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Perspective

Monitoring the mortality impact of COVID-19 in Europe: What can be learned from 2009 influenza H1N1p mortality studies?

Lisa Staadegaard[a], Robert J. Taylor[b], Peter Spreeuwenberg[a], Saverio Caini[a], Lone Simonsen[c], John Paget[a,*]

[a] Netherlands Institute for Health Services Research (Nivel), Utrecht, The Netherlands
[b] Independent Consultant, Portland, ME, USA
[c] Roskilde University, Roskilde, Denmark

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ABSTRACT

Objectives: Understanding the proportion of pandemic deaths captured as 'laboratory-confirmed' deaths is crucial. We assessed the ability of laboratory-confirmed deaths to capture mortality in the EU during the 2009 pandemic, and examined the likelihood that these findings are applicable to the SARS-CoV-2 pandemic.

Methods: We present unpublished results from the Global Pandemic Mortality (GLaMOR) project, in which country-specific mortality estimates were made for the 2009 influenza H1N1p pandemic. These estimates were compared with laboratory-confirmed deaths during the 2009 pandemic to estimate the ability of surveillance systems to capture pandemic mortality.

Results: For the 2009 influenza H1N1p pandemic, we estimated that the proportion of true pandemic deaths captured by laboratory-confirmed deaths was approximately 67%. Several differences between the two pandemics (e.g. age groups affected) make it unlikely that this capture rate will be equally high for SARS-CoV-2.

Conclusion: The surveillance of laboratory-confirmed deaths in the EU during the 2009 pandemic was more accurate than previously assumed. We hypothesize that this method is less reliable for SARS-CoV-2. Near-real-time excess all-cause mortality estimates, routinely compiled by EuroMOMO, probably offer a better indicator of pandemic mortality. We urge more countries to join this project and that national-level absolute mortality numbers are presented.

Background

On March 11, 2020 the World Health Organization (WHO) characterized COVID-19, caused by SARS-CoV-2, as a global pandemic (WHO, 2020a). Understanding the pandemic's mortality impact is critical to the public health response. It is clear that the number of laboratory-confirmed deaths is growing rapidly, but it is not clear what proportion of the true number of pandemic deaths the laboratory-confirmed count represents, because some deaths caused by the virus may instead be attributed to underlying diseases, while others may be attributed to COVID-19 without laboratory confirmation.

Similar questions arose during the 2009 H1N1p influenza pandemic (WHO, 2009; Briand et al., 2011). Countries were asked to report laboratory-confirmed pandemic cases and deaths to WHO (Briand et al., 2011). Such data are not typically used to monitor seasonal influenza activity. Instead, most European countries monitoring influenza cases rely on syndromic community- and/or hospital-based surveillance systems and laboratory data (Paget et al., 2007). Retrospective data analyses periodically assess the mortality impact of seasonal influenza at a country, regional, and global level (Iuliano et al., 2018; Paget et al., 2019).

During the H1N1p pandemic, ECDC published a daily update of laboratory-confirmed H1N1p cases and deaths (ECDC, 2009). Two later publications (Dawood et al., 2012; Simonsen et al., 2013), using different methods to estimate the regional and global mortality burden of H1N1p, concluded that only about 10% of the true global excess mortality burden had been captured by directly counting laboratory-confirmed pandemic deaths. One of these studies, the WHO-funded Global Influenza Mortality Burden project (GLaMOR) project, applied a multivariate linear regression model to estimate respiratory pandemic excess mortality in 21 global countries (including eight from the EU), and used these to

* Corresponding author. Present address: Nivel, Otterstraat 118, 3513 CR, Utrecht, The Netherlands.
E-mail address: j.paget@nivel.nl (J. Paget).

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impute the respiratory mortality burden for all world countries in order to generate regional and global mortality burden estimates (Simonsen et al., 2013).

Here we compare the GLaMOR country-level estimates for the EU (including the UK) with the laboratory-confirmed H1N1p deaths reported to ECDC through January 2010. We discuss these findings in the context of the debate about laboratory-confirmed COVID-19 deaths and the current pandemic's true mortality burden.

