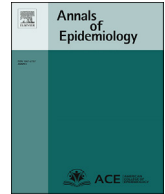




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Brief communication

Leveraging epidemiological principles to evaluate Sweden's COVID-19 response



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ABSTRACT

In the response to COVID-19, countries have implemented response strategies along a continuum of population- and venue-level specificity ranging from suppression to mitigation strategies. Suppression strategies generally include population-wide shelter-in-place mandates or lockdowns, closure of nonessential physical venues, travel bans, testing and contact tracing, and quarantines. Sweden followed a mitigation strategy focused on risk-tailored approaches to mitigate specific acquisition risks among the elderly, minimizing the disruption to education and the delivery of other health care services, and recommendations for social distancing to minimize the disease burden. To date, Sweden has reported higher case counts and attributable mortality than other Scandinavian countries and lower than other Northern European countries. However, there are several limitations with comparison given heterogeneity in testing strategies, suspected and confirmed case definitions, and assessment of attributable mortality. The decisions in Sweden also reflect social priorities such as equity being a foundational principle of Swedish social systems. Consistently, in-person education for those aged less than 16 years continued throughout. Notably, the mitigation strategy did not eliminate the inequitable impacts of COVID-19 cases and mortality in Sweden with higher-exposure and generally lower-income occupations being associated with higher risks intersecting with these communities often residing in more dense multigenerational households. From January 1 to November 15, there has been a 1.8% increase in all-cause mortality in 2020 compared with the average of 2015–2019, representing an excess of 14.3 deaths per 100,000 population. However, the final assessment of excess deaths in Sweden in 2020 including stratification by age and integration of secular trends can only be calculated in the coming years. In response to increasing cases in the fall of 2020, Sweden has continued to leverage business-oriented regulations and public-oriented guidelines for social distancing rather than police-enforced mandates. Ultimately, pandemics present no winners. Countries have implemented a range of different COVID-19 prevention and mitigation strategies responsive to their own priorities and legal systems including equity and the balancing of competing health priorities. Given these varied approaches, countries that pursued elimination, suppression, or mitigation strategies can collaboratively learn from both successes and challenges of the different strategies to inform COVID-19 and future pandemic responses.

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Introduction

In the responses to COVID-19, countries have implemented response strategies along a continuum of population and venue-level specificity. The most common response has been a suppression strategy popularly called “The Hammer and the Dance,” where the “hammer” consists of population-wide shelter-in-place mandates or lockdowns, closing nonessential physical venues, travel bans, combined with testing and contact tracing, is alternated with the “dance,” consisting of testing, contact tracing, quarantines, and sustained travel bans [1, 2]. In contrast, Sweden has followed a mitigation strategy, including instituting risk-tailored strategies to mitigate acquisition risks among the elderly, minimizing the disruption to education and the delivery of other healthcare services, and general public health measures to minimize the disease burden across the whole population [3]. The overarching goal of the Swedish mitigation strategy has been to implement a response that could be sustained over a longer time horizon while minimizing the COVID-19 associated morbidity and mortality [4]. Moreover, the mitigation strategy was intended to avoid amplifying the potential and realized socioeconomic inequities associated with suppression strategies combined with adverse consequences on competing health, education, and developmental risks over the short, medium, and long term [5–8]. There has been widespread criticism of the mitigation approach employed in Sweden generally focused on higher reported attributable mortality compared to other Scandinavian countries and lower than other Northern European countries [9–12]. The comparisons of both case counts and attributable mortality across countries have been common throughout the COVID-19 pandemic. However, these comparisons may be of limited utility given heterogeneity across multiple domains, including testing, assessment of attributable mortality, viral introduction timelines, environmental determinants, and socioeconomic differences that may drive differential transmission and mortality, as well as the assessment of those differences. In terms of testing, the sensitivity and specificity of polymerase chain reaction (PCR)-based viral assays and serological assays may vary by sample collection processes, by time in relation to infection, and by laboratory handling processes [13, 14]. Nosology is a field of science focused on attributing causes of death [15]. Over time, strategies to effectively compare attribute mortality across countries will be elucidated but currently remain limited [16]. For example, some

