoke Styling in Contemporary Make-up Advertising

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The negative impacts of tobacco on morbidity and mortality continue on the global stage, with an annual death toll of over 8 million [1]. The WHO's Framework Convention on Tobacco Control (FCTC) has proven to be pivotal in helping combat tobacco [2]. A crucial component of the FCTC is a comprehensive tobacco advertising ban. A major success of the FCTC can, for example, be seen in Western Europe, where direct tobacco advertising has largely been eliminated.

Portrayals of smoking in various media continue to be an issue, ranging from Hollywood blockbusters and network dramas to graphic novels [3–5]. However, another important but overlooked phenomenon is what may be termed 'smoke styling'. This involves the portrayal or use of another product in a manner that is effectively coded as a tobacco product. Examples can include lipstick or mascara held to mimic a cigarette or a cigar.

Examples of this can be seen in the two adverts below. The first of these is for Charlotte Tilbury, a hugely popular brand among young women, in which a woman holds lipstick in the same manner, as though holding a cigarette (Figure 1).

The second image (Figure 2), from L'Oréal, features a woman holding mascara in a manner to mimic a cigar.

These images effectively glamorize smoking, without using tobacco products directly. Nonetheless, in their use of smoke styling, they conflate would-be tobacco products with sexuality, sensuality, confidence, power, beauty, slimness, celebrity, and youth among women. Tobacco manufacturers have long fine-tuned the appeal of cigarette packaging [6]. Such tactics can include slim cigarettes and packet shape, including lipstick-style packaging [7–9]. It is clear that cosmetics manufacturers, situated in the global beauty industry, are adopting reciprocal tactics. Such advertising needs to be 'named and shamed'.

Figure 1. Smoke Styling Imagery From A Charlotte Tilbury Lipstick Advertisement. (2019 advert on Charlotte Tilbury's official YouTube channel)

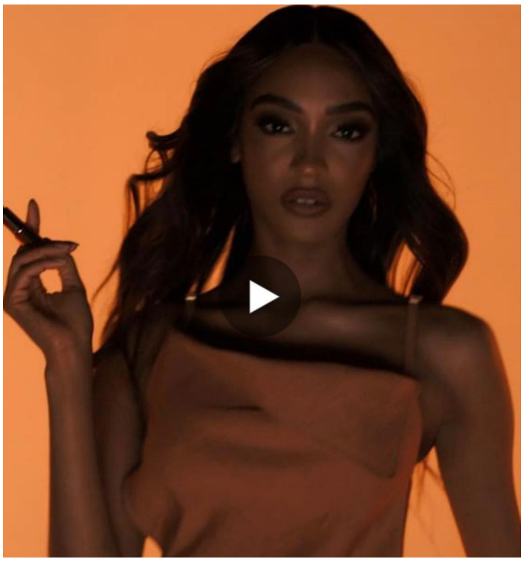

Figure 2: Smoke Styling Imagery from A L'Oréal Mascara Advertisement. (2025 advert on one of Ireland's State television channels, RTE)

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COMPETING INTEREST

None declared.

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