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# **BMJ Open**

#### The Burden of Lower Respiratory Infections and the Risk Factors across Regions in Ethiopia: Global Burden of Diseases Study 1990-2019

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Complete List of Authors:	Yigezu, Amanuel; Ethiopian Public Health Institute Misganaw, Awoke; University of Washington, Department of Health Metrics Sciences; Ethiopian Public Health Association, Getnet, Fentabil; Jigjiga University; Ethiopian Public Health Institute Berheto, Tezera; Ethiopian Public Health Institute Walker, Ally ; University of Washington, Department of Health Metrics Sciences Zergaw, Ababi; Ethiopian Public Health Institute; Addis Ababa University College of Health Sciences, Department of Health Systems and Policy Gobena, Firehiwot ; Ethiopian Health Insurance Service Haile, Muluken ; Ethiopian Health Insurance Service Hailu, Alemayehu; University of Bergen, Department of Global Public Health and Primary Care Medicine Memirie, Solomon Tessema; Addis Ababa University, Addis Center for Ethics and Priority Setting; Harvard University, Harvard T.H. Chan School of Public Health Tolosa, Dereje ; Ethiopian Health Insurance Service Abate, Semagn Mekonnen; Dilla University College of Health Sciences, Department of Anesthesiology Molla Adane, Mesafint; Bahir Dar University College of Medical and Health Sciences Akalu, Gizachew ; St Paul's Hospital Millennium Medical College; Addis Ababa University College of Health Sciences Akliu, Addis ; Arba Minch University College of Health Science, Adult health nursing; Gebru, Zeleke; Arba Minch University College of Health Science, Adult health nursing; Gebru, Zeleke; Arba Minch University, public health; Arba minch university Asemahagn, Mulusew; Bahir Dar University College of Medical and Health Sciences, School of Public Health; Attaw, Daniel; Madda Walabu University, public health Belete, Melaku; Wollo University Hailemariam, Tekleberhan; Mekelle University Hailemariam, Tekleberhan; Mekelle University Yirga, Alemeshet; Bahir Dar University Yirga, Alemeshet; Bahir Dar University Yirga, Alemeshet; Bahir Dar University Hailemariam, Tekleberhan; Mekelle University Yirga, Alemeshet; Bahir Dar University Hailemariam, Tekleberhan; Mekelle University Yirga, Alemeshet; Bahir Dar University, Pub				

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	Demeke, Feleke ; Bahir Dar University College of Medical and Health Sciences Desta, Abebaw ; University of Gondar Ena, Lankamo; Arba Minch University, Eyayu, Tahir; Debre Tabor University, Department of Medical Laboratory Sciences Fentaw, Zinabu; Wollo University, Department of Epidemiology and Biostatistics; Wollo University, Epidemiology and Biostatistics Gargamo, Daniel ; Wolaita Sodo University Gebrehiwot, Mesfin ; Wollo University Gebremichael, Mathewos ; Arba Minch University Getachew, Melaku ; Haramaya University College of Health and Medical Sciences Molla, Getahun ; University of Gondar, University of Gondar Hospital Sahiledengle, Biniyam; Madda Walabu University, Public Health Beyene, Bereket; Arba Minch University Sibhat, Migbar; Dilla University College of Health Sciences, Nursing; Sidamo, Negussie ; Arba Minch University, Public Health Solomon, Damtew ; Madda Walabu University Solomon, Yonatan ; Dire Dawa University Wagaye, Birhanu; Wollo University; Ethiopian Public Health Institute Wedajo, Shambel; Wollo University, Weldemariam, Melat; Arba Minch University, Department of Medical Laboratory Sciences Yismaw, Yazachew ; Bahir Dar University Naghavi, Moshen; University of Washington School of Public Health,
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- 1 The Burden of Lower Respiratory Infections and the Risk Factors across Regions in Ethiopia:
- 2 Global Burden of Diseases Study 1990-2019

3 Ethiopia Subnational-Level Lower Respiratory Infections Burden collaborators

Amanuel Yigezu<sup>\*</sup>,<sup>1</sup> Awoke Misganaw<sup>\*</sup>,<sup>2,1</sup> Fentabil Getnet,<sup>1,3</sup> Tezera Moshago Berheto,<sup>4</sup> Ally Walker,<sup>5</sup> Ababi Zergaw,<sup>6,1</sup> Firehiwot Abebe Gobena,<sup>7</sup> Muluken Argaw Haile,<sup>8</sup> Alemayehu Hailu,<sup>9</sup> Solomon Tessema Memirie,<sup>10</sup> Dereje Mengistu Tolosa,<sup>11</sup> Semagn Mekonnen Abate,<sup>12</sup> Mesafint Molla Adane,<sup>13</sup> Gizachew Taddesse Akalu,<sup>14,15</sup> Addis Aklilu,<sup>16</sup> Dejene Tsegaye Alem,<sup>17</sup> Zeleke Gebru,<sup>18</sup> Mulusew Andualem Asemahagn,<sup>19</sup> Daniel Atlaw,<sup>20</sup> Tewachew Awoke,<sup>21</sup> Hunegnaw Abebe<sup>22</sup>, Melaku Ashagrie Belete,<sup>23</sup> Tekleberhan Hailemariam,<sup>24</sup> Alemeshet Yirga,<sup>25</sup> Setognal Birara Aychiluhm,<sup>26</sup> Belay Boda Abule Bodicha,<sup>27</sup> Chuchu Churko,<sup>18</sup> Feleke Mekonnen Demeke,<sup>21</sup> Abebaw Alemayehu Desta,<sup>28</sup> Lankamo Ena,<sup>29</sup> Tahir Eyayu,<sup>30</sup> Zinabu Fentaw,<sup>31</sup> Daniel Baza Gargamo,<sup>32</sup> Mesfin Damtew Gebrehiwot,<sup>33</sup> Mathewos Alemu Gebremichael,<sup>34</sup> Melaku Getachew,<sup>35</sup> Getahun Molla,<sup>36</sup> Biniyam Sahiledengle,<sup>37</sup> Bereket Beyene,<sup>38</sup> Migbar Sibhat,<sup>39</sup> Negussie Boti Sidamo,<sup>18</sup> Damtew Solomon,<sup>40</sup> Yonatan Solomon,<sup>41</sup> Birhanu Wagaye,<sup>42,43</sup> Shambel Wedajo,<sup>22</sup> Melat Weldemariam,<sup>16</sup> Yazachew Yismaw,<sup>44,45</sup> Mohsen Naghavi.<sup>5,2</sup> 

<sup>24</sup> <sub>25</sub> 16 \*Joint first authors

## 26 27 17 Affiliations 28

<sup>1</sup>National Data Management Center for Health (NDMC), Ethiopian Public Health Institute, Addis Ababa, Ethiopia; <sup>2</sup>Department of Health Metrics Sciences, School of Medicine, University of Washington, Seattle, WA, USA; <sup>3</sup>Department of Epidemiology, Jigjiga University, Jigjiga, Ethiopia; <sup>4</sup>HIV and TB Research Directorate, Ethiopian Public Health Institute, Addis Ababa, Ethiopia: <sup>5</sup>Institute for Health Metrics and Evaluation, University of Washington, Seattle, WA, USA; <sup>6</sup>Department of Health Systems and Policy, Addis Ababa University, Addis Ababa, Ethiopia; <sup>7</sup> Ethiopian Health Insurance Service, Addis Ababa, Ethiopia; <sup>8</sup>Program Section, Ethiopian Health Insurance Service, Addis Ababa, Ethiopia; <sup>9</sup>Department of Global Public Health and Primary Care, University of Bergen, Bergen, Norway; <sup>10</sup>Addis Center for Ethics and Priority Setting, Addis Ababa University, Addis Ababa, Ethiopia; <sup>11</sup>Ethiopian Health Insurance Service, Ministry of Health, Addis Ababa, Ethiopia; <sup>12</sup>Department of Anesthesiology, Dilla University, Addis Ababa, Ethiopia; <sup>13</sup>College of Medicine and Health Sciences, Bahir Dar University, Bahir Dar, Ethiopia; <sup>14</sup>Department of Microbiology, Immunology and Parasitology, St. Paul's Hospital Millennium Medical College, Addis Ababa, Ethiopia; <sup>15</sup>Department of Microbial, Cellular and Molecular Biology, Addis Ababa University, Addis Ababa, Ethiopia; <sup>16</sup>Department of Medical Laboratory Sciences, Arba Minch University, Arba Minch, Ethiopia; <sup>17</sup>Department of Nursing, Debre Markos University, Debremarkos, Ethiopia; <sup>18</sup>School of Public Health, Arba Minch University, Arba Minch, Ethiopia; <sup>19</sup>School of Public Health, Bahir Dar University, Bahir Dar, Ethiopia; <sup>20</sup>Department of Biomedical Science, Madda Walabu University, Bale Robe, Ethiopia; <sup>21</sup>Department of Medical Laboratory Sciences, Bahir Dar University, Bahir Dar, Ethiopia; <sup>22</sup>Department of Public Health, Wollo University, Dessie, Ethiopia; <sup>23</sup>Department of Medical Laboratory Sciences, Wollo University, Dessie, Ethiopia; <sup>24</sup>Department of Medical Physiology, 

Mekelle University, Mekelle, Ethiopia; <sup>25</sup>School of Health Science, Bahir Dar University, Bahir Dar, Ethiopia; <sup>26</sup>Department of Public Health, Samara University, Samara, Ethiopia; <sup>27</sup>Department of Biomedical Sciences, Arba Minch University, Arba Minch, Ethiopia; <sup>28</sup>Department of Surgical Nursing, University of Gondar, Gondar, Ethiopia; <sup>29</sup>Department of Comprehensive Nursing, Arba Minch University, Arba Minch, Ethiopia; <sup>30</sup>Department of Medical Laboratory Sciences, Debre Tabor University, Debre Tabor, Ethiopia; <sup>31</sup>Department of Epidemiology and Biostatistics, Wollo University, Dessie, Ethiopia; <sup>32</sup>Department of Pediatrics and Neonatal Nursing, Wolaita Sodo University, Wolaita Sodo, Ethiopia; <sup>33</sup>Department of Environmental Health, Wollo University, Dessie, Ethiopia; <sup>34</sup>Department of Epidemiology and Biostatistics, Arba Minch University, Arba Minch, Ethiopia; <sup>35</sup>Department of Emergency and Critical Care Medicine, Haramaya University, Harar, Ethiopia; <sup>36</sup>Department of Epidemiology and Biostatistics, University of Gondar, Gondar, Ethiopia; <sup>37</sup>Department of Public Health, Madda Walabu University, Bale Robe, Ethiopia; <sup>38</sup>Department of Nursing, Arba Minch University, Arba Minch, Ethiopia; <sup>39</sup>Department of Pediatrics and Child Health Nursing, Dilla University, Dilla, Ethiopia; <sup>40</sup>Department of Anatomy, Madda Walabu University, Bale Robe, Ethiopia; <sup>41</sup>Department of Nursing, Dire Dawa University, Dire Dawa, Ethiopia; <sup>42</sup>College of Medicine and Health Sciences, Wollo University, Dessie, Ethiopia; <sup>43</sup>Water, Sanitation and Hygiene Unit, Ethiopian Public Health Institute, Addis Ababa, Ethiopia; <sup>44</sup>Department of Pharmacology, Bahir Dar University, Bahir Dar, Ethiopia; <sup>45</sup>Pharmacy Department, Alkan Health Science, Business and Technology College, Bahir Dar, Ethiopia. 

- Corresponding Author: Amanuel Yigezu; yigezuamanuel@yahoo.com 5.02071
  - Submitting Author: Awoke Misganaw

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3 4	71	Abstract
5	72	Objective: This analysis is to present the burden and trends of morbidity and mortality due to
7 8	73	LRIs, their contributing risk factors, and the disparity across administrative regions and cities from
9 10	74	1990 to 2019.
11 12 13	75	Design: This analysis is part of a collaborative and comparable systematic Global Burden of
14 15	76	Disease (GBD 2019) study.
16 17	77	Study setting: The study includes nine region states and two chartered cities of Ethiopia
18 19 20	78	Outcome Measures: We calculated incidence, death, and years of life lost (YLLs) due to LRIs
20 21 22	79	and contributing risk factors using all accessible data sources. We calculated 95% uncertainty
23 24	80	intervals (UI) for the point estimates.
25 26	81	Results: In 2019, LRIs incidence, death, and YLLs among all age groups were 8313.7 (95% UI:
27 28 29	82	7757.6-8918), 59.4 (49.8-71.4) and 2404.5 (2059.4-2833.3) per 100000 people, respectively.
30 31	83	From 1990, the corresponding decline rates were 39%, 61%, and 76%, respectively. Children
32 33 34 35 36 37 38	84	under the age of five years account for 20% of episodes, 42% of mortalities, and 70% of the YLL
	85	of the total burden of LRIs in 2019. The mortality rate was significantly higher in predominantly
	86	pastoralist regions-Benishangul-Gumuz 101.8 (84.0-121.7) and Afar 103.7 (86.6-122.6). The
39 40	87	Somali region showed the least decline in mortality rates. More than three-fourths of under-five
41 42	88	child deaths due to LRIs were attributed to malnutrition. Household air pollution from solid fuel
43 44 45	89	attributed to nearly half of the risk factors for all age mortalities due to LRIs in the country.
46 47	90	Conclusion: In Ethiopia, LRIs have reduced significantly across the regions over the years (except
48 49	91	in elders), however are still the third leading cause of mortality, disproportionately affecting
50 51 52	92	children younger than five years old, and predominantly pastoralist regions. Interventions need to
52 53 54	93	consider leading risk factors, targeted age groups and pastoralist and cross-border communities.
55 56	94	Keywords: Lower respiratory infections, regions, chartered cities, Ethiopia
57 58		3
59 60		For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml

#### What is already known on this topic

Lower respiratory infections (LRIs) remain a significant contributor to Ethiopia's morbidity and mortality. LRIs are one of the leading causes of under-five mortality and are expected to increase because of the current conflict, internal displacements, health care service interruption and the COVID-19 pandemic. This work is among the first to present a comprehensive analysis of LRIs effect on morbidity and mortality, and their risk factors across all the regional states of Ethiopia over an extended time period to support health decision making at subnational levels.

#### 102 What this study adds

This is the first collaborative effort to provide the effects of LRIs and its risk factors on morbidity and mortality for Ethiopia's nine regions and two chartered cities from 1990 to 2019. This analysis highlights substantial decline morbidities and mortalities caused by LRIs over the last three decades, as well as the disparities between regions and chartered cities, and the opportunity to reduce LRIs burden of premature mortality by addressing specific geographic locations, risk factors and age-groups with cost-effective interventions.

## 109 How this study might affect research, practice or policy

The results identify regions and segments of the population highly affected by LRIs , and the leading risk factors contributing to premature mortalities. These could be potential priorities for action against LRIs that would reduce premature mortality. There is a need to enhance strategies addressing predominantly pastoralist regions and cross-border communities and for quality healthcare services in underserved areas. Although morbidity and mortality have shown improvements over the past three decades, LRIs burden is still high in parts of Ethiopia.

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### 117 INTRODUCTION

Lower Respiratory Infections (LRIs) have been a predominant health problem worldwide, causing more than 2.3 million deaths in 2016 alone, amounting to a mortality rate of 32.2 per 100,000 people (1). LRIs comprise diseases of the lower airways such as pneumonia, bronchitis, and bronchiolitis, among others (2). Nearly all (99%) of LRI deaths occur in low and middle income countries and highly affect children under the age of 5 years (3). In sub-Sahara African countries, the mortality rate is 66.4 per 100,000 people, which is four times the mortality rate in East Asia and twice the global average (2).

Ethiopia ranked in the top three African countries in the number of under-five child deaths from LRIs (4). To prevent child death from LRIs and other diseases in early life, Ethiopia has been implementing the "Integrated management of childhood illness" program since 1997 which was scaled up to the national level in 2007 (5). LRIs, and pneumonia in particular, have been among the top three leading causes of childhood mortality in the country (6). Among LRIs' aetiologies, S. pneumonia contributed to more deaths than the other LRIs aetiologies combined (3). In 2011, the country introduced 10-valent pneumococcal conjugate vaccine (PCV 10) into its national immunization program to reduce the burden of Streptococcal pneumonia (7).

Morbidity and mortality from LRIs are attributable to multiple underlying factors. Malnutrition is one of the main underlying risk factors (8, 9). The other main attributable factor are poor living conditions that include household crowding, parental smoking, high use of household solid fuel/biomass consumption, poor ventilation, and lack of hand-washing facilities (10-12). In addition, bottle feeding also contributes to the burden of LRIs in children (13).

138 The flagship Ethiopian Health Extension Program (HEP) has been the backbone of the country's139 health system strategies to reduce the burden of LRIs and other diseases through preventive and

health promotion activities at the community level. The HEP has also improved broader access to
health care, availability of essential antibiotics, and immunization mainly to the rural population
since 2004 (14). In 2010, the country also introduced the "integrated community case
management" (ICCM) approach to treat pneumonia through trained health cadres of health
extension workers (HEWs) implementing HEP (15).

Currently, Ethiopia is implementing its Health Sector Transformation Plan-2 (HSTP-2) which is adapted from the Sustainable Development Goals. Some of the aims include increasing the proportion of under-five children with pneumonia who received antibiotics from 48% to 69% and improving full vaccination coverage from 44% to 69% between 2020 and 2025 (16). Commitment to international goals such as The Global Action Plan for the Prevention and Control of Pneumonia and Diarrhoea by 2025 could be reached if enough investment is made in high LRI burden countries like Ethiopia (17).

As Ethiopia is a country of stark contrasts in socioeconomic, epidemiological, and geographical variations, estimating disease burden at the regional level could provide valid and reliable information to inform policy decisions, including efficient resource allocation to match the burden in the subnational states. Hence, this paper presents the 2019 Global Burden of Diseases, Injuries, and Risk Factors study (GBD) results on the burden, trends and regional variations of LRIs in Ethiopia from 1990 to 2019.

5 158 METHODS

Ethiopia is the second-most populous country in Africa next to Nigeria, with an estimatedpopulation of 112 million in 2019 (18). More than half of the country's population is under 20, and

<sup>159</sup> Study Setting

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over 80% of the population resides in rural areas (19). The country is subdivided into ten regional states (Afar, Amhara, Benishangul-Gumuz, Gambella, Harari, Oromia, Somali, Sidama, Southern Nations and Nationalities and Peoples (SNNP), and Tigray) and two chartered cities (Addis Ababa and Dire Dawa). During this study, Sidama was a zonal administration under the SNNP region. Oromia, Amhara, and SNNP are the highly populated regions. In this study, we classified the regions into urban (Addis Ababa, Dire Dawa, and Harari), agrarian (Oromia, Amhara, SNNP, Tigray), and pastoralist (Benishangul-Gumuz, Afar, Gambella, and Somali). The healthcare system of the country is a three-tiered system consisting of primary, secondary, and tertiary levels of healthcare delivery units with 21,154 functioning health facilities and 159,545 health workforce in 2019 (16). The primary health care unit (PHCU) consists of health posts (staffed by HEWs), health centres, and primary hospitals. The secondary level of care consists of general hospitals and the tertiary level of care includes national referral hospitals which provide specialized services Lien (16).

#### **Data Sources and Analysis**

The analysis and findings of LRIs presented in this paper were produced by the Ethiopia Subnational Burden of Disease Initiative, a collaborative endeavour between the National Data Management Center for Health (NDMC) at the Ethiopian Public Health Institute (EPHI) and the Institute for Health Metrics and Evaluation (IHME), as part of GBD. The details of the methodology were described elsewhere (20). In brief, woreda (district) level geographic boundary mapping of regions and cities was used because woredas were relatively stable government structures (compared to lower or higher level administrative structures) during political or government changes and through the three census years (1984, 1994, and 2007). First, the analysis was estimated by mapping population and demography at the district level by time and region. 

Then, the data sources were mapped by regions before processing the data in the GBD analysis based on GBD protocol. EPHI, in collaboration with IHME, gathered all accessible data sources by location for Ethiopia and all regions and cities that included census, demographic surveillance, household surveys, diseases registry, health service utilization, disease notification, and other data for this analysis. A comprehensive description of data sources, quality, and modelling for GBD 2019 has been reported on the following online portal: (http://ghdx.healthdata.org/gbd-2019/data-

- 191 input-sources).
- **192 GBD Methods and Tools**

The GBD details are reported elsewhere (21). Diseases and injuries within the GBD were organized into levels: Level 1 being the broadest causes of death and disability to Level 4 being the most specific. Within the three Level 1 causes (communicable, maternal, neonatal, and nutritional diseases; non-communicable diseases; and injuries), there were 174 Level 3 causes. The GBD 2019 study has estimated the burden of disease, including LRIs, for Ethiopia's national and subnational states. LRIs comprise diseases of the lower airways such as pneumonia, bronchitis, and bronchiolitis, among others (2). LRI mortality was estimated by age, sex, geography, and year using a modelling platform called the Cause of Death Ensemble model. LRI morbidity, including incidence, was modelled using a meta-regression platform known as DisMod-MR, a Bayesian, hierarchical, mixed-effects meta-regression platform (22). Years of life lost (YLLs) were computed by multiplying cause-specific deaths by the life expectancy at the age of death (23, 24). Population risk assessments over time and among risks were estimated using the comparative risk assessment approach developed for the GBD study (25, 26). The GBD risk factors were categorized as follows: Level 1 risk factors are behavioural, environmental, occupational, and 

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3 4 5	207	metabolic; Level 2 risk factors include 20 clusters of risks; Level 3 consists of 52 clusters of risks;
5 6 7	208	and Level 4 contains 69 specific risk factors (21).
8 9 10 11	209	Presentation of results
12 13 14	210	We present the burden of LRIs in Ethiopia and its regional states using incidence, deaths, and
14 15 16	211	YLLs categorized by sex, age groups, and year. We used numbers, rates, and percent change for
10 17 18	212	the quantification of the burden. We also estimated the risk factors contributing to LRIs in Ethiopia
19 20	213	and the percent change between 1990 and 2019. We reported GBD causes and risk factors using
21 22 23	214	level 3 classifications, with 95% Uncertainty Intervals (UI). Additional tables and figures are
24 25 26	215	attached in the supplementary appendix.
27 28 29	216	Patient and public involvement
30 31 32 33	217	Patients and the public were not involved in this study.
34 35 36	218	RESULTS
37 38 39	219	Morbidity Due to LRIs
40 41 42	220	In 2019, an estimated 6,628,673.6 (95% UI: 6,108,786.2–7,230,986.3) new cases of LRIs occurred
43 44	221	in Ethiopia resulting in an age-standardized incidence rate of 8313.7 per 100,000 people (7757.6–
45 46 47	222	8918). Out of the total LRI episodes, 22% (1,448,680.0 new cases [1,150,089.8–1,799,704.4]) of
47 48 49	223	new cases occurred among children younger than 5 years, yielding an annual incidence rate of
50 51	224	8685.0 per 100,000 children (6895.1–10,789.8). In adults older than 70 years, there were 725,273.3
52 53 54	225	(640,315.4–837,746.3) new cases of LRIs with an annual incidence of 38,394.4 per 100,000 people
55 56	226	(33,896.9–44,348.5) (Appendix Table 1 and Table 2).
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Compared to national estimates, a significantly lower age-standardized incidence rate of LRIs per 100,000 people was observed in the chartered cities (6788.1 [6285.1-7339.1] in Addis Ababa, 7148.8 [6634.6–7750.7] in Dire Dawa), and in Harari region (7190.5 [6684.1–7718.6]). The highest rates of age-standardized incidence per 100,000 people were observed in Afar (9350.2 [8648.8-10,157.4]), Somali (9220.0 [8515.9-10,046.4]), and Benishangul-Gumuz (9054.6 [8394.2–9766.0]) although not significant compared to the national estimate (Figure 1; Figure 2; Appendix Table 2). In children younger than 5 years, the lowest incidence rates were observed in Addis Ababa (4927.2 [3812.5–6231.8]), Harari (6821.6 [5373.5–8607.3]), and Gambella (6791.1 [5370.4–8460.1]) per 100,000 people, substantially below the national estimate. The highest incidence of LRIs per 100,000 children were recorded in Benishangul-Gumuz (10,481.8 [8269.5-13,219.0]), Somali (10,062.7 [7949.6–12,802.8]), Afar (9365.5 [7421.7–11,714.7]), and Oromia (9039.4 [7080.5– 11,277.7]). The age-standardized decline rate between 1990 and 2019 was 39% for both sexes, and it was 56% in under-five children and 13% in adults older than 70. The lowest decline in age-standardized incidence rate was in Somali (19%); while it was between 38% and 44% for the remaining regions (Appendix Table 2). In children younger than 5, the incidence rates increased slightly between 1990 and 1995, except in Addis Ababa and Amhara region. The highest decline rates were found between the years 2005 and 2015 across all regions (Appendix Figure 1). Mortality due to LRIs 

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In 2019, LRIs caused 46,300.7 (95% UI: 39,515-54,642) deaths in Ethiopia, giving the age-248 standardized mortality rate of 86.4 (75.3-97.6) per 100,000 people. Under-five mortality accounted 249 for 42% (19.591.8 [14.018.4–26.899.0]) of all deaths due to LRIs which resulted in a mortality 250 rate of 117.4 (84.0–161.2) per 100,000 children. Of the under-five deaths, 71% (13,919.0 [9946.0– 251 18,860.0]) occurred in the first year of life. In adults older than 70 years, LRIs caused 14,627.6 252 253 (12,393.7–16,892.8) deaths, which was a mortality rate of 774.3 (656–894.2) deaths per 100,000 adults (Table 1; Appendix Table 3). 254 In 2019, the number of deaths in all age groups by region were highest in Oromia (18,206 [15,193– 255

257 [3007.4–4959.4]), followed by Tigray (2551.4 [2090.3–3028.6]), Afar (706.2 [567.7–869.6]),

21745]), Amhara (9525 [7530-11872]), SNNP (9494 [7713-11649]), and Somali (3907.5

258 Benishangul-Gumuz (619 [470.7–803.0]), Dire Dawa (154.6 [120.6–193.8]) and Gambella (123.2

259 [98.2–151.9]). Harari (93.1 [73.8–116.0) had the lowest number of deaths. (Appendix Table 3).

