of effectiveness on a transmission outcome. Studies that assessed the effect of testing or diagnosis on disease outcomes via treatment, but did not assess a transmission outcome, were not included. We focused on interventions implemented among the general population rather than in specific settings; these were from anywhere in the world and published any time after 1 January 2020 until the end of 2022. From 26 720 titles and abstracts, 1181 were reviewed as full text, and 25 met our inclusion criteria. These 25 studies included one randomized control trial (RCT) and the remaining 24 analysed empirical data and made some attempt to control for confounding. Studies included were categorized by the type of intervention: contact tracing (seven studies); specific testing strategies (12 studies); strategies for isolating cases/contacts (four studies); and 'test, trace, isolate' (TTI) as a part of a package of interventions (two studies). None of the 25 studies were rated at low risk of bias and many were rated as serious risk of bias, particularly due to the likely presence of uncontrolled confounding factors, which was a major challenge in assessing the independent effects of TTI in observational studies. These confounding factors are to be expected from observational studies during an on-going pandemic, when the emphasis was on reducing the epidemic burden rather than trial design. Findings from these 25 studies suggested an important public health role for testing followed by isolation, especially where mass and serial testing was used to reduce transmission. Some of the most compelling analyses came from examining fine-grained within-country data on contact tracing; while broader studies which compared behaviour between countries also often found TTI led to reduced transmission and mortality, this was not universal. There was limited evidence for the benefit of isolation of cases/contacts away from the home environment. One study, an RCT, showed that daily testing of contacts could be a viable strategy to replace lengthy quarantine of contacts. Based on the scarcity of robust empirical evidence, we were not able to draw any firm quantitative conclusions about the quantitative impact of TTI interventions in different epidemic contexts. While the majority of studies found that testing, tracing and isolation reduced transmission, evidence for the scale of this impact is only available for specific scenarios and hence is not necessarily generalizable. Our review therefore emphasizes the need to conduct robust experimental studies that help inform the likely quantitative impact of different TTI interventions on transmission and their optimal design. Work is needed to support such studies in the context of future emerging epidemics, along with assessments of the cost-effectiveness of TTI interventions, which was beyond the scope of this review but will be critical to decision-making.

This article is part of the theme issue 'The effectiveness of non-pharmaceutical interventions on the COVID-19 pandemic: the evidence'.

1. Introduction

Preventing people who have an infectious disease from making contact with others has been one of the cornerstones of public health practice since antiquity [1]. During the COVID-19 pandemic substantial efforts were made by many countries to identify people who were potentially infectious through the use of polymerase chain reaction (PCR) tests or lateral flow viral antigen tests, to isolate these people from others, and to trace and quarantine their contacts—who were also potentially infected. In theory, test, trace and isolate (TTI) methods can work well when the incidence of disease is low, and the generation time is long [2]. The low level of infection means that limited public health resources can be targeted to where they are most needed, and the long generation time means that isolation of the infected individual can occur before many secondary infections are generated. In addition, contact tracing—finding likely secondary infections due to their contact with the identified case—may help to more rapidly identify and prevent further onward transmission from these new infections and further target public health resources. Such testing has been common within public health responses to sexually transmitted infections [3], which often conform to the ideal of low incidence, slow transmission and ease of identifying

sexual contacts (although the recent outbreak of Mpox is a counterexample due to the difficulty of identifying the sexual contacts of some of those who were affected [4]).

Testing followed by isolation of the identified infected individual has the potential to break chains of transmission and limit the spread of SARS-CoV-2; when coupled with contact tracing to form TTI there is the potential to accelerate this process. Compared to interventions that aim to reduce transmission through blanket reductions to social contacts, such as stay-at-home orders or workplace and educational closures, TTI interventions aim to identify and prevent contacts between infectious and susceptible people only. They can therefore be seen as more specific strategies compared to population wide social contact reductions, but which could come at a cost to sensitivity and thus epidemic control, if identifying and preventing these contacts is incomplete or delayed. However, as with many public health interventions, there can be a complex range of practical and contextual issues that may affect the strength of the effect. These can be broadly broken down into three categories that relate to: (i) the specific nature of the TTI practices that are employed, (ii) how members of the public engage with these practices and (iii) the current status of the pandemic. In the first category, we include factors such as the speed and sensitivity of the testing mechanism, as well as the speed and accuracy of any contact tracing. The second category includes the public's ability and willingness to follow testing guidance (e.g. testing on early symptoms or testing before entering specific settings) and the extent to which the population is able to adhere to isolation rules [5]. The third category includes the prevalence of infection and the transmissibility of the specific variants that are circulating, as well as the presence of other non-pharmaceutical interventions (NPIs) that reduce the risk of transmission.