countries have included COVID-19 attributable mortality with only confirmed cases, whereas others have included probable cases based on symptoms [16]. Moreover, some countries have included cases confirmed or probable where COVID-19 was assumed to be the cause of death, whereas others have included all cases where someone died with COVID-19 irrespective of whether it directly caused the death. Each decision will greatly affect attributable mortality and limit the utility of comparisons of mortality estimates across countries. Leveraging core epidemiologic principles, we present an interim assessment of empiric successes and failures of Sweden’s mitigation strategy.

Risk-tailored strategies

The goal of “flattening the curve” was integral to both viral mitigation and viral suppression strategies, with the primary aim of avoiding overwhelming healthcare systems to facilitate effective clinical management of people infected with SARS-CoV-2. The difference between risk-tailored approaches in a mitigation strategy was the focus on identifying populations expected to have more severe clinical courses to implement focused interventions compared to universal interventions in suppression strategies. Thus, given early data on age-related increased morbidity and mortality, there was a goal to prioritize the protection of the elderly with specific recommendations to support physical distancing among elderly and their direct contacts (especially caregivers), with less focus on younger populations at less risk of severe illness or death [4, 17]. Notably, despite the same overarching strategy across Sweden, regions within the country experienced significantly different epidemic trajectories in the first wave, likely explained by a combination of heterogeneity in viral introduction timelines into different regions, potential differences in localized implementation of the venue, and individual-level interventions, and heterogeneity in transmission networks based on working and living conditions (Fig. 1). Nonetheless, even in Stockholm, intensive care unit (ICU) capacity was never reached during the first wave, and a temporary COVID-19 field hospital with 140 beds built in Stockholm was never used [18].

Correlates of exposure, such as seroprevalence, can be used to perform an interim internal assessment of the success of age-tailored approaches and can also allow external comparisons with other countries. In a Swedish seroprevalence survey

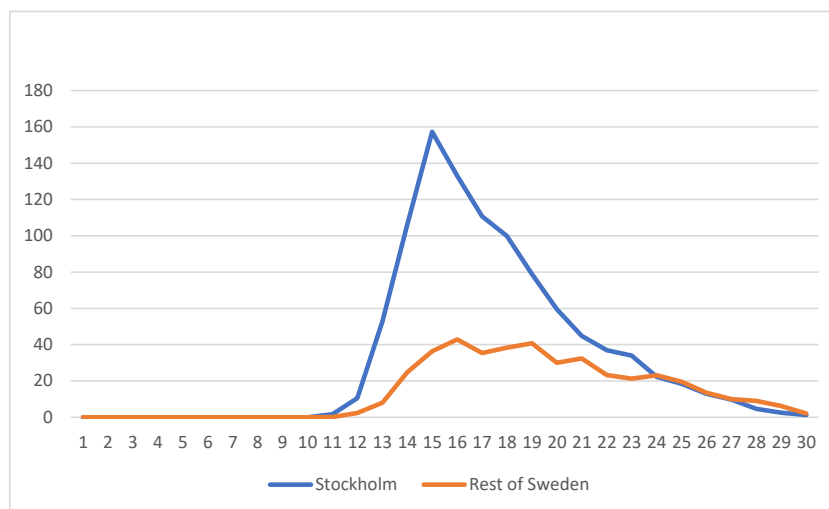


Fig. 1. Weekly COVID19 deaths/million.