260 Between 1990 and 2019, the age-standardized mortality rate declined by 61%, and the decline in

under-five children and adults over 70 years was 86% and 30%, respectively (Table 1).

3	262	Table 1: Lower Respiratory Infections mortality rates and percentage changes between 1990 and 2019 in Ethiopia, both sexes, with different age
4 5	263	groups

5	Age standardized			Children younger than 5			People older than 70		
7 Location	Deaths per 100 000	Deaths per 100 000	Cha-	Deaths per 100 000	Deaths per 100 000	Cha-	Deaths per 100 000	Deaths per 100 000	Cha-
8 9	people [95% UI],	people [95% UI],	nge,	children [95% UI], 1990	children [95% UI],	Nge,%	people [95% UI],	people [95% UI],	nge,%
10	1990	2019	%		2019		1990	2019	
Addis Ababa	163.4[134.6-206.9]	59.4[49.8-71.4]	64	441.5[320.4-602.7]	23.4[14.1-36.4]	95	909.2[669.5-1264.6]	503.6[410.5-633.7]	45
1 <b>D</b> romia	241.3[188.5-292.8]	89.3[75.9-103.1]	63	920.7[629.5-1264.1]	122.3[84.8-171]	87	1174.1[842.8-1543]	849.5[687.3-1009]	28
14 Amhara 15	197.7[163.5-236.5]	74.3[59.4-91]	62	691.3[531.7-883.4]	94.9[55.6-146.1]	87	1017.9[755.4-1324]	682.7[537.4-857.9]	33
18NNPs	243.7[196.4-296.9]	98.9[83.8-116.6]	59	971.9[697.2-1273.2]	118.4[79-168.5]	88	1161.3[584.7-822.3]	845.4[685.6-018.1]	28
「不 <sub>igray</sub> 18	242.7[200.5-292]	84.6[69.2-100.1]	65	780.4[593.5-1009.1]	67.2[43.5-98.3]	92	1166.7[838.2-1586]	788.6[637.9-956.8]	33
Harari	240.2[182.6-303.1]	77[63-92.5]	68	1146.7[730-1604.1]	89.9[51.1-138]	93	762.3[412-1223.7]	694.3[551.9-849]	9
20 <sub>A far</sub> 21	244.8[186.5-316.9]	103.7[86.6-122.6]	58	723.7[481.5-1023.7]	101.7[65-152.4]	86	1010[658-1541.7]	917.6[720.6-146.8]	10
Somali	147.6[113.8-192.6]	97.5[79.2-118.6]	34	455.9[313-628.5]	197.3[135-279.8]	57	798.8[519.2-1177.6]	765.1[588.8-972.4]	5
23BG	284.1[221.8-358.1]	101.8[84-121.7]	64	1266.4[846.7-790.9]	215.1[141.4-311]	84	975.3[656.5-1379.3]	671.9[532.7-848.7]	32
Dire Dawa	220.1[171.6-270.9]	69.9[56.5-84]	68	1084.2[689.1-503.2]	83.7[44.7-135.9]	93	868.7[604.5-1205.5]	621.3[496.4-766.1]	29
2Gambella	231.5[176.8-297.4]	82.4[68.3-97.1]	64	1265.5[805.4-764.3]	57[32.4-89.6]	96	739.6[477.7-1074.9]	678.3[540.4-835.3]	9
Éthiopia*	223[184.7-264.3]	86.4[75.3-97.6]	61	822.2[635-1051.2]	117.4[84-161.2]	86	1092.3[844-1391.5]	774.3[656-894.2]	30

N.B: all changes are in decreasing percent. SNNPs: Southern Nations, Nationalities, and Peoples; BG: Benishangul-Gumuz; \*national estimate 

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In Ethiopia, the age-standardized mortality rate was higher among males (100.6 [84.1-121.4]) than
females (71.8 [60.2–82.9]) (Appendix Table 4).

In 1990, the age-standardized mortality rate per 100,000 people was the highest in Benishangul-Gumuz (284.1 [221.8–358.1]), Afar (244.8 [186.5–316.9]) and SNNP (243.7 [196.4–296.9]), although it is not significantly different from the national estimate. On the other hand, the lowest age standardized mortality rate was exhibited in Somali (147.6 [113.8–192.6]). Although the value was not significantly different from the national value in 1990, Addis Ababa showed the second lowest age-standardized mortality rate (163.4 [134.6–206.9]) (Table 1).

275 In 2019, the age-standardized mortality rate per 100,000 people was significantly lower in Addis Ababa (59.4 [49.8–71.4]) when compared to other regions, although not significantly lower than 276 277 Gambella and other urban areas (Harari and Dire Dawa). Dire Dawa showed a significantly lower age-standardized mortality rate when compared to Benishangul-Gumuz, Afar, and SNNP. 278 Compared to the national estimate, the regions of Afar (103.7 [86.6–122.6]) and Benishangul-279 Gumuz (101.8 [84.0-121.7]) recorded the highest age-standardized mortality rates per 100,000 280 people, although the difference is not statistically significant (Table 1). Compared to the 1990s, 281 there was a 58% to 68% decrease in the age-standardized mortality rates across all regions. 282 However, the Somali region recorded a 34% reduction in mortality rates (Table 1 and Figure 3). 283

Among children below the age of 5, the mortality rate per 100,000 people was significantly lower in Addis Ababa (23.4 ([14.1–36.4]) than other regions, although it was not significantly less than Gambella in 2019. The mortality rate was the highest in Benishangul-Gumuz (215.1 [141.4– 311.0]), Somali (197.3 [135.2–279.8]), and Oromia (122.3 [84.8–171.0]) despite being not significantly higher than the national estimate (Table 1). Dire Dawa showed a significantly lower mortality rate than Benishangul-Gumuz and Somali. Harari had a significantly lower mortality rate

than Benishangul-Gumuz. For all regions, the mortality rate declined for children younger than 5years between 1990 and 2019 by between 84% (in Benishangul-Gumuz) and 96% (in Gambella),
except in Somali, which showed a 57% decline (Table 1). The mortality rate increased slightly
between 1990 and 1995 and between 2010 and 2015 in Somali region (Appendix Figure 2).

The mortality rate in adults older than 70 was the lowest in Addis Ababa (503.6 [410.5–633.7]). Other regions and cities have not shown a statistically significant difference from the national estimate. The decline in mortality rates between 1990 and 2019 is below 50% across all regions (Table 1). The mortality rate increased in Afar and Somali between 2005 and 2019 and in Gambella between 1990 and 2005 (Appendix Figure 3).

**Premature Mortality due to LRIs** 

In 2019, premature death due to LRIs was 2,445,093.7 (95% UI: 1,934,420.8–3,119,838.6) YLLs, yielding an age-standardized rate of 2404.5 per 100,000 people (2059.4–2833.3). Compared to 1990, the age-standardized YLL rate declined by 76% in 2019. In parallel, 70% of all premature mortality occurred in children younger than five, which accounted for 1,721,122.3 (1,231,032.1– 2,362,958.7) YLLs. The YLL rate of 72,055.4 (55,718.5–92,064) per 100,000 under-five children in 2019 declined by 86% compared to the YLL rate in 1990. Adults over 70 years contributed 8% of all YLLs due to LRIs (194,756.2 [165,462.0-225,502.1]), yielding a rate of 10,309.9 (8759.2-11,937.6) YLLs per 100,000 people (Table 2; Appendix Table 5 and Table 6). 

Compared to 1990, the number of YLLs has decreased by 70% in all age groups and by 76% in
children younger than five in 2019. However, the number of YLLs has increased by 45% in adults
older than 70 (Appendix Table 5).

311	The age-standardized YLL rate was significantly lower in Addis Ababa (1285.6 [1065–1561.8])
312	in 2019 compared to the national average. The highest age standardized YLL rate were in
313	Benishangul-Gumuz (3571.1 [2772.4–4510.7]), Somali (3236.4 [2537.4–4006]), and Afar (2824.6
314	[2323–3414]), although not statistically significant compared to the national estimate (Table 2).
245	In shildren second and for second Addie Alasha (20(0 [1252, 2017,5]) had a significant da laser
315	In children younger than five years, Addis Ababa (2069 [1253–3217.5]) had a significantly lower
316	YLL rate than the national estimate. The YLL rate was observed to be the lowest in Gambella
317	(5031.8 [2867.2–7885.7]), although not significantly lower than the national estimate (Table 2).
318	

319	Table 2: Lower Respiratory Infections YLL rates and percentage changes between 1990 and 2019 in Ethiopia, both sexes, with different age
320	groups

	Age-standardized		Children younger than 5 years			People older than 70			
Locatio	YLL per 100,000	YLL per 100,000	Ch	YLL per 100,000	YLL per 100,000	Ch	YLL per 100,000	YLL per 100,000	Ch
n	people,1990	people, 2019	а	people,1990	people, 2019	a	people,1990	people, 2019	a
			nge ,%			nge ,%			nge ,%
Addis	6362.2(5161.9-	1285.6(1065-	80	38824.7(28230.1-	2069(1253-	95	13587(9985.4-	6857.1(5545.8-	50
Ababa	7847.9)	1561.8)		53092.4)	3217.5)		18978.3)	8721.2)	
Oromia	11217.6(8517-	2433.8(2042.2-	78	80610.7(55103.7-	10742.8(7456.7-	87	18754.2(13297.1-	11119.7(8939.1-	41
	14318)	2879.5)		110696)	15039.6)		24843)	13305)	
Amhara	8690.4(7146.3-	2016.4(1551.4-	77	60663.3(46712.5-	8355(4898.9-	87	15950.4(11723.4-	9059.7(7063.2-	44
	10453.8)	2541.8)		77511.5)	12845)		21059.7)	11529.2)	
SNNPs	11633(9119.4-	2698.1(2243.5-	77	85114.7(61203.2-	10409.3(6968.1-	88	18842.6(13166.1-	11736.6(9426.7-	38
	14477.9)	3250.2)		111502.1)	14819.3)		26081)	14238.6)	
Tigray	10346.4(8522.9-	1977.1(1593.9-	81	68509.3(52185.7-	5927.9(3839.4-	92	19502.8(13914.1-	10486.8(8439.5-	47
	12340.3)	2395)		88712.2)	8676.8)		26751.2)	12765.3)	
Harari	12826.5(9336.5-	2060.4(1595.6-	84	100421.7(63898.7	7922.5(4518.7-	93	11782.6(6360.4-	9260.4(7338.7-	22
	16985.4)	2623.1)		-140467.8)	12117.2)		19341.1)	11340.3)	
Afar	10993.5(8520.8-	2824.6(2323-	74	63570.5(42296.6-	8943.7(5734.6-	86	16925.5(10923.7-	11867.1(9346-	30
	14193.6)	3414)		89769)	13390.2)		26001.7)	14716.9)	
Somali	6286.9(4860.5-	3236.4(2537.4-	49	40088.1(27543.7-	17314.3(11890.7-	57	11953.6(7599.2-	10246(7797.8-	15
	7970)	4006)		55109)	24530)		17885.5)	13150.6)	
BG	14965.1(11197.4-	3571.1(2772.4-	76	110847.2(74368-	18868.3(12442.9-	83	16397.3(10917-	9541.9(7476.9-	42
	19998.6)	4510.7)		156588.4)	27281.8)		23228.5)	12112.3)	
Dire	11749.7(8605.4-	1832.8(1407.3-	84	94905.3(60458.5-	7371.3(3953-	93	13207.9(9219.6-	8371(6616.3-	37
Dawa	15249.5)	2363.1)		131584.5)	11962.1)		18328.2)	10408.2)	
Gambel	13175.8(9291-	1937.4(1567.6-	85	110783.8(70576-	5031.8(2867.2-	96	11811.4(7673.5-	10030.9(7730.2-	16
la	17411)	2344.6)		154304.1)	7885.7)		17012.5)	12664.9)	
Ethiopi	10189.1(8347.5-	2404.5(2059.4-	76	72055.4(55718.5-	10318.6(7380.4-	86	17415.9(13362.7-	10309.9(8759.2-	41
a*	12201.8)	2833.3)		92064)	14166.6)		22228.5)	11937.6)	

321 SNNPs: Southern Nations, Nationalities, and Peoples; BG: Benishangul-Gumuz; \*national estimate

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The age-standardized premature mortality rate between 1990 and 2019 showed a continuous decline in all regions, except Somali. Benishangul-Gumuz showed the highest burden between 1990 and 2019 (Figure 4).

The change in premature mortality in children younger than five was significant throughout the years. However, the reduction in premature mortality among adults older than 70 was not as significant (Appendix Figure 4 and Figure 5).

#### **Risk Factors**

Across all population groups, about half (48%) of the mortalities (measured in rates) due to LRIs in Ethiopia were attributed to household air pollution from solid fuel. In addition, lack of access to a hand-washing facility (23%), childhood wasting (23%), low birth weight (9%), short gestation period (7%), and ambient particulate matter pollution (6%) were also risk factors for mortality due to LRIs. The contribution of the risk factors to death due to LRIs in all regions was similar to the national estimate, except in Addis Ababa, where lack of access to hand-washing facilities, ambient particulate matter pollution, and low temperature were the main contributing factors. Ambient particulate matter pollution was also relatively higher in Dire Dawa, Harari, and Tigray regions (Appendix Figure 6). 

In children younger than five, more than three-fourths of deaths due to LRIs were attributed to childhood wasting (54%) stunting (12%), and child underweight (10%) in Ethiopia. In addition, 50% of the LRIs mortalities were attributed to household air pollution from solid fuel. Lack of access to hand-washing facilities (23%), low birth weight (23%), short gestation period (17%), high (4%) or low temperature (4%), absence of exclusive breastfeeding (4%) were also the risk factors with evident contribution. The distribution of risk factors varied among the regions. Child

wasting, low birth weight, and pre-term birth were the contributing factors of mortality in Addis
Ababa. In Harari and Dire Dawa, child wasting, lack of access to hand-washing facilities, pre-term
birth, and household air pollution from solid fuels contributed more to the death from LRIs than
the other risk factors in 2019. All the risk factors except for ambient particulate air matter and low
temperature were the highest in Somali and Benishangul-Gumuz (Appendix Figure 7).

#### **Discussion**

The findings from this study indicate that although the burden of LRIs, measured in incidence or mortality rates, have shown a significant decline, they are still the third leading cause of death after neonatal disorders and diarrheal diseases in 2019 in Ethiopia. Cities and predominantly urban areas had lower mortality rates than predominantly pastoralist regions of the country. The rate of decline in mortality between 1990 and 2019 varied slightly across regions and chartered cities. The mortality rate decreased by more than three-fourths among children under the age of five and only by one-third among adults older than 70 between 1990 and 2019. Half of LRIs mortalities are attributed to household air pollution from solid fuels in all age groups. About three-fourths of LRIs in children were attributed to malnutrition. 

The mortality rate of LRIs among children below the age of 5 has declined by 86% between 1990 and 2019. This decline could be attributed to improvements in living conditions, access to healthcare, and immunization. The national health delivery infrastructure has grown from 2,600 health facilities in 1997 to 21,154 facilities, including 314 hospitals, 3,678 health centers, and 17,162 health posts and private health facilities in 2019. As a result, the health workforce has increased from 46,000 in 2007 to 159,545 in 2019 (16). The introduction of HEP since 2004 to provide preventive, health promotion, and curative treatment for pneumonia, malaria and diarrhoea

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had improved health outcomes for children (14). Moreover, Ethiopia has been implementing holistic child health improvement programs like IMCI since 1997 (15) and ICCM (5). Vaccination against Streptococcus pneumonia, which is responsible for about half of the LRIs mortality in African countries, with the PCV 10 vaccine since 2011 helped reduce the burden of LRIs (4). In addition, improved socioeconomic conditions have supported the reduction of the burden of LRIs in the country (27).

Despite the achievements reached in improving child health outcomes in Ethiopia, children are still disproportionately affected by LRIs. Out of the total burden of LRIs, 42% of all the deaths were among children younger than five. In that regard, this study has shown that one out of ten child deaths are due to LRIs. However, another study estimated that pneumonia alone shared about 17% of all deaths in children younger than five years (28). Among children under five, children younger than one carry the highest burden of LRIs. Furthermore, the mortality rate among children younger than one (397.7 per 100,000 people) was more than nine times higher than that of children between one and four years old (43 per 100,000 people). Although most studies on the high burden of LRIs corroborate our findings, the findings from Global Health Observatory (GHO) estimated a much higher mortality rate than the estimates of this study (i.e. 481.9 in children less than one year and 51.1 per 1000,000 population in children between one and four years) (8). Although we could not explain why this variation occurs, the estimates from GBD are also less than the estimate from findings of the Child Health Epidemiology Reference Group (CHERG), which is primarily due to the difference in the types of data used (29). 

387 Urban areas of the country, mainly Addis Ababa and Dire Dawa, had significantly lower mortality 388 rates than pastoralist areas such as Benishangul-Gumuz and Somali. These regional variations 389 could be attributed to gaps in availability and access to healthcare and socioeconomic status

differences among the subnational states. A previously conducted study indicated that disease burden is high among people in the poorest wealth quintile and people located mainly in Afar, Somali, Oromia, SNNP, and Benishangul-Gumuz and also have the lowest level of health service utilization (30). The rural area of the country has less healthcare coverage and utilization than the urban areas. The coverage of all basic vaccination is 43% in the country. Across the regions, the coverage of all basic vaccination is lowest in Afar (20%) and highest in Addis Ababa (83%). Coverage of pentavalent vaccines in children is 72% among the urban population while it is 56% among the rural population (15, 28). There is a variation in the performance of immunization across regions. Addis Ababa, Ethiopia's capital has PCV3 coverage of 93% among 1-year-olds in 2019, whereas this coverage is only 23% in Afar and Somali. The wasting rate in Somali was 21% in children under five, while it was just 2% in Addis Ababa in 2019 (31) 

In addition to children, LRIs affects people older than 70 years. The number of people dying from LRIs increased over the years in people older than 70 years, partly due to the increase in the aging population. However, the mortality rate declined by 30% between 1990 and 2019 (3, 32). The incidence rate did not show a significant improvement across the study years, showing only 15% reductions between 1990 and 2019. Among the regions, Somali and Afar have recorded an increased incidence rate between 1990 and 2019. This could partly be explained by poor accessibility and availability of health facilities in the regions (31).

Wasting, stunting, and underweight were major risk factors contributing to the death of children
younger than five years due to LRIs (33-35). More than 37% of children under five are stunted,
with a higher percentage in rural areas (41%) than in urban areas (26%). Similarly, the prevalence
of child underweight and wasting is 21% in the rural and 7% in the urban parts of Ethiopia (36).
This indicates that more investment is needed to reduce the burden on malnutrition among children

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and in the rural parts of the country to attain better health outcomes, protecting against LRIs.
Although the prevalence of stunting, wasting, and underweight has decreased markedly over time,
they are still major risk factors for death caused by LRIs. In the Millennium Development Goals
(MDG) era, between 1990 and 2015, about half of the deaths averted due to LRIs were attributed
to improvement in the nutritional status of children (reduction in wasting and stunting) (15).

Ambient particulate matter and household air pollution from solid fuel use were the two essential components of air pollution. Household air pollution from solid fuel use the was the second leading risk factor for LRIs, and ambient particulate matter is the eight leading risk factor among the top ten risk factors for LRIs (37-39). This indicates that improvement in socio-demographic factors will have a more substantial contribution as the use of electricity and natural gas for cooking increases (3).

To reduce the burden of LRIs, both national and global efforts are underway. The Global Action Plan for the Prevention and Control of Pneumonia and Diarrhoea (GAPPD), established by the World Health Organization, set goals in 2013 to reduce child LRI mortality rates to below 3 in 1,000 live births and to reduce severe LRI incidence by 75% of the 2010 baseline by 2025. To achieve these goals, reaching 90% of children with full-dose vaccine coverage, 90% access to pneumonia treatment, 50% coverage of exclusive breastfeeding in the first six months, and exclusive breastfeeding promotion were set as prerequisites (17). However, a 6% average annual mortality reduction was recorded between 2000 and 2018 in Ethiopia. With this, the country can only reach the 2025 GAPPD target in 2035, ten years behind the target, according to the Maternal and Child Epidemiology Estimation Group (MICE) estimation (28). 

Ethiopia's major health sector strategic plan, the Health Sector Transformation Plan-2 (HSTP-2)
for the year 2021-2024, aims to reduce the infant mortality rate to 35, the neonatal mortality rate

to 21 and the children under-5 mortality rate to 43 per 1,000 live births. Similarly, the 2030 Sustainable Development Goals (SDG) has set targets to reduce childhood mortality significantly. These targets can be achieved if the country implements high-impact priority curative and preventive interventions against LRIs (40). To achieve this, concerted action to improve policies, increase investment, foster innovations, and scale-up evidence-based interventions has paramount importance. Parallel to this, an estimated \$274 billion for health is required to achieve the healthrelated SDGs by 2030 in 67 low and middle-income countries, including Ethiopia. One of the strategies to mobilize the needed resources is to increase government expenditure by 15% and share the population's costs through taxes or insurances (41). 

This study is not without limitations; limitations in the GBD methods also apply to this study. One of the limitations is the incompleteness of data. A previously conducted study showed that most countries in Africa, including Ethiopia, have had a vast amount of incomplete vital records data (42). This increases the uncertainty in the estimates, which might compromise the accuracy of the findings and reduce the use of these findings for policy decision-making (1). However, to improve the quality of the estimates, the best available data are used and GBD estimates are continuously updated.

#### **Conclusion**

Despite the substantial reduction in morbidity and mortality at national and regional states, LRIs still remain one of the leading causes of the burden of disease in Ethiopia. Children and elders are still disproportionately affected by LRIs. The burden of illness and death due to LRIs varies across regional states in Ethiopia, with lower rates in cities and predominantly urban areas while predominantly pastoralist areas of the country have higher rates. Efforts should be made to tackle Page 25 of 47

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the major risk factors contributing to death by LRIs. Improving child nutrition, access to immunization and curative health services, as well as universal electrification to reduce indoor air pollution will be very useful strategies to reduce deaths due to LRIs in Ethiopia. Furthermore, improvement in socioeconomic factors will also help to reduce LRI burden at national and regional levels. To reach the targets set at the national and international level, mobilizing resources to health and improving the provision of health services to the community according to the needs of the regions is of paramount importance.

## 465 List of abbreviations

EPHI: Ethiopian Public Health Institute; GAPPD: Global Action Plan for the Prevention and
Control of Pneumonia and Diarrhoea GBD: Global Burden of Disease; GHO: Global Health
Observatory; HSTP: Health Sector Transformation Plan; ICCM: integrated community case
management; IHME: Institute of Health and Metric Evaluation; LRIs: Lower Respiratory
Infections; NDMC: National Data Management Center for health; PCV: Pneumococcal Conjugate
Vaccine; SDG: Sustainable Development Goals; SNNPs: Southern Nations, Nationalities and
Peoples; UI: Uncertainty Interval; WHO: World Health Organization; YLL: Years of Life Lost.

