Title: A non-inferiority randomised controlled trial to assess the risk of onward infection transmission from contacts of confirmed COVID-19 cases who use daily lateral flow tests to enable exemption from isolation compared to standard self-isolation

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Summary [300]

Background: In the UK, during the study period all COVID-19 contacts were required to self-isolate for 10 days, which had adverse impacts. Avoiding the need to self-isolate for those who remain uninfected would be beneficial to society. We investigated whether using daily lateral flow devices (LFDs) to test for COVID-19 with removal of self-isolation for 24 hours if negative was a safe alternative to self-isolation by determining tertiary attack rates in study groups.

Methods: We conducted a non-inferiority randomised controlled trial (Research Registry ID:6809) in adult contacts identified during COVID-19 contact tracing. Consented participants were randomised to self-isolation (SI; single PCR, 10 days isolation) or daily contact-testing (DCT; 7 LFDs, 2 PCRs, no isolation if negative on LFD); participants from a household were assigned to the same arm. Participants were prospectively followed-up with the impact of each intervention on onward transmission determined from routinely collected contact tracing data for COVID-19 participants, and tertiary cases arising from their contacts. Attack rates were derived from cluster-robust standard error Bernoulli regression models. Questionnaires were sent at recruitment and at the end of testing/self-isolation to assess behaviours.

Findings: 49,623 individuals consented to participate with final arm allocations of 26,123 DCT (52.6%) and 23,500 SI participants (47.4%). Overall. 4,561 participants tested positive by PCR (secondary cases); 2,359 (10.0%) in the SI arm and 2,202 (8.4%) in the DCT arm. Tertiary attack rates (among secondary contacts) were 7.49% in SI arm and 6.40% in DCT arm (difference of -1.09 % (95% Confidence Interval -2.16% to -0.03%)). 124,010 valid LFD results were reported from 20,795 (79.6%) DCT participants with 1,132 (5.4%) reporting a positive result. Using DCT released each participant from self-isolation for an average of 5.4 days, (total time released:121,115 days).

Interpretation: DCT with 24-hour exemption from self-isolation for essential activities appears to be non-inferior to self-isolation.

Introduction

In England, the NHS Test and Trace (NHSTT) programme provides access to testing and contact tracing for close contacts of confirmed COVID-19 cases (1). At the time of this study (April-July 2021) all contacts, vaccinated and unvaccinated were required to isolate for 10 days from the date of exposure to the primary case. In August 2021, vaccinated contacts and those under 18 years and 6 months were no longer required to isolate but unvaccinated adult contacts were required by legislation self-isolate for 10 days from the date of their last exposure to the case. All COVID-19 contacts have been offered a single PCR test, irrespective of symptoms since March 2021 (2); however only half of identified contacts performed this test. Most contacts of COVID-19 cases modify their behaviours and contact with other people. However, full adherence to self-isolation guidance in England remains between 50-80% (3-5), reducing the effectiveness of isolation on viral transmission. Strategies for improving self-isolation compliance have been developed, including provision of financial or other incentives and penalties (6). However, such strategies do not consider the wider economic, social and well-being impacts of self-isolation (7).

Strategies that target self-isolation more effectively to contacts who become infected, while allowing those without infection to continue with essential activities, would help society return to greater normality while continuing to reduce onward transmission. Improving case ascertainment through the identification of asymptomatic, pauci-symptomatic and pre-sympromatic cases could help target isolation most effectively and, potentially, improve adherence to self-isolation guidance (8-10). Asymptomatic, rapid antigenic testing using lateral flow devices (LFDs) for COVID-19 is widely available in the UK (11-12), with low cost, rapid turn-around times, and delivery outside of a routine laboratory environment. Such tests could be suitable to support a structured programme of testing contacts of cases (8-10).

Two previous feasibility and acceptability studies demonstrated the potential benefits of a structured programme of daily testing of contacts using either a single PCR (13) or a 'test to enable' approach using daily LFDs plus one PCR as part of the contact tracing process in England (14-17). However, these studies were not designed to assess the risk of onward transmission. The use of daily contact testing using LFDs as an alternative to self-isolaton was explored in a school-based study, which reported that the use of daily LFDs was non-inferior to self-isolation for control of COVID-19 transmission (18). Here we report the results of a non-inferiority randomised controlled trial of adult, close contacts of COVID-19 cases to test whether using daily LFDs with 24-hour exemption from self-isolation following each negative LFD result, in combination with 2 PCR tests, was a safe alternative to self-isolation combined with a single PCR test.