conducted among approximately 1600 individuals in each age group during April–May 2020, 3.1% of those 65 and older had developed antibodies, compared to 6.5% among those 20–64 and 5.7% among those aged 0–19 [19]. In contrast, in the Spanish National Seroprevalence Survey of 61,000 participants, those over 65 were most likely to have antibodies with 6.0% (>65), compared to 5.3% (20–64), and 3.4% (0–19) [20]. Among other countries, Iran and Japan had similar age-distribution as observed in Spain, while Switzerland reported estimates more like Sweden [21–23]. Notably, the sensitivity of serological assessments as correlates of exposure remains of potential limited utility, particularly in the context of asymptomatic and mild infections [24]. In addition, there may be survival bias among the elderly people included in seroprevalence surveys. However, both of these biases are likely conserved across countries, facilitating comparison [10]. The age-based seroprevalence trends suggest that in the first wave of COVID-19, the elderly in Sweden were relatively less likely to have been exposed compared to Spain, likely in part attributable to a combination of different prevention and mitigation strategies and underlying contact patterns by age.

Throughout the world, some of the highest levels of COVID-19 mortality have been observed among residents in long-term care facilities (LTCF). In Stockholm, people above the age of 70 living in LTCFs had a COVID-19 hazard ratio of 4.1 (95% CI 3.5–4.9), compared to those living independently at home. While LTCF residents may generally be less healthy than those living independently, the equivalent hazard ratio risk for mortality from other causes was 2.6 demonstrating specific COVID-19 related mortality (95% CI 2.3–3.0) [25–27]. Notably, the risk of mortality has not been equal across all LTCF—with data emerging in Canada that LTCF that are more densely populated and for-profit having higher COVID-19 case and mortality risks [25, 26]. Specifically, for-profit LTCF status was associated with a nearly 80% increase in the total number of COVID-19 deaths (adjusted risk ratio/aRR 1.78, 95% CI 1.03–3.07) among residents after adjusting for health region-characteristics [25]. In addition, increased crowding of LTCF was associated with a 72% increase in infection risks (aRR 1.72, 95% CI 1.11–2.65) among residents [26]. Characterizing the role of client density and profit status of LTCF in Sweden may provide insight into risks of infection and mortality in these facilities and potential intervention strategies. In a risk-tailored approach such as in Sweden, more attention should have been given to interventions in LTCF to address the inadequate supply and effective use of personal protective equipment, limited staff testing, inadequate education, excess staff rotation, and suboptimal cohorting. Notably, the limited implementation of these measures early in the epidemic combined with potential pre-existing LTCF-specific risks such as crowding and profit status likely contributed to significant COVID-19 attributable morbidity and mortality in Sweden.

Given significant outbreaks in long-term care facilities and differential risks for mortality, 68% of all COVID-19 related mortality in Sweden has been among those 80 years of age and older, which is similar to other European settings. This high proportion of COVID-19 related deaths may also reflect the limited use of ICU among older populations. In Sweden, 9.1%, 8.5%, 1.6%, and 0.1% of individuals age 60–69, 70–79, 80–89, and 90 years and over diagnosed with COVID-19, respectively, were cared for in the ICU [28]. As there were sufficient resources in the ICUs throughout the response, no one was declined admission based on capacity. Potential explanations include that some COVID-19 patients, families, and providers declined ICU admission, given the potential for limited benefit for those with significant comorbidities [29]. For example, in one region of Sweden, only 15% of nonhospital COVID-19 deaths reported COVID-19 as the primary cause of death. In addition, a study of the Swedish Register of Palliative Care

suggested that patients that died in LTCF without hospital admission were significantly older and less symptomatic with improved palliative management when cared for in the context of LTCF as compared to in-hospital care [30].

Structural inequities were apparent in the unequal distribution of the risk of COVID-related mortality in Sweden. In a study of people in Stockholm over age 70, there was a 60% increase in COVID-19-related case-fatality rates (95% CI 1.3–2.0) if living in a multigenerational household with someone of working age as compared to living alone or with someone above the age of 65 or under the age of 16 [27]. In addition, there were higher levels of mortality among people living in more densely populated and generally low-income parts of Stockholm compared to mortality in Stockholm overall. Notably, the increases in mortality among low-income communities also reflect increases in non-COVID-19 mortality related, reflecting shared inequities in mortality risks in Sweden [31]. There were particularly high rates of mortality among people who had recently immigrated to Sweden that appeared to reflect intersections of high risk occupational and residential risks [31, 32]. The challenges of the prevention of both COVID-19 infections and secondary mortality in multigenerational households has been nearly a universal phenomenon irrespective of whether viral mitigation or suppression strategies were implemented, suggesting the need for equity considerations with dedicated resources for economically marginalized communities across all approaches [27, 33].