473 Ethics approval and consent to participate

474 This manuscript was produced as part of the GBD Collaborator Network and in accordance with475 the GBD Protocol.

**Consent for publication** 

477 Not applicable.

#### 478 Availability of data and material

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479 All relevant data are submitted with this manuscript.

#### 480 **Competing interests**

481 The authors declare that they have no competing interests.

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486 Authors' contributions

Please see appendix section C for more detailed information about individual author contributions
to the research, divided into the following categories: providing data or critical feedback on data
sources; developing methods or computational machinery; providing critical feedback on methods
or results; drafting the manuscript or revising it critically for important intellectual content; and

- 491 managing the estimation or publications process
- 492 **Declarations**

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- 497 **References**

498 1. Global, regional, and national age-sex specific mortality for 264 causes of death, 1980499 2016: a systematic analysis for the Global Burden of Disease Study 2016. Lancet (London,

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England). 2017 Sep 16;390(10100):1151-210. PubMed PMID: 28919116. Pubmed Central
PMCID: PMC5605883. Epub 2017/09/19. eng.

502 2. Troeger C, Blacker B, Khalil IA, Rao PC, Cao J, Zimsen SRM, et al. Estimates of the
503 global, regional, and national morbidity, mortality, and aetiologies of lower respiratory infections
504 in 195 countries, 1990–2016: a systematic analysis for the Global Burden of Disease
505 Study 2016. The Lancet Infectious Diseases. 2018;18(11):1191-210.

Moradi-Lakeh M, El Bcheraoui C, Charara R, Khalil I, Afshin A, Kassebaum NJ, et al.
Burden of lower respiratory infections in the Eastern Mediterranean Region between 1990 and
2015: findings from the Global Burden of Disease 2015 study. International Journal of Public
Health. 2018 2018/05/01;63(1):97-108.

Reiner RC, Welgan CA, Casey DC, Troeger CE, Baumann MM, Nguyen QP, et al.
 Identifying residual hotspots and mapping lower respiratory infection morbidity and mortality in
 African children from 2000 to 2017. Nature Microbiology. 2019 2019/12/01;4(12):2310-8.

513 5. Miller NP, Amouzou A, Tafesse M, Hazel E, Legesse H, Degefie T, et al. Integrated
514 community case management of childhood illness in Ethiopia: implementation strength and quality
515 of care. Am J Trop Med Hyg. 2014;91(2):424-34. PubMed PMID: 24799369. Epub 05/05. eng.

516 6. Alamneh YM, Adane F. Magnitude and Predictors of Pneumonia among Under-Five
517 Children in Ethiopia: A Systematic Review and Meta-Analysis. Journal of Environmental and
518 Public Health. 2020 2020/05/30;2020:1606783.

519 7. Wondimu A, Cao Q, Wilschut JC, Postma MJ. Factors associated with the uptake of newly
520 introduced childhood vaccinations in Ethiopia: the cases of rotavirus and pneumococcal conjugate
521 vaccines. BMC Public Health. 2019 2019/12/10;19(1):1656.

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522 8. Gonakoti S, Osifo IF. Protein-Energy Malnutrition Increases Mortality in Patients Hospitalized With Bacterial Pneumonia: A Retrospective Nationwide Database Analysis. Cureus. 523 2021 Jan 12;13(1):e12645. PubMed PMID: 33585131. Pubmed Central PMCID: PMC7876587. 524 Epub 2021/02/16. eng. 525 Yeo HJ, Byun KS, Han J, Kim JH, Lee SE, Yoon SH, et al. Prognostic significance of 9. 526 527 malnutrition for long-term mortality in community-acquired pneumonia: a propensity score matched analysis. The Korean journal of internal medicine. 2019 Jul;34(4):841-9. PubMed PMID: 528 30685962. Pubmed Central PMCID: PMC6610202. Epub 2019/01/29. eng. 529 10. Adane MM, Alene GD, Mereta ST, Wanyonyi KL. Prevalence and risk factors of acute 530 lower respiratory infection among children living in biomass fuel using households: a community-531 Northwest based cross-sectional study in Ethiopia. BMC Public Health. 2020 532 2020/03/19;20(1):363. 533 Adane MM, Alene GD, Mereta ST, Wanyonyi KL. Effect of improved cookstove 11. 534 intervention on childhood acute lower respiratory infection in Northwest Ethiopia: a cluster-535 randomized controlled trial. BMC Pediatrics. 2021 2021/01/04;21(1):4. 536 Keleb A, Sisay T, Alemu K, Ademas A, Lingerew M, Kloos H, et al. Pneumonia remains 12. 537 a leading public health problem among under-five children in peri-urban areas of north-eastern 538 Ethiopia. PLOS ONE. 2020;15(9):e0235818. 539 Ahmed KY, Page A, Arora A, Ogbo FA, Global M, Child Health Research c. Associations 540 13. 541 between infant and young child feeding practices and acute respiratory infection and diarrhoea in Ethiopia: A propensity score matching approach. PLOS ONE. 2020;15(4):e0230978. 542

Page 29 of 47

### BMJ Open

1 2			
2 3 4	543	14.	Assefa Y, Gelaw YA, Hill PS, Taye BW, Van Damme W. Community health extension
5 6 7 8 9 10 11 12 13 14 15	544	progra	m of Ethiopia, 2003–2018: successes and challenges toward universal coverage for primary
	545	health	care services. Globalization and Health. 2019 2019/03/26;15(1):24.
	546	15.	Ruducha J, Mann C, Singh NS, Gemebo TD, Tessema NS, Baschieri A, et al. How Ethiopia
	547	achiev	ed Millennium Development Goal 4 through multisectoral interventions: a Countdown to
	548	2015 c	case study. Lancet Glob Health. 2017;5(11):e1142-e51. PubMed PMID: 29025635. eng.
16 17 18	549	16.	Federal Ministry of Health. Health Sector Transformation Plan 2020/21-2024/25 (2013
19 20	550	EFY -	2017 EFY), Addis Ababa Ethiopia. 2020.
21 22	551	17.	Unicef, World Health O. Ending preventable child deaths from pneumonia and diarrhoea
23 24 25 26 27	552	by 202	25 : the integrated global action plan for pneumonia and diarrhoea (GAPPD) 2013. Available
	553	from:	https://apps.who.int/iris/handle/10665/79200.
28 29	554	18.	World B. World Bank data catalog. [Washington, D.C.]: World Bank.
30 31 32	555	19.	CSA. Ethiopia. central statstical agency. 2020.
32 33 34 35 36	556	20.	Misganaw ANMWAMAHGAZBTMWEAKJHEGTWTKDDA. Progress in health among
	557	region	s of Ethiopia, 1990-2019: a subnational country analysis for the Global Burden of Disease
37 38 30	558	Study	2019. Lancet Lancet (London, England). 2022;399(10332):1322-35. English.
40 41	559	21.	Murray CJL, Aravkin AY, Zheng P, Abbafati C, Abbas KM, Abbasi-Kangevari M, et al.
42 43 44 45	560	Globa	burden of 87 risk factors in 204 countries and territories, 1990–2019: a systematic
	561	analys	is for the Global Burden of Disease Study 2019. The Lancet. 2020;396(10258):1223-49.
40 47 48	562	22.	Collaborators GL. Estimates of the global, regional, and national morbidity, mortality, and
49 50	563	aetiolo	ogies of lower respiratory tract infections in 195 countries: a systematic analysis for the
51 52	564	Globa	Burden of Disease Study 2015. Lancet Infect Dis. 2017;17(11):1133-61. PubMed PMID:
55 55	565	28843	578. Epub 08/23. eng.
56 57			

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DALYs GBD, Collaborators H. Global, regional, and national disability-adjusted life-years
(DALYs) for 315 diseases and injuries and healthy life expectancy (HALE), 1990-2015: a
systematic analysis for the Global Burden of Disease Study 2015. Lancet (London, England).
2016;388(10053):1603-58. PubMed PMID: 27733283. eng.

570 24. Dicker D, Nguyen G, Abate D, Abate KH, Abay SM, Abbafati C, et al. Global, regional,
571 and national age-sex-specific mortality and life expectancy, 1950–2017: a systematic
572 analysis for the Global Burden of Disease Study 2017. The Lancet. 2018;392(10159):1684-735.

573 25. Lim SS, Vos T, Flaxman AD, Danaei G, Shibuya K, Adair-Rohani H, et al. A comparative
574 risk assessment of burden of disease and injury attributable to 67 risk factors and risk factor clusters
575 in 21 regions, 1990-2010: a systematic analysis for the Global Burden of Disease Study 2010.
576 Lancet (London, England). 2012;380(9859):2224-60. PubMed PMID: 23245609. eng.

577 26. Collaborators GBDRF, Forouzanfar MH, Alexander L, Anderson HR, Bachman VF,
578 Biryukov S, et al. Global, regional, and national comparative risk assessment of 79 behavioural,
579 environmental and occupational, and metabolic risks or clusters of risks in 188 countries, 1990580 2013: a systematic analysis for the Global Burden of Disease Study 2013. Lancet (London,
581 England). 2015;386(10010):2287-323. PubMed PMID: 26364544. Epub 09/11. eng.

582 27. Shibre G, Zegeye B, Idriss-Wheeler D, Yaya S. Trends of inequalities in care seeking
583 behavior for under-five children with suspected pneumonia in Ethiopia: evidence from Ethiopia
584 demographic and health surveys (2005–2016). BMC Public Health. 2021 2021/02/01;21(1):258.

585 28. UNICEF. Fighting for Breath in Ethiopia: a call to action to stop children dying from
586 pneumonia. 2020.

587 29. Kovacs SD, Mulholland K, Bosch J, Campbell H, Forouzanfar MH, Khalil I, et al.
588 Deconstructing the differences: a comparison of GBD 2010 and CHERG's approach to estimating

Page 31 of 47

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#### **BMJ** Open

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- 3 4	589
5 6	590
7 8	591
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45 46	607
47 48	608
49 50 51	609
51 52 53	610
55 55	
56	
57	
58 59	
60	

the mortality burden of diarrhea, pneumonia, and their etiologies. BMC Infectious Diseases. 2015
2015/01/16;15(1):16.

591 30. Federal Ministry of Health E. EVIDENCE SYSTHESIS BASED ON DHS KEY MCH
592 AND NUTRITION INDICATORS. 2019.

593 31. Health FDRoE-Mo. Mini Demographic and Health Survey 2019. 2019.

Sourcea RA, José BPS, Malta DC, Passos VMA, França EB, Teixeira RA, et al. Burden of
disease by lower respiratory tract infections in Brazil, 1990 to 2015: estimates of the Global Burden
of Disease 2015 study. Revista brasileira de epidemiologia = Brazilian journal of epidemiology.
2017 May;20Suppl 01(Suppl 01):171-81. PubMed PMID: 28658381. Epub 2017/06/29. Carga de
doença por infecções do trato respiratório inferior no Brasil, 1990 a 2015: estimativas do estudo
Global Burden of Disease 2015. por

600 eng.

Salam RA, Das JK, Bhutta ZA. Current issues and priorities in childhood nutrition, growth,
and infections. The Journal of nutrition. 2015 May;145(5):1116S-22S. PubMed PMID: 25833888.
Pubmed Central PMCID: PMC4410495. Epub 2015/04/03. eng.

Akombi BJ, Agho KE, Hall JJ, Wali N, Renzaho AMN, Merom D. Stunting, Wasting and
Underweight in Sub-Saharan Africa: A Systematic Review. International journal of environmental
research and public health. 2017 Aug 1;14(8). PubMed PMID: 28788108. Pubmed Central
PMCID: PMC5580567. Epub 2017/08/10. eng.

608 35. Ibrahim MK, Zambruni M, Melby CL, Melby PC. Impact of Childhood Malnutrition on
609 Host Defense and Infection. Clinical microbiology reviews. 2017 Oct;30(4):919-71. PubMed
610 PMID: 28768707. Pubmed Central PMCID: PMC5608884. Epub 2017/08/05. eng.

36. Fantay Gebru K, Mekonnen Haileselassie W, Haftom Temesgen A, Oumer Seid A, Afework Mulugeta B. Determinants of stunting among under-five children in Ethiopia: a multilevel mixed-effects analysis of 2016 Ethiopian demographic and health survey data. BMC Pediatrics. 2019 2019/06/01;19(1):176. Dherani M, Pope D, Mascarenhas M, Smith KR, Weber M, Bruce N. Indoor air pollution 37. from unprocessed solid fuel use and pneumonia risk in children aged under five years: a systematic review and meta-analysis. Bulletin of the World Health Organization. 2008 May;86(5):390-8C. PubMed PMID: 18545742. Pubmed Central PMCID: PMC2647443. Epub 2008/06/12. eng. 38. Kurmi OP, Lam KB, Ayres JG. Indoor air pollution and the lung in low- and medium-income countries. The European respiratory journal. 2012 Jul;40(1):239-54. PubMed PMID: 22362845. Epub 2012/03/01. eng. 39. Burnett RT, Pope CA, 3rd, Ezzati M, Olives C, Lim SS, Mehta S, et al. An integrated risk function for estimating the global burden of disease attributable to ambient fine particulate matter exposure. Environmental health perspectives. 2014 Apr;122(4):397-403. PubMed PMID: 24518036. Epub 2014/02/13. eng. 40. Federal Ministry of Health Addis Ababa E. Health Sector Transformation Plan 2015/16 -2019/20 (2008-2012 EFY). . August 2015. . Stenberg K, Hanssen O, Edejer TT-T, Bertram M, Brindley C, Meshreky A, et al. 41. Financing transformative health systems towards achievement of the health Sustainable Development Goals: a model for projected resource needs in 67 low-income and middle-income

631 countries. The Lancet Global Health. 2017;5(9):e875-e87.

1 2 3	<b>633</b>	42 - Puess P. de Courten M. Crohem WI. Leffemme L. McCouv Pinns A. Sankoh O.A. et al.
4 5	032	42. Byass P, de Courten M, Oranam WJ, Lananine L, McCaw-Binns A, Sankon OA, et al.
6 7	633	Reflections on the global burden of disease 2010 estimates. PLoS Med. 2013;10(7):e1001477-e.
8 9	634	PubMed PMID: 23843748. Epub 07/02. eng.
10 11 12	635	
13 14	636	
15 16 17 18 19 20 21 22 23 24 25 26 27 28 29 30 31 32 33 34 35 36 37 38 39 40 41 42 43 44 45 46 47 48 49 50 51 52 53		
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4	637	Figure 1: Incidence of lower respiratory infections per 100,000 people in Ethiopia and its regions
6	638	in 2019.
7 8 9 10	639 640	Figure 2: Trend in age-standardized incidence rate of LRIs per 100,000 people in Ethiopia, 1990-2019
10 11 12	641	Figure 3: Trend in LRIs age-standardized mortality rates per 100,000 people in Ethiopia, 1990-
13 14 15	642	2019
16 17 18	643 644	Figure 4: Trend in LRIs age standardized years of life lost rates per 100,000 people in Ethiopia, 1990-2019
19         20         21         22         23         24         25         26         27         28         29         30         31         32         33         34         35         36         37         38         39         40         41         42         43         44         45         46         47         48         950         51         52         53	645	
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Figure 1: Incidence of lower respiratory infections per 100,000 people in Ethiopia and its regions in 2019.

Key: U5: children younger than 5 years; 70+: adults older than 70 years; ASR: Age-standardized rates; AA: Addis Ababa; DD: Dire Dawa; SNNPs: Southern Nations and Nationalities and Peoples; BG: Benishangul Gumuz





Figure 2: Trend in age-standardized incidence rate of LRIs per 100,000 people in Ethiopia, 1990-

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# 1990-2019



respiratory infections in Ethiopia, 1990-2019



Appendix figure 3: Adults older than 70 years mortality rate per 100,000 populations for lower respiratory infections in Ethiopia, 1990-2019



Appendix figure 4: Children younger than 5 years YLL per 100,000 populations for lower respiratory
 infections in Ethiopia, 1990-2019



Appendix figure 5: Adults older than 70 years YLL per 100,000 populations for lower respiratory infections in Ethiopia, 1990-2019 



Appendix figure 6: Attribution of the risk factors to LRIs death rate per 100,000 population in all age groups between 1990 and 2019 for Ethiopia and its regions, both sexes, number of death, 2019. SNNPs: Southern Nations, Nationalities, and Peoples.

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Addis Ababa	3.63	0.82	0.64	8.35	0.00	1.75	8.86	3.29	4.27	1.32	0.31	7.98
Oromia	6.41	14.75	11.45	67.14	2.34	60.08	25.95	6.05	28.32	5.25	1.66	21.03
Amhara	5.40	13.01	9.84	48.10	2.02	46.86	23.47	5.46	21.99	2.81	1.36	18.88
SNNPs	6.36	16.67	13.77	63.88	5.03	57.68	21.95	4.12	27.49	5.28	1.38	18.31
Tigray	5.03	6.15	5.75	29.88	1.87	29.89	20.59	2.00	15.32	1.91	0.79	17.45
Harari	9.12	7.21	5.80	43.66	0.01	25.51	19.63	2.74	19.30	5.00	1.62	17.18
Afar	4.88	11.42	11.57	52.76	15.77	53.12	28.03	0.26	23.50	5.49	1.33	22.31
Somali	5.40	18.08	20.92	121.83	16.76	110.21	39.76	1.46	46.07	13.99	3.18	31.30
Benishangul-Gumuz	12.63	28.22	22.25	125.72	17.81	105.51	30.75	2.22	50.23	8.05	2.61	24.89
Dire Dawa	9.38	5.50	5.64	42.47	1.11	23.88	19.72	1.42	18.88	3.67	1.50	16.71
Gambella	4.75	3.13	3.08	25.92	6.16	23.51	18.20	0.18	13.02	2.86	0.60	15.31
Ethiopia	6.06	14.39	11.93	64.00	4.28	58.22	25.08	4.73	27.20	5.22	1.58	20.40

بد per 100,000 por . دthiopia and its regions, b. . vationalities, and Peoples. Appendix figure 7: Attribution of the risk factors to LRIs death rate per 100,000 population in children younger than 5 years between 1990 and 2019 for Ethiopia and its regions, both sexes, number of death, 2019. SNNPs: Southern Nations, Nationalities, and Peoples. 

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		All ages		Children younger	than 5 years		People above 70		
Location	Episode, (95%UI),1990	Episode, (95%UI),2019	Change, %	Episode, (95%UI),1990	Episode, (95%UI),2019	Change, %	Episode, (95% UI),1990	Episode, (95%UI),2019	Change,%
Addis Ababa	194122.9(1754 03.8-213856.2)	176027.6(162152.3 -190557.8)	10	44940.6(35673.3 -56859.6)	14522.3(11237-18367.5)	68	8099.5(6891.6- 9463.2)	24034.2(20749.5- 27702.3)	196**
Oromia	2164243.7(195 7719.5- 2397957.9)	2597863.9(237208 9.2-2859925.6)	20	739239.6(57847 7-935022.8)	613676.6(480687.2- 765626.5)	17	110627.2(95303. 7-129579.9)	292179.4(254670.4- 342438.5)	164**
Amhara	1508431.4(136 8059.8- 1671550.1)	1400682.4(128532 3-1530939.8)	8	423999.3(33470 0.8-538426.8)	261397.4(206754.7- 327889.7)	39	116332.8(98774. 4-137194.5)	198977.5(173809.4- 229925.5)	71**
SNNPs	1235554.9(110 8317.9- 1368520.3)	1330491.5(121717 6.7-1452694.1)	7	421825.6(33508 7.1-526155.2)	307771.3(248326.4- 385053.7)	28	68084.5(57450- 79640.8)	99723(88168.3- 113438)	46**
Tigray	360795.1(3282 76.3-400714.9)	409829.8(376290.4 -445030.2)	13	109047.9(86435. 2-137691.1)	69958.2(55210.7- 87468.6)	36	20653.3(17469.9 -24256.6)	62677.2(53933.1- 72927.6)	203**
Harari	15145.9(13618. 9-16851.9)	13765.3(12657- 15054.7)	10	4693.6(3691.4- 5990.1)	2188.4(1723.8-2761.3)	54	307.2(259.6-357)	1614.8(1396-1863.6)	425**
Afar	113506.8(1023 17-126084.3)	113210.3(102987.9 -124578)	1	32991.6(25672.4 -42147.6)	26177.2(20744.1- 32743.3)	21	2640.2(2212.5- 3150.9)	7222.5(6246.8-8559.1)	173**
Somali	300306.3(2689 88-336331.8)	463220.4(420429.8 -516009.4)	54	103526.3(81391. 3-131352.8)	126089.6(99611.9- 160423.3)	21**	6182.3(5316- 7370.4)	30203.2(25942.8- 35038.5)	388**
BG	68501.6(61804. 9-75736.4)	71675.7(64972.1- 79105.8)	4	20970.5(16626.7 -26454.5)	18175.6(14339.5- 22922.1)	14	3288.9(2784.8- 3911.4)	4311.3(3743.8-5113.9)	31**
Dire Dawa	30607.1(27359. 8-34252.2)	26221.1(24010.1- 28647.8)	15	9547.4(7523- 12185)	4387.7(3439.6-5583.9)	55	1274.8(1090.1- 1483.5)	2840.1(2469-3289.5)	122**
Gambella	19687.9(17723. 9-21945.7)	25685.2(23516.6- 28093.2)	30**	6747.7(5338.7- 8613.7)	4335.4(3428.4-5400.9)	36	1568.1(1316.6- 1825.8)	1489.6(1281.4-1737.3)	6
Ethiopia*	6010904.2(546 7801.6- 6648644.3)	6628673.6(610878 6.2-7230986.3)	10**	1917530.8(1518 850.1- 2400978.5)	1448680.4(1150089.8- 1799704.4)	25	339059.4(29349 1.9-387514.2)	725273.3(640315.4- 837746.3)	113**

SNNP: Southern Nations, Nationalities, and Peoples; BG: Benishangul Gumuz; \*country's estimate; \*\*percentage increase between 1990 and 2019

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Appendix table 2: Rate and percentage changes of episodes attributable to LRIs in 1990 and 2019 for Ethiopia and its regions, both sexes

	Age standardized			Children younger	than 5 years		People above70			
Location	Episode per 100,000 people (95%UI),1990	Episode per 100,000 people (95% UI),2019	Change,%	Episode per 100,000 people (95% UI),1990	Episode per 100,000 people (95% UI),2019	Change,%	Episode per 100,000 people (95% UI),1990	Episode per 100,000 people (95% UI),2019	Change,%	
Addis 0Ababa	11373(10484.2- 12197.4)	6788.1(6285.1- 7339.1)	40	14666.9(11642.4- 18556.9)	4927.2(3812.5- 6231.8)	67	35138(29897.7- 41054.2)	30748.4(26546- 35441.2)	13	
1Oromia 2	14613.1(13525.9- 15725.8)	8659.9(8040.1- 9411.6)	41	22232(17397.2- 28120)	9039.4(7080.5- 11277.7)	60	46498.3(40057.6- 54464.4)	41564.6(36228.7- 48714.4)	11	
<sup>3</sup> Amhara 4 -	12826.4(11830- 13882.8)	7716.9(7162.3- 8321.3)	40	16487.1(13014.7- 20936.6)	8061.7(6376.4- 10112.3)	52	43580(37002.4- 51395.2)	35377.7(30902.9- 40880.2)	19	
<sup>5</sup> SNNPs 6	13591.9(12538.6- 14646.8)	8235.5(7670.5- 8846.4)	39	20106.4(15972- 25079.3)	8427.1(6799.4- 10543.2)	59	44628.1(37657.5- 52203.1)	36616.1(32373.5- 41652)	18	
Tigray 8	13927.2(12858.2- 15100.7)	8663.8(8034- 9382.3)	38	19185.4(15207- 24224.8)	8342.1(6583.5- 10430.1)	57	43748.4(37005.1- 51381)	40859(35158.8- 47541.2)	7	
0 <sup>Harari</sup>	13014.6(11941- 14066.7)	7190.5(6684.1- 7718.6)	45	19672.6(15471.9- 25106.9)	6821.6(5373.5- 8607.3)	66	33916.7(28665.1- 39416.7)	32797.4(28354- 37850.7)	4	
2 <sup>Afar</sup>	15245.7(14050.8- 16525.6)	9350.1(8648.8- 10157.4)	39	21151.6(16459.1- 27021.7)	9365.5(7421.7- 11714.7)	56	39849(33393.8- 47557.2)	44368.7(38375.2- 52580.1)	11**	
4 <sup>Somali</sup> 5	11482.7(10638.1- 12368.7)	9220(8515.8- 10046.3)	20	16792.9(13202.4- 21306.6)	10062.7(7949.6- 12802.8)	41	32748.3(28159.7- 39042.1)	41031.2(35243.4- 47600)	25**	
6BG 7	15628.1(14481- 16809.3)	9054.6(8394.2- 9766)	42	22041.1(17475.5- 27805)	10481.8(8269.5- 13219)	53	42911.6(36334.5- 51032.5)	37592.7(32643.9- 44591.2)	13	
8Dire Dawa 9	12806.6(11807.9- 13871.4)	7148.8(6634.6- 7750.7)	44	19968.2(15734.3- 25484.7)	7191.5(5637.6- 9152.1)	64	38333(32779.4- 44607)	32033.6(27847.4- 37101.4)	17	
0Gambella 1	13623.1(12637.4- 14572.4)	7575.8(7002.3- 8128.2)	44	21419.8(16947.2- 27343.2)	6791.1(5370.4- 8460.1)	69	40197.8(33751.8- 46803.7)	32657.1(28093.9- 38087.2)	19	
2Ethiopia* 3	13619.7(12640.8- 14588.6)	8313.7(7757.6- 8918)	39	19486.4(15434.9- 24399.3)	8685.3(6895.1- 10789.8)	56	44092.2(38166.5- 50393.4)	38394.4(33896.9- 44348.5)	13	

SNNP: Southern Nations, Nationalities, and Peoples; BG: Benishangul Gumuz; \*country's estimate; \*\*percentage increase between 2019 and 1990

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Appendix table 3: Number and percentage changes of death attributable to LRIs in 1990 and 2019 for Ethiopia and its regions, both sexes.

