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Low-Threshold Testing for SARS-CoV-2 (COVID-19) in Long-Term Care Facilities Early in the First Pandemic Wave, the Twente Region, the Netherlands: A Possible Factor in Reducing Morbidity and Mortality

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Abstract

During the first wave of the COVID-19 pandemic, there was a shortage of SARS-CoV-2 diagnostic tests, and testing patients with mild symptoms (low-threshold testing) was not recommended in the Netherlands. Despite these guidelines, to protect those who were most at risk, low-threshold testing was advocated and offered to the majority of long-term care institutions in the *Twente* region. In this manner, 144 healthcare workers and 96 residents tested SARS-CoV-2-positive and were isolated before the same service was provided nationwide by public health services. Strikingly, excess mortality rate in the *Twente* region 1 month after the introduction of this strategy was found to be 62%–89% lower than that in neighboring regions, which may be explained by this divergent testing strategy. In an emerging pandemic, early implementation of a liberal testing policy may be more effective than restricted testing in settings with a high death rate.

Keywords

COVID-19, mortality, home and community-based care and services, decision making, pandemic, long-term care, SARS-CoV-2 diagnostic testing

What this paper adds

- Low-threshold testing in LTC facilities was performed on a large scale intended to diminish the impact of the first pandemic wave on a whole region, a strategy which has not been performed elsewhere in the Netherlands in the first pandemic wave, as far as we know.
- Because this mitigation strategy did not comply with the national stringent testing policy a unique situation arose, in which its possible effect on the outcome of the pandemic in the region could directly be compared with neighboring regions.
- Early identification and isolation of potential sources for virus transmission in LTC facilities have putatively prevented many cases of severe disease and deaths of older persons in the first pandemic wave, explaining the lower excess death number in the *Twente* region as compared to its neighboring regions.

Applications of study findings

- In a viral pandemic crisis where the older persons are most at risk for severe disease and death, LTC facilities are prone for disaster, and maximal gain in numbers of lives spared may be made by focusing on preventing virus transmission in these facilities.

Introduction

The outbreak of a novel beta-coronavirus, SARS-CoV-2, which started in December 2019 in Wuhan, China, rapidly spread worldwide, causing COVID-19 disease with primary symptoms of fever, cough, shortness of breath, and fatigue (Guan et al., 2020). The Netherlands encountered its first case on February 27, 2020, in the province of Brabant (National Institute for Public Health and the Environment (RIVM), 2020). The other 11 Dutch provinces reported the first cases in the ensuing 2 weeks; the *Twente* region in the province of Overijssel on March 3, 2020 (RIVM, 2020).

Governmental measures to halt viral spread were issued, including social distancing, public advice to work at home, and a ban on gatherings of 100 people or more before the outbreak was declared a pandemic by the World Health Organization (WHO) on March 12. Thus, the national strategy shifted toward mitigation. At that time, it was clear that the groups that were most at risk for serious disease and death were older adults and those with underlying diseases (Porcheddu et al., 2020; Wang et al., 2020). All efforts were focused on their protection and prevention of the healthcare system from becoming overwhelmed.

However, clear guidelines on how to accomplish this task at a regional level was lacking. Furthermore, an imminent shortage of the national capacity to test for SARS-CoV-2 infection, and a very stringent national case definition that required both fever and respiratory symptoms to be present as a prerequisite for testing, led to very low numbers of healthcare personnel and older adults in the local LTC facilities and home-based care being tested by the local health authorities. This strongly increased the risk of virus circulation in these facilities, since it was already known that less than half of the SARS-CoV-2 infected patients may present with a fever. In general, older adults may have an absent or blunted fever response to infection in 20–30% (Guan et al., 2020; Norman, 2000), and the majority of SARS-CoV-2 infected patients present with only mild and non-specific symptoms. Moreover, people with only mild COVID-19 symptoms can be infectious to others (World Health Organization (WHO), 2020; Wölfel et al., 2020). Furthermore, case reports suggest possible transmission in asymptomatic cases (Bai et al., 2020; Rothe et al., 2020). However, national guidelines recommended healthcare workers (HCWs) with mild symptoms without a fever to continue working without being tested for SARS-CoV-2, while HCWs with fever had to stay at home without being tested either (Dutch Broadcasting Foundation (NOS), 2020). Thus, LTC facilities seem to be prone to large outbreaks of COVID-19.