(a) Uses of testing, tracing and isolating

During the COVID-19 pandemic, testing and/or TTI were used in a complex and overlapping range of situations (figure 1), which changed as the epidemic progressed:

1) *Focused testing of symptomatic and high-risk individuals* especially during the early phase of an in-country outbreak, when infection is rare, to contain the spread and prevent transmission among the wider population. This was the case in the UK during the early outbreak, when symptomatic individuals, in combination with other specific travel histories and contact-based criteria, were tested and manual contact tracing performed [6]. In some countries, an intensive TTI system was implemented that aimed to fully contain re-introduced epidemics following periods of zero or very low transmission.
2) *Mass testing of those with symptomatic respiratory disease* to identify SARS-CoV-2 infection, such that individuals could take appropriate action including home isolation and authorities could organize contact tracing. In the UK, this was deployed from May 2020 to April 2022, with minor differences across the four nations [7]; prior to an increase in testing capacity, the UK had adopted a less specific approach of asking everyone with a new onset cough or fever to isolate [8].
3) *Mass testing of those entering healthcare or other vulnerable settings* such as care homes [9]. Here, the aim was to block the interaction between vulnerable susceptible people and those who were infectious, thereby reducing transmission to individuals most likely to suffer severe consequences.
4) *Mass asymptomatic testing of all individuals*, in an attempt to identify both symptomatic and asymptomatic infections and hence dramatically reduce the amount of circulating infection [10].
5) *Regular asymptomatic testing to identify all infectious individuals in workplace and educational settings*. In the UK, this process required healthcare workers [11], care home workers [9,12] and secondary school children [13] to perform regular (twice weekly) tests using lateral flow devices (LFDs) in attempts to minimize spread.

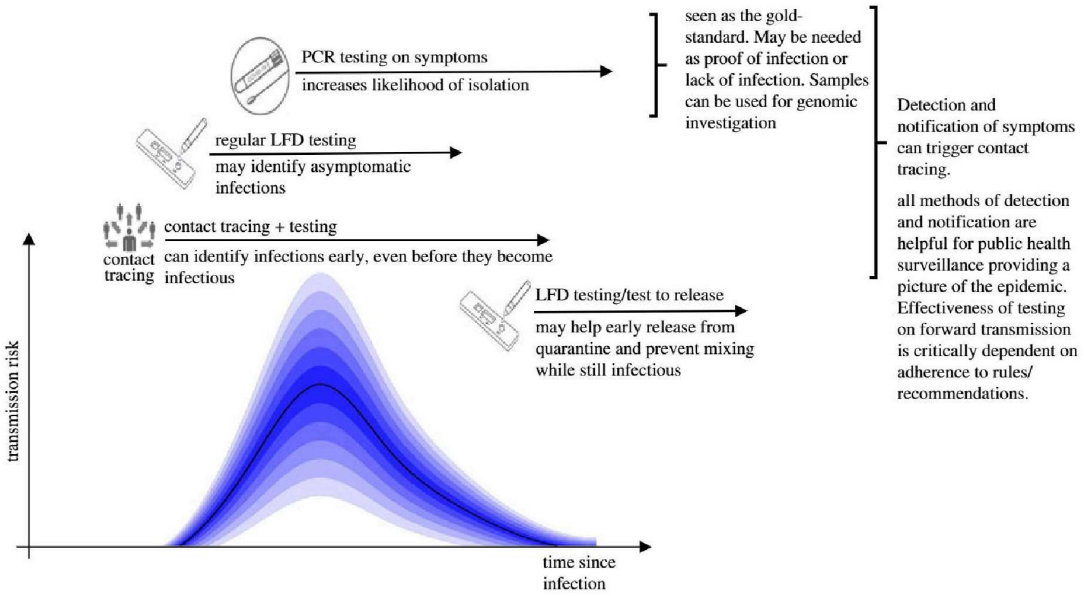

Figure 1. Infographic of the timing and variability in transmission risk from an infected individual with the time since infection, showing the potential timing of symptomatic testing, regular testing, testing following contact tracing and test to release. Early tests combined with isolation were hypothesized to truncate the risk of onward transmission. LFD, lateral flow device; PCR, polymerase chain reaction.

6) *The requirement of a negative test result to undertake particular activities or enter particular settings* [14,15]. Of these, the need for negative tests before international travel was common [16–18].
7) *Testing of identified at-risk individuals*. While the previous testing protocols are concerned with identifying infections, tests could also be used to reduce the time spent in isolation; either to inform the safe early release from isolation [19] or testing at-risk contacts rather than asking them to isolate [20]. In January 2022, the UK advised that people could end self-isolation after 5 days, if they had two negative lateral flow tests taken on consecutive days [21].

Two main forms of diagnostic test were used throughout the COVID-19 pandemic: LFDs and PCR tests [22,23]. PCR and LFD have different targets for detecting SARS-CoV-2: PCR is a laboratory-based system that amplifies and detects viral RNA; LFDs detect the viral antigen [24]. Extensive studies have shown that in general, PCR tests have a higher sensitivity at lower viral loads, thus detecting infections early, as well as beyond the period of high infectiousness, while LFDs are most sensitive when sampled viral load is highest, which is at times of high transmission risk [25–27]. While LFDs have lower sensitivity over the full course of infection, they have the substantial advantage that they provide a rapid assessment (within 15–30 min) that can be performed in the home environment. Here, we do not focus on the differences between PCR- and LFD-based testing, which will be context-dependent, but instead consider the impact that all forms of testing may have on reducing transmission.

When investigating the impact of testing, it is important to consider the wider context of the outbreak, including the presence of other control measures, the incidence of infection and the characteristics of the dominant variant. Control interventions such as mask-use, social distancing or other NPIs aim to reduce the level of transmission from infectious to susceptible individuals, while vaccination aims to reduce the number of susceptible individuals in the population. All of these control measures might help to reduce transmission, such that that TTI can be less effective and still maintain containment or control. PCR testing and manual contact-tracing are highly intensive activities, such that when there is a high incidence of infection resources can become