The Role of Age Distribution, Time Lag Between Reporting and Death, and Healthcare System Capacity in Case Fatality Estimates of COVID-19

P. Vanella[1,2,3], C. Wiessner[4], A. Holz[4], G. Krause[1,2,5], A. Möhl[4], S. Wiegel[4], B. Lange[1,2,5], H. Becher[4]

[1] Epidemiology Department, Helmholtz Centre for Infection Research (HZI), Brunswick, Germany

[2]Hannover Biomedical Research School (HBRS), Hannover, Germany

[3]Chair of Empirical Methods in Social Science and Demography, University of Rostock, Rostock, Germany

[4]Institute of Medical Biometry and Epidemiology, University Medical Center Hamburg-Eppendorf (UKE), Hamburg, Germany

[5]German Center for Infection Research (DZIF), Brunswick, Germany

Motivation

- Case fatalities of COVID-19 reported in different countries vary
- Case Fatality Risk (CFR) estimated by dividing cumulative number of deaths by cumulative number of cases
- CFR estimates known to be biased
- CFR estimates are influenced by factors influencing the actual lethality and those biasing the estimates

Factors influencing CFR Estimates

- Factors influencing lethality:
  - Population structure: Higher CFR given an older population with a higher load of comorbidities
  - Healthcare system: Higher CFR due to a low healthcare capacity in connection with additional demand for intensive care beds during a pandemic
- Factors that bias CFR estimate:
  - Surveillance and testing:
    - A Overestimation of CFR due to undercounting of infections because of poor surveillance and poor testing capacities
    - B Underestimation of CFR due to low capacities and poor methods to record age-specific deaths, resulting in an undercounting of deaths due to the specific disease
    - C Overestimation of CFR, if deaths are attributed to the specific disease, regardless of the actual cause of death
  - Time Lags: Underestimation of CFR due to ignoring the time between infection and death (some cases did not have "the time to die yet")

Aims

1. Quantify the difference in during-epidemic case fatality due to COVID-19 between the countries Germany, Italy, France, and Spain attributed to differences in the age structure among the reported cases
2. Investigate the time lag between case reporting and death and its effect on CFR estimation
3. Discuss the association between CFR and the healthcare system capacity