5	All age			Children younger than 5	5		People above 70 years				
<sup>6</sup> Location 7 8	death, (95% UI),1990	death, (95%UI),2019	Cha nge,%	death, (95% UI), 1990	Death, (95% UI),2019	Cha nge, %	Death , (95% UI),1990	Death, (95%UI),20 19	Cha nge,%		
9 Addis 1 Ababa	2159.3(1731.9-2690.7)	918.8(767.4- 1116.9)	58	1353(981.9-1846.7)	69.1(41.7-107.4)	95	209.5(154.3-291.5)	393.6(320.9 -495.3)	87**		
1 Dromia 12	40004.4(29432.4-51942.2)	18206.1(15193.3- 21745.4)	55	30614.3(20932.5- 42033.5)	8306.2(5763.5-11611.8)	73	2793.5(2005.1- 3673)	5971.6(483 1.7-7093.4)	113**		
1≩mhara 14	25449.3(20869.5-30724.8)	9525.5(7530.5- 11872.2)	63	17780.1(13674.3- 22720.1)	3079.5(1805.3-4737.3)	83	2717.2(2016.4- 3535.8)	3839.9(302 2.6-4825.6)	41**		
1 <b>\$</b> NNPs 16	26044.7(20108-33017)	9494.7(7713.5- 11649)	-64	20390.6(14627.6- 26712.9)	4326.6(2891.3-6157.2)	79	1771.7(1254.5- 2417.6)	2302.6(186 7.3-2772.8)	29**		
1 <b>T</b> igray 18	6463.8(5272.1-7762.9)	2551.4(2090.3- 3028.6)	61	4436(3373.5-5736)	564.2(364.9-825)	88	550.8(395.7-749.1)	1209.7(978. 5-1467.8)	119**		
1 <b>9</b> Harari 20	336(233.3-448.8)	93.1(73.8-116)	73	273.5(174.1-382.7)	28.8(16.4-44.3)	90	6.9(3.7-11)	34.1(27.1- 41.8)	395**		
21Afar 22	1717.5(1300.7-2243.4)	706.2(567.7- 869.6)	-59	1128.9(751.1-1596.7)	284.2(182.5-426)	75	66.9(43.5-102.1)	149.3(117.3 -186.6)	123**		
2\$omali 24	3603.8(2620-4713.6)	3907.5(3007.4- 4959.4)	#N/A	2811.1(1929.6-3874.8)	2472.2(1695.2-3506.8)	13	150.8(98-222.3)	563.1(433.4 -715.8)	273**		
2∯G 26	1549.2(1131.1-2097)	619(470.7-803)	61	1204.8(805.6-1703.9)	373(245.3-539.3)	70	74.7(50.3-105.7)	77(61.1- 97.3)	3**		
2⊅ire Dawa 28	632.3(445.5-830.9)	154.6(120.6- 193.8)	76	518.4(329.5-718.7)	51(27.3-82.9)	91	28.8(20.1-40)	55(44-67.9)	90**		
2 <b>6</b> Gambella	475.9(328.5-635.7)	123.2(98.2-151.9)	75	398.6(253.7-555.7)	36.4(20.7-57.2)	91	28.8(18.6-41.9)	30.9(24.6- 38.1)	7**		
∃Ethiopia* 32 33	108436.6(87669-132758.3)	46300.7(39515.8- 54642.2)	58	80909.9(62491.6- 103448.8)	19591.8(14018.4-26899)	76	8400.1(6490.3- 10700.9)	14627.6(12 393.7- 16892.8)	74**		

SNNP: Southern Nations, Nationalities, and Peoples; BG: Benishangul Gumuz; \*country's estimate; \*\*percentage increase between 2019 and 1990

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Appendix table 4: Age standardized mortality rate, Ethiopia and its regions, by sex, 2019.

	Age standardized mortality rate per 100,000 people, 2019	
Location	Female	Male
Addis Ababa	47(35.5-62.5)	73.6(55-98.3)
Oromia	77.3(62-92.4)	100.3(79.9-123.5)
Amhara	57.9(44.1-73.7)	92.5(70.5-122.1)
SNNPs	79.2(63.5-95.2)	118.8(94.3-146.3)
Tigray	73.2(55.9-93.5)	96.9(74.8-122.3)
Harari	63(49-79.9)	95.7(72.5-123.4)
Afar	112.4(87.3-142.3)	98.7(76.9-127.3)
Somali	88.3(69-111.4)	101.7(77.2-130.7)
Benishangul-Gumuz	109.2(82.6-138.8)	95.8(74.6-124.1)
Dire Dawa	56.2(42.5-71.3)	85.4(67.3-109.5)
Gambella	47.9(34.6-60.1)	120.2(95.6-149.5)
Ethiopia	71.8(60.2-82.9)	100.6(84-121.4)

Appendix table 5:	Number and percentage	e changes of YLL	attributable to I	LRIs in 199	90 and 2019	for	Ethiopia and	its regions,	both sexes

	all age			Children younger the	an 5 years	People above 70			
	YLL, (95%UI),1990	YLL, (95%UI),2019	Chan	YLL, (95%UI),1990	YLL, (95%UI),1990 YLL, (95%UI),2019 Chan		YLL,	YLL,	Chan
			ge,%			ge,%	(95%UI),1990	(95%UI),2019	ge,%
Addis	149543.9(115542.6-	29703.1(23833.4-	81	118961.7(86499.1-	6098.2(3693.1-	95	3131.8(2301.7-	5359.8(4334.8-	71**
Ababa	195437)	36855.7)		162678.7)	9483.3)		4374.6)	6816.8)	
Oromia	3019031.9(2144916.	981808.4(748459.2-	68	2680397.2(1832260.	729313.8(506226.4-	73	44619.5(31636-	78166.1(62837.5	75**
	2-4057496.3)	1278135)		4-3680767.1)	1021016.9)		59105.6)	-93527.9)	
Amhar	1813522.3(1445106.	428277.8(309674.7-	77	1560078.3(1201305.	270909.2(158846-	83	42578.2(31294.7-	50955.1(39726.1	19**
а	4-2246142.2)	583000.2)		4-1993362.8)	416496.1)		56216.9)	-64844.6)	
<b>SNNPs</b>	1993643.3(1489598.	543135.8(405565.6-	73	1785675.1(1284021	380166.4(254486.8-	79	28746.2(20086.2-	31964.4(25673.6	11**
	4-2577052.3)	711397.4)		-2339272.5)	541224.9)		39789.1)	-38778.5)	

1															
3	Tigray	455613.4	4(364406.1-	96429.9(74139.8	8-	79 389	399.3(296618.1-	497	12.6(32198.3	3-	88	9207.1(656	8.7-	16086.6(12946.	2 74**
+		569702.	1)	122350.5)		504	230.2)	727	764.9)			12629.1)		-19581.8)	
•	Harari	26755.3	(17866.5-	4273.6(2999.1-		85 239	59.3(15245.4-	254	1.6(1449.6-		90	106.7(57.6-	-175.1)	455.9(361.3-	327**
		36380.3	)	5798.4)		335	13.8)	388	37.3)					558.3)	
	Afar	124052(	89386.4-	39507.6(29535.5	5-	69 991	55.3(65972.9-	249	998.1(16028.5	5-	75	1121.4(723	.7-	1931.7(1521.3-	72**
		166880.	5)	52178.5)		140	018.8)	374	26.3)			1722.7)		2395.6)	
	Somali	281532.	2(201275.3-	266379.4(19366	9.7-	6 247	138.5(169803.8-	216	5954(148995.	2-	13	2256.6(143	4.6-	7542.1(5740-	234**
0		374880.	8)	357880.7)		339	740.3)	307	7369.5)			3376.4)		9680.2)	
1	BG	119211.	2(83517.3-	42245.6(30388.8	8-	-65 105	463.5(70756-	327	18.1(21576.4	4-	69	1256.7(836	.7-	1094.3(857.5-	13
2		165095.	7)	57591.8)		148	983.1)	473	307.2)			1780.3)		1389.1)	
3	Dire	50024.5	(33464.5-	7267.7(5038-		86 453	77.4(28907.2-	449	97.4(2411.8-		91	439.2(306.0	<u>5</u> -	742.1(586.6-	68**
4	Dawa	67580.6	)	10264.7)		629	14.9)	729	98.3)			609.5)		922.8)	
5	Gambel	37680.8	24783.6-	6064.4(4389.3-		84 348	99.5(22233.1-	321	2.2(1830.4-		91	460.7(299.3	3-	457.5(352.6-	1
6	la	51516.1	)	7853.6)		486	09.4)	503	34.1)			663.6)		577.6)	
7	Ethiopi	8070611	.3(6356905.	2445093.7(1934	420.	70 709	0505.4(5482895.	172	21122.3(1231	032.	76	133924.6(1	02756.	194756.2(16546	5 45**
8	a*	2-10091	563.7)	8-3119838.6)		7-9	059421.2)	1-2	362958.7)			8-170932.9	)	2-225502.1)	
9	SNNP: S	outhern N	lations. Nation	alities, and Pec	pples: F	3G: Benish:	angul Gumuz: *c	ount	rv's estimat	e: **r	percento	ige increase	betwee	n 2019 and 1990	)
0	2111112				·P····, -		ingui commu, c			-, p			0000000		
1															
, 2	Appendix	table 6:	Rate and perc	entage changes	of YL	L attributa	ble to LRIs in 1	990	and 2019 f	for Et	hiopia	and its regi	ions, bo	oth sexes.	
2	II.			8 8							.1				
4	all age				Child	ren younge	than 5 years			Peop	le abov	e 70			
Location	YLL per	100,000	YLL per	Change,%	YLL	per 100,000	YLL per 100,0	000	Change,%	YLL	per 100	,000	YLL per	100,000	Change,%
5	people,19	990	100,000 peopl	e,	peopl	e,1990	people, 2019		0	peop	le.1990	· ·	people, 2	2019	U /
0	1 1 /		2019	,	1 1	,			-	1	, ,		/		
Addis	6362.2(5	161.9-	1285.6(1065-	80	38824	.7(28230.1-	6857.1(5545.8	3-	95	1358	7(9985.	4-			50
Ababa	7847.9)		1561.8)	00	53092	2.4)	8721.2)	-		1897	8.3)		6857.1(5	545.8-8721.2)	
Oromia	11217.6(	8517-	2433 8(2042.2	2- 78	80610	7(55103 7-	11119 7(8939	1-	87	1875	$\frac{42(132)}{42(132)}$	97 1-			41
0.101111	14318)	0017	2879.5)	,0	11069	96)	13305)		07	2484	3)		11119.70	8939.1-13305)	
<del>1</del> Amhara	8690 4(7	146 3-	2016 4(1551 4	L- 77	60663	3(46712 5-	9059 7(7063 2	)_	87	1595	0.4(117)	23.4-	9059 7(7	063 2-	44
2	10453.8)	110.0	2541.8)	. , ,	77511	5)	11529 2)	-	07	2105	97)	2011	11529 2	003.2	
3 SNNPs	11633(01	194-	2698 1(2243 5	5- 77	85114	7(61203.2-	11726 6(0426	7	00	199/	$\frac{2}{2} \frac{6}{6} \frac{131}{2}$	66 1	11736.60	01267	20
							1 / 10 0.94 /0	/- !	00	1004				74/11/5	18

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11340.3)

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19502.8(13914.1-

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9260.4(7338.7-

12765.3)

11340.3)

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<del>87</del> Harari 88 39 40

85 Tigray 86

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1977.1(1593.9-

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Afar	10993.5(8520.8-	2824.6(2323-	74	63570.5(42296.6-	11867.1(9346-	86	16925.5(10923.7-	1186/.1(9346-14/16.9)	30
4	14193.6)	3414)		89769)	14716.9)		26001.7)		
<sup>5</sup> Somali	6286.9(4860.5-	3236.4(2537.4-	49	40088.1(27543.7-	10246(7797.8-	57	11953.6(7599.2-	10246(7797.8-13150.6)	15
б	7970)	4006)		55109)	13150.6)		17885.5)		
7BG	14965.1(11197.4-	3571.1(2772.4-	76	110847.2(74368-	9541.9(7476.9-	83	16397.3(10917-	9541.9(7476.9-	42
8	19998.6)	4510.7)		156588.4)	12112.3)		23228.5)	12112.3)	
9 Dire Dawa	11749.7(8605.4-	1832.8(1407.3-	84	94905.3(60458.5-	8371(6616.3-	93	13207.9(9219.6-	8371(6616.3-10408.2)	37
10	15249.5)	2363.1)		131584.5)	10408.2)		18328.2)		
1 Gambella	13175.8(9291-	1937.4(1567.6-	85	110783.8(70576-	10030.9(7730.2-	96	11811.4(7673.5-	10030.9(7730.2-	16
12	17411)	2344.6)		154304.1)	12664.9)		17012.5)	12664.9)	
1 <b>E</b> thiopia*	10189.1(8347.5-	2404.5(2059.4-	76	72055.4(55718.5-	10309.9(8759.2-	86	17415.9(13362.7-	10309.9(8759.2-	41
14	12201.8)	2833.3)		92064)	11937.6)		22228.5)	11937.6)	

nd Peoples; BG: Beinsnergen SNNP: Southern Nations, Nationalities, and Peoples; BG: Benishangul Gumuz; \*country's estimate; \*\*percentage increase between 2019 and 1990 

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# **Appendix:** Authors

# Providing data or critical feedback on data sources

Semagn Mekonnen Abate, Mesafint Molla Adane, Addis Aklilu, Dejene Tsegaye Alem, Mulusew A Asemahagn, Hunegnaw Abebe, Melaku Ashagrie Belete, Tekleberhan Hailemariam, Tezera Moshago Berheto, Belay Boda Abule Bodicha, Daniel Baza Gargamo, Alemayehu Hailu, Awoke Misganaw, Mohsen Naghavi, Negussie Boti Sidamo, Yonatan Solomon, Shambel Wedajo, Melat Weldemariam, Amanuel Yigezu, Fentabil Getnet, and Yazachew Yismaw.

# Developing methods or computational machinery

Semagn Mekonnen Abate, Tezera Moshago Berheto, Alemayehu Hailu, Mohsen Naghavi, Negussie Boti Sidamo, and Amanuel Yigezu.

# Providing critical feedback on methods or results

Semagn Mekonnen Abate, Mesafint Molla Adane, Gizachew Taddesse Akalu, Addis Aklilu, Dejene Tsegaye Alem, Zeleke Gebru, Mulusew Andualem Asemahagn, Daniel Atlaw, Tewachew Awoke, Hunegnaw Abebe, Melaku Ashagrie Belete, Tekleberhan Hailemariam, Tezera Moshago Berheto, Alemeshet Yirga, Setognal Birara Aychiluhm, Belay Boda Abule Bodicha, Chuchu Churko, Feleke Mekonnen Demeke, Abebaw Alemayehu Desta, Lankamo Ena, Tahir Eyayu, Zinabu Fentaw, Daniel Baza Gargamo, Mesfin Damtew Gebrehiwot, Mathewos Alemu Gebremichael, Melaku Getachew, Ababi Zergaw, Alemayehu Hailu, Getahun Molla, Awoke Misganaw, Mohsen Naghavi, Biniyam Sahiledengle, Bereket Beyene, Migbar Sibhat, Negussie Boti Sidamo, Damtew Damtew Solomon, Yonatan Solomon, Birhanu Wagaye, Shambel Wedajo, Melat Weldemariam, Amanuel Yigezu, Fentabil Getnet, and Yazachew Yismaw.

# Drafting the work or revising is critically for important intellectual content

Semagn Mekonnen Abate, Gizachew Taddesse Akalu, Mulusew A Asemahagn, Daniel Atlaw, Niguss Cherie Bekele, Melaku Ashagrie Belete, Tezera Moshago Berheto, Setognal Birara Aychiluhm, Belay Boda Abule Bodicha, Chuchu Churko, Tahir Eyayu, Zinabu Fentaw, Daniel Baza Gargamo, Melaku Getachew, Ababi Zergaw, Firehiwot Abebe Gobena, Muluken Argaw Haile, Alemayehu Hailu, Solomon Tessema Memirie, Awoke Misganaw, Mohsen Naghavi, Biniyam Sahiledengle, Bereket Beyene, Negussie Boti Sidamo, Yonatan Solomon, Dereje Mengistu Tolosa, Birhanu Wagaye, Ally Walker, Amanuel Yigezu, and Fentabil Getnet.

# Managing the estimation or publications process

Semagn Mekonnen Abate, Awoke Misganaw, Mohsen Naghavi, Negussie Boti Sidamo, and Amanuel Yigezu.

# **BMJ Open**

# The burden of lower respiratory infections and associated risk factors across regions in Ethiopia: A subnational analysis of the Global Burden of Diseases 2019 Study

Journal:	BMJ Open
Manuscript ID	bmjopen-2022-068498.R1
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Complete List of Authors:	Yigezu, Amanuel; Ethiopian Public Health Institute Misganaw, Awoke; University of Washington, Department of Health Metrics Sciences; Ethiopian Public Health Association, Getnet, Fentabil; Jigjiga University; Ethiopian Public Health Institute Berheto, Tezera; Ethiopian Public Health Institute Walker, Ally ; University of Washington, Department of Health Metrics Sciences Zergaw, Ababi; Ethiopian Public Health Institute; Addis Ababa University College of Health Sciences, Department of Health Systems and Policy Gobena, Firehiwot ; Ethiopian Health Insurance Service Haile, Muluken ; Ethiopian Health Insurance Service Hailu, Alemayehu; University of Bergen, Department of Global Public Health and Primary Care Medicine Memirie, Solomon Tessema; Addis Ababa University, Addis Center for Ethics and Priority Setting; Harvard University, Harvard T.H. Chan School of Public Health Tolosa, Dereje ; Ethiopian Health Insurance Service Abate, Semagn Mekonnen; Dilla University College of Health Sciences, Department of Anesthesiology Molla Adane, Mesafint; Bahir Dar University College of Medical and Health Sciences Akalu, Gizachew ; St Paul's Hospital Millennium Medical College; Addis Ababa University College of Health Sciences Akliu, Addis ; Arba Minch University College of Health Science, Adult health nursing; Gebru, Zeleke; Arba Minch University, public health; Arba minch university Asemahagn, Mulusew; Bahir Dar University College of Medical and Health Sciences, School of Public Health; Ataw, Daniel; Madda Walabu University, public health; Arba minch university Abebe, Hunegnaw ; Wollo University, public health Belete, Melaku; Wollo University Hailemariam, Tekleberhan; Mekelle University Hailemariam, Tekleberhan; Mekelle University Yirga, Alemeshet; Bahir Dar University, Public Health Bodicha, Belay ; Arba Minch University, Public Health Bodicha, Belay ; Arba Minch University, Public Health Bodicha, Belay ; Arba Minch University, Public Health

	Demeke, Feleke ; Bahir Dar University College of Medical and Health Sciences Desta, Abebaw ; University of Gondar Ena, Lankamo; Arba Minch University, Eyayu, Tahir; Debre Tabor University, Department of Medical Laboratory Sciences Fentaw, Zinabu; Wollo University, Department of Epidemiology and Biostatistics; Wollo University, Epidemiology and Biostatistics Gargamo, Daniel ; Wolaita Sodo University Gebrehiwot, Mesfin ; Wollo University Gebrenichael, Mathewos ; Arba Minch University Getachew, Melaku ; Haramaya University College of Health and Medical Sciences Molla, Getahun ; University of Gondar, University of Gondar Hospital Sahiledengle, Biniyam; Madda Walabu University, Public Health Beyene, Bereket; Arba Minch University Sibhat, Migbar; Dilla University College of Health Sciences, Nursing; Sidamo, Negussie ; Arba Minch University, Public Health Solomon, Damtew ; Madda Walabu University Solomon, Yonatan ; Dire Dawa University Wagaye, Birhanu; Wollo University; Ethiopian Public Health Institute Wedajo, Shambel; Wollo University, Weldemariam, Melat; Arba Minch University, Department of Medical Laboratory Sciences Yismaw, Yazachew ; Bahir Dar University Naghavi, Moshen; University of Washington School of Public Health,
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review on

1 The burden of lower respiratory infections and associated risk factors across regions in Ethiopia:

- 2 A subnational analysis of the Global Burden of Diseases 2019 Study

3 Ethiopia Subnational-Level Lower Respiratory Infections Burden collaborators

Amanuel Yigezu<sup>\*</sup>,<sup>1</sup> Awoke Misganaw<sup>\*</sup>,<sup>2,1</sup> Fentabil Getnet,<sup>1,3</sup> Tezera Moshago Berheto,<sup>4</sup> Ally Walker,<sup>5</sup> Ababi Zergaw,<sup>6,1</sup> Firehiwot Abebe Gobena,<sup>7</sup> Muluken Argaw Haile,<sup>8</sup> Alemayehu Hailu,<sup>9</sup> Solomon Tessema Memirie,<sup>10</sup> Dereje Mengistu Tolosa,<sup>11</sup> Semagn Mekonnen Abate,<sup>12</sup> Mesafint Molla Adane,<sup>13</sup> Gizachew Taddesse Akalu,<sup>14,15</sup> Addis Aklilu,<sup>16</sup> Dejene Tsegaye Alem,<sup>17</sup> Zeleke Gebru,<sup>18</sup> Mulusew Andualem Asemahagn,<sup>19</sup> Daniel Atlaw,<sup>20</sup> Tewachew Awoke,<sup>21</sup> Hunegnaw Abebe<sup>22</sup>, Melaku Ashagrie Belete,<sup>23</sup> Tekleberhan Hailemariam,<sup>24</sup> Alemeshet Yirga,<sup>25</sup> Setognal Birara Aychiluhm,<sup>26</sup> Belay Boda Abule Bodicha,<sup>27</sup> Chuchu Churko,<sup>18</sup> Feleke Mekonnen Demeke,<sup>21</sup> Abebaw Alemayehu Desta,<sup>28</sup> Lankamo Ena,<sup>29</sup> Tahir Eyayu,<sup>30</sup> Zinabu Fentaw,<sup>31</sup> Daniel Baza Gargamo,<sup>32</sup> Mesfin Damtew Gebrehiwot,<sup>33</sup> Mathewos Alemu Gebremichael,<sup>34</sup> Melaku Getachew,<sup>35</sup> Getahun Molla,<sup>36</sup> Biniyam Sahiledengle,<sup>37</sup> Bereket Beyene,<sup>38</sup> Migbar Sibhat,<sup>39</sup> Negussie Boti Sidamo,<sup>18</sup> Damtew Solomon,<sup>40</sup> Yonatan Solomon,<sup>41</sup> Birhanu Wagaye,<sup>42,43</sup> Shambel Wedajo,<sup>22</sup> Melat Weldemariam,<sup>16</sup> Yazachew Yismaw,<sup>44,45</sup> Mohsen Naghavi.<sup>5,2</sup> 