We hypothesized that the limited number of diagnostic tests available could best be used to prevent the introduction and spread of virus in the LTC facilities in the *Twente* region, as early in the pandemic wave and in as many facilities as possible. This would limit SARS-CoV-2 caused severe disease and deaths cases among its residents, and potentially contribute to flattening of the epidemic curve in the region. Most importantly, HCWs with only minimal symptoms in the absence of fever needed to stop working, and immediately test for SARS-CoV-2 (low-threshold testing), to prevent transmission of the virus, and to minimize disruption of health care continuity. As of March 19, 2020, seven of the *Twente* region's largest institutions providing LTC and home-based care, for an estimated 17,000 older adults including 5600 residents, collectively, were approached by the regional medical microbiology laboratory and advised on a maximal containment strategy including low-threshold testing for SARS-CoV-2. Although the stringent national testing policy for HCWs was liberalized as of March 25 (Table 1), similar low-threshold testing by public health services in the Netherlands was provided only after April 9 (Center for Infectious Disease Control (LCI), 2020). Here, we aimed to evaluate the results of low-threshold testing for SARS-CoV-2 in LTC facilities in the *Twente* region early in the first pandemic wave, and gauge its effect on mortality rate as published by the RIVM and Statistics Netherlands (CBS).

Methods

Strategy Set Up and Implementation

On March 17, the medical staff and the director of the regional medical microbiology laboratory agreed on the proposed strategy to provide low-threshold testing for SARS-CoV-2 immediately to LTC facilities in the region. Hereafter, physical attendance by a clinical microbiologist of the outbreak management team (Coronavirus Crisis Team [CCT]) meetings in the LTC institutions was arranged through existing

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Table 1. Timeline of changes in the national stringent testing policy, and actions that facilitated testing accessibility during the study period.

Date	Study timeline	Change in the national testing policy
March 3, 2020	First COVID-19 case detected in the *Twente* region	
March 17, 2020	The strategy of low-threshold testing for long-term care institutions was conceived	
March 19, 2020	Inclusion of the first of seven participating institutions	
March 25, 2020		The national policy of not testing HCWs with respiratory symptoms for SARS-CoV-2 in the absence of a fever, was adjusted, allowing testing if certain pre-requisites were met: There should have been contact with residents, symptoms needed to continue for at least 24 hours, the HCWs could not be assigned alternative work and needed to work, and only if tests were available. If symptoms resolved with 24 hours at home, the HCWs were to continue to work (De Boer, 2020)
March 26, 2020	Inclusion of the last of seven participating institutions	
April 6, 2020		Public health services throughout the country installed sampling facilities for primary care HCWs, increasing testing accessibility
April 8, 2020		The national guidelines recommended that if testing was performed it was *preferred* that the HCWs should stay at home (LCI, 2020)
April 9, 2020	Peak of the COVID-19 pandemic in the *Twente* region	All HCWs with respiratory symptoms in absence of fever were allowed to be tested directly by public health services according to national guidelines, although the 24 hours of symptoms criterium was retained (LCI, 2020)

Note. HCWs: Healthcare workers.