Crude CFRs of GER,ITA,FRA,ESP

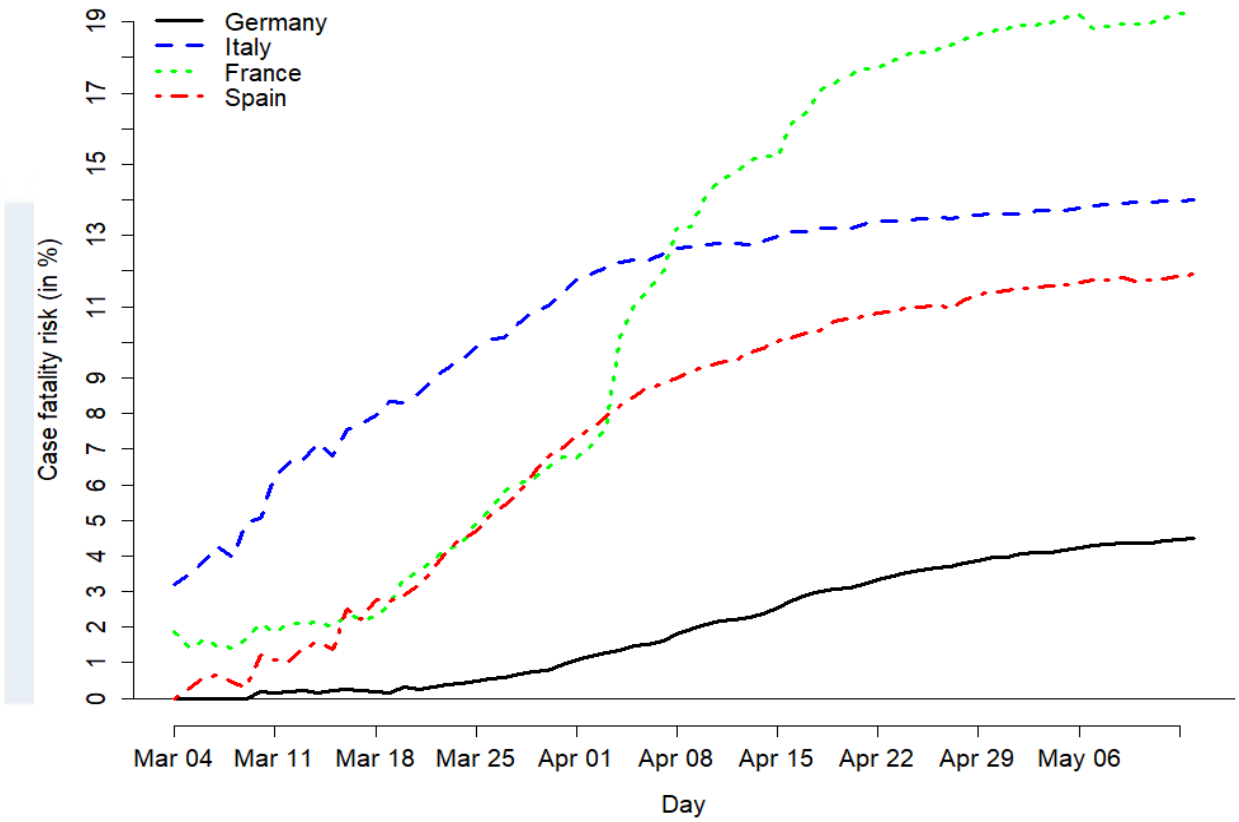

Figure 1: Crude Case Fatality Risk Estimates due to COVID-19 between March 4^{th} and May 14^{th}, 2020 (Sources: European Centre for Disease Prevention and Control; Own computation and design)

Data

- Study period was early phase of the pandemic in Europe, namely March 4^{th} to May 14^{th}, 2020
- Aim 1:
  - Weekly official reports on COVID-19 specific cases and deaths by age groups for Germany (Robert Koch Institut), Italy (Istituto Superiore di Sanità), France (Santé publique France), and Spain (Instituto de Salud Carlos III)
  - European Standard Population (Federal Health Reporting)
- Aim 2:
  - Daily Case and Death Numbers for the Study countries provided by European Centre for Disease Prevention and Control (ECDC)
- Aim 3:
  - Estimates of the available critical care beds from OECD
  - Daily estimates of hospitalizations and needed critical care beds for COVID-19 patients from Institute for Health Metrics and Evaluation (IHME)

Methods I

- Aim 1:
  1. Calculate crude weekly age group-specific CFR CFR_{ijk} for age group i, country j, and day k:

$$CFR_{ijk} = \frac{d_{ijk}}{n_{ijk}} \tag{1}$$

with

- d_{ijk} being the cumulated number of deaths in age group i in country j on day k,
- n_{ijk} being the corresponding number of cases

  2. Compute age-standardized CFR by weighting CFR_{ijk} with population weights w_i:

$$\widetilde{CFR}_{jk} = \sum_i w_i \cdot CFR_{ijk} \tag{2}$$

  3. Divide $\widetilde{CFR}_{jk}$ of Italy, France in Spain by Germany's to receive age-standardized CFR ratios

Methods II

- Aim 2:
  1. Calculate CFR for cases lagged by Δ days:

$$CFR_{k,\Delta} = \frac{d_{.jk}}{n_{.jk-\Delta}} \tag{3}$$

     for $\Delta = 0, .., 10$
  2. Graphically determine values of Δ, for which $CFR_{k,\Delta}$ appears to converge to the final CFR

Methods III

- Aim 3:
  1. Define Daily hospitalization fatality:

$$H_{jk} = \frac{\delta_{jk}}{\sum_{\kappa=k-14}^{k} h_{j\kappa}} \tag{4}$$

     with
     - δ_{jk} being the number of deaths on day k,
     - $h_{j\kappa}$ being the number of hospitalizations on day j
  2. Graphically investigate association of H_{jk} with demand and supply of intensive care unit capacity of said country