2526 17 \*Joint first authors

# 282918 Affiliations

<sup>1</sup>National Data Management Center for Health (NDMC), Ethiopian Public Health Institute, Addis Ababa, Ethiopia; <sup>2</sup>Department of Health Metrics Sciences, School of Medicine, University of Washington, Seattle, WA, USA; <sup>3</sup>Department of Epidemiology, Jigjiga University, Jigjiga, Ethiopia: <sup>4</sup>HIV and TB Research Directorate, Ethiopian Public Health Institute, Addis Ababa, Ethiopia; <sup>5</sup>Institute for Health Metrics and Evaluation, University of Washington, Seattle, WA, USA; <sup>6</sup>Department of Health Systems and Policy, Addis Ababa University, Addis Ababa, Ethiopia; <sup>7</sup> Ethiopian Health Insurance Service, Addis Ababa, Ethiopia; <sup>8</sup>Program Section, Ethiopian Health Insurance Service, Addis Ababa, Ethiopia; <sup>9</sup>Department of Global Public Health and Primary Care, University of Bergen, Bergen, Norway; <sup>10</sup>Addis Center for Ethics and Priority Setting, Addis Ababa University, Addis Ababa, Ethiopia; <sup>11</sup>Ethiopian Health Insurance Service, Ministry of Health, Addis Ababa, Ethiopia; <sup>12</sup>Department of Anesthesiology, Dilla University, Addis Ababa, Ethiopia; <sup>13</sup>College of Medicine and Health Sciences, Bahir Dar University, Bahir Dar, Ethiopia; <sup>14</sup>Department of Microbiology, Immunology and Parasitology, St. Paul's Hospital Millennium Medical College, Addis Ababa, Ethiopia; <sup>15</sup>Department of Microbial, Cellular and Molecular Biology, Addis Ababa University, Addis Ababa, Ethiopia; <sup>16</sup>Department of Medical Laboratory Sciences, Arba Minch University, Arba Minch, Ethiopia; <sup>17</sup>Department of Nursing, Debre Markos University, Debremarkos, Ethiopia; <sup>18</sup>School of Public Health, Arba Minch University, Arba Minch, Ethiopia; <sup>19</sup>School of Public Health, Bahir Dar University, Bahir Dar, Ethiopia; <sup>20</sup>Department of Biomedical Science, Madda Walabu University, Bale Robe, Ethiopia; <sup>21</sup>Department of Medical Laboratory Sciences, Bahir Dar University, Bahir Dar, Ethiopia; <sup>22</sup>Department of Public Health, Wollo University, Dessie, 

Ethiopia; <sup>23</sup>Department of Medical Laboratory Sciences, Wollo University, Dessie, Ethiopia; <sup>24</sup>Department of Medical Physiology, Mekelle University, Mekelle, Ethiopia; <sup>25</sup>School of Health Science, Bahir Dar University, Bahir Dar, Ethiopia; <sup>26</sup>Department of Public Health, Samara University, Samara, Ethiopia; <sup>27</sup>Department of Biomedical Sciences, Arba Minch University, Arba Minch, Ethiopia; <sup>28</sup>Department of Surgical Nursing, University of Gondar, Gondar, Ethiopia; <sup>29</sup>Department of Comprehensive Nursing, Arba Minch University, Arba Minch, Ethiopia; <sup>30</sup>Department of Medical Laboratory Sciences, Debre Tabor University, Debre Tabor, Ethiopia; <sup>31</sup>Department of Epidemiology and Biostatistics, Wollo University, Dessie, Ethiopia; <sup>32</sup>Department of Pediatrics and Neonatal Nursing, Wolaita Sodo, University, Wolaita Sodo, Ethiopia; <sup>33</sup>Department of Environmental Health, Wollo University, Dessie, Ethiopia; <sup>34</sup>Department of Epidemiology and Biostatistics, Arba Minch University, Arba Minch, Ethiopia; <sup>35</sup>Department of Emergency and Critical Care Medicine, Haramaya University, Harar, Ethiopia; <sup>36</sup>Department of Epidemiology and Biostatistics, University of Gondar, Gondar, Ethiopia; <sup>37</sup>Department of Public Health, Madda Walabu University, Bale Robe, Ethiopia; <sup>38</sup>Department of Nursing, Arba Minch University, Arba Minch, Ethiopia; <sup>39</sup>Department of Pediatrics and Child Health Nursing, Dilla University, Dilla, Ethiopia; <sup>40</sup>Department of Anatomy, Madda Walabu University, Bale Robe, Ethiopia; <sup>41</sup>Department of Nursing, Dire Dawa University, Dire Dawa, Ethiopia; <sup>42</sup>College of Medicine and Health Sciences, Wollo University, Dessie, Ethiopia; <sup>43</sup>Water, Sanitation and Hygiene Unit, Ethiopian Public Health Institute, Addis Ababa, Ethiopia; <sup>44</sup>Department of Pharmacology, Bahir Dar University, Bahir Dar, Ethiopia; <sup>45</sup>Pharmacy Department, Alkan Health Science, Business and Technology College, Bahir Dar, Ethiopia. 

- Corresponding Author: Amanuel Yigezu; yigezuamanuel@yahoo.com iez oni
- Submitting Author: Awoke Misganaw

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# 73 Abstract

> **Objective:** This analysis is to present the burden and trends of morbidity and mortality due to 75 lower respiratory infections, their contributing risk factors, and the disparity across 76 administrative regions and cities from 1990 to 2019.

77 Design: This analysis used Global Burden of Disease 2019 framework to estimate morbidity and 78 mortality outcomes of lower respiratory infection and its contributing risk factors. The Global 79 Burden of Disease study uses all available data sources and Cause of Death Ensemble model to 80 estimate deaths from lower respiratory infection and a Meta-Regression Disease Modeling 81 technique to estimate lower respiratory infection non-fatal outcomes with 95% uncertainty 82 intervals.

83 Study setting: The study includes nine region states and two chartered cities of Ethiopia

Outcome Measures: We calculated incidence, death, and years of life lost (YLLs) due to LRIs
and contributing risk factors using all accessible data sources. We calculated 95% uncertainty
intervals (UI) for the point estimates.

**Results:** In 2019, LRIs incidence, death, and YLLs among all age groups were 8,313.7 (95% UI: 7,757.6–8,918), 59.4 (49.8–71.4) and 2,404.5 (2059.4–2833.3) per 100,000 people, respectively. From 1990, the corresponding decline rates were 39%, 61%, and 76%, respectively. Children under the age of five years account for 20% of episodes, 42% of mortalities, and 70% of the YLL of the total burden of LRIs in 2019. The mortality rate was significantly higher in predominantly pastoralist regions-Benishangul-Gumuz 101.8 (84.0-121.7) and Afar 103.7 (86.6-122.6). The Somali region showed the least decline in mortality rates. More than three-fourths of under-five child deaths due to LRIs were attributed to malnutrition. Household air pollution from solid fuel attributed to nearly half of the risk factors for all age mortalities due to LRIs in the country.

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**Conclusion:** In Ethiopia, LRIs have reduced significantly across the regions over the years (except in elders), however are still the third leading cause of mortality, disproportionately affecting children younger than five years old, and predominantly pastoralist regions. Interventions need to consider leading risk factors, targeted age groups and pastoralist and cross-border communities. *Keywords*: Lower respiratory infections, regions, chartered cities, Ethiopia Strengths and limitations of this study The analysis has considered political, government and administrative changes of regional states and cities over the years to map available data and populations The analysis used all available data identified through an extensive collaboration effort and • involving more than 700 leading researchers and policy makers from Ethiopia When data were not available for a particular regional states or city, the modelling process used data from other locations borrowing strength from geographic locations and time, and use predictive covariates However, limited quality data availability and accessibility for the analysis resulted in wider 95% Uncertainty Intervals which largely affect policy debates, prioritization, and health decisions. **INTRODUCTION** Lower Respiratory Infections (LRIs) have been a predominant health problem worldwide, causing more than 2.3 million deaths in 2016 alone, amounting to a mortality rate of 32.2 per 

100,000 people (1). LRIs comprise diseases of the lower airways such as pneumonia, bronchitis,
and bronchiolitis, among others (2). Nearly all (99%) of LRI deaths occur in low- and middleincome countries and highly affect children under the age of five years (3). In sub-Sahara
African countries, the mortality rate is 66.4 per 100,000 people, which is four times the mortality
rate in East Asia and twice the global average (2).

Ethiopia ranked in the top three African countries in the number of under-five child deaths from LRIs (4). To prevent child death from LRIs and other diseases in early life, Ethiopia has been implementing the "Integrated Management of Childhood Illness" program since 1997 later scaled up to the national level in 2007 (5). LRIs, and pneumonia in particular, have been among the top three leading causes of childhood mortality in the country (6). Among LRIs' aetiologies, S. pneumonia contributed to more deaths than the other LRIs aetiologies combined (3). In 2011, the country introduced 10-valent pneumococcal conjugate vaccine (PCV 10) into its national immunization program to reduce the burden of Streptococcal pneumonia (7). 

Morbidity and mortality from LRIs are attributable to multiple underlying factors. Malnutrition is one of the main underlying risk factors (8, 9). The other main attributable factor are poor living conditions that include household crowding, parental smoking, high use of household solid fuel/biomass consumption, poor ventilation, and lack of hand-washing facilities (10-12). In addition, bottle feeding also contributes to the burden of LRIs in children (13).

The flagship Ethiopian Health Extension Program (HEP) has been the backbone of the country's health system strategies to reduce the burden of LRIs and other diseases through preventive and health promotion activities at the community level. The HEP has also improved broader access to health care, availability of essential antibiotics, and immunization mainly to the rural population since 2004 (14). In 2010, the country also introduced the "integrated community case

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management" (ICCM) approach to treat pneumonia through trained health cadres of health
extension workers (HEWs) implementing HEP (15).

Currently, Ethiopia is implementing its Health Sector Transformation Plan-2 (HSTP-2) which is adapted from the Sustainable Development Goals. Some of the aims include increasing the proportion of under-five children with pneumonia who received antibiotics from 48% to 69% and improving full vaccination coverage from 44% to 69% between 2020 and 2025 (16). Commitment to international goals such as The Global Action Plan for the Prevention and Control of Pneumonia and Diarrhoea by 2025 could be reached if enough investment is made in high LRI burden countries like Ethiopia (17).

As Ethiopia is a country of stark contrasts in socioeconomic, epidemiological, and geographical variations, estimating disease burden at the regional level could provide valid and reliable information to inform policy decisions, including efficient resource allocation to match the burden in the subnational states. Hence, this article presents the 2019 Global Burden of Diseases, Injuries, and Risk Factors study (GBD) results on the burden, trends and regional variations of LRIs in Ethiopia from 1990 to 2019.

154 METHODS

# 155 Study Setting

Ethiopia is the second-most populous country in Africa next to Nigeria, with an estimated population of 112 million in 2019 (18). More than half of the country's population is under 20, and over 80% of the population resides in rural areas (19). The country is subdivided into ten regional states (Afar, Amhara, Benishangul-Gumuz, Gambella, Harari, Oromia, Somali, Sidama, Southern Nations and Nationalities and Peoples (SNNP), and Tigray) and two chartered cities

(Addis Ababa and Dire Dawa). During this study, Sidama was a zonal administration under the SNNP region. Oromia, Amhara, and SNNP are the highly populated regions. In this study, we classified the regions into urban (Addis Ababa, Dire Dawa, and Harari), agrarian (Oromia, Amhara, SNNP, Tigray), and pastoralist (Benishangul-Gumuz, Afar, Gambella, and Somali). The socio-economy of the regions such as income per person, educational attainment, and total fertility rate (TFR) varies as measured in socio-demographic index (SDI) (20) (Figure 1).

The healthcare system of the country is a three-tiered system consisting of primary, secondary, and tertiary levels of healthcare delivery units with 21,154 functioning health facilities and 159,545 health workforce in 2019 (16). The primary health care unit (PHCU) consists of health posts (staffed by HEWs), health centres, and primary hospitals. The secondary level of care consists of general hospitals and the tertiary level of care includes national referral hospitals ie. which provide specialized services (16). 

**Data Sources and Analysis** 

The analysis and findings of LRIs presented in this analysis were produced by the Ethiopia Subnational Burden of Disease Initiative, a collaborative endeavour between the National Data Management Center for Health (NDMC) at the Ethiopian Public Health Institute (EPHI) and the Institute for Health Metrics and Evaluation (IHME), as part of GBD. The details of the methodology were described elsewhere (21). In brief, woreda (district) level geographic boundary mapping of regions and cities was used because woredas were relatively stable government structures (compared to lower or higher level administrative structures) during political or government changes and through the three census years (1984, 1994, and 2007). First, the analysis was estimated by mapping population and demography at the district level by 

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time and region. Then, the data sources were mapped by regions before processing the data in the GBD analysis based on GBD protocol. EPHI, in collaboration with IHME, gathered all accessible data sources by location for Ethiopia and all regions and cities that included census, demographic surveillance, household surveys, diseases registry, health service utilization, disease notification, and other data for this analysis. A comprehensive description of data sources, quality, and modelling for GBD 2019 has been reported on the following online portal: (http://ghdx.healthdata.org/gbd-2019/data-input-sources). This study outputs predates the COVID-19 and civil war occurred in the northern and other parts of the country and does not include the impact of COVID-19 or civil war. 

**GBD Methods and Tools** 

The GBD details are reported elsewhere (22). Diseases and injuries within the GBD were organized into levels: Level 1 being the broadest causes of death and disability to Level 4 being the most specific. Within the three Level 1 causes (communicable, maternal, neonatal, and nutritional diseases; non-communicable diseases; and injuries), there were 174 Level 3 causes. The GBD 2019 study has estimated the burden of disease, including LRIs, for Ethiopia's national and subnational states. LRIs comprise diseases of the lower airways such as pneumonia, bronchitis, and bronchiolitis, among others (2). LRI mortality was estimated by age, sex, geography, and year using a modelling platform called the Cause of Death Ensemble model. LRI morbidity, including incidence, was modelled using a meta-regression platform known as DisMod-MR, a Bayesian, hierarchical, mixed-effects meta-regression platform (23). Years of life lost (YLLs) were computed by multiplying cause-specific deaths by the life expectancy at the age of death (24, 25). Population risk assessments over time and among risks were estimated using the comparative risk assessment approach developed for the GBD study (26, 27). The

> GBD risk factors were categorized as follows: Level 1 risk factors are behavioural, environmental, occupational, and metabolic; Level 2 risk factors include 20 clusters of risks; Level 3 consists of 52 clusters of risks; and Level 4 contains 69 specific risk factors. All metrics were estimated separately for Ethiopia's nine regions and two chartered cities, and are presented with their 95% uncertainty intervals (UIs). All estimates produced for GBD report 95% uncertainty intervals (UIs) that account for sampling and non-sampling error associated with data and various assumptions of the modelling process and are derived from the 2.5th and 97.5th percentiles of 1000 draws(22, 28).

**Presentation of results** 

We present the burden of LRIs in Ethiopia and its regional states using incidence, deaths, and YLLs categorized by sex, age groups, and year. We used numbers, rates, and percent change for the quantification of the burden. We also estimated the risk factors contributing to LRIs in Ethiopia and the percent change between 1990 and 2019. We reported GBD causes and risk factors using level 3 classifications, with 95% Uncertainty Intervals (UI). Additional tables and figures are attached in the supplementary materials.

222 Patient and public involvement

223 Patients and the public were not involved in the design of the study.

- **RESULTS** 
  - 225 Morbidity Due to LRIs

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In 2019, an estimated 6,628,673.6 (95% UI: 6,108,786.2-7,230,986.3) new cases of LRIs occurred in Ethiopia resulting in an age-standardized incidence rate of 8,313.7 per 100,000 people (7,757.6-8,918). Out of the total LRI episodes, 22% (1,448,680.0 new cases [1,150,089.8–1,799,704.4]) of new cases occurred among children younger than 5 years, yielding an annual incidence rate of 8,685.0 per 100,000 children (6,895.1–10,789.8). In adults older than 70 years, there were 725,273.3 (640,315.4-837,746.3) new cases of LRIs with an annual incidence of 38,394.4 per 100,000 people (33,896.9–44,348.5) (Figure 2; Supplemental Table 1 and Table 2). 

Compared to national estimates, a significantly lower age-standardized incidence rate of LRIs per 100,000 people was observed in the chartered cities (6,788.1 [6,285.1–7,339.1] in Addis Ababa, 7,148.8 [6,634.6–7,750.7] in Dire Dawa), and in Harari region (7,190.5 [6,684.1– 7,718.6]). The highest rates of age-standardized incidence per 100,000 people were observed in Afar (9,350.2 [8,648.8–10,157.4]), Somali (9,220.0 [8,515.9–10,046.4]), and Benishangul-Gumuz (9,054.6 [8,394.2–9,766.0]) although not significant compared to the national estimate (Figure 2; Supplemental Figure 1 and Table 2).

In children younger than 5 years, the lowest incidence rates were observed in Addis Ababa (4,927.2 [3,812.5–6,231.8]), Harari (6,821.6 [5,373.5–8,607.3]), and Gambella (6,791.1 [5,370.4–8460.1]) per 100,000 people, substantially below the national estimate. The highest incidence of LRIs per 100,000 children were recorded in Benishangul-Gumuz (10,481.8 [8,269.5–13,219.0]), Somali (10,062.7 [7,949.6–12,802.8]), Afar (9,365.5 [7,421.7–11,714.7]), and Oromia (9,039.4 [7,080.5–11,277.7]).

The age-standardized decline rate between 1990 and 2019 was 39% for both sexes, and it was
56% in under-five children and 13% in adults older than 70. The lowest decline in age-

standardized incidence rate was in Somali (19%); while it was between 38% and 44% for the
remaining regions (Supplemental Table 2).

In children younger than 5, the incidence rates increased slightly between 1990 and 1995, except in Addis Ababa and Amhara region. The highest decline rates were found between the years 2005 and 2015 across all regions (Supplemental Figure 2).

# 254 Mortality due to LRIs

In 2019, LRIs caused 46,300.7 (95% UI: 39,515–54,642) deaths in Ethiopia, giving the agestandardized mortality rate of 86.4 (75.3-97.6) per 100,000 people. Under-five mortality accounted for 42% (19,591.8 [14,018.4–26,899.0]) of all deaths due to LRIs which resulted in a mortality rate of 117.4 (84.0–161.2) per 100,000 children. Of the under-five deaths, 71% (13,919.0 [9,946.0–18,860.0]) occurred in the first year of life. In adults older than 70 years, LRIs caused 14,627.6 (12,393.7–16,892.8) deaths, which was a mortality rate of 774.3 (656– 894.2) deaths per 100,000 adults (Table 1; Supplemental Table 3).

In 2019, the number of deaths in all age groups by region were highest in Oromia (18,206 [15,193–21,745]), Amhara (9525 [7,530–11872]), SNNP (9,494 [7,713–11,649]), and Somali (3,907.5 [3,007.4–4,959.4]), followed by Tigray (2,551.4 [2,090.3–3,028.6]), Afar (706.2 [567.7–869.6]), Benishangul-Gumuz (619 [470.7–803.0]), Dire Dawa (154.6 [120.6–193.8]) and Gambella (123.2 [98.2–151.9]). Harari (93.1 [73.8–116.0) had the lowest number of deaths. (Supplemental Table 3).

Between 1990 and 2019, the age-standardized mortality rate declined by 61%, and the decline in
under-five children and adults over 70 years was 86% and 30%, respectively (Table 1 and

270 Supplemental Figure 3).

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	271	Table 1: Lower Respiratory Infections mortality rates and percentage changes between 1990 and 2019 in Ethiopia, both sexes, with different age
4 5	272	groups

6	Age standardized		Children younger than 5			People older than 70		
Location	Deaths per 100 000	Deaths per 100 000	Deaths per 100 000	Deaths per 100 000	Cha-	Deaths per 100 000	Deaths per 100 000	Cha-
8 9	people [95% UI],	people [95% UI],	children [95% UI], 1990	children [95% UI],	Nge,%	people [95% UI],	people [95% UI],	nge,%
10	1990	2019		2019		1990	2019	
Addis Ababa	163.4[134.6-206.9]	59.4[49.8-71.4]	441.5[320.4-602.7]	23.4[14.1-36.4]	95	909.2[669.5-1264.6]	503.6[410.5-633.7]	45
Ogromia	241.3[188.5-292.8]	89.3[75.9-103.1]	920.7[629.5-1264.1]	122.3[84.8-171]	87	1174.1[842.8-1543]	849.5[687.3-1009]	28
Amhara 15	197.7[163.5-236.5]	74.3[59.4-91]	691.3[531.7-883.4]	94.9[55.6-146.1]	87	1017.9[755.4-1324]	682.7[537.4-857.9]	33
<b>SennPs</b>	243.7[196.4-296.9]	98.9[83.8-116.6]	971.9[697.2-1273.2]	118.4[79-168.5]	88	1161.3[584.7-822.3]	845.4[685.6-018.1]	28
Tigray 18	242.7[200.5-292]	84.6[69.2-100.1]	780.4[593.5-1009.1]	67.2[43.5-98.3]	92	1166.7[838.2-1586]	788.6[637.9-956.8]	33
Harari	240.2[182.6-303.1]	77[63-92.5]	1146.7[730-1604.1]	89.9[51.1-138]	93	762.3[412-1223.7]	694.3[551.9-849]	9
Alfar 21	244.8[186.5-316.9]	103.7[86.6-122.6]	723.7[481.5-1023.7]	101.7[65-152.4]	86	1010[658-1541.7]	917.6[720.6-146.8]	10
<b>So</b> mali	147.6[113.8-192.6]	97.5[79.2-118.6]	455.9[313-628.5]	197.3[135-279.8]	57	798.8[519.2-1177.6]	765.1[588.8-972.4]	5
<b>B</b> G 24	284.1[221.8-358.1]	101.8[84-121.7]	1266.4[846.7-790.9]	215.1[141.4-311]	84	975.3[656.5-1379.3]	671.9[532.7-848.7]	32
Dire Dawa	220.1[171.6-270.9]	69.9[56.5-84]	1084.2[689.1-503.2]	83.7[44.7-135.9]	93	868.7[604.5-1205.5]	621.3[496.4-766.1]	29
Cambella	231.5[176.8-297.4]	82.4[68.3-97.1]	1265.5[805.4-764.3]	57[32.4-89.6]	96	739.6[477.7-1074.9]	678.3[540.4-835.3]	9
Éthiopia*	223[184.7-264.3]	86.4[75.3-97.6]	822.2[635-1051.2]	117.4[84-161.2]	86	1092.3[844-1391.5]	774.3[656-894.2]	30

N.B: all changes are in decreasing percent. SNNPs: Southern Nations, Nationalities, and Peoples; BG: Benishangul-Gumuz; \*national estimate 

 

> In Ethiopia, the age-standardized mortality rate was higher among males (100.6 [84.1-121.4]) than females (71.8 [60.2–82.9]) (Supplemental Table 4). In 1990, the age-standardized mortality rate per 100,000 people was the highest in Benishangul-Gumuz (284.1 [221.8-358.1]), Afar (244.8 [186.5-316.9]) and SNNP (243.7 [196.4-296.9]), although it is not significantly different from the national estimate. On the other hand, the lowest age standardized mortality rate was exhibited in Somali (147.6 [113.8–192.6]). Although the value was not significantly different from the national value in 1990, Addis Ababa showed the second lowest age-standardized mortality rate (163.4 [134.6-206.9]) (Table 1). In 2019, the age-standardized mortality rate per 100,000 people was significantly lower in Addis Ababa (59.4 [49.8–71.4]) when compared to other regions, although not significantly lower than Gambella and other urban areas (Harari and Dire Dawa). Dire Dawa showed a significantly

> lower age-standardized mortality rate when compared to Benishangul-Gumuz, Afar, and SNNP.
> Compared to the national estimate, the regions of Afar (103.7 [86.6–122.6]) and BenishangulGumuz (101.8 [84.0–121.7]) recorded the highest age-standardized mortality rates per 100,000
> people, although the difference is not statistically significant (Table 1). Compared to the 1990s,
> there was a 58% to 68% decrease in the age-standardized mortality rates across all regions.
> However, the Somali region recorded a 34% reduction in mortality rates (Supplemental Figure 3).