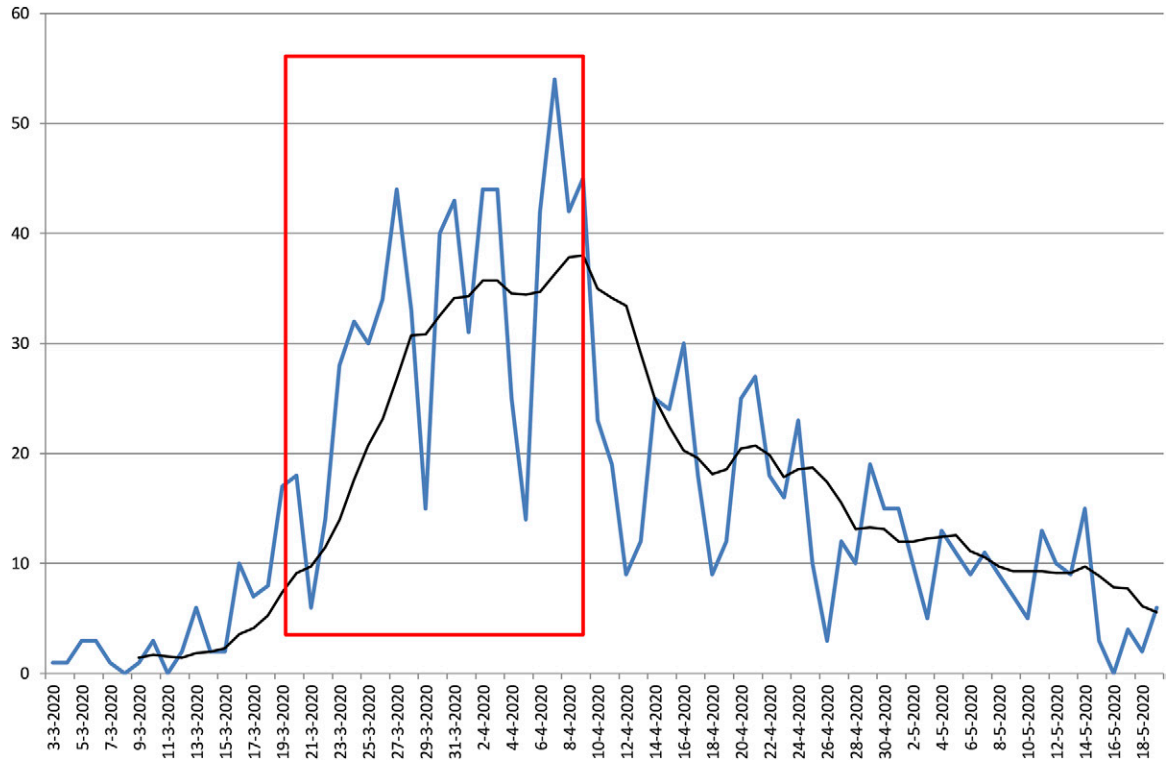

Figure 1. The first pandemic wave in the *Twente* region. Numbers of SARS-CoV-2-positive cases per day for the *Twente* region, starting from the firstly identified case on March 3 (blue line), with the 7-day average given (black line). The red box presents the time period in which low-threshold testing in regionally long-term care institutions was performed before similar testing became available by public health services.

Table 2. Estimated numbers of healthcare workers and residents in the participating long-term care institutions.

Institution	Number of HCWs[a]	Number of residents[a]	Total
1	4209	1251	5460
2	2400	772	3172
3	1800	946	2746
4	2000	681	2681
5	2323	1022	3345
6	2436	720	3156
7	706	257	963
Total	13,438	5649	19,087

[a]Due to the, sometimes, rapidly changing bed occupancy in the LTC facilities the estimated numbers of HCWs and residents per institution were based on previous year reports and replies to our questionnaires to the institutions, and comprised the number of residents under the national Long-term Care Act (WLZ). HCWs: Healthcare workers.

contacts with the institutions' infection control professionals. Participating institutions were selected because they had an infection prevention professional in service, which in practice reflected the size of the institution. Time pressure, capacity issues, and political discussion prevented scaling up this sample size to include smaller LTC institutions in the region. In this manner, between March 19 and March 26, about 2 weeks before the peak of SARS-CoV-2 infections in the *Twente* region, occurring on approximately April 9 (see also Figure 1), CCT meetings of seven LTC institutions in the *Twente* region were attended, and the advice to implement the following containment measures was given. These measures were largely based on the current pandemic experience of other institutions (Lee et al., 2020), and some of these contradicted the national advice at that time.