Results of Aim 1

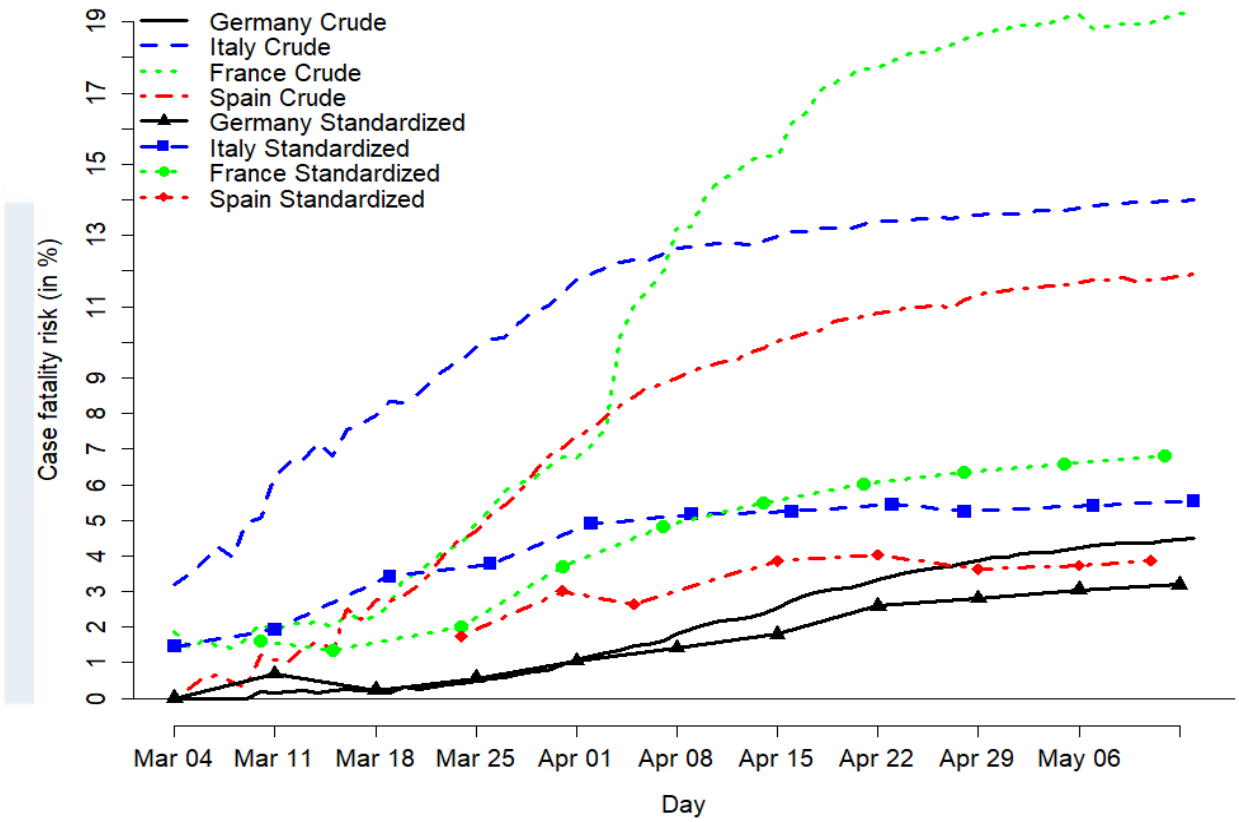

Figure 2: Crude and age-standardized CFR estimates (Sources: Robert Koch Institut; Istituto Superiore di Sanità; Santé publique France; Istituto de Salud Carlos III; GBE-Bund; Own computation and design)