Among children below the age of five, the mortality rate per 100,000 people was significantly lower in Addis Ababa (23.4 ([14.1–36.4]) than other regions, although it was not significantly less than Gambella in 2019. The mortality rate was the highest in Benishangul-Gumuz (215.1 [141.4–311.0]), Somali (197.3 [135.2–279.8]), and Oromia (122.3 [84.8–171.0]) despite being not significantly higher than the national estimate (Table 1). Dire Dawa showed a significantly

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lower mortality rate than Benishangul-Gumuz and Somali. Harari had a significantly lower mortality rate than Benishangul-Gumuz. For all regions, the mortality rate declined for children younger than 5-years between 1990 and 2019 by between 84% (in Benishangul-Gumuz) and 96% (in Gambella), except in Somali, which showed a 57% decline (Table 1). The mortality rate increased slightly between 1990 and 1995 and between 2010 and 2015 in Somali region (Supplemental Figure 4).

The mortality rate in adults older than 70 was the lowest in Addis Ababa (503.6 [410.5–633.7]). Other regions and cities have not shown a statistically significant difference from the national estimate. The decline in mortality rates between 1990 and 2019 is below 50% across all regions (Table 1). The mortality rate increased in Afar and Somali between 2005 and 2019 and in Gambella between 1990 and 2005 (Supplemental Figure 5).

310 Premature Mortality due to LRIs

In 2019, premature death due to LRIs was 2,445,093.7 (95% UI: 1,934,420.8–3,119,838.6) YLLs, yielding an age-standardized rate of 2404.5 per 100,000 people (2059.4–2833.3). Compared to 1990, the age-standardized YLL rate declined by 76% in 2019. In parallel, 70% of all premature mortality occurred in children younger than five, which accounted for 1,721,122.3 (1,231,032.1-2,362,958.7) YLLs. The YLL rate of 72,055.4 (55,718.5-92,064) per 100,000 under-five children in 2019 declined by 86% compared to the YLL rate in 1990. Adults over 70 years contributed 8% of all YLLs due to LRIs (194,756.2 [165,462.0–225,502.1]), yielding a rate of 10,309.9 (8759.2–11,937.6) YLLs per 100,000 people (Table 2; Supplemental Table 5 and Table 6).

Compared to 1990, the number of YLLs has decreased by 70% in all age groups and by 76% in

children younger than five in 2019. However, the number of YLLs has increased by 45% in adults older than 70 (Supplemental Table 5). The age-standardized YLL rate was significantly lower in Addis Ababa (1,285.6 [1,065-1,561.8]) in 2019 compared to the national average. The highest age standardized YLL rate were in Benishangul-Gumuz (3,571.1 [2,772.4–4,510.7]), Somali (3,236.4 [2,537.4–4,006]), and Afar (2,824.6 [2,323–3,414]), although not statistically significant compared to the national estimate (Table 2).

In children younger than five years, Addis Ababa (2,069 [1,253–3,217.5]) had a significantly lower YLL rate than the national estimate. The YLL rate was observed to be the lowest in Gambella (5,031.8 [2,867.2–7,885.7]), although not significantly lower than the national estimate (Table 2). 

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	Age-standardized		Children younger th	Children younger than 5 years			People older than 70		
Locatio	YLL per 100,000	YLL per 100,000	YLL per 100,000	YLL per 100,000	Cha	YLL per 100,000	YLL per 100,000	Cha	
n	people,1990	people, 2019	people,1990	people, 2019	nge,	people,1990	people, 2019	nge,	
					%			%	
Addis	6362.2(5161.9-	1285.6(1065-	38824.7(28230.1-		95	13587(9985.4-	6857.1(5545.8-	50	
Ababa	7847.9)	1561.8)	53092.4)	2069(1253-3217.5)		18978.3)	8721.2)		
Oromia	11217.6(8517-	2433.8(2042.2-	80610.7(55103.7-	10742.8(7456.7-	87	18754.2(13297.1-	11119.7(8939.1-	41	
	14318)	2879.5)	110696)	15039.6)		24843)	13305)		
Amhara	8690.4(7146.3-	2016.4(1551.4-	60663.3(46712.5-		87	15950.4(11723.4-	9059.7(7063.2-	44	
	10453.8)	2541.8)	77511.5)	8355(4898.9-12845)		21059.7)	11529.2)		
SNNPs	11633(9119.4-	2698.1(2243.5-	85114.7(61203.2-	10409.3(6968.1-	88	18842.6(13166.1-	11736.6(9426.7-	38	
	14477.9)	3250.2)	111502.1)	14819.3)		26081)	14238.6)		
Tigray	10346.4(8522.9-	1977.1(1593.9-	68509.3(52185.7-	5927.9(3839.4-	92	19502.8(13914.1-	10486.8(8439.5-	47	
	12340.3)	2395)	88712.2)	8676.8)		26751.2)	12765.3)		
Harari	12826.5(9336.5-	2060.4(1595.6-	100421.7(63898.7-	7922.5(4518.7-	93	11782.6(6360.4-	9260.4(7338.7-	22	
	16985.4)	2623.1)	140467.8)	12117.2)		19341.1)	11340.3)		
Afar	10993.5(8520.8-	2824.6(2323-3414)	63570.5(42296.6-	8943.7(5734.6-	86	16925.5(10923.7-	11867.1(9346-	30	
	14193.6)		89769)	13390.2)		26001.7)	14716.9)		
Somali	6286.9(4860.5-	3236.4(2537.4-	40088.1(27543.7-	17314.3(11890.7-	57	11953.6(7599.2-	10246(7797.8-	15	
	7970)	4006)	55109)	24530)		17885.5)	13150.6)		
BG	14965.1(11197.4-	3571.1(2772.4-	110847.2(74368-	18868.3(12442.9-	83	16397.3(10917-	9541.9(7476.9-	42	
	19998.6)	4510.7)	156588.4)	27281.8)		23228.5)	12112.3)		
Dire	11749.7(8605.4-	1832.8(1407.3-	94905.3(60458.5-	7371.3(3953-	93	13207.9(9219.6-	8371(6616.3-	37	
Dawa	15249.5)	2363.1)	131584.5)	11962.1)		18328.2)	10408.2)		
Gambell	13175.8(9291-	1937.4(1567.6-	110783.8(70576-	5031.8(2867.2-	96 <	11811.4(7673.5-	10030.9(7730.2-	16	
a	17411)	2344.6)	154304.1)	7885.7)		17012.5)	12664.9)		
Ethiopia	10189.1(8347.5-	2404.5(2059.4-	72055.4(55718.5-	10318.6(7380.4-	86	17415.9(13362.7-	10309.9(8759.2-	41	
*	12201.8)	2833.3)	92064)	14166.6)		22228.5)	11937.6)		

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Table 2: Lower Respiratory Infections YLL rates and percentage changes between 1990 and 2019 in Ethiopia, both sexes, with different age
 groups

335 SNNPs: Southern Nations, Nationalities, and Peoples; BG: Benishangul-Gumuz; \*national estimate

The age-standardized premature mortality rate between 1990 and 2019 showed a continuous decline in all regions, except Somali. Benishangul-Gumuz showed the highest burden between 1990 and 2019 (Figure 3).

The change in premature mortality in children younger than five was significant throughout the years. However, the reduction in premature mortality among adults older than 70 was not as significant (Supplemental Figure 6 and Figure 7).

# **Risk Factors**

Across all population groups, about half (48%) of the mortalities (measured in rates) due to LRIs in Ethiopia were attributed to household air pollution from solid fuel. In addition, lack of access to a hand-washing facility (23%), childhood wasting (23%), low birth weight (9%), short gestation period (7%), and ambient particulate matter pollution (6%) were also risk factors for mortality due to LRIs. The contribution of the risk factors to death due to LRIs in all regions was similar to the national estimate, except in Addis Ababa, where lack of access to hand-washing facilities, ambient particulate matter pollution, and low temperature were the main contributing factors. Ambient particulate matter pollution was also relatively higher in Dire Dawa, Harari, and Tigray regions (Supplemental Figure 8). 

In children younger than five, more than three-fourths of deaths due to LRIs were attributed to childhood wasting (54%) stunting (12%), and child underweight (10%) in Ethiopia. In addition, 50% of the LRIs mortalities were attributed to household air pollution from solid fuel. Lack of access to hand-washing facilities (23%), low birth weight (23%), short gestation period (17%), high (4%) or low temperature (4%), absence of exclusive breastfeeding (4%) were also the risk factors with evident contribution. The distribution of risk factors varied among the regions. Child
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wasting, low birth weight, and pre-term birth were the contributing factors of mortality in Addis Ababa. In Harari and Dire Dawa, child wasting, lack of access to hand-washing facilities, preterm birth, and household air pollution from solid fuels contributed more to the death from LRIs than the other risk factors in 2019. All the risk factors except for ambient particulate air matter and low temperature were the highest in Somali and Benishangul-Gumuz (Supplemental Figure 9). When we examine the trend from 1990 to 2019, there is no significant reduction in the risk factors (Supplemental Figure 10).

## 366 Discussion

The findings from this study indicate that although the burden of LRIs, measured in incidence or mortality rates, have shown a significant decline, they are still the third leading cause of death after neonatal disorders and diarrheal diseases in 2019 in Ethiopia. Cities and predominantly urban areas had lower mortality rates than predominantly pastoralist regions of the country. The rate of decline in mortality between 1990 and 2019 varied slightly across regions and chartered cities. The mortality rate decreased by more than three-fourths among children under the age of five and only by one-third among adults older than 70 between 1990 and 2019. Half of LRIs mortalities are attributed to household air pollution from solid fuels in all age groups. About three-fourths of LRIs in children were attributed to malnutrition. 

The mortality rate of LRIs among children below the age of five has declined by 86% between 1990 and 2019. This decline could be attributed to improvements in living conditions, access to healthcare, and immunization. The national health delivery infrastructure has grown from 2,600 health facilities in 1997 to 21,154 facilities, including 314 hospitals, 3,678 health centers, and 17,162 health posts and private health facilities in 2019. As a result, the health workforce has

increased from 46,000 in 2007 to 159,545 in 2019 (16). The introduction of HEP since 2004 to provide preventive, health promotion, and curative treatment for pneumonia, malaria and diarrhoea had improved health outcomes for children (14). Moreover, Ethiopia has been implementing holistic child health improvement programs like IMCI since 1997 (15) and ICCM (5). Vaccination against Streptococcus pneumonia, which is responsible for about half of the LRIs mortality in African countries, with the PCV 10 vaccine since 2011 helped reduce the burden of LRIs (4). In addition, improved socioeconomic conditions have supported the reduction of the burden of LRIs in the country (29). 

Despite the achievements reached in improving child health outcomes in Ethiopia, children are still disproportionately affected by LRIs. Out of the total burden of LRIs, 42% of all the deaths were among children younger than five. In that regard, this study has shown that one out of ten child deaths are due to LRIs. However, another study estimated that pneumonia alone shared about 17% of all deaths in children younger than five years (30). Among children under five, children younger than one carry the highest burden of LRIs. Furthermore, the mortality rate among children younger than one (397.7 per 100,000 people) was more than nine times higher than that of children between one and four years old (43 per 100,000 people). Although most studies on the high burden of LRIs corroborate our findings, the findings from Global Health Observatory (GHO) estimated a much higher mortality rate than the estimates of this study (i.e. 481.9 in children less than one year and 51.1 per 1000,000 population in children between one and four years) (8). Although we could not explain why this variation occurs, the estimates from GBD are also less than the estimate from findings of the Child Health Epidemiology Reference Group (CHERG), which is primarily due to the difference in the types of data used (31). 

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Urban areas of the country, mainly Addis Ababa and Dire Dawa, had significantly lower mortality rates than pastoralist areas such as Benishangul-Gumuz and Somali. These regional variations could be attributed to gaps in availability and access to healthcare and socioeconomic status differences among the subnational states. A previously conducted study indicated that disease burden is high among people in the poorest wealth quintile and people located mainly in Afar, Somali, Oromia, SNNP, and Benishangul-Gumuz and also have the lowest level of health service utilization (32). The rural area of the country has less healthcare coverage and utilization than the urban areas. The coverage of all basic vaccination is 43% in the country. Across the regions, the coverage of all basic vaccination is lowest in Afar (20%) and highest in Addis Ababa (83%). Coverage of pentavalent vaccines in children is 72% among the urban population while it is 56% among the rural population (15, 30). There is a variation in the performance of immunization across regions. Addis Ababa, Ethiopia's capital has PCV3 coverage of 93% among 1-year-olds in 2019, whereas this coverage is only 23% in Afar and Somali. The wasting rate in Somali was 21% in children under five, while it was just 2% in Addis Ababa in 2019 (33) 

In addition to children, LRIs affects people older than 70 years. The number of people dying from LRIs increased over the years in people older than 70 years, partly due to the increase in the aging population. However, the mortality rate declined by 30% between 1990 and 2019 (3, 34). The incidence rate did not show a significant improvement across the study years, showing only 15% reductions between 1990 and 2019. Among the regions, Somali and Afar have recorded an increased incidence rate between 1990 and 2019. This could partly be explained by poor accessibility and availability of health facilities in the regions (33).

Wasting, stunting, and underweight were major risk factors contributing to the death of children
younger than five years due to LRIs (35-37). More than 37% of children under five are stunted,

with a higher percentage in rural areas (41%) than in urban areas (26%). Similarly, the prevalence of child underweight and wasting is 21% in the rural and 7% in the urban parts of Ethiopia (38). This indicates that more investment is needed to reduce the burden on malnutrition among children and in the rural parts of the country to attain better health outcomes, protecting against LRIs. Although the prevalence of stunting, wasting, and underweight has decreased markedly over time, they are still major risk factors for death caused by LRIs. In the Millennium Development Goals (MDG) era, between 1990 and 2015, about half of the deaths averted due to LRIs were attributed to improvement in the nutritional status of children (reduction in wasting and stunting) (15). 

Ambient particulate matter and household air pollution from solid fuel use were the two essential components of air pollution. Household air pollution from solid fuel use the was the second leading risk factor for LRIs, and ambient particulate matter is the eight leading risk factor among the top ten risk factors for LRIs (39-41). Our analysis also showed that there is a poor progress in the reductions of risk factors across the year, which shows there is a weak attempt in reducing the risk factors to prevent the population from LRIs. This indicates that improved use of electricity and natural gas for cooking and also appropriate investment in interventions that helps to reduce these risk factors will contribute to the reduction in the burden of the LRIs. (3).

To reduce the burden of LRIs, both national and global efforts are underway. The Global Action Plan for the Prevention and Control of Pneumonia and Diarrhoea (GAPPD), established by the World Health Organization, set goals in 2013 to reduce child LRI mortality rates to below 3 in 1,000 live births and to reduce severe LRI incidence by 75% of the 2010 baseline by 2025. To achieve these goals, reaching 90% of children with full-dose vaccine coverage, 90% access to pneumonia treatment, 50% coverage of exclusive breastfeeding in the first six months, and

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exclusive breastfeeding promotion were set as prerequisites (17). However, a 6% average annual
mortality reduction was recorded between 2000 and 2018 in Ethiopia. With this, the country can
only reach the 2025 GAPPD target in 2035, ten years behind the target, according to the
Maternal and Child Epidemiology Estimation Group (MICE) estimation (30).

Ethiopia's major health sector strategic plan, the Health Sector Transformation Plan-2 (HSTP-2) for the year 2021-2024, aims to reduce the infant mortality rate to 35, the neonatal mortality rate to 21 and the children under-5 mortality rate to 43 per 1,000 live births. Similarly, the 2030 Sustainable Development Goals (SDG) has set targets to reduce childhood mortality significantly. These targets can be achieved if the country implements high-impact priority curative and preventive interventions against LRIs (42). To achieve this, concerted action to improve policies, increase investment, foster innovations, and scale-up evidence-based interventions has paramount importance. Parallel to this, an estimated \$274 billion for health is required to achieve the health-related SDGs by 2030 in 67 low and middle-income countries, including Ethiopia. One of the strategies to mobilize the needed resources is to increase government expenditure by 15% and share the population's costs through taxes or insurances (43). 

This study is not without limitations; limitations in the GBD methods also apply to this study and limitations on Ethiopia subnational burden of disease that includes scarcity of quality data is published elsewhere (28).. When data on causes of death, morbidity or risk factors were not available for a particular regional state such as Afar or Somali, GBD modelled estimates use data from other locations and predictive covariates. Data sources such as household surveys have both sampling and non-sampling errors that account and led a wider 95% uncertainty intervals which might compromise the accuracy of the findings and reduce the use of these findings for policy

decision-making (1). Causes of mortality data sources used were mainly from verbal autopsy and sibling history having recall bias, broader category of causes of death report or poor generalizability to regional states (44). We used the best available data identified through an extensive collaboration effort and involving more than 700 leading researchers and policy makers from Ethiopia. The generation of estimates and their interpretation have benefited from intensive subnational review workshops and consultative meetings with domain experts.

# 478 Conclusion

Despite the substantial reduction in morbidity and mortality at national and regional states, LRIs still remain one of the leading causes of the burden of disease in Ethiopia. Children and elders are still disproportionately affected by LRIs. The burden of illness and death due to LRIs varies across regional states in Ethiopia, with lower rates in cities and predominantly urban areas while predominantly pastoralist areas of the country have higher rates. Efforts should be made to tackle the major risk factors contributing to death by LRIs. Improving child nutrition, access to immunization and curative health services, as well as universal electrification to reduce indoor air pollution will be very useful strategies to reduce deaths due to LRIs in Ethiopia. Furthermore, improvement in socioeconomic factors will also help to reduce LRI burden at national and regional levels. To reach the targets set at the national and international level, mobilizing resources to health and improving the provision of health services to the community according to the needs of the regions is of paramount importance. 

491 List of abbreviations

492 EPHI: Ethiopian Public Health Institute; GAPPD: Global Action Plan for the Prevention and 493 Control of Pneumonia and Diarrhoea GBD: Global Burden of Disease; GHO: Global Health

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Observatory; HSTP: Health Sector Transformation Plan; ICCM: integrated community case
management; IHME: Institute of Health and Metric Evaluation; LRIs: Lower Respiratory
Infections; NDMC: National Data Management Center for health; PCV: Pneumococcal
Conjugate Vaccine; SDG: Sustainable Development Goals; SNNPs: Southern Nations,
Nationalities and Peoples; UI: Uncertainty Interval; WHO: World Health Organization; YLL:
Years of Life Lost.

# 500 Ethics approval and consent to participate

501 This manuscript was produced as part of the GBD Collaborator Network and in accordance with502 the GBD Protocol.

#### 503 **Consent for publication**

504 Not applicable.

# 505 Availability of data and material

506 All relevant data are submitted with this manuscript.

### 507 **Competing interests**

508 The authors declare that they have no competing interests.

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- 513 Authors' contributions

514 Authors contribution

Providing data or critical feedback on data sources Semagn Mekonnen Abate, Mesafint Molla Adane, Addis Aklilu, Dejene Tsegave Alem, Mulusew A Asemahagn, Hunegnaw Abebe, Melaku Ashagrie Belete, Tekleberhan Hailemariam, Tezera Moshago Berheto, Belay Boda Abule Bodicha, Daniel Baza Gargamo, Alemayehu Hailu, Awoke Misganaw, Mohsen Naghavi, Negussie Boti Sidamo, Yonatan Solomon, Shambel Wedajo, Melat Weldemariam, Amanuel Yigezu, Fentabil Getnet, and Yazachew Yismaw. Developing methods or computational machinery Semagn Mekonnen Abate, Tezera Moshago Berheto, Alemayehu Hailu, Mohsen Naghavi, Negussie Boti Sidamo, and Amanuel Yigezu. Providing critical feedback on methods or results Semagn Mekonnen Abate, Mesafint Molla Adane, Gizachew Taddesse Akalu, Addis Aklilu, Dejene Tsegaye Alem, Zeleke Gebru, Mulusew Andualem Asemahagn, Daniel Atlaw, Tewachew Awoke, Hunegnaw Abebe, Melaku Ashagrie Belete, Tekleberhan Hailemariam, Tezera Moshago Berheto, Alemeshet Yirga, Setognal Birara Aychiluhm, Belay Boda Abule Bodicha, Chuchu Churko, Feleke Mekonnen Demeke, Abebaw Alemayehu Desta, Lankamo Ena, Tahir Eyayu, Zinabu Fentaw, Daniel Baza Gargamo, Mesfin Damtew Gebrehiwot, Mathewos Alemu Gebremichael, Melaku Getachew, Ababi Zergaw, Alemayehu Hailu, Getahun Molla, Awoke Misganaw, Mohsen Naghavi, Biniyam Sahiledengle, Bereket Beyene, Migbar Sibhat, Negussie Boti Sidamo, Damtew Damtew Solomon, Yonatan Solomon, Birhanu Wagaye, Shambel Wedajo, Melat Weldemariam, Amanuel Yigezu, Fentabil Getnet, and Yazachew Yismaw. Drafting the work or revising is critically for important intellectual content 

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539	Aychiluhm, Belay Boda Abule Bodicha, Chuchu Churko, Tahir Eyayu, Zinabu Fentaw, Daniel
540	Baza Gargamo, Melaku Getachew, Ababi Zergaw, Firehiwot Abebe Gobena, Muluken Argaw
541	Haile, Alemayehu Hailu, Solomon Tessema Memirie, Awoke Misganaw, Mohsen Naghavi,
542	Biniyam Sahiledengle, Bereket Beyene, Negussie Boti Sidamo, Yonatan Solomon, Dereje
543	Mengistu Tolosa, Birhanu Wagaye, Ally Walker, Amanuel Yigezu, and Fentabil Getnet.
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552	References
553	1. Global, regional, and national age-sex specific mortality for 264 causes of death, 1980-
554	2016: a systematic analysis for the Global Burden of Disease Study 2016. Lancet (London,
555	England). 2017 Sep 16;390(10100):1151-210. PubMed PMID: 28919116. Pubmed Central
556	PMCID: PMC5605883. Epub 2017/09/19. eng.
557	2. Troeger C, Blacker B, Khalil IA, Rao PC, Cao J, Zimsen SRM, et al. Estimates of the
558	global, regional, and national morbidity, mortality, and aetiologies of lower respiratory infections

in 195 countries, 1990–2016: a systematic analysis for the Global Burden of Disease
Study 2016. The Lancet Infectious Diseases. 2018;18(11):1191-210.

3. Moradi-Lakeh M, El Bcheraoui C, Charara R, Khalil I, Afshin A, Kassebaum NJ, et al.
Burden of lower respiratory infections in the Eastern Mediterranean Region between 1990 and
2015: findings from the Global Burden of Disease 2015 study. International Journal of Public
Health. 2018 2018/05/01;63(1):97-108.

Keiner RC, Welgan CA, Casey DC, Troeger CE, Baumann MM, Nguyen QP, et al.
Identifying residual hotspots and mapping lower respiratory infection morbidity and mortality in
African children from 2000 to 2017. Nature Microbiology. 2019 2019/12/01;4(12):2310-8.

568 5. Miller NP, Amouzou A, Tafesse M, Hazel E, Legesse H, Degefie T, et al. Integrated 569 community case management of childhood illness in Ethiopia: implementation strength and 570 quality of care. Am J Trop Med Hyg. 2014;91(2):424-34. PubMed PMID: 24799369. Epub 571 05/05. eng.

572 6. Alamneh YM, Adane F. Magnitude and Predictors of Pneumonia among Under-Five
573 Children in Ethiopia: A Systematic Review and Meta-Analysis. Journal of Environmental and
574 Public Health. 2020 2020/05/30;2020:1606783.

575 7. Wondimu A, Cao Q, Wilschut JC, Postma MJ. Factors associated with the uptake of
576 newly introduced childhood vaccinations in Ethiopia: the cases of rotavirus and pneumococcal
577 conjugate vaccines. BMC Public Health. 2019 2019/12/10;19(1):1656.

578 8. Gonakoti S, Osifo IF. Protein-Energy Malnutrition Increases Mortality in Patients
579 Hospitalized With Bacterial Pneumonia: A Retrospective Nationwide Database Analysis.
580 Cureus. 2021 Jan 12;13(1):e12645. PubMed PMID: 33585131. Pubmed Central PMCID:
581 PMC7876587. Epub 2021/02/16. eng.

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#### **BMJ** Open

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Yeo HJ, Byun KS, Han J, Kim JH, Lee SE, Yoon SH, et al. Prognostic significance of
 malnutrition for long-term mortality in community-acquired pneumonia: a propensity score
 matched analysis. The Korean journal of internal medicine. 2019 Jul;34(4):841-9. PubMed
 PMID: 30685962. Pubmed Central PMCID: PMC6610202. Epub 2019/01/29. eng.