Methods

Study design and recruitment

The study design was a two-arm, non-inferiority non-blinded randomised controlled trial. Adults (≥ 18 years), vaccinated and unvaccinated, identified as contacts of confirmed COVID-19 cases, living in England, were offered participation in the study (Supplementary Figure 1 and Supplementary methods). Participants were not eligible to participate if they were; symptomatic at recruitment; under travel associated quarantine; participating in a workplace DCT programme; resident in a prison or social care institution; a contact of a case with a variant of concern (VOC; between 29-April–7-June-2021 only; removed after this date to ensure generalisability for Delta); or did not provide an email address. Individuals were recruited through the routine contact tracing process and selected sequentially. Information on eligibility criteria were self-reported. Self-reported age, postcode, VOC, and travel criteria were confirmed using data collected by NHSTT during contact tracing. Recruitment was performed daily from 29-April to 28-July-2021 with eligible contacts invited to take part via recruitment phone calls or via SMS/emails containing a link to self-register online. There was no limit on daily recruitment; however, due to intermittent limitations in the number of kits available, enrolment was restricted between 26–29-June, 03-12-July and 19-26-July. A sub-set of participants were interviewed after completing testing/self-isolation as part of a nested qualitative component to the study, which is reported elsewhere (19).

Ethical approval was granted by Public Health England Research Ethics and Governance Group (ref:NR0235) and the protocol was registered with the Research Registry (ID:6809). Informed consent was obtained during recruitment.

Sample size calculation

Allowing for attrition and testing compliance, 40,000 participants were required to generate 3,170 secondary contacts based on a non-inferiority sample size calculation using a significance level of 0.05, power of 80%, ratio of group sizes 1:1, and design effect of 1.2, derived from a difference of proportions of 6.3% in DCT vs. 8.2% in general population comparator as reported in (14). At the study mid-point, the sample size was inflated to 50,000 to account for a lower than expected detection of COVID-19 in contacts, suspected to be related to vaccination.

Randomisation

Participants were randomly assigned to either the DCT arm (daily contact testing with 7 self-administered LFDs with release for 24 hours based on a negative LFD result) or the Standard Isolation (SI) arm (a single self-taken PCR swab and self-isolation for 10 days), with randomisation occurring at the point of consent based on a system-generated timestamp for a participant. Contacts from the same household were assigned to the arm of the first member of the household recruited, irrespective of the outcome of randomisation.

Procedures and data collection

Demographic data were collected at recruitment using a secure electronic questionnaire (SnapSurvey, Snap 11 Professional) and downloaded twice daily to produce lists for test kit postage and messaging. Kits were posted via NHSTT home delivery channels. Within 24 hours of recruitment, participants with a valid mobile number and/or email address were informed of their assigned study arm and sent a link to a short, voluntary, anonymous baseline questionnaire. On day 7, a link was sent with a completion of study questionnaire. Reminder messages were sent after 48 hours.

Participants in both arms were asked to take a self-sample for PCR on day of kit arrival and return it by post. DCT participants were asked to perform their first LFD on day of kit arrival and then on each of the following 6 days, reporting results daily to a secure study portal (SnapSurvey). Reported results were submitted to the national results database in compliance with infectious disease notification regulations. On reporting their first negative LFD, DCT-participants were assigned a flag in the NHSTT contact tracing system to prevent isolation checks and access to self-isolation support payments. A second PCR swab was requested for DCT participants on receipt of an LFD-positive result or on the day of their last LFD (if all previous LFDs were negative). All participants were legally required to self-isolate for 10 days if PCR-positive. No formal restrictions were placed on study

participants in the DCT arm during periods free from self-isolation; however, participants were advised to minimise contact and undertake only essential activities.

Outcomes

The primary outcome was to determine if DCT was inferior to SI by ascertaining the proportion of secondary contacts (close contacts of COVID-19 positive study participants), who became COVID-19 cases (tertiary cases) in each arm.