(1) Low-threshold testing for all HCWs and residents. National guidelines advised residents to be tested only if fever was one of the symptoms; personnel were not to be tested at all, but were instructed to stay at home if fever was present. From April 9 onwards, national guidelines allowed all HCWs with respiratory symptoms to be tested directly, including those without a fever.
(2) Instruction for HCWs to stop working when symptomatic, even with minimal symptoms, while awaiting test results. National guidelines advised those without fever to continue working without using any personal protective equipment. Only from April 8 onwards, national guidelines suggested that HCWs should stay at home until the test results were available.
(3) For a fast turnaround time, in-house sampling of personnel and residents was recommended. Only from April 6 onward publicly accessible testing facilities became available.
(4) A lock-down for visitors, if not already implemented by the institution. An official (national) lock-down was announced on March 19.
(5) Movement restrictions within LTC facilities (internal lock-down), at least for the first 2 weeks after closing the doors, to minimize the spread of the already introduced virus.
(6) Regular surveillance to identify symptomatic residents early.
(7) Isolation of the positively tested individuals, combined with contact tracing and quarantining high risk contacts.
(8) Monitoring hand hygiene and measuring temperature of healthcare personnel to identify those with fever at the entrance of the building.
(9) Counteract reintroduction of SARS-CoV-2 by adopting the European Centre for Disease Prevention and Control criteria for hospital discharge for residents and following a 3-day symptom-free period for personnel after at least a 7–8 day period from onset, with the possibility of testing. In contrast, national guidelines advised a 1-day symptom-free period and no testing.

Laboratory Testing for SARS-CoV-2

Healthcare workers with mild symptoms only were tested. HCWs with fever were to stay at home and not subjected to testing. Residents with mild symptoms and those with fever were also tested. The estimated numbers of HCWs and residents in the included long-term care institutions are listed in Table 2.

A real-time reverse-transcription polymerase chain reaction (RT-PCR) test, which detects the E gene from SARS-CoV-2 as provided by the RIVM, and is described elsewhere (Corman et al., 2020), was performed on pharyngeal and nasopharyngeal swabs either sampled separately, or if necessary, due to a supply shortage, sampled from both locations using a single swab.

SARS-CoV-2 RT-PCR tests were performed 7 days a week by the regional microbiology laboratory; at first three times a day, later on continuously except for at night, with results being communicated hourly to the applicants until approximately 11.00 in the evening.

Data Analysis

Test results for SARS-CoV-2 of HCWs of the participating LTC institutions from March 19 to April 21 were extracted from the regional microbiology laboratory's database (GLIMS, version 9.5.25; CliniSys/MIPS, Gent, Belgium),

Table 3. Proportion of positive test results among healthcare workers and residents tested for SARS-CoV-2 in the seven participating long-term care institutions according to the period.

	Proportion of positive tests per testing period			
	March 19–April 9, 2020[a]		March 19–April 21, 2020[b]	
Institution	HCWs	Residents	HCWs	Residents
1	33/246 (13%)	17/82 (21%)	59/750 (8%)	23/139 (17%)
2	47/315 (15%)	47/151 (31%)	61/440 (14%)	57/212 (27%)
3	8/111 (7%)	9/64 (14%)	10/151 (7%)	9/77 (12%)
4	27/222 (12%)	7/55 (13%)	35/295 (12%)	9/100 (9%)
5	8/49 (16%)	7/45 (16%)	19/88 (22%)	8/60 (13%)
6	12/82 (15%)	2/22 (9%)	18/147 (12%)	3/33 (9%)
7	9/49 (18%)	7/31 (23%)	13/71 (18%)	13/49 (27%)
Total	144/1074 (13%)	96/450 (21%)	215/1942 (11%)	122/670 (18%)

Note. HCWs = Healthcare workers.

[a]The period from 19 March to 9 April, 2020 is the period during which low-threshold testing was performed by the regional microbiology laboratory and the long-term care institutions in the *Twente* region, before comparable low-threshold testing was provided by the public health services.

[b]The period from 19 March to 21 April, 2020 is the period from the start of low-threshold testing in the *Twente* region until approximately the end of the first 6 weeks of the pandemic in the Netherlands (19 April, 2020), and corresponds to the period for which the excess in death rates was evaluated by Kunst et al., 2020.

and the number of positively tested individuals was determined. Individuals with a postal code outside the *Twente* region or those who had a repeated test while already proven SARS-CoV-2-positive were excluded. The results were also plotted against time and the timing of low-threshold testing provided by the regional microbiology laboratory and public health services.

The date that public health services provided a matching testing strategy for HCWs was set on April 9, considering the adaptations in the national testing policy that were made in that time (Table 1). To clarify the numbers of SARS-CoV-2-positive HCWs identified using low-threshold testing who would have been missed otherwise had the national guidelines been followed, a period selection was made from March 19 to April 9. The numbers of SARS-CoV-2-positive HCWs in this period was determined in each institution, and the total number was used to estimate possible effects of low-threshold testing on the outcome of the pandemic in the *Twente* region.