Findings

The final 2009 WHO H1N1p pandemic update, published on August 6, 2010, stated that 18 449 laboratory-confirmed pandemic A(H1N1) deaths had been reported globally (WHO, 2010). In contrast, the GLaMOR project put the number of influenza-associated respiratory excess deaths about an order of magnitude higher, at 123 000–203 000 globally (Simonsen et al., 2013). This was in broad agreement with the second excess mortality modeling study by CDC, estimating 201 200 (105 700–395 600) associated respiratory deaths, with an additional 83 300 (46 000–179 900) associated cardiovascular deaths (Dawood et al., 2012). These estimates show that laboratory-confirmed mortality surveillance only captured approximately 10% of all global H1N1p-associated mortality and thus greatly underestimated the actual burden.

Though not previously published, the GLaMOR project generated single-country estimates. These add up to an estimated 3369 (range 2695–4031) influenza-associated deaths in the EU (including the UK). As of January 18, 2010, ECDC had recorded a total of 2269 laboratory-confirmed H1N1p deaths in the EU, of which half were from four countries: UK (16%), France (13%), Spain (12%) and Italy (9%) (ECDC, 2010). For the entire EU region, national laboratory-based mortality surveillance captured 67% of these pandemic deaths, showing wide variation between countries, with agreement ranging from –80% to +47% (Table 1).

Discussion

Our analysis shows that laboratory-confirmed H1N1p deaths in Europe were not wildly different from excess mortality estimates, despite variability between EU countries. In the case of the ongoing SARS-CoV-2 pandemic, however, there are reasons to believe that laboratory-confirmed death surveillance may be a less accurate estimate of COVID-19 mortality. First, the sheer scale of the current pandemic is far larger: November 11, 2020, 254 459 COVID-19 deaths had been reported to ECDC, compared with 2269 deaths overall during the H1N1p pandemic (ECDC, 2010, 2020). The age groups with the highest mortality are also different, which might cause serious case ascertainment issues. For example, a recent study estimated that in five EU countries (Belgium, France, Ireland, Norway, and Spain) approximately 42–57% of COVID-19 deaths have occurred in 'care homes', where testing appears to occur less systematically (Comas-Herrera et al., 2020); interestingly, in Belgium all deaths of those previously experiencing clinical COVID-19 symptoms in nursing homes have been attributed to COVID-19 without laboratory confirmation (Sciensano, 2020). Meanwhile, shortages have prevented widespread testing of suspected deaths, as urged by WHO (WHO, 2020b). Together, these factors are likely to cause a far lower capture rate for COVID-19 deaths in the confirmed tally, and inconsistent measurement across the EU region (Leon et al., 2020). Though the progressive increase in testing capacity for contact tracing purposes could introduce important time-dependent biases in mortality surveillance, it may have also raised the proportion of deaths captured, which could lead to more reliable figures over time.

Optimal public health policies in response to the pandemic are of the highest importance, and accurate COVID-19 burden estimates (including deaths) are essential for making the best possible decisions. Currently, most populations are still susceptible, and with no vaccine the economic disruption of the measures currently available to contain the spread of the infection (i.e. more or less restrictive social distancing) will bring a huge socio-economic cost.

Table 1
Number of deaths in the EU during the 2009 influenza pandemic and the estimated net capture rate.

	Country	Respiratory deaths (<65 and 85% rule)[a]	Laboratory-confirmed deaths (2009 pandemic)	Net capture
European Union	Austria	74	24	–67%
	Belgium	86	17	–80%
	Bulgaria	126	35	–72%
	Croatia	34	26	–23%
	Czechia	105	77	–27%
	Denmark	43	30	–29%
	Finland	31	41	+31%
	France	224	290	+30%
	Germany	205	178	–13%
	Greece	141	93	–33%
	Hungary	136	57	–58%
	Ireland	39	22	–43%
	Italy	489	210	–57%
	Latvia	26	31	+18%
	Lithuania	53	19	–64%
	Netherlands	133	54	–59%
	Poland	260	138	–47%
	Portugal	105	83	–21%
	Romania	425	107	–75%
	Slovakia	65	38	–42%
	Spain	208	271	+31%
	Sweden	70	25	–64%
	UK	246	362	+47%
	Other[b]	48	41	+17%
	Total	3369	2269	–33%

[a] Lower-bound 2009 estimate determined by proportionally projecting the under-65 age group estimate to all ages, using data from laboratory surveillance indicating that 85% of confirmed pandemic deaths occurred in the under 65 age group (Simonsen et al., 2013).
[b] Countries with fewer than 20 estimated deaths during the 2009 pandemic (Cyprus, Estonia, Luxembourg, Malta, Slovenia).