Results of Aim 2

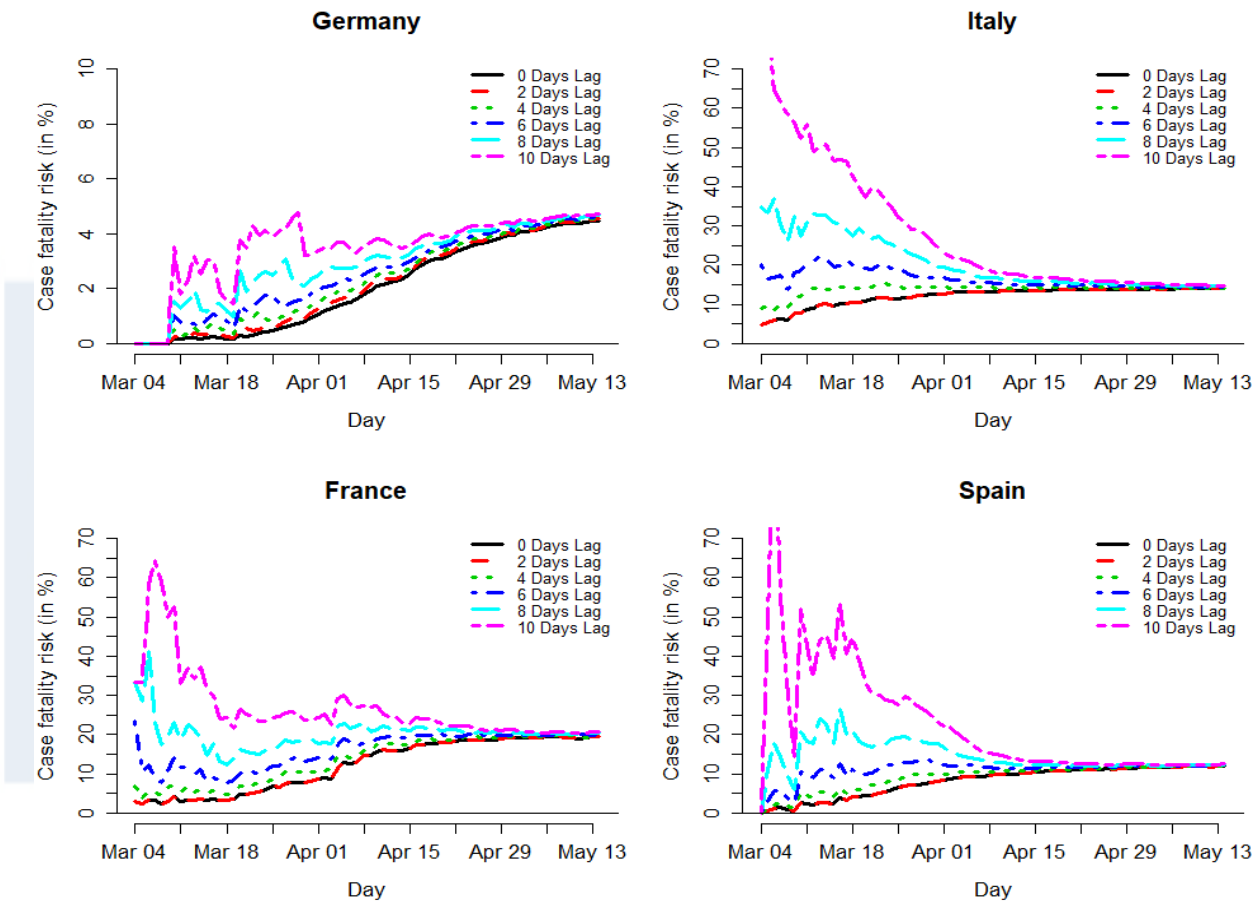

Figure 3: Crude CFR estimates for Germany, Italy, France and Spain with different time lags (Sources: ECDC; Own computation and design)