Similar to the HCWs' data collection, the test results of the residents were retrieved. However, it was not known which of the residents tested had a fever and would also have been tested according to the national guidelines. Therefore, the possible contribution of SARS-CoV-2-positive residents with only mild symptoms to the reduction of virus transmission, morbidity, and mortality was largely left out of the discussion.

To estimate the timing of the pandemic wave from March 19 to April 21 in the *Twente* region, the total number of SARS-CoV-2-positive patients per day was extracted from the regional microbiology laboratory's database, using the given postal codes of the patients' living address.

Publicly available data from the RIVM and CBS on COVID-19-related deaths and excess deaths (Kunst et al., 2020; RIVM, 2020), and population size (CBS, 2020a) were used to calculate the number of registered COVID-19-related deaths per inhabitant on April 21, and excess deaths per inhabitant on April 19 for the *Twente* region and the rest of the Overijssel province (*Salland* region and *Kop van Overijssel*), as well as the *Achterhoek* region and the province of Utrecht. Excess deaths were defined as the difference between the observed numbers of deaths and the expected numbers of deaths if there would not have been a pandemic, and used as an approximation of the true number of COVID-19-related deaths in absence of widespread testing for SARS-CoV-2. In addition, the dates of the first case in each region were retrieved.

Results

Laboratory Results of Low-Threshold Testing for SARS-CoV-2 in the Twente *Region*

The exact dates the institutions were first advised on low-threshold testing and other mitigation measures varied per institution, with the earliest on March 19 and latest on March 26 (starting dates for each of the institutions are indicated in supplemental figure 1 by the rear end of the red arrow). Until April 9, all institutions had multiple HCWs and residents tested, with a total of 1074 HCWs and 450 residents (Table 3), while the daily numbers of persons tested varied per institution (Supplemental Figure 1). Not all institutions started testing HCWs and residents with minimal symptoms at the same time, possibly because the institutions were advised for such testing at different times, the organization of sampling facilities takes certain time and effort, and there

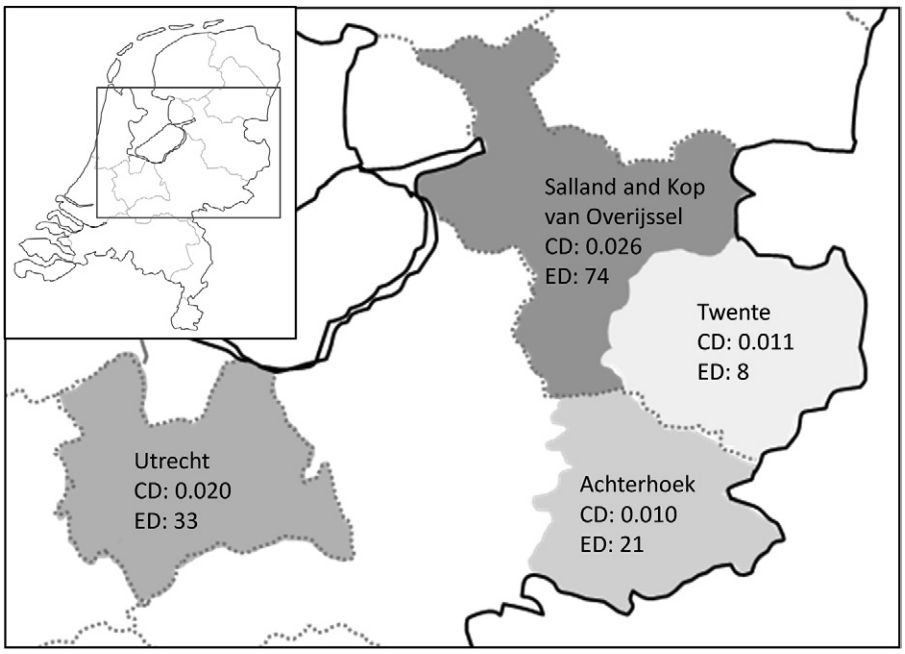

Figure 2. Regional differences in COVID-19-related deaths and excess deaths. The regions for which the percentages of COVID-19-related deaths (CD) per inhabitant and percentages of excess deaths (ED) are given (see also the text) are depicted in shades of gray. Dotted lines represent the boundaries of the Dutch provinces (insert).

should be HCWs and residents who are presenting with minimal symptoms.