If the laboratory-confirmed count is inadequate, other timely data on SARS-CoV-2 mortality are needed. This is where studies of excess all-cause mortality can help. Several studies in Italy and Spain have shown large numbers of excess deaths in certain cities and regions (Economist, 2020). While the number of laboratory-confirmed deaths is dependent on testing capacity and policy choices, all-cause mortality is free of such bias, as it is consistently registered for all deaths. The excess mortality approach has its own limitations and can overestimate the mortality burden attributed to the virus (Li et al., 2018). However, excess all-cause mortality calculated in a timely fashion potentially provides the most objective estimate of the mortality burden of a pandemic. If all-cause mortality suddenly far exceeds the historical baseline when the pandemic arrives, as it has during the COVID-19 period, one can be reasonably sure the pandemic is to blame.

Fortunately, the EuroMOMO network, based at the Statens Serum Institut in Copenhagen, collects timely age-specific mortality data from 24 European countries on a weekly basis. Created in 2009, both to monitor seasonal influenza mortality and for pandemic preparedness and response (Mazick et al., 2010), EuroMOMO publishes aggregate numbers of deaths for the entire region, adjusted for incomplete data. These timely estimates, created using a common mathematical algorithm, are standardized and presented with z-scores. This is a major asset, allowing for comparison of weekly differences across countries (EuroMOMO, no date).

The EuroMOMO surveillance system is a valuable resource for understanding pandemic mortality. For example, the data show clearly that no excess mortality is observable in children and young adults. Because EuroMOMO uses a common mathematical algorithm to compute the COVID-19 burden for Europe, measures of excess mortality and impact are standardized and can be compared across countries. This standardization allows calculation and plotting of z-score graphs to easily see which countries have experienced high COVID-19 mortality and which have not.

It is of great public health interest to see how these differences between countries evolve over the following weeks and months, and on this basis we encourage all WHO Euro countries to contribute mortality data to EuroMOMO. Furthermore, we urge participating countries to explore the possibility of allowing EuroMOMO to present absolute mortality numbers and population rates (per 100 000) for individual countries, which would be of considerable added value (Leon et al., 2020). Doing so could provide public health and government policy makers with useful insights as they seek to manage the COVID-19 pandemic's terrible human and economic burden.

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Conflicts of interest

LSt, RT, SC, LSi, and PS declare no competing interests. JP declares that Nivel has received unrestricted research grants from WHO, Sanofi Pasteur, and the Foundation for Influenza Epidemiology.

Ethical approval

None required.

References

Briand S, Mounts A, Chamberland M. Challenges of global surveillance during an influenza pandemic Available at: https://www.who.int/influenza/surveillance_monitoring/Challenges_global_surveillance.pdf [Accessed 23 March 2020]. 2011.

Comas-Herrera A, Zalakaín J, Lemmon E, Henderson D, Litwin C, Hsu AT, et al. Mortality associated with COVID-19 outbreaks in care homes: early international evidence Available at: https://ltccovid.org/wp-content/uploads/2020/06/Mortality-associated-with-COVID-21-May-1.pdf [Accessed 20 April 2020]. LTCcovid.org; 2020.

Dawood FS, Iuliano AD, Reed C, Meltzer MI, Shay DK, Cheng PY, et al. Estimated global mortality associated with the first 12 months of 2009 pandemic influenza A H1N1 virus circulation: a modelling study. Lancet Infect Dis 2012;12(9):687–95, doi:http://dx.doi.org/10.1016/S1473-3099(12)70121-4.

ECDC. Timeline on the pandemic (H1N1) 2009 Available at: https://www.ecdc.europa.eu/en/seasonal-influenza/2009-influenza-h1n1-timeline [Accessed 30 March 2020]. 2009.