Social equity

Equity is a fundamental determinant in social systems in Sweden, exemplified specifically by its provision of both universal education and healthcare. Consequently, in its response to COVID-19, Sweden has attempted to minimize the inequities that result from universal lockdown mandates, as such mandates potentially concentrate COVID-19 among lower socioeconomic communities given those in higher socioeconomic classes are more likely to be able to work remotely. Specific interventions included the provision of paid leave from the first day of illness to essential workers to avoid undue pressures to continue working while under quarantine or isolation. Similarly, financial support was provided to people in multigenerational households facilitating temporary relocations to mitigate risks of onward transmission to household contacts [4].

Equitable and continuous universal access to healthcare services has been integral to the Swedish approach of mitigation. COVID-19 is not the only important health problem, and major healthcare interruptions have been reported in suppression strategy countries, some with immediate and others with long-term costs to human health and wellbeing. This includes significant declines in child vaccination coverage [34, 35], reduced cancer screening [36, 37], significant increases of out of hospital cardiac arrest and perinatal mortality [38, 39], delays in elective and nonurgent surgical procedures, more overdose deaths than in recorded history [40, 41], increased malnutrition [42], increased mental health stressors and suicidal ideation [43, 44], and interruptions to the prevention of other infectious diseases. Notably, there may also have been positive consequences from lockdowns such as fewer traffic accidents, more outdoor-oriented activities, fewer preterm deliveries [45], and fewer deaths from other infectious diseases prevented from reduced contact rates and improved hand hygiene [46].

The mitigation-based approach in Sweden appeared to limit the breadth of health disruption facilitating the overall health and wellbeing of Swedes. Specifically, in Sweden, a health report showed no significant declines in mental health during the pandemic compared to earlier time periods [47]. Moreover, there were no reported decreases in childhood vaccination rates [48].

However, during the height of COVID-19 transmission, cancer screening was paused. For example, 18 out of 21 health regions did not maintain the usual level of mammography screenings [49]. Consequently, in Stockholm, the number of cancer diagnoses were down by 30% during April and May of 2020 [50]. Thus, even in the context of a mitigation strategy, there are interruptions to the provision of both preventive and therapeutic services with catch-up efforts urgently needed. Ultimately, comparing all-cause mortality from both non-COVID and COVID causes will be relevant to inform the benefits of mitigation versus suppression strategies [16]. In Sweden, from January 1 to November 15, there was a 1.8% increase in all-cause mortality in 2020 compared to the same time period from 2015 to 2019, representing an excess of 14.3/100,000 (Fig. 2) [51]. This represents an excess of 1479 deaths, which is less than the 6410 COVID-19 deaths during the same period [28]. Further analyses are required to characterize the actual number of excess deaths in Sweden, including stratification by age and adjusted for secular trends are needed to interpret COVID-19-attributable mortality in Sweden compared to previous years in Sweden and across countries.

Even in the context of universal healthcare in Sweden, the mitigation strategy has not eliminated the inequitable impacts of COVID-19 [52]. In Sweden, the highest COVID-19 risks were found among taxi, transit drivers, restaurant workers, translators, ambulatory service workers, firefighters, building caretakers, and janitors, with estimated relative risks ranging from 1.4 to 4.8 [53]. In Stockholm, COVID-19 mortality was higher among people with lower income, less formal education, more crowded living arrangements, and among recent immigrants to Sweden [27, 32]. To date, there are no data available regarding transmission within Swedish homeless shelters, refugee intake centers, or jails, although in other countries, there have been significant disparities in these settings due to dense living arrangements and suboptimal IPAC [7]. Multiple Phase III COVID-19 vaccine trials are underway with promising preliminary data in the prevention of symptomatic COVID-19 [54]. COVID-19 vaccination has begun in the United Kingdom and likely soon to initiate in multiple other countries though not expected to achieve widespread coverage among adults until the summer of 2021. Importantly, equitable vaccination strategies are needed to avoid exacerbating disparities given historical inequities including differential health literacy and medical mistrust [55].