The advising and deploying the low-threshold testing in the LTC institutions was carried out in the upward phase of the pandemic wave in the *Twente* region. While the same level of low-threshold testing was provided by the public health services on April 9, the epidemic curve was already flattening (Figure 1). On April 8, the cumulative number of SARS-CoV-2-positive cases in the *Twente* region was 700 out of 3398 individuals tested (data not shown), and a total of 144 HCWs and 96 residents from the seven LTC institutions were identified as SARS-CoV-2-positive (Table 3), constituting 34% of the SARS-CoV-2-positive cases registered until April 9 in the *Twente* region (240/700).

During the period from March 19 to April 21, a shortage in test capacity as a result of early low-threshold testing was not encountered, nor in the time that followed until the writing of this manuscript. The average turnaround time was estimated to be 6 h. Only from April 7 to April 9 it was longer (up to 48 hrs) when running a test to outsource part of the COVID-19 diagnostics to another laboratory as an emergency strategy.

Analysis of Public Data on COVID-19-Related Deaths and Excess Deaths

The percentage of COVID-19-related deaths per inhabitant in the *Twente* region on April 21 was 0.011% (72/630,940 (CBS, 2020a; Lindeman, 2020)), which was 2.4 times lower than that in the other part of Overijssel province (*Salland* region and Kop van *Overijssel* region; 139/532,015: 0.026% (CBS, 2020a; RIVM, 2020)) to the West and North-West, but 1.2 times higher than that of the *Achterhoek* region (39/401,183: 0.009% on April 22 (CBS, 2020a; Regional Media Center [REGIO8], 2020)) to the Southwest, and 1.8 times lower than in Utrecht province (277/1,356,757: 0.020% (CBS, 2020a; RIVM, 2020)) (Figure 2). However, the percentage of excess deaths in the *Twente* region on April 19, measuring 8%, was the lowest in comparison to each of these regions (21–74%) (Figure 2 (CBS, 2020b; Kunst et al., 2020)). The first COVID-19 case in the *Twente* region was detected on March 3, which was 4 days ahead of the *Salland* region and Kop van *Overijssel* region, and 2 days ahead of the *Achterhoek* region (Haggeman, 2020; Municipal Health Service (GGD), 2020). In Utrecht, the first COVID-19 case was detected on February 29, 3 days ahead of the *Twente* region (and thereby Overijssel province) (RIVM, 2020).

Discussion

By introducing low-threshold testing in seven LTC facilities in the *Twente* region, 144 HCWs infected with SARS-CoV-2 were identified and isolated in the 14 days before comparable low-threshold testing became available through the public health services on April 9. Without this strategy, these HCWs would have continued working, which conformed to the national guidelines, at least until April 8, when it was recommended that if testing was performed, the HCWs should preferably stay at home (LCI, 2020).

It is difficult to assess how many transmissions from HCWs to residents may have been prevented. With an estimated basic reproduction number (R0; representing the number of persons that one infected person will transmit the virus to) between 0.7 and 1.0 at that time (Van Dissel, 2020), calculated for the whole of the Netherlands, 101 to 144 secondary infections may have been prevented. However, considering the intensive contact with people who are most susceptible to infection, while the use of personal protective equipment such as masks and goggles was not advised by national guidelines, the transmission rate within the LTC facilities would likely have been much higher. Therefore, an R0 of 2–3 may be more realistic, which is known for SARS-CoV-2 in a susceptible population (Van Dissel, 2020), and possibly 288 to 432 transmissions may have been prevented. Even in the absence of secondary and further transmissions, which is unlikely because multiple transmission generations have been described during the early outbreak in Germany, which included cases with often mild or non-specific symptoms (Böhmer et al., 2020), this could alter the epidemic curve in the *Twente* region. Instead of the 556 SARS-CoV-2-positive cases (excluding 144 HCWs from a total of 700 (data not shown)) registered on April 8, 844 to 988 cases might have occurred. Assuming for convenience that these extra cases would have all been registered cases on April 8 (which is likely an overestimation), with an actual case count of 225 on March 26, this would imply a doubling time in the *Twente* region approaching the doubling time of 6.4 days calculated for the original Wuhan outbreak (i.e., in an unprepared population) (Wu et al., 2020). In the *Twente* region, the actual doubling time on March 26 was 3–4 days (case count on March 22: 105; March 26: 225), but on April 8 11–12 days (case count on March 27: 256; April 8: 541), showing that the pandemic wave was slowed down in that period.