ECDC. 2009 influenza A (H1N1) pandemic — daily update (18 January 2010). 2010.

ECDC. COVID-19 situation update for the EU/EEA and the UK, as of 12 November 2020 Available at: https://www.ecdc.europa.eu/en/cases-2019-ncov-eueea [Accessed 12 November 2020]. 2020.

Economist. Fatal flaws — Covid-19's death toll appears higher than official figures suggest Available at: https://www.economist.com/graphic-detail/2020/04/03/covid-19s-death-toll-appears-higher-than-official-figures-suggest [Accessed 9 April 2020]. 2020.

http://www.euromomo.eu/EuroMOMO (no date). Available at: [Accessed 23 March 2020].

Iuliano AD, Roguski KM, Chang HH, Muscatello DJ, Palekar R, Tempia S, et al. Estimates of global seasonal influenza-associated respiratory mortality: a modelling study. Lancet 2018;391(10127):1285–300, doi:http://dx.doi.org/10.1016/S0140-6736(17)33293-2.

Leon DA, Shkolnikov VM, Smeeth L, Magnus P, Pechholdová M, Jarvis CI, et al. COVID-19: a need for real-time monitoring of weekly excess deaths. Lancet 2020;e81, doi:http://dx.doi.org/10.1016/S0140-6736(20)30933-8.

Li L, Wong JY, Wu P, Bond HS, Lau EHY, Sullivan SG, et al. Heterogeneity in estimates of the impact of influenza on population mortality: a systematic review. Am J Epidemiol 2018;187(2):378–88, doi:http://dx.doi.org/10.1093/aje/kwx270.

Paget J, Marquet R, Meijer A, van der Velden K, et al. Influenza activity in Europe during eight seasons (1999–2007): an evaluation of the indicators used to measure activity and an assessment of the timing, length and course of peak activity (spread) across Europe. BMC Infect Dis 2007;7(1):141, doi:http://dx.doi.org/10.1186/1471-2334-7-141.

Mazick A, Gergonne B, Wuillaume F, Danis K, Vantarakis A, Uphoff H, et al. Higher all-cause mortality in children during autumn 2009 compared with the three previous years: pooled results from eight European countries. Eurosurveillance 2010;15(5):1–4, doi:http://dx.doi.org/10.2807/ese.15.05.19480-en.

Paget J, Spreeuwenberg P, Charu V, Taylor RJ, Iuliano AD, Bresee J, et al. Global mortality associated with seasonal influenza epidemics: new burden estimates and predictors from the GLaMOR project. J Glob Health 2019;9(2):1–12, doi:http://dx.doi.org/10.7189/jogh.09.020421.

Sciensano. COVID-19-EPIDEMIOLOGISCH BULLETIN VAN 5 MEI 2020 Available at: https://epistat.wiv-isp.be/covid [Accessed 6 May 2020]. 2020.

Simonsen L, Spreeuwenberg P, Lustig R, Taylor RJ, Fleming DM, Kroneman M, et al. Global mortality estimates for the 2009 influenza pandemic from the GLaMOR project: a modeling study. PLoS Med 2013;10(11)e1001558, doi:http://dx.doi.org/10.1371/journal.pmed.1001558.

WHO. World now at the start of 2009 influenza pandemic. World Health Organization; 2009 Available at: https://www.who.int/mediacentre/news/statements/2009/h1n1_pandemic_phase6_20090611/en/#:~:te [Accessed 30 March 2020].

WHO. Pandemic (H1N1) 2009 — update 112. World Health Organization; 2010 Available at: https://www.who.int/csr/don/2010_08_06/en/ [Accessed 23 March 2020].

WHO. WHO Director-General's opening remarks at the media briefing on COVID-19–11 March 2020 Available at: https://www.who.int/dg/speeches/detail/who-director-general-s-opening-remarks-at-the-media-briefing-on-covid-19—11-march-2020 [Accessed 23 March 2020]. 2020.

WHO. WHO Director-General's opening remarks at the media briefing on COVID-19–16 March 2020 Available at: https://www.who.int/dg/speeches/detail/who-director-general-s-opening-remarks-at-the-media-briefing-on-covid-19—16-march-2020 [Accessed 7 April 2020]. 2020.