Secondary outcomes of the study were to determine the feasibility and acceptability of each strategy by measuring uptake and compliance with testing, ascertaining the proportion of positive results, describing the concordance of PCR and LFD results, describing participant behaviours during the study period, establishing the number of working days enabled for DCT-participants and understanding factors influencing the use of tests, understanding of test results, and how tests inform behavioural decisions (reported in (19)).

Data analysis

Data submitted to the study LFD portal and recruitment portal were analysed as of 14-August-2021, with PCR data analysed as of 8-September-2021. Data were analysed in Stata version 15 and R Studio version 4.0.0. Recruitment data were enriched using routinely collected NHSTT contact tracing data and deterministically linked to PCR results from national laboratory surveillance, study LFD results, the national LFD result portal and to immunisation data from the National Immunisation Management System (NIMS) using a combination of identifiers. PCR results from all participants were restricted to tests with a specimen date in the 90 days prior to recruitment (to adjust for extended PCR positivity) to 14 days after recruitment. Fully and one dose vaccinated individuals were defined as those vaccinated more than 14 days prior to recruitment. Where NIMS vaccination status was unknown, self-reported vaccination status was used.

Participants were excluded if they met the exclusion criteria, if no address was provided, or the same participant was registered multiple times (with an alternative contact tracing ID) within 3 days. Descriptive analyses determined associations by chi-squared and rank sum tests, with a p-value of <0.001 used to assign significance due to the large study population. The second behavioural questionnaire was analysed as three groups (SI, DCT–tested positive, DCT–no positive test). For both behavioural questionnaires, proportions were calculated among participants, who provided a least one response to a question and were compared using chi-squared tests.

Attack rates were derived from participants (primary contacts), who tested positive for SARS-CoV-2 by PCR in the 2 days before and 14 days after recruitment (secondary cases). SI participants who reported LFDs to the study portal were excluded (n=43). Participants were deterministically linked to case episodes in CTAS and their named close contacts identified. Potential transmission events were defined as contact records matched to a subsequent case record with symptom onset (test date if asymptomatic) between 2-14 days (inclusive) after the exposure date. Where the contact was in the household, the date of symptom onset (test date if asymptomatic) of the exposer was taken as the exposure date. Where multiple case-contact exposures could have resulted in transmission, rules-based prioritisation (preferring household exposures, and most recent exposures) identified a single most likely potential transmission event. The attack rate was the proportion of contacts of participants (secondary contacts) that were identified as potential transmission events, leading to tertiary cases. Attack rates were derived from Bernoulli regression models with cluster-robust standard errors. The simplest 'unadjusted' model used arm as the only covariate. The second 'unadjusted' model added household exposure and its interaction with arm, while the third 'unadjusted' model instead added vaccine status (0 or 1; 2 doses) and its interaction. 'Adjusted' versions of these models were obtained by adding household exposure, vaccine status and ability to work from home. Interactions were tested for significance by Wald tests with significance level of 0.05. Sensitivity analyses restricted to DCT-participants who submitted LFD results to the study portal (as a proxy for compliance) and the first household member recruited (to account for allocation to the same arm for multiple household members) and with both restrictions were performed. An independent unadjusted masked analysis was also performed.

Results

57,430 unique contacts of confirmed cases of COVID-19 consented to participation in the study (Figure 1). 60.2% of participants self-enrolled digitally (n=34,580) and 39.8% enrolled via telephone calls (n=22,850). 54,923/57,430 (95.6%) consenting individuals were eligible for inclusion (n=1,169 had no address or contact information, n=369 met exclusion criteria, n=969 were duplicate participants. 27,741 participants were randomised into the DCT arm (50.5%) and 27,182 into the SI arm (49.5%). 5,300 participants withdrew after randomisation (2,634 (49.7%) DCT-participants and 2,666 SI-participants); common reasons for withdrawing were dissatisfaction with arm allocation (n=1,453), being at the end of isolation (n=770), having a previous PCR test (n=568), and already testing positive (n=453; Supplementary Table 1). Household members were grouped into the same study arm after randomisation, with final arm allocations being 26,123 DCT-participants (52.6%) and 23,500 SI-participants (47.4%).