The *Twente* region passed its peak of infections 6–7 days earlier than the rest of Overijssel Province (*Salland* region and *Kop van Overijssel* region), which peaked on April 16 (highest average of positives in the last 7 days) (RIVM, 2021; see also Figure 1). It is tempting to speculate that low-threshold testing in LTC institutions may have played a role in flattening the epidemic curve in the *Twente* region, in addition to the other measures taken at the national and institutional levels. In a modeling study of the pandemic in China, however, early detection and isolation of positively tested individuals was estimated to have prevented more infections than travel restriction and contact reduction did (5-fold vs. 2.6-fold), while combined measures were the most effective and rapid (Lai et al., 2020). The timing of these interventions was crucial, showing a 66–95% reduction in cases if measures were taken 1–3 weeks earlier (Lai et al., 2020). Similarly, all seven LTC institutions had their first SARS-CoV-2-positive HCWs detected using low-threshold testing between March 26 and March 31, more than a week before comparable low-threshold testing was offered by the public health services on April 9. This timing difference likely increased the impact of low-threshold testing on virus spread.

The extent to which low-threshold testing influenced the outcome of the pandemic in the region as a whole remains uncertain. Because the majority of COVID-19-related deaths were among older adults (Porcheddu et al., 2020), and published case-fatality rates in LTC facilities were high (27.8–33.7%) (McMichael et al., 2020; Stall et al., 2020), any significant effect would be expected to be seen in the number of COVID-19-related deaths and/or excess deaths in the region. In addition, excess deaths in the Netherlands in the first 6 weeks of the pandemic was found to be high among the 75–95 years age group and LTC residents (Kunst et al., 2020). Compared to the other parts of Overijssel province and Utrecht province, the number of COVID-19-related deaths per inhabitant in the *Twente* region was 2.4 and 1.8 times lower, respectively, while in the Achterhoek region it was 1.2 times higher (Figure 2). However, because of the restricted testing policy at that time, and a national advice not to test residents with symptoms if already two of their ward mates were proven as COVID-19 cases, excess deaths numbers may be a more reliable representation of COVID-19-related mortality. Several other studies suggest that many COVID-19 deaths were unrecognized during the first pandemic wave, including one study which estimated that 24% of all COVID-19 deaths were unrecognized, and 82% of these unrecognized deaths were among individuals aged 65 years and older (Dutey-Magni et al., 2021; Iuliano et al., 2021; Scortichini et al., 2021). The excess mortality rate in the *Twente* region was 2.6 times (62%) to 9.3 times (89%) lower than in all these regions. This suggests a higher underdiagnosis of COVID-19-related deaths in the *Achterhoek* region. In a population modeling study, home isolation in combination with household quarantine and social distancing of those over 70 years old yielded the highest mortality reduction of up to 50% (Ferguson et al., 2020). Low-threshold testing in the seven LTC institutions enabled the isolation of SARS-CoV-2-positive HCWs and residents with minimal symptoms and quarantining of contacts, which would not have been accomplished otherwise, and might explain the strong reduction in excess mortality rate in the *Twente* region.

There are some limitations to the presented argumentation. The exact symptoms in the HCWs were not always recorded, and it cannot be ascertained that some of the HCWs in SARS-CoV-2-positive group had a fever and should not have been implicated in calculations on the effect of low-threshold testing on virus transmission. However, we did not account for the effect of SARS-CoV-2-positive residents with only mild symptoms, which constituted an unknown proportion of the 96 SARS-CoV-2-positive residents who would otherwise not have been isolated, on the reduction of virus transmission within the LTC facilities. Possible transmission by asymptomatic individuals may not have been prevented by low-threshold testing. However, the chances of secondary transmission by asymptomatic individuals

are probably lower than those by symptomatic individuals, with an estimated relative risk of 0.35, while the number of asymptomatic individuals was estimated to be 20% (Buitrago-Garcia et al., 2020). The pandemic may have started earlier in other regions, allowing more deaths to accumulate. This could be the case for Utrecht province, which saw its first case on February 29 (RIVM, 2020). However, when matched for a similar timespan (by omitting 11 deaths from the last 3 days) the COVID-19-related death percentage in the *Twente* region was still 1.78 times lower. Importantly, because of the low scale of testing at that time, the first detected case may not have accurately predicted the start of the pandemic in a region.