Education

An example of a strategic decision based on the principle of equity was the decision to keep childcare and elementary schools open throughout the height of the pandemic, for children ages 1 to 15, while most high schools and universities used remote teaching until

mid-June. In contrast, a common intervention in many countries included the closure of all schools for in-person teaching with exclusive reliance on virtual education. Aggravation of inequities with childcare and school closures are inevitable as it is more difficult for low-income families to support home education; they may be forced to quit work to stay home with young children, leave them with other families, or ask grandparents who are particularly vulnerable to COVID-19 to help. The inadvertently increased reliance on grandparents may have explained both higher relative exposure via serological assessments and mortality in Spain as compared to Sweden. In contrast, high-income families may have access to better resources for virtual education, including faster internet, better equipment, and access to private tutoring or educational “pods” [56].

Arguments often used to support continued school closures have been those in which children are seen as potential vectors of COVID-19, putting teachers and other staff at excess risk. Real-world data from Sweden in the spring of 2020 can be informative. Despite continuously open daycare and schools (ages 1–15), the relative risk of a COVID-19 diagnosis was 0.9 (95% CI 0.7–1.1) for 157,000 daycare teachers, 1.1 (95% CI 0.9–1.3) for 105,000 primary school teachers compared to all employed adults (with the exception of healthcare workers) [57]. The corresponding odds of COVID-19 infection for 30,357 high school teachers who worked from home was 0.7 (95% CI 0.5–1.0) [57]. A recent study reinforced that high school teachers who worked remotely had lower odds of infection compared to those who taught in person [58].

There was no additional household risk for those over 70 in Stockholm associated with coresiding with children still in school during the pandemic [27]. This was consistent with no observed increases in hospitalizations among parents of children with in-person school compared to those with older children being taught virtually [58]. Out of 1.8 million children in daycare centers and primary schools, ages 1–15, there were zero COVID-19 deaths and eight ICU admissions (incidence 1/230,000) by mid-June when summer vacation started. Since many infected children are asymptomatic/mildly symptomatic and unlikely to be tested, the number of actual infections remains unknown. Therefore, the 468 reported cases (incidence = 1/3900) is an underestimate of true incidence [57]. Sweden did close high schools and universities. Among older students, there have been zero COVID-19 deaths in the 16–19 age group, and 9 deaths among those 20–29 years old, although it is unclear to what extent comorbidities contributed to mortality to those in this age group (incidence = 1/147,000) [28].

Discussion

Rapidly emerging infectious pandemics represent periods of instability in any affected country. After the 2009 H1N1 influenza