586 10. Adane MM, Alene GD, Mereta ST, Wanyonyi KL. Prevalence and risk factors of acute
587 lower respiratory infection among children living in biomass fuel using households: a
588 community-based cross-sectional study in Northwest Ethiopia. BMC Public Health. 2020
589 2020/03/19;20(1):363.

590 11. Adane MM, Alene GD, Mereta ST, Wanyonyi KL. Effect of improved cookstove
591 intervention on childhood acute lower respiratory infection in Northwest Ethiopia: a cluster592 randomized controlled trial. BMC Pediatrics. 2021 2021/01/04;21(1):4.

593 12. Keleb A, Sisay T, Alemu K, Ademas A, Lingerew M, Kloos H, et al. Pneumonia remains
 594 a leading public health problem among under-five children in peri-urban areas of north-eastern
 595 Ethiopia. PLOS ONE. 2020;15(9):e0235818.

596 13. Ahmed KY, Page A, Arora A, Ogbo FA, Global M, Child Health Research c. 597 Associations between infant and young child feeding practices and acute respiratory infection 598 and diarrhoea in Ethiopia: A propensity score matching approach. PLOS ONE. 599 2020;15(4):e0230978.

600 14. Assefa Y, Gelaw YA, Hill PS, Taye BW, Van Damme W. Community health extension
601 program of Ethiopia, 2003–2018: successes and challenges toward universal coverage for
602 primary healthcare services. Globalization and Health. 2019 2019/03/26;15(1):24.

603 15. Ruducha J, Mann C, Singh NS, Gemebo TD, Tessema NS, Baschieri A, et al. How
604 Ethiopia achieved Millennium Development Goal 4 through multisectoral interventions: a

2		
3 4	605	Countdown to 2015 case study. Lancet Glob Health. 2017;5(11):e1142-e51. PubMed PMID:
5 6 7	606	29025635. eng.
7 8 9	607	16. Federal Ministry of Health. Health Sector Transformation Plan 2020/21-2024/25 (2013
10 11	608	EFY - 2017 EFY), Addis Ababa Ethiopia. 2020.
12 13	609	17. Unicef, World Health O. Ending preventable child deaths from pneumonia and diarrhoea
14 15 16	610	by 2025 : the integrated global action plan for pneumonia and diarrhoea (GAPPD) 2013.
17 18	611	Available from: https://apps.who.int/iris/handle/10665/79200.
19 20	612	18. World Bank. World Bank data catalog. [Washington, D.C.]: World Bank.
21 22 23	613	19. central statstical agency. Ethiopian statistical service. 2020. Available from:
23 24 25	614	http://www.statsethiopia.gov.et/.
26 27	615	20. Burden of Disease Unit (BoD) NDMCNfh, Ethiopia Public Health Institute. Ethiopia
28 29	616	Health Atlas, 2021 2021. Available from: https://ndmc.ephi.gov.et/national-health-atlas/.
30 31 32	617	21. Misganaw ANMWAMAHGAZBTMWEAKJHEGTWTKDDA. Progress in health
33 34	618	among regions of Ethiopia, 1990-2019: a subnational country analysis for the Global Burden of
35 36	619	Disease Study 2019. Lancet Lancet (London, England). 2022;399(10332):1322-35.
37 38 39	620	22. Murray CJL, Aravkin AY, Zheng P, Abbafati C, Abbas KM, Abbasi-Kangevari M, et al.
40 41	621	Global burden of 87 risk factors in 204 countries and territories, 1990–2019: a
42 43	622	systematic analysis for the Global Burden of Disease Study 2019. The Lancet.
44 45	623	2020;396(10258):1223-49.
40 47 48	624	23. Collaborators GL. Estimates of the global, regional, and national morbidity, mortality,
49 50	625	and aetiologies of lower respiratory tract infections in 195 countries: a systematic analysis for the
51 52	626	Global Burden of Disease Study 2015. Lancet Infect Dis. 2017;17(11):1133-61. PubMed PMID:
53 54 55	627	28843578. Epub 08/23. eng.
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DALYs GBD, Collaborators H. Global, regional, and national disability-adjusted lifeyears (DALYs) for 315 diseases and injuries and healthy life expectancy (HALE), 1990-2015: a
systematic analysis for the Global Burden of Disease Study 2015. Lancet (London, England).
2016;388(10053):1603-58. PubMed PMID: 27733283. eng.

632 25. Dicker D, Nguyen G, Abate D, Abate KH, Abay SM, Abbafati C, et al. Global, regional,
633 and national age-sex-specific mortality and life expectancy, 1950–2017: a systematic
634 analysis for the Global Burden of Disease Study 2017. The Lancet. 2018;392(10159):1684-735.

Lim SS, Vos T, Flaxman AD, Danaei G, Shibuya K, Adair-Rohani H, et al. A
comparative risk assessment of burden of disease and injury attributable to 67 risk factors and
risk factor clusters in 21 regions, 1990-2010: a systematic analysis for the Global Burden of
Disease Study 2010. Lancet (London, England). 2012;380(9859):2224-60. PubMed PMID:
23245609. eng.

Collaborators GBDRF, Forouzanfar MH, Alexander L, Anderson HR, Bachman VF,
Biryukov S, et al. Global, regional, and national comparative risk assessment of 79 behavioural,
environmental and occupational, and metabolic risks or clusters of risks in 188 countries, 19902013: a systematic analysis for the Global Burden of Disease Study 2013. Lancet (London,
England). 2015;386(10010):2287-323. PubMed PMID: 26364544. Epub 09/11. eng.

645 28. Misganaw A, Naghavi M, Walker A, Mirkuzie AH, Giref AZ, Berheto TM, et al.
646 Progress in health among regions of Ethiopia, 1990–2019: a subnational country
647 analysis for the Global Burden of Disease Study 2019. The Lancet. 2022;399(10332):1322-35.

Shibre G, Zegeye B, Idriss-Wheeler D, Yaya S. Trends of inequalities in care seeking
behavior for under-five children with suspected pneumonia in Ethiopia: evidence from Ethiopia
demographic and health surveys (2005–2016). BMC Public Health. 2021 2021/02/01;21(1):258.

Page 34 of 57

#### **BMJ** Open

30. Fighting for Breath in Ethiopia: a call to action to stop children dying from pneumonia
[Internet]. 2020. Available from: stoppneumonia.org/wp-content/uploads/2019/11/Ethiopia2019-Web\_updated.pdf.

Kovacs SD, Mullholland K, Bosch J, Campbell H, Forouzanfar MH, Khalil I, et al.
Deconstructing the differences: a comparison of GBD 2010 and CHERG's approach to
estimating the mortality burden of diarrhea, pneumonia, and their etiologies. BMC Infectious
Diseases. 2015 2015/01/16;15(1):16.

658 32. Federal Ministry of Health Ethiopia. Evidence Synthesis based on DHS key maternal and659 child health and nutrition indicators. 2019.

660 33. Federal Democratic Republic of Ethiopia-Ministry of Health. Mini Demographic and 661 Health Survey 2019. 2019.

Gorrêa RA, José BPS, Malta DC, Passos VMA, França EB, Teixeira RA, et al. Burden of
disease by lower respiratory tract infections in Brazil, 1990 to 2015: estimates of the Global
Burden of Disease 2015 study. Revista brasileira de epidemiologia = Brazilian journal of
epidemiology. 2017 May;20Suppl 01(Suppl 01):171-81. PubMed PMID: 28658381. Epub
2017/06/29. Carga de doença por infecções do trato respiratório inferior no Brasil, 1990 a 2015:
estimativas do estudo Global Burden of Disease 2015. por

668 eng.

Salam RA, Das JK, Bhutta ZA. Current issues and priorities in childhood nutrition,
growth, and infections. The Journal of nutrition. 2015 May;145(5):1116S-22S. PubMed PMID:
25833888. Pubmed Central PMCID: PMC4410495. Epub 2015/04/03. eng.

672 36. Akombi BJ, Agho KE, Hall JJ, Wali N, Renzaho AMN, Merom D. Stunting, Wasting and
673 Underweight in Sub-Saharan Africa: A Systematic Review. International journal of

Page 35 of 57

1

#### **BMJ** Open

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environmental research and public health. 2017 Aug 1;14(8). PubMed PMID: 28788108. 674 Pubmed Central PMCID: PMC5580567. Epub 2017/08/10. eng. 675 37. Ibrahim MK, Zambruni M, Melby CL, Melby PC. Impact of Childhood Malnutrition on 676 Host Defense and Infection. Clinical microbiology reviews. 2017 Oct;30(4):919-71. PubMed 677 PMID: 28768707. Pubmed Central PMCID: PMC5608884. Epub 2017/08/05. eng. 678 679 38. Fantay Gebru K, Mekonnen Haileselassie W, Haftom Temesgen A, Oumer Seid A, Afework Mulugeta B. Determinants of stunting among under-five children in Ethiopia: a 680 multilevel mixed-effects analysis of 2016 Ethiopian demographic and health survey data. BMC 681 Pediatrics. 2019 2019/06/01;19(1):176. 682 39. Dherani M, Pope D, Mascarenhas M, Smith KR, Weber M, Bruce N. Indoor air pollution 683 from unprocessed solid fuel use and pneumonia risk in children aged under five years: a 684 systematic review and meta-analysis. Bulletin of the World Health Organization. 2008 685 May;86(5):390-8C. PubMed PMID: 18545742. Pubmed Central PMCID: PMC2647443. Epub 686

<sup>33</sup> 687 2008/06/12. eng.

688 40. Kurmi OP, Lam KB, Ayres JG. Indoor air pollution and the lung in low- and medium689 income countries. The European respiratory journal. 2012 Jul;40(1):239-54. PubMed PMID:
690 22362845. Epub 2012/03/01. eng.

41. Burnett RT, Pope CA, 3rd, Ezzati M, Olives C, Lim SS, Mehta S, et al. An integrated risk
function for estimating the global burden of disease attributable to ambient fine particulate
matter exposure. Environmental health perspectives. 2014 Apr;122(4):397-403. PubMed PMID:
24518036. Epub 2014/02/13. eng.

695 42. Federal Ministry of Health Addis Ababa E. Health Sector Transformation Plan 2015/16 696 2019/20 (2008-2012 EFY). August 2015.

43. Stenberg K, Hanssen O, Edejer TT-T, Bertram M, Brindley C, Meshreky A, et al. Financing transformative health systems towards achievement of the health Sustainable Development Goals: a model for projected resource needs in 67 low-income and middle-income countries. The Lancet Global Health. 2017;5(9):e875-e87. 44. Vos T, Lim SS, Abbafati C, Abbas KM, Abbasi M, Abbasifard M, et al. Global burden of 369 diseases and injuries in 204 countries and territories, 1990–2019: a systematic analysis for the Global Burden of Disease Study 2019. The Lancet. 2020;396(10258):1204-22. 

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5 6	708	Figure 2: Incidence of lower respiratory infections per 100,000 people in Ethiopia and its
7 8 0	709	regions in 2019.
9 10 11	710	Figure 3: Trend in LRIs age standardized years of life lost rates per 100,000 people in Ethiopia,
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Figure 2: Incidence of lower respiratory infections per 100,000 people in Ethiopia and its regions in 2019.







1990-2019

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2 3	1	Supplementary material to "The burden of lower respiratory infections and associated risk
4	1 2	factors across regions in Ethionia: A subnational analysis of the Global Burden of Diseases
5	2	2019 Study"
7	5	2019 Study
8	4	This supplementary material provides supplemental figures and tables more detailed results for
9 10	5	""The burden of lower respiratory infections and associated risk factors across regions in
10	6	Ethiopia: A subnational analysis of the Global Burden of Diseases 2019 Study"
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24 25	15	1990-2019
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28 29	18	Supplemental Figure 5: Adults older than 70 years mortality rate per 100,000 populations for lower
30	19	respiratory infections in Ethiopia, 1990-2019
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32 33	21	respiratory infections in Ethiopia, 1990-2019
34	22	Supplemental Figure 8: Attribution of the rick factors to LRIs death rate per 100,000 population in all
35	23	age groups between 1990 and 2019 for Ethiopia and its regions, both sexes, number of death, 2019.
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38 39	25	Supplemental Figure 10: Trends in the risk factors between 1990 and 2019 for all ages for Ethiopia8
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53 54	35	for Ethiopia and its regions, both sexes
55	36	Supplemental Table 6: Rate and percentage changes of YLL attributable to LRIs in 1990 and 2019 for
56	37	Ethiopia and its regions, both sexes
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47 Supplemental Figure 2: Children under 5 years of age incidence rate per 100,000 populations due
48 to LRI in Ethiopia, 1990- 2019





# Supplemental Figure 3: Trend in LRIs age-standardized mortality rates per 100,000 people in Ethiopia, 1990-2019



Supplemental Figure 4: Children younger than 5 years mortality rate per 100,000 populations for
 lower respiratory infections in Ethiopia, 1990-2019









Supplemental Figure 7: Adults older than 70 years YLL per 100,000 populations for lower
 respiratory infections in Ethiopia, 1990-2019

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Addis Ababa	1.4	4	0.1	0.1	0.7	0	1.7	0.7	3.7	4.8	0.1	0.4	0.7	1
Oromia	0.6	2.5	2.5	1.9	11.2	0.9	21.6	4.3	2.2	10.3	0.9	0.6	3.5	1.3
Amhara	0.4	2.5	1.8	1.4	6.7	0.9	19.8	3.3	2.4	9.5	0.4	0.6	2.6	0.4
SNNPs	0.8	2.4	2.7	2.2	10.2	1.8	19.9	3.5	1.4	9.6	0.8	0.5	2.9	0.9
Tigray	0.7	3.3	0.8	0.8	4	1.1	17.7	2.8	1.2	9.4	0.3	0.5	2.4	0.4
Harari	1	3.8	0.9	0.7	5.3	0	9.6	2.4	1.1	7.6	0.6	0.6	2.1	3.2
Afar	0.4	2.1	1.8	1.9	8.5	6.3	21	4.5	0.1	9.4	0.9	0.6	3.6	1.4
Somali	0.3	1.6	3.3	3.8	22.2	4.8	31.6	7.2	0.4	13.3	2.5	0.9	5.7	1.8
Benishangul-Gumuz	0.4	3.4	4.5	3.5	20	4.7	27.7	4.9	0.6	13.3	1.3	0.7	4	0.8
Dire Dawa	0.9	3.6	0.7	0.7	5.1	0.4	8.3	2.4	0.5	6.9	0.4	0.5	2	2.1
Gambella	0.8	2.2	0.4	0.4	3.2	2.5	9.3	2.2	0.1	5.4	0.4	0.3	1.9	2.1
Ethiopia	0.6	2.5	2.2	1.8	9.9	1.4	20.5	3.9	1.9	9.9	0.8	0.6	3.2	1



in all age groups between 1990 and 2019 for Ethiopia and its regions, both sexes, number of

78 death, 2019. SNNPs: Southern Nations, Nationalities, and Peoples.

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Addis Ababa	3.63	0.82	0.64	8.35	0.00	1.75	8.86	3.29	4.27	1.32	0.31	7.98
Oromia	6.41	14.75	11.45	67.14	2.34	60.08	25.95	6.05	28.32	5.25	1.66	21.03
Amhara	5.40	13.01	9.84	48.10	2.02	46.86	23.47	5.46	21.99	2.81	1.36	18.88
SNNPs	6.36	16.67	13.77	63.88	5.03	57.68	21.95	4.12	27.49	5.28	1.38	18.31
Tigray	5.03	6.15	5.75	29.88	1.87	29.89	20.59	2.00	15.32	1.91	0.79	17.45
Harari	9.12	7.21	5.80	43.66	0.01	25.51	19.63	2.74	19.30	5.00	1.62	17.18
Afar	4.88	11.42	11.57	52.76	15.77	53.12	28.03	0.26	23.50	5.49	1.33	22.31
Somali	5.40	18.08	20.92	121.83	16.76	110.21	39.76	1.46	46.07	13.99	3.18	31.30
Benishangul-Gumuz	12.63	28.22	22.25	125.72	17.81	105.51	30.75	2.22	50.23	8.05	2.61	24.89
Dire Dawa	9.38	5.50	5.64	42.47	1.11	23.88	19.72	1.42	18.88	3.67	1.50	16.71
Gambella	4.75	3.13	3.08	25.92	6.16	23.51	18.20	0.18	13.02	2.86	0.60	15.31
Ethiopia	6.06	14.39	11.93	64.00	4.28	58.22	25.08	4.73	27.20	5.22	1.58	20.40
Supplemental	l Figure 9. A	ttribut	ion of	the ris	sk fact	ors to	I RIS (	leath r	ate nei	r 100 (	000  po	nulation

Supplemental Figure 9: Attribution of the risk factors to LRIs death rate per 100,000 population
in children younger than 5 years between 1990 and 2019 for Ethiopia and its regions, both sexes,
number of death, 2019. SNNPs: Southern Nations, Nationalities, and Peoples.

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# Tables

Supplemental Table 1: Number and percentage changes of episode attributable to LRIs in 1990 and 2019 for Ethiopia, its regions, both sexes

		All ages		Children younger	than 5 years		People above 70			
Location	Episode,	Episode,	Change,	Episode,	Episode, (95% UI),2019	Change,	Episode,	Episode,	Change,%	
	(95%UI),1990	(95%UI),2019	%	(95%UI),1990		%	(95%UI),1990	(95%UI),2019		
Addis	194122.9(1754	176027.6(162152.3	10	44940.6(35673.3	14522.3(11237-18367.5)	68	8099.5(6891.6-	24034.2(20749.5-	196**	
Ababa	03.8-213856.2)	-190557.8)		-56859.6)			9463.2)	27702.3)		
Oromia	2164243.7(195	2597863.9(237208	20	739239.6(57847	613676.6(480687.2-	17	110627.2(95303.	292179.4(254670.4-	164**	
	7719.5-	9.2-2859925.6)		7-935022.8)	765626.5)		7-129579.9)	342438.5)		
	2397957.9)									
Amhara	1508431.4(136	1400682.4(128532	8	423999.3(33470	261397.4(206754.7-	39	116332.8(98774.	198977.5(173809.4-	71**	
	8059.8-	3-1530939.8)	· · · · ·	0.8-538426.8)	327889.7)		4-137194.5)	229925.5)		
	1671550.1)									
SNNPs	1235554.9(110	1330491.5(121717	7	421825.6(33508	307771.3(248326.4-	28	68084.5(57450-	99723(88168.3-	46**	
	8317.9-	6.7-1452694.1)		7.1-526155.2)	385053.7)		79640.8)	113438)		
	1368520.3)									
Tigray	360795.1(3282	409829.8(376290.4	13	109047.9(86435.	69958.2(55210.7-	36	20653.3(17469.9	62677.2(53933.1-	203**	
	76.3-400714.9)	-445030.2)		2-137691.1)	87468.6)		-24256.6)	72927.6)		
Harari	15145.9(13618.	13765.3(12657-	10	4693.6(3691.4-	2188.4(1723.8-2761.3)	54	307.2(259.6-357)	1614.8(1396-1863.6)	425**	
	9-16851.9)	15054.7)		5990.1)						
Afar	113506.8(1023	113210.3(102987.9	1	32991.6(25672.4	26177.2(20744.1-	21	2640.2(2212.5-	7222.5(6246.8-8559.1)	173**	
	17-126084.3)	-124578)		-42147.6)	32743.3)		3150.9)			
Somali	300306.3(2689	463220.4(420429.8	54	103526.3(81391.	126089.6(99611.9-	21**	6182.3(5316-	30203.2(25942.8-	388**	
	88-336331.8)	-516009.4)		3-131352.8)	160423.3)		7370.4)	35038.5)		
BG	68501.6(61804.	71675.7(64972.1-	4	20970.5(16626.7	18175.6(14339.5-	14	3288.9(2784.8-	4311.3(3743.8-5113.9)	31**	
	9-75736.4)	79105.8)		-26454.5)	22922.1)		3911.4)			
Dire Dawa	30607.1(27359.	26221.1(24010.1-	15	9547.4(7523-	4387.7(3439.6-5583.9)	55	1274.8(1090.1-	2840.1(2469-3289.5)	122**	
	8-34252.2)	28647.8)		12185)			1483.5)			
Gambella	19687.9(17723.	25685.2(23516.6-	30**	6747.7(5338.7-	4335.4(3428.4-5400.9)	36	1568.1(1316.6-	1489.6(1281.4-1737.3)	6	
	9-21945.7)	28093.2)		8613.7)			1825.8)			
Ethiopia*	6010904.2(546	6628673.6(610878	10**	1917530.8(1518	1448680.4(1150089.8-	25	339059.4(29349	725273.3(640315.4-	113**	
	7801.6-	6.2-7230986.3)		850.1-	1799704.4)		1.9-387514.2)	837746.3)		
	6648644.3)			2400978.5)						

SNNP: Southern Nations, Nationalities, and Peoples; BG: Benishangul Gumuz; \*country's estimate; \*\*percentage increase between 1990 and 2019