A few other regions, such as the northern Dutch provinces Groningen, Friesland, and Drenthe also had low numbers of excess deaths, but these also had an exceptionally low incidence of proven SARS-CoV-2 infections (Kunst et al., 2020; RIVM, 2020). In the case of the *Twente* region, it has been recognized in a nationwide study that the excess mortality rate has been strikingly low, while other parameters indicated that it was not spared from the pandemic. For instance, the estimated seroprevalence in *Twente* was higher than that in the rest of Overijssel province (Kunst et al., 2020).

Differences in the number of deaths may be partially attributable to differences in the number of older adults between regions. However, the number of people aged 65 or older living in the *Twente* region on January 1, 2020, was estimated to be higher than that in the rest of Overijssel Province (*Salland* region and *Kop van Overijssel*) or in the *Achterhoek* region (Supplemental Figure 2) (CBS, 2020c). The proportion of persons aged 65 or older in the total population in the region exceeded that of the *Twente* region only in the *Achterhoek* region, by a factor of 1.19 (Supplemental Figure 2). This seems too small an increase to explain the 2.6-fold difference in excess mortality between these regions.

The direct influence of other possible regional differences, such as socio-economic status, population density, healthcare availability, and hospital avoidance on excess mortality, is harder to gauge and it was not evaluated in this study. A previous study showing 40% excess mortality in the whole of the Netherlands in the first 6 weeks of the pandemic, revealed no significant differences in household incomes or welfare levels, but a higher excess mortality rate among those with a migration background (Kunst et al., 2020). The latter group, however, constituted a small proportion of the total number of excess death cases, making it unlikely to explain the large geographic differences in excess mortality rate. The earlier passing of the peak in the *Twente* region as compared to the rest of Overijssel province could be an argument for low-threshold testing. However, Utrecht Province reached its peak already on March 31. Yet, the incidence of positively tested individuals was declined less steeply in Utrecht Province than in the *Twente* region and the rest of Overijssel province, suggesting other dynamics underlying this process (RIVM, 2021; see also Figure 1).

Finally, it could not be fully excluded that low-threshold testing in the upgoing phase of the pandemic wave has been applied in LTC facilities elsewhere in the Netherlands, as it has been in at least one hospital (Daily of the North (DvhN), 2020). However, in general, low-threshold testing at that time was discouraged (RTV Noord, 2020).

While there was little research data available at the beginning of the pandemic to guide an optimal response, experiences from others emphasize the importance of early testing and isolation in LTC facilities during this phase. In a LTC facility in West Virginia, the most helpful strategies managing outbreaks, and limiting virus spread and deaths, included early testing and isolation (Shrader et al., 2021). In an Austrian study, it was concluded that delayed recognition of COVID-19-positive cases due to mild or non-specific symptoms contributed to virus transmission in multiple facilities, emphasizing the importance of low-threshold testing (Zollner-Schwetz et al., 2021). Low-threshold testing of HCWs in a hospital early in the pandemic enabled the identification of asymptomatic and mildly symptomatic SARS-CoV-2-positive HCWs, when easily accessible public facilities were absent, preventing further spread of the infection (Menting et al., 2021). In a comparative study, explaining the 270-fold lower death rate in aged care homes in Australia than in the United Kingdom, an earlier lock-down and higher level of testing to prevent new cases may have played a role in saving lives (Chan et al., 2021).

In conclusion, in a phase of pandemic mitigation with limited test resources, low-threshold testing amongst other interventions may have significantly contributed to the reduction of virus transmission and deaths in the *Twente* region. Low-threshold testing in specific groups early in the pandemic wave may be a more efficient and effective strategy than restricted testing.

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Supplemental Material

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