Baseline characteristics

There were no statistical differences in the sex, age, regional distribution or ethnicity, vaccination status or the presence of a COVID-19 case in the household between the two arms (Table 1 and Supplementary Table 2). DCT-participants were significantly less likely to work outside of the home (40.1% vs. 43.2%; ; p=<0.001). 41.7% of DCT-participants and 36.1% of SI-participants had more than one household member in the study or registered more than once during recruitment (p=<0.001).

Transmission from participants who became cases

Of the 49,623 participants (primary contacts), 2,359 (10.0%) reported at least one positive PCR result in the SI arm and 2,202 (8.4%) in the DCT arm in the period between 2 days prior to recruitment and 14 days after recruitment, hereafter referred to as secondary cases. 4,561 were linked to 4,615 cases in the NHSTT contact tracing database (where a case had multiple records, all were included). 3,710/4,615 cases (80.4%) reported at least one contact (secondary contacts); 1,948/2,385 (81.7%) PCR-positive SI-participants and 1,762/2,230 (79.0%) PCR-positive DCT-participants (Table 2). In total, 10,115 secondary contacts were reported; 5,206 contacts reported by SI-participants and 4,909 contacts reported by DCT-participants. Of these secondary contacts, 704 became tertiary cases (390 from SI-participants and 314 from DCT-participants).

Overall, 2.19 secondary contacts were reported per secondary case (2.18 per case in the SI arm and 2.20 per case in the DCT arm; no statistical difference), with the majority of these being household contacts (1.94 household secondary contacts per case in SI arm and 1.93 in DCT arm). The number of tertiary cases per secondary case was 0.14 in the DCT arm and 0.16 in the SI arm. Attack rates among secondary contacts were 7.49% in the SI arm and 6.40% in the DCT arm. The percentage difference between the arms was -1.09 % (95% Confidence Interval (CI): -2.16% to -0.03%), suggesting that DCT is non-inferior to SI (Table 3).

Attack rates among secondary household contacts of secondary cases were 6.9% in the DCT arm and 8.0% in the SI arm, though not significantly different (percentage difference: -1.10%; CI: -2.26% to 0.06%). Attack rates amongst non-household secondary contacts did not differ between the DCT arm (2.98%) and the SI arm (3.52%) (percentage difference: -0.54% (CI: -2.72% to 1.64%)).

Attack rates did not significantly differ between arms for secondary contacts who were unvaccinated or partially vaccinated (6.93% in DCT arm and 7.78% in SI arm; percentage difference:-0.85% (CI: -2.34% to 0.64%)). The difference was greater in magnitude, but not significant for fully vaccinated secondary contacts (5.72% in DCT arm vs 7.06% in SI arm; percentage difference:-1.33% (95% CI -2.84% to 0.17%)).

Results from models testing arm and household exposure interaction and arm and vaccination status interaction were not significant (Table 3).

LFD testing uptake and compliance

Between 30-April and 9-August-2021, 124,010 unique LFD test results were reported to the study portal from 20,795 DCT-participants (79.6%;). 5,328 DCT-participants did not report LFD results to the study portal; of

whom 1,300 reported at least one result to the national, non-study portal (Supplementary Table 3). These 5,328 participants were excluded from subsequent analyses because it was unknown if these individuals intended to follow the 24-hour release approach given the widespread use of LFD testing in England. Demographic characteristics differed significantly between people who did and did not report an LFD result to the portal. Individuals in lower index of multiple deprivation (IMD) deciles, minority ethnicity background and those unable to work from home were less likely to report a result (Supplementary Table 4). 19,663/20,795 DCT-participants (94.6%) reported only negative and/or void LFD results and 1,132/20,795 DCT-participants (5.4%) reported at least one positive LFD result.

A sensitivity analysis removed DCT-participants who had not submitted an LFD result to the study portal (Supplementary Table 5 and 6), again indicating that DCT was non-inferior to SI (attack rates: 7.49% in the SI arm and 6.00% in the DCT arm). A separate sensitivity analysis which restricted to the first person recruited in the household (Supplementary Table 7 and 8) also indicated that DCT was non-inferior to SI (attack rates: 7.15% in the SI arm and 6.45% in the DCT arm). Results of a further sensitivity analysis that combined both restrictions, considering only the first person recruited in the household after exclusion of those DCT-participants who had not submitted a LFD result to the study portal, was also consistent with results of the main analysis (Supplementary Table 9 and 10).