Change,%

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100,000       Episode per         6UI),1990       100,000 peop         (95%UI),2019         34.2-       6788.1(6285.         7339.1)         525.9-       8659.9(8040.         9411.6)         830-       7716.9(7162         8321.3)         538.6-       8235.5(7670         8846.4)	Ie         Change,%           9         -           1-         40           1-         41           3-         40	Episode per 100,000 people (95% UI),1990 14666.9(11642.4- 18556.9) 22232(17397.2- 28120) 16487.1(13014.7- 22036.6)	Episode per 100,000 people (95% UI),2019 4927.2(3812.5- 6231.8) 9039.4(7080.5- 11277.7) 8061.7(2276.4)	Change,%	Episode per 100,000 people (95% UI),1990 35138(29897.7- 41054.2) 46498.3(40057.6-	Episode per 100,000 people (95% UI),2019 30748.4(26546- 35441.2) 41564.6(36228.7-	Cha 13
34.2-         6788.1(6285.           7339.1)         525.9-           \$659.9(8040.           9411.6)           830-           7716.9(7162)           8321.3)           538.6-           8235.5(7670)           8846.4)	1-     40       1-     41       3-     40	14666.9(11642.4- 18556.9) 22232(17397.2- 28120) 16487.1(13014.7- 22926.6)	4927.2(3812.5- 6231.8) 9039.4(7080.5- 11277.7)	67	35138(29897.7- 41054.2) 46498.3(40057.6-	30748.4(26546- 35441.2) 41564.6(36228.7-	13
525.9- 9411.6) 830- 7716.9(7162.: 8321.3) 538.6- 8235.5(7670.: 8846.4)	1- 41 3- 40	22232(17397.2- 28120) 16487.1(13014.7-	9039.4(7080.5- 11277.7)	<i>c</i> 0	46498.3(40057.6-	41564.6(36228.7-	
830- 830- 7716.9(7162 8321.3) 538.6- 8235.5(7670 8846.4)	3- 40	16487.1(13014.7-	90617(62764	60	54464.4)	48714.4)	11
538.6- 8235.5(7670.: 8846.4)	- 20	20936.6)	8061.7(6376.4-10112.3)	52	43580(37002.4- 51395.2)	35377.7(30902.9- 40880.2)	19
,	5- 39	20106.4(15972- 25079.3)	8427.1(6799.4- 10543.2)	59	44628.1(37657.5- 52203.1)	36616.1(32373.5- 41652)	18
858.2- 9382.3)	38	19185.4(15207- 24224.8)	8342.1(6583.5- 10430.1)	57	43748.4(37005.1- 51381)	40859(35158.8- 47541.2)	7
941- 7190.5(6684. 7718.6)	1- 45	19672.6(15471.9- 25106.9)	6821.6(5373.5- 8607.3)	66	33916.7(28665.1- 39416.7)	32797.4(28354- 37850.7)	4
050.8- 9350.1(8648.8 10157.4)	8- 39	21151.6(16459.1- 27021.7)	9365.5(7421.7- 11714.7)	56	39849(33393.8- 47557.2)	44368.7(38375.2- 52580.1)	11*
538.1- 9220(8515.8- 10046.3)	20	16792.9(13202.4- 21306.6)	10062.7(7949.6- 12802.8)	41	32748.3(28159.7- 39042.1)	41031.2(35243.4- 47600)	25*
481- 9054.6(8394.2 9766)	2- 42	22041.1(17475.5- 27805)	10481.8(8269.5- 13219)	53	42911.6(36334.5- 51032.5)	37592.7(32643.9- 44591.2)	13
807.9- 7148.8(6634.0 7750.7)	6- 44	19968.2(15734.3- 25484.7)	7191.5(5637.6- 9152.1)	64	38333(32779.4- 44607)	32033.6(27847.4- 37101.4)	17
537.4- 7575.8(7002.3 8128.2)	3- 44	21419.8(16947.2- 27343.2)	6791.1(5370.4- 8460.1)	69	40197.8(33751.8- 46803.7)	32657.1(28093.9- 38087.2)	19
540.8- 8313.7(7757.6 8918)	6- 39	19486.4(15434.9- 24399.3)	8685.3(6895.1- 10789.8)	56	44092.2(38166.5- 50393.4)	38394.4(33896.9- 44348.5)	13
	941-         7190.5(6684.           7718.6)         9350.1(8648.)           0050.8-         9350.1(8648.)           10157.4)         638.1-           9220(8515.8-           10046.3)           481-         9054.6(8394.)           9766)           807.9-         7148.8(6634.)           7750.7)             8313.7(7757.)            8918)           :hern Nations, Nationaliti	941- $7190.5(6684.1-$ $7718.6)$ 45050.8-9350.1(8648.8- 10157.4)39638.1-9220(8515.8- 10046.3)20481-9054.6(8394.2- 9766)429766)807.9-7148.8(6634.6- 7750.7)637.4-7575.8(7002.3- 8128.2)448128.2)8313.7(7757.6- 8918)398918)	941-7190.5( $6684.1-$ 7718.6)4519672.6( $15471.9-$ 25106.9)050.8-9350.1( $8648.8-$ 10157.4)3921151.6( $16459.1-$ 27021.7)638.1-9220( $8515.8-$ 10046.3)2016792.9( $13202.4-$ 21306.6)481-9054.6( $8394.2-$ 9766)4222041.1( $17475.5-$ 27805)807.9-7148.8( $6634.6-$ 7750.7)4419968.2( $15734.3-$ 25484.7).637.4-7575.8( $7002.3-$ 8128.2)4421419.8( $16947.2-$ 27343.2).640.8-8313.7( $7757.6-$ 8918)3919486.4( $15434.9-$ 24399.3).hern Nations, Nationalities, and Peoples; BG: Benishangul	941-7190.5(6684.1- 7718.6)4519672.6(15471.9- 25106.9)6821.6(5373.5- 8607.3)050.8-9350.1(8648.8- 10157.4)3921151.6(16459.1- 27021.7)9365.5(7421.7- 11714.7)638.1-9220(8515.8- 10046.3)2016792.9(13202.4- 21306.6)10062.7(7949.6- 12802.8)481-9054.6(8394.2- 9766)4222041.1(17475.5- 27805)10481.8(8269.5- 13219)807.9-7148.8(6634.6- 7750.7)4419968.2(15734.3- 25484.7)7191.5(5637.6- 9152.1)637.4-7575.8(7002.3- 8128.2)4421419.8(16947.2- 27343.2)6791.1(5370.4- 8460.1)640.8-8313.7(7757.6- 8918)3919486.4(15434.9- 24399.3)8685.3(6895.1- 10789.8)thern Nations, Nationalities, and Peoples; BG: Benishangul Gumuz; *country's es	941-7190.5(6684.1- 7718.6)4519672.6(15471.9- 25106.9)6821.6(5373.5- 8607.3)66050.8-9350.1(8648.8- 10157.4)3921151.6(16459.1- 27021.7)9365.5(7421.7- 11714.7)56638.1-9220(8515.8- 10046.3)2016792.9(13202.4- 21306.6)10062.7(7949.6- 12802.8)41481-9054.6(8394.2- 9766)4222041.1(17475.5- 27805)10481.8(8269.5- 13219)53807.9-7148.8(6634.6- 7750.7)4419968.2(15734.3- 25484.7)7191.5(5637.6- 9152.1)64637.4-7575.8(7002.3- 8128.2)4421419.8(16947.2- 27343.2)6791.1(5370.4- 8460.1)69640.8-8313.7(7757.6- 8918)3919486.4(15434.9- 24399.3)8685.3(6895.1- 10789.8)56hern Nations, Nationalities, and Peoples; BG: Benishangul Gumuz; *country's estimate; **pe	941-7190.5(6684.1- 7718.6)4519672.6(15471.9- 25106.9)6821.6(5373.5- 8607.3)33916.7(28665.1- 39416.7)050.8-9350.1(8648.8- 10157.4)3921151.6(16459.1- 27021.7)9365.5(7421.7- 11714.7)39849(33393.8- 47557.2)638.1-9220(8515.8- 10046.3)2016792.9(13202.4- 21306.6)10062.7(7949.6- 12802.8)32748.3(28159.7- 39042.1)481-9054.6(8394.2- 9766)4222041.1(17475.5- 27805)10481.8(8269.5- 13219)42911.6(36334.5- 51032.5)807.9-7148.8(6634.6- 7750.7)4419968.2(15734.3- 25484.7)7191.5(5637.6- 9152.1)38333(32779.4- 444007)637.4-7575.8(7002.3- 8128.2)4421419.8(16947.2- 27343.2)6791.1(5370.4- 8460.1)40197.8(33751.8- 46803.7)640.8-8313.7(7757.6- 8918)3919486.4(15434.9- 24399.3)8685.3(6895.1- 10789.8)44092.2(38166.5- 50393.4)hern Nations, Nationalities, and Peoples; BG: Benishangul Gumuz; *country's estimate; **percentage increase	941-7190.5(6684.1- 7718.6)4519672.6(15471.9- 25106.9)6821.6(5373.5- 8607.3)33916.7(28665.1- 39416.7)32797.4(28354- 37850.7)050.8-9350.1(8648.8- 10157.4)3921151.6(16459.1- 27021.7)9365.5(7421.7- 11714.7)39849(33393.8- 5644368.7(38375.2- 52580.1)633.1-9220(8515.8- 10046.3)2016792.9(13202.4- 21306.6)10062.7(7949.6- 12802.8)32748.3(28159.7- 41031.2(35243.4- 47600)481-9054.6(8394.2- 9766)4222041.1(17475.5- 27805)10481.8(8269.5- 13219)42911.6(36334.5- 51032.5)37592.7(32643.9- 44591.2)807.9-7148.8(6634.6- 7750.7)4419968.2(15734.3- 27343.2)7191.5(5637.6- 9152.1)44607)37101.4)637.4-7575.8(7002.3- 8128.2)4421419.8(16947.2- 27343.2)6791.1(5370.4- 8460.1)40197.8(33751.8- 6932657.1(28093.9- 38087.2)640.8-8313.7(7757.6- 8918)391948.4(15434.9- 24399.3)8685.3(6895.1- 10789.8)44092.2(38166.5- 50393.4)38394.4(33896.9- 44348.5)hern Nations, Nationalities, and Peoples; BG: Benishangul Gumuz; *country's estimate; **percentage increase between 2019 and .

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1				Children vounger then	People above 70 years				
;	All age		~	Ciniuren younger than s					
Location	death, (95% UI),1990	death, (95%UI),2019	Cha nge,%	death, (95% UI), 1990	Death, (95% UI),2019	Cha nge, %	Death , (95%UI),1990	Death, (95%UI),20 19	Cha nge,%
Addis Ababa	2159.3(1731.9-2690.7)	918.8(767.4- 1116.9)	58	1353(981.9-1846.7)	69.1(41.7-107.4)	95	209.5(154.3-291.5)	393.6(320.9 -495.3)	87**
Oromia	40004.4(29432.4-51942.2)	18206.1(15193.3- 21745.4)	55	30614.3(20932.5- 42033.5)	8306.2(5763.5-11611.8)	73	2793.5(2005.1- 3673)	5971.6(483 1.7-7093.4)	113**
Amhara 3	25449.3(20869.5-30724.8)	9525.5(7530.5- 11872.2)	63	17780.1(13674.3- 22720.1)	3079.5(1805.3-4737.3)	83	2717.2(2016.4- 3535.8)	3839.9(302 2.6-4825.6)	41**
SNNPs	26044.7(20108-33017)	9494.7(7713.5- 11649)	-64	20390.6(14627.6- 26712.9)	4326.6(2891.3-6157.2)	79	1771.7(1254.5- 2417.6)	2302.6(186 7.3-2772.8)	29**
Tigray 7	6463.8(5272.1-7762.9)	2551.4(2090.3- 3028.6)	61	4436(3373.5-5736)	564.2(364.9-825)	88	550.8(395.7-749.1)	1209.7(978. 5-1467.8)	119**
Harari 9	336(233.3-448.8)	93.1(73.8-116)	73	273.5(174.1-382.7)	28.8(16.4-44.3)	90	6.9(3.7-11)	34.1(27.1- 41.8)	395**
20Afar 21	1717.5(1300.7-2243.4)	706.2(567.7- 869.6)	-59	1128.9(751.1-1596.7)	284.2(182.5-426)	75	66.9(43.5-102.1)	149.3(117.3 -186.6)	123**
2 <mark>3</mark> omali 23	3603.8(2620-4713.6)	3907.5(3007.4- 4959.4)	#N/A	2811.1(1929.6-3874.8)	2472.2(1695.2-3506.8)	13	150.8(98-222.3)	563.1(433.4 -715.8)	273**
2 <b>4</b> 8G 25	1549.2(1131.1-2097)	619(470.7-803)	61	1204.8(805.6-1703.9)	373(245.3-539.3)	70	74.7(50.3-105.7)	77(61.1- 97.3)	3**
2 <b>D</b> ire Dawa 27	632.3(445.5-830.9)	154.6(120.6- 193.8)	76	518.4(329.5-718.7)	51(27.3-82.9)	91	28.8(20.1-40)	55(44-67.9)	90**
2 <b>&amp;</b> Gambella 29	475.9(328.5-635.7)	123.2(98.2-151.9)	75	398.6(253.7-555.7)	36.4(20.7-57.2)	91	28.8(18.6-41.9)	30.9(24.6- 38.1)	7**
8 <b>Œ</b> thiopia* 31 32	108436.6(87669-132758.3)	46300.7(39515.8- 54642.2)	58	80909.9(62491.6- 103448.8)	19591.8(14018.4-26899)	76	8400.1(6490.3- 10700.9)	14627.6(12 393.7- 16892.8)	74**

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	Age standardized mortality rate per 100,000 p	eople, 2019
Location	Female	Male
Addis Ababa	47(35.5-62.5)	73.6(55-98.3)
Oromia	77.3(62-92.4)	100.3(79.9-123.5)
Amhara	57.9(44.1-73.7)	92.5(70.5-122.1)
SNNPs	79.2(63.5-95.2)	118.8(94.3-146.3)
Tigray	73.2(55.9-93.5)	96.9(74.8-122.3)
Harari	63(49-79.9)	95.7(72.5-123.4)
Afar	112.4(87.3-142.3)	98.7(76.9-127.3)
Somali	88.3(69-111.4)	101.7(77.2-130.7)
Benishangul-Gumuz	109.2(82.6-138.8)	95.8(74.6-124.1)
Dire Dawa	56.2(42.5-71.3)	85.4(67.3-109.5)
Gambella	47.9(34.6-60.1)	120.2(95.6-149.5)
Ethiopia	71.8(60.2-82.9)	100.6(84-121.4)
SNNP: Southern Nations	Nationalities, and Peoples	10

# Supplemental Table 5: Number and percentage changes of YLL attributable to LRIs in 1990 and 2019 for Ethiopia and its regions, both sexes

	all age		Children younger th	an 5 years	People above 70				
	YLL, (95%UI),1990	YLL, (95%UI),2019	Chan	YLL, (95%UI),1990	YLL, (95%UI),2019	Chan	YLL,	YLL,	Chan
			ge,%			ge,%	(95%UI),1990	(95% UI),2019	ge,%
Addis	149543.9(115542.6-	29703.1(23833.4-	81	118961.7(86499.1-	6098.2(3693.1-	95	3131.8(2301.7-	5359.8(4334.8-	71**
Ababa	195437)	36855.7)		162678.7)	9483.3)		4374.6)	6816.8)	
Oromia	3019031.9(2144916.	981808.4(748459.2-	68	2680397.2(1832260.	729313.8(506226.4-	73 📂	44619.5(31636-	78166.1(62837.5	75**
	2-4057496.3)	1278135)		4-3680767.1)	1021016.9)		59105.6)	-93527.9)	
Amhar	1813522.3(1445106.	428277.8(309674.7-	77	1560078.3(1201305.	270909.2(158846-	83	42578.2(31294.7-	50955.1(39726.1	19**
а	4-2246142.2)	583000.2)		4-1993362.8)	416496.1)		56216.9)	-64844.6)	
SNNPs	1993643.3(1489598.	543135.8(405565.6-	73	1785675.1(1284021	380166.4(254486.8-	79	28746.2(20086.2-	31964.4(25673.6	11**
	4-2577052.3)	711397.4)		-2339272.5)	541224.9)		39789.1)	-38778.5)	
Tigray	455613.4(364406.1-	96429.9(74139.8-	79	389399.3(296618.1-	49712.6(32198.3-	88	9207.1(6568.7-	16086.6(12946.2	74**
	569702.1)	122350.5)		504230.2)	72764.9)		12629.1)	-19581.8)	
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4		166880.5)	52178.5)		140018.8)	37426.3)		1722.7)	2395.6)		
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15	SNNP: Southern Nationalities, and Peoples: BG: Benishangul Gumuz: *country's estimate: ** <i>percentage increase between 2019 and 1990</i>										

SNNP: Southern Nations, Nationalities, and Peoples; BG: Benishangul Gumuz; \*country's estimate; \*\*percentage increase between 2019 and 1990

Supplemental Table 6: Rate and percentage changes of YLL attributable to LRIs in 1990 and 2019 for Ethiopia and its regions, both sexes.

18	Supplemental Table 6: Rate and percentage changes of YLL attributable to LRIs in 1990 and 2019 for Ethiopia and its regions, both sexes.											
19	all age			Children younger t	han 5 years		People above 70					
2 <b>9Location</b> 21 22	YLL per 100,000 people,1990	YLL per 100,000 people, 2019	Change,%	YLL per 100,000 people,1990	YLL per 100,000 people, 2019	Change,%	YLL per 100,000 people,1990	YLL per 100,000 people, 2019	Change,%			
2≩Addis 2∕Ababa	6362.2(5161.9- 7847.9)	1285.6(1065- 1561.8)	80	38824.7(28230.1- 53092.4)	6857.1(5545.8- 8721.2)	95	13587(9985.4- 18978.3)	6857.1(5545.8-8721.2)	50			
2 <b>D</b> romia 26	11217.6(8517- 14318)	2433.8(2042.2- 2879.5)	78	80610.7(55103.7- 110696)	11119.7(8939.1- 13305)	87	18754.2(13297.1- 24843)	11119.7(8939.1-13305)	41			
2 <b>A</b> mhara 28	8690.4(7146.3- 10453.8)	2016.4(1551.4- 2541.8)	77	60663.3(46712.5- 77511.5)	9059.7(7063.2- 11529.2)	87	15950.4(11723.4- 21059.7)	9059.7(7063.2- 11529.2)	44			
2 <b>\$</b> NNPs 30	11633(9119.4- 14477.9)	2698.1(2243.5- 3250.2)	77	85114.7(61203.2- 111502.1)	11736.6(9426.7- 14238.6)	88	18842.6(13166.1- 26081)	11736.6(9426.7- 14238.6)	38			
3¶Tigray 32	10346.4(8522.9- 12340.3)	1977.1(1593.9- 2395)	81	68509.3(52185.7- 88712.2)	10486.8(8439.5- 12765.3)	92	19502.8(13914.1- 26751.2)	10486.8(8439.5- 12765.3)	47			
3 <b>3</b> Harari 34	12826.5(9336.5- 16985.4)	2060.4(1595.6- 2623.1)	84	100421.7(63898.7- 140467.8)	9260.4(7338.7- 11340.3)	93	11782.6(6360.4- 19341.1)	9260.4(7338.7- 11340.3)	22			
3∯far 36	10993.5(8520.8- 14193.6)	2824.6(2323- 3414)	74	63570.5(42296.6- 89769)	11867.1(9346- 14716.9)	86	16925.5(10923.7- 26001.7)	11867.1(9346-14716.9)	30			
3≯omali 38	6286.9(4860.5- 7970)	3236.4(2537.4- 4006)	49	40088.1(27543.7- 55109)	10246(7797.8- 13150.6)	57	11953.6(7599.2- 17885.5)	10246(7797.8-13150.6)	15			
<mark>зф</mark> б 40	14965.1(11197.4- 19998.6)	3571.1(2772.4- 4510.7)	76	110847.2(74368- 156588.4)	9541.9(7476.9- 12112.3)	83	16397.3(10917- 23228.5)	9541.9(7476.9- 12112.3)	42			

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)	SINING. SOUTHERIN	Nations, Mational	illes, and	reopies, b0. benisha	igui Guinuz, "cour	illy s esti	male, * percentage incr	ease between 2019 and 19	90
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- ২	This facto mateur				priction y ingeetion	<i>per</i> 100,0	oo population jor the je		percentus
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## Authors contributions

# Providing data or critical feedback on data sources

Semagn Mekonnen Abate, Mesafint Molla Adane, Addis Aklilu, Dejene Tsegaye Alem, Mulusew A Asemahagn, Hunegnaw Abebe, Melaku Ashagrie Belete, Tekleberhan Hailemariam, Tezera Moshago Berheto, Belay Boda Abule Bodicha, Daniel Baza Gargamo, Alemayehu Hailu, Awoke Misganaw, Mohsen Naghavi, Negussie Boti Sidamo, Yonatan Solomon, Shambel Wedajo, Melat Weldemariam, Amanuel Yigezu, Fentabil Getnet, and Yazachew Yismaw.

# Developing methods or computational machinery

Semagn Mekonnen Abate, Tezera Moshago Berheto, Alemayehu Hailu, Mohsen Naghavi, Negussie Boti Sidamo, and Amanuel Yigezu.

# Providing critical feedback on methods or results

Semagn Mekonnen Abate, Mesafint Molla Adane, Gizachew Taddesse Akalu, Addis Aklilu, Dejene Tsegaye Alem, Zeleke Gebru, Mulusew Andualem Asemahagn, Daniel Atlaw, Tewachew Awoke, Hunegnaw Abebe, Melaku Ashagrie Belete, Tekleberhan Hailemariam, Tezera Moshago Berheto, Alemeshet Yirga, Setognal Birara Aychiluhm, Belay Boda Abule Bodicha, Chuchu Churko, Feleke Mekonnen Demeke, Abebaw Alemayehu Desta, Lankamo Ena, Tahir Eyayu, Zinabu Fentaw, Daniel Baza Gargamo, Mesfin Damtew Gebrehiwot, Mathewos Alemu Gebremichael, Melaku Getachew, Ababi Zergaw, Alemayehu Hailu, Getahun Molla, Awoke Misganaw, Mohsen Naghavi, Biniyam Sahiledengle, Bereket Beyene, Migbar Sibhat, Negussie Boti Sidamo, Damtew Damtew Solomon, Yonatan Solomon, Birhanu Wagaye, Shambel Wedajo, Melat Weldemariam, Amanuel Yigezu, Fentabil Getnet, and Yazachew Yismaw.

# Drafting the work or revising is critically for important intellectual content

Semagn Mekonnen Abate, Gizachew Taddesse Akalu, Mulusew A Asemahagn, Daniel Atlaw, Niguss Cherie Bekele, Melaku Ashagrie Belete, Tezera Moshago Berheto, Setognal Birara Aychiluhm, Belay Boda Abule Bodicha, Chuchu Churko, Tahir Eyayu, Zinabu Fentaw, Daniel Baza Gargamo, Melaku Getachew, Ababi Zergaw, Firehiwot Abebe Gobena, Muluken Argaw Haile, Alemayehu Hailu, Solomon Tessema Memirie, Awoke Misganaw, Mohsen Naghavi, Biniyam Sahiledengle, Bereket Beyene, Negussie Boti Sidamo, Yonatan Solomon, Dereje Mengistu Tolosa, Birhanu Wagaye, Ally Walker, Amanuel Yigezu, and Fentabil Getnet.

# Managing the estimation or publications process

Semagn Mekonnen Abate, Awoke Misganaw, Mohsen Naghavi, Negussie Boti Sidamo, and Amanuel Yigezu.

# STROBE Statement-checklist of items that should be included in reports of observational studies

	Item No.	Recommendation	Page No. (Line No.)
Title and abstract	1	(a) Indicate the study's design with a commonly used term in the title or the abstract	1 (1-2)
		(b) Provide in the abstract an informative and balanced summary of what was done and what was	4 and 5 (73-
		found	89)
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	7 (140-147)
Objectives	3	State specific objectives, including any prespecified hypotheses	7 ( 148-153)
Methods		6	
Study design	4	Present key elements of study design early in the paper	10 (194-214)
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure,	8 and 9 (175-
		follow-up, and data collection	192)
Participants	6	(a) Cohort study—Give the eligibility criteria, and the sources and methods of selection of	
		participants. Describe methods of follow-up	
		Case-control study—Give the eligibility criteria, and the sources and methods of case	
		ascertainment and control selection. Give the rationale for the choice of cases and controls	
		Cross-sectional study-Give the eligibility criteria, and the sources and methods of selection of	8 and 9 (175-
		participants	192)
		(b) Cohort study—For matched studies, give matching criteria and number of exposed and	
		unexposed	
		Case-control study—For matched studies, give matching criteria and the number of controls per	
		case	
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers.	9 and 10 (194-
		Give diagnostic criteria, if applicable	214)
Data sources/	8*	For each variable of interest, give sources of data and details of methods of assessment	8 and 9 (175-
measurement		(measurement). Describe comparability of assessment methods if there is more than one group	192)
Bias	9	Describe any efforts to address potential sources of bias	10 (211-214)
Study size	10	Explain how the study size was arrived at	8 (175-184)

Continued on next page

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Quantitative	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which	9 (200-206)	
variables		groupings were chosen and why		
Statistical	12	(a) Describe all statistical methods, including those used to control for confounding	9 (200-206)	
methods		(b) Describe any methods used to examine subgroups and interactions	10 (211-214)	
		(c) Explain how missing data were addressed	9 and 10	
			(194-214)	
		(d) Cohort study—If applicable, explain how loss to follow-up was addressed		
		Case-control study—If applicable, explain how matching of cases and controls was addressed		
		Cross-sectional study—If applicable, describe analytical methods taking account of sampling		
		strategy		
		( <u>e</u> ) Describe any sensitivity analyses	10 (211-214)	
Results				
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined	10 (216-221)	
		for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed		
		(b) Give reasons for non-participation at each stage		This is a population level
		(c) Consider use of a flow diagram		
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on	7 and 8	Described in the method sect
		exposures and potential confounders	(156-168)	
		(b) Indicate number of participants with missing data for each variable of interest		This is a population level s
		(c) <i>Cohort study</i> —Summarise follow-up time (eg, average and total amount)	12-19 (255-	
			361	
Outcome data	15*	Cohort study—Report numbers of outcome events or summary measures over time		
		Case-control study-Report numbers in each exposure category, or summary measures of exposure		
		Cross-sectional study-Report numbers of outcome events or summary measures	12-19 (255-	
			361	
Main results	16	(a) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision	12-19 (255-	
		(eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were	361	
		included		
		(b) Report category boundaries when continuous variables were categorized	12-19 (255-	
			361	
		(c) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time		
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Other analyses	17	Report other analyses done-eg analyses of subgroups and interactions, and sensitivity analyses	12-19 (255-
			361
Discussion			
Key results	18	Summarise key results with reference to study objectives	19 (363-
-			371)
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss	23 and 24
		both direction and magnitude of any potential bias	(461-471)
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of	19-23 (373-
		analyses, results from similar studies, and other relevant evidence	460)
Generalisability	21	Discuss the generalisability (external validity) of the study results	24 (475-
			486)
Other information	on		
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the	25 (506-
C		original study on which the present article is based	508)
*Give informatio Note: An Explan- checklist is best u	n sep ation 1sed i	parately for cases and controls in case-control studies and, if applicable, for exposed and unexposed groups and Elaboration article discusses each checklist item and gives methodological background and published n conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmed	in cohort and cross-sectional studies. examples of transparent reporting. The STRO licine.org/, Annals of Internal Medicine at
*Give informatio <b>Note:</b> An Explan- checklist is best u http://www.annal	n sep ation ised i	arately for cases and controls in case-control studies and, if applicable, for exposed and unexposed groups and Elaboration article discusses each checklist item and gives methodological background and published n conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmec /. and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at w	in cohort and cross-sectional studies. examples of transparent reporting. The STROP licine.org/, Annals of Internal Medicine at ww.strobe-statement.org.
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