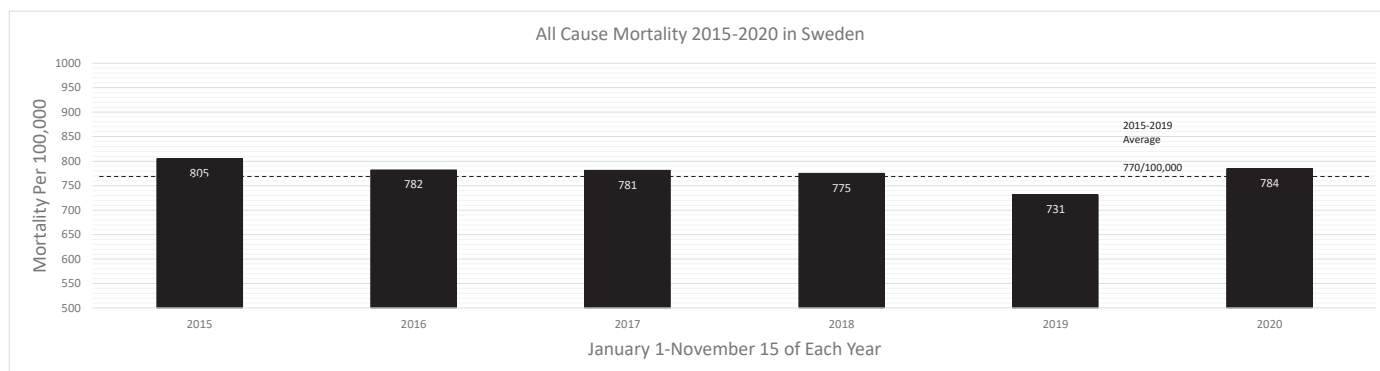


Fig. 2. Weekly COVID19 deaths/million.

pandemic, many countries developed pandemic preparedness plans to be better prepared for the next challenge [59]. While COVID-19 is not a pandemic influenza virus, the preparedness plans for a highly transmissible lipid-enveloped respiratory virus likely remained relevant as a starting point for COVID-19 response strategies [60, 61]. Notably, Sweden was an exception in keeping to the general outline of its preparedness plan, calling for a sustainable pandemic response with rapid identification of those most vulnerable, specific structural intervention strategies to mitigate identified risks, strategies to minimize all-cause mortality in the long term, education and empowerment of the population, avoid close contacts for those over 70, hand hygiene, maintain physical and social distancing where possible, and stay home if sick, with the provision of financial support via the national insurance system from the first missed day from work [4].

While Sweden's approach has often been described as passive or "laissez-faire," risk-adaptive approaches actually require greater effort from public health authorities with rapid identification of determinants of infection, development, and implementation of specific interventions, as compared to implementing non-adaptive population-wide mandates [9]. With the arrival of autumn, SARS-CoV-2 has returned to Europe along with most Northern climates as was generally predicted given the seasonal nature of similar lipid-enveloped viruses [62]. The resurgence in COVID-19 cases in many countries has led to the reimplementing of restrictions, including broad lockdown mandates being termed "circuit-breakers" or "fire break." Countries or subnational areas with higher case counts appear to be different than those observed in spring of 2020, such as the country of Czech Republic and parts of northern England. Sweden began the autumn with a reopening of high schools and some universities and a return to office work for some urban professionals. The transmission dynamics of COVID-19 reflected this change, with incidence rates of infection increasing throughout September and October among those 20–59 and relatively limited transmission to date among those 0–19 and 70+. Consequently, there have been increases in ICU admission during November accompanied with increases in mortality that remain, to date, generally consistent with historical seasonal trends. In response to increasing cases, Sweden has implemented business-oriented regulations such as not selling alcohol after 2200, but continues to leverage recommended guidelines for social distancing for the public rather than the police-enforced mandates in place in several countries across Europe and North America [63]. The differential rate of severe case resurgence observed across Sweden and other countries is to be expected given the heterogeneities in differential levels of population immunity that have arisen either as a consequence of public health interventions or due to chance [64–67]. For example, Uppsala has experienced a higher relative morbidity resurgence compared to Stockholm, which was more affected during the spring as regards both morbidity and mortality. However, more data are needed before we can properly assess the potential role of herd immunity across subsets of the population and within heterogeneous contact networks in reducing local population-level COVID-19 transmission.

Health systems are complex. In this context, minimizing deaths from COVID-19 over the long-term is critical, but so too is minimizing all-cause mortality and the preservation of other health and social services. Pandemics present no winners. The final assessment of different strategies can only be made after accounting for country-level heterogeneities in COVID-19 transmission, morbidity, and mortality and likely informed by the speed by which effective vaccines ultimately achieved widespread coverage. Until then, countries that pursued elimination, suppression, or mitigation strategies can collaboratively learn from both successes and challenges of the different strategies to inform COVID-19 and future pandemic responses.

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