Results of Aim 3

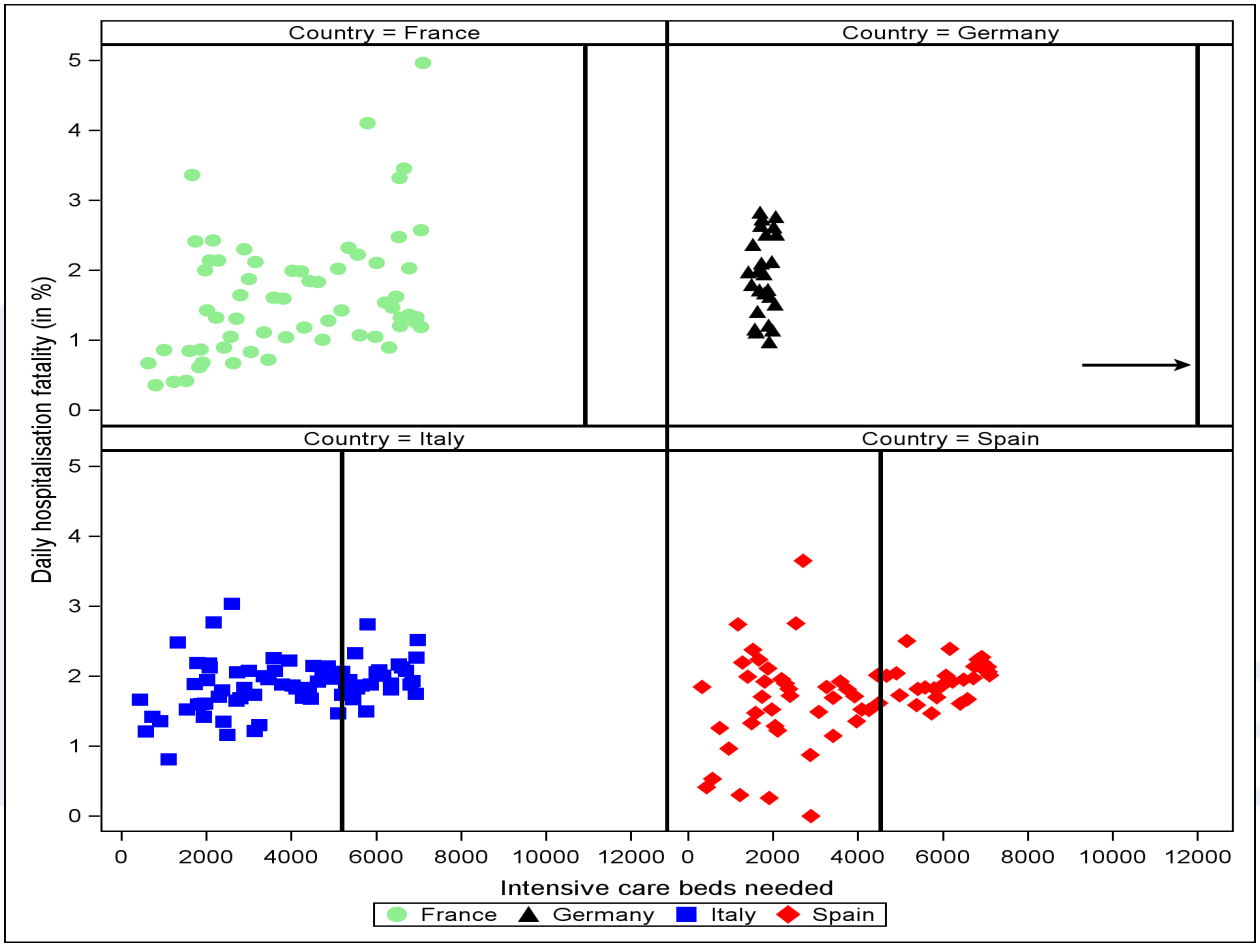

Figure 4: Daily hospitalization fatality relative to intensive care beds needed for COVID-19 patients (Sources: ECDC; OECD; IHME; Own computation and design)

Discussion

- Large proportion of international differences in CFR attributed to demographics of cases
- CFR estimates strongly biased at peak phases of pandemic due to lags between reporting and death
- Slight evidence for association between ICU capacity and fatality of hospitalized cases, when demand is close to or even exceeds available bed capacities; needs further investigation
- Others factors not investigated here might explain differences to some extent as well
  - Environmental factors
  - Differences in overall mortality between countries
  - Surveillance system capacities for COVID-19, e.g., underestimation of cases due to underdetection of asymptomatic or mild cases
  - Not all tests show the same sensitivity
  - Capacities for lab tests at peak times exceeded

Limitations

- Detailed age-specific data on cases and deaths for many countries not available at all or not regularly, especially during early phase of pandemic
- Even if so, age groups mostly very rough and not consistent among different countries
- No joint analysis with comorbidities due to a lack of information in the data
- Information on needed ICU beds not combined with demographics of the patients
- Data on daily healthcare capacities for COVID-19 patients not available, thus approximation by OECD data
- Case detection ratio unknown

Outlook

- Update of analysis looming
- Study period?
- Adjust analyses by weekly test data, which in the meantime has been published
- Merge separate analyses into one regression analysis
- Add stochastic elements to the deterministic analysis we have conducted thus far

Thanks for your attention!

Questions or Remarks?

patrizio.vanella@helmholtz-hzi.de