Days of self-isolation exemption enabled by DCT

For DCT participants who worked outside of the home and did not test LFD or PCR-positive during their testing period (n=7,457) the number of days free from self-isolation and therefore the number of work days enabled through DCT were estimated at up to 44,089 days (average of 5.9 days per participant). Overall, the number of days free from self-isolation among DCT-participants who reported LFDs, was estimated as 121,115 days (average of 5.4 days per participant).

PCR testing uptake and compliance

62,190 valid PCR results with specimen dates 2 days before recruitment to 14 days post recruitment (to cover a full incubation period) were obtained from 34,958 participants using England's national laboratory surveillance system; 17,344/23,457 (73.9%) from SI-participants and 17,614/20,795; (84.7%) from DCT-participants (Table 4), 316 results were void (0.5%).

The median number of PCR tests taken by participants during this time period was 2 for both arms (SI: IQR=2; Range: 0-9 and DCT: IQR=1; Range 0-8), with 12,061 (68.5%) of DCT-participants submitting two or more PCR swabs in the 14 days following recruitment, as directed by the study protocol. Of 17,614 DCT-participants who submitted an LFD to the study portal, 1,647 had a positive PCR result (9.4%).

Behavioural survey

31,660 (63%) participants responded to the baseline questionnaire; 17,694 in the SI and 13,966 in the DCT arm; 69% of all respondents reported participating in the study as they wanted to avoid self-isolating if possible (Supplementary Table 11).

20,004 (40%) participants responded to the end of study questionnaire (8,807 SI-participants, 754 in the DCT – tested positive group and 10,443 in the DCT–no positive test; Table 5). 82% of individuals in the SI arm reported much less contact with non-household contacts in the previous 7 days compared with the week prior, as did 84% of individuals in the DCT – tested positive group. In the DCT-no positive test group, 57% reported much less contact, with 11% of participants reporting having much or slightly more contact.

Participants were asked about any reasons for leaving home whilst self-isolating. The most common response was to take a COVID-19 test (87% of those who reported a reason in both groups). The proportion of participants who reported at least one other activity outside of the home whilst self-isolating was similar between the SI and DCT-tested positive groups (16% and 17% respectively, p=0.80).

In the SI group most respondents (79%) were very or completely confident in the accuracy of their test results. This level of confidence was reported by 64% of participants in the DCT–tested positive group and 83% in the DCT-no positive test group.

Discussion

As the COVID-19 pandemic continues to have a major impact on health and society, it is important to make efforts to reduce transmission. While self-isolation of confirmed cases and their contacts can be effective, it is also disruptive for society and causes adverse impacts for individuals, given the practical, financial, and psychological challenges associated with sustained and repeated self-isolation. To address these challenges, it has been proposed that innovative approaches could limit self-isolation to those who are infected, whilst allowing those without infection to return to greater normality (14, 20). While previous studies showed that DCT was acceptable to participants (14-16), they were not powered to assess the potential transmission risk to others.

Here we present results of the first randomised controlled trial in a general population of close contacts of COVID-19 cases comparing self-isolation to DCT with 24 hours exemption from self-isolation after a negative LFD result. By ascertaining the proportion of contacts of PCR-positive study participants who became tertiary cases in each arm, we demonstrated that DCT was a safe alternative to SI regarding onwards transmission of SARS-CoV-2, with a difference in attack rates of -1.09% amongst contacts of secondary cases, indicating non-inferiority of DCT. Consistent with this finding, the number of observed tertiary cases per secondary case was 0.14 in the DCT arm and 0.16 in the SI arm. Attack rates among contacts of DCT-participants, who had received two vaccine doses (>14 days before recruitment) also showed non-inferiority compared to SI-participants, with an unadjusted difference between DCT and SI arms (SI as baseline) of -1.33%. This suggests DCT would be of value among fully vaccinated people. Although there was some imbalance in the study arms due to household clustering, a sensitivity analysis restricted to the first person recruited also showed DCT was non-inferior to SI. Other sensitivity analyses adjusting for non-reporting of LFD results supported the plausibility of DCT non-inferiority.

While the study did not set out to change behaviour, individuals in the DCT group who reported only negative test results did not report significantly more contacts that those who were self-isolating, with the majority of contacts reported by participants in both arms being household contacts. This study occurred prior to the removal of all social restrictions. It is possible that DCT may perform differently in the absence of any social restrictions when cases are likely to have a higher number of close contacts beyond the household.

