

Dangerous to claim “no clear association” between intergenerational relationships and COVID-19

Jennifer Beam Dowd^{a,b,1}, Per Block^{a,b}, Valentina Rotondi^{a,b}, and Melinda C. Mills^{a,b}

Arpino et al. (1) report the failure of aggregate data to show an association between intergenerational relationships (IR) and COVID-19 mortality. We hypothesized that high mortality in countries like Italy may stem from the interaction of early infection seeding, high levels of IR, and older population age structures (2). High levels of IR alone are not sufficient to drive mortality, and thus the analyses by Arpino et al. do not provide a test of this hypothesis.

First, initial infection seeding is a necessary precondition for any association between IR and COVID-19 mortality. At the extreme of no infections, no level of IR contact could spread it. Initial community seeding is partly random; some transmission chains die and others are amplified by superspreading (3). Initial seeding of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) was strongly connected to international travel hubs like Milan and New York City (3, 4). Greece has similarly high levels of IR compared to Italy (5) but was not seeded at the same time. Similarly, within Italy, Lombardy was heavily affected by early infections while other regions remained relatively untouched prior to lockdown. Given these dynamics, there is no reason to expect aggregate-level correlations between IR and COVID-19 mortality.

Additionally, the choice of the case fatality rate (CFR)—deaths over confirmed cases—as the outcome of interest is questionable since it differs strongly with age, age structure, and testing across populations (2, 6). CFRs reported by ref. 1 range from 2.35 to 18.52% between European countries and 4.74 to 18.30% between Italian regions—numbers hard to explain without considering testing. Furthermore, CFR conceptually

measures lethality of infection rather than deaths/population and thus does not reflect overall mortality burden. CFRs can be identical across countries with both very high and low deaths. If used as a proxy for a high proportion of older deaths, it is crude and potentially biased; deaths or excess deaths per population are preferable (7).

Finally, the authors report a negative correlation between IR and CFR within Italy. Besides the differences in initial infections by region mentioned above, levels of IR are high throughout Italy, restricting variation in the key exposure. This is akin to the adage that in a population where everyone smokes, genetics will be the strongest predictor of lung cancer. Again, presenting area-level correlations within Italy reveals little about the underlying IR and COVID-19 association.

As the authors note, only individual-level data can properly test the role of IR in SARS-CoV-2 transmission and mortality. A recent study from Sweden found that older persons living with working-age individuals had higher COVID-19 mortality compared to “old-only” households (8). Ongoing household surveys of living arrangements and intergenerational contacts will provide further understanding of these dynamics. Until then, it is crucial to be mindful of risks to older adults physically interacting with younger relatives. Undermining these precautions based on inadequate analyses is potentially dangerous. Social connectedness and psychological well-being among young and old are vital. Nonetheless, viral transmission does not heed a lack of aggregate-level correlations; it ultimately relies on person-to-person contact.

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^aLeverhulme Centre for Demographic Science, University of Oxford, Oxford OX1 1JD, United Kingdom; and ^bNuffield College, University of Oxford, Oxford OX1 1NF, United Kingdom

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¹To whom correspondence may be addressed. Email: jennifer.dowd@sociology.ox.ac.uk.

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