Compliance with testing was high with 80% of DCT-participants submitting at least one LFD result, higher than the 70.2% observed in the pilot study (14). Furthermore, 73.9% of SI-participants and 84.7% of DCT-participants had at least one PCR test during the study, higher than the 40% return rate reported in a previous study (13). Currently in England, it is recommended that all close COVID-19 contacts take a PCR test, with compliance in the general population lower than in our study (48.2% of household contacts and 36.3% of non-household contacts in the general population 0-10 days after exposure; in an email from P. Patrzylas (piotr.patrzylas@phe.gov.uk) in November 2021). The usage of LFDs was common for participants in the SI arm. Many non-reporting individuals from the DCT arm and individuals in the SI arm submitted at least one LFD to the non-study result portal, which may suggest LFDs provided reassurance to SI-participants, as well as DCT-participants. This was adjusted for in a sensitivity analysis, with similar findings.

DCT-participants living in more socioeconomically deprived areas and those from minority ethnic backgrounds were less likely to report an LFD result, aligning with previous findings (14,16). The ineligibility of DCT-participants for isolation support payments may have resulted in lower compliance among participants in lower socioeconomic groups (4). Prior to introducing any DCT policy it will be important to engage with disadvantaged communities to further understand and address barriers to testing and reporting.

The average number of close contacts reported was low (2.7 contacts per case), consistent with the national experience (20). Around 80% of secondary cases (participants who tested positive by PCR) provided details of

their contacts to NHSTT, which was comparable to figures for overall compliance with the contact tracing programme (20). During the study period 30-50% of contacts notified to NHSTT in England were non-household contacts (20). This was substantially higher than the proportion of non-household contacts reported in the study for both arms (~12%), with the number of non-household contacts per case near-equivalent between arms. This lower number of non-household contacts may indicate increased caution as described in qualitative analysis (19) or ascertainment bias towards being early in isolation period. Study participants were aware of their contact status prior to becoming cases and therefore may have different behaviours to the general case population, which includes cases who were not previously aware of their contact status. Although additional freedom was offered to DCT-participants, individuals in the DCT arm were still advised to limit contact and that they should only engage in essential activities. Behavioural data suggest that DCT-participants limited their contact with others and remained cautious in their behaviours despite enjoying additional freedom (19). For example, 57% of DCT-participants reported having much less contact with people they did not live with in the last seven days, compared to the week before, with only 11% of DCT-participants reporting having much or slightly more contact. In contrast, around 80% of participants in both the SI arm and the DCT–positive test group reported much less contact with non-household contacts, with compliance with self-isolation comparable to estimates from a study conducted by ONS (5).

The key strengths of this RCT include its large size, the real-life setting using existing contact tracing systems and validity of the transmission measure due to the use of named contacts identified by their exposers. There are, however, some limitations. We relied on self-notification of close contacts, which could lead to under ascertainment, particularly of non-household contacts. These limitations are also limitations of the existing contact tracing system. Furthermore, it was not possible to assess the risk of transmission beyond named close contacts. The attack rates should be considered minimum estimates because only contacts who access testing can subsequently be identified as a case and because, to avoid mismatching, the process to identify transmission was highly specific. Despite freedoms allowed, DCT-participants were still advised to minimise contact and national restrictions were in place at the time of our study, which may have reduced likelihood of onward transmission. There was a skew in the DCT arm towards individuals who were able to work from home, which again would limit opportunities for non-household transmission. Differences in the number of contacts within workplaces and non-household settings could not be fully explored by this work due to national COVID-19 restrictions in place during the study period. Findings may not be generalisable to children, however, other work has investigated DCT in schools (20).

The study was undertaken as part of real-life management of contacts of COVID-19 cases, providing evidence of the impact that a DCT policy would have, if introduced. Nearly two years since the identification of SARS-CoV-2, the pandemic continues to have a significant impact on individuals and society. Developing public health interventions that mitigate both viral transmission and the wider impacts on health, wellbeing, prosperity, and society, including those arising from self-isolation, is essential. This study shows the potential benefits of daily testing while minimising the need for self-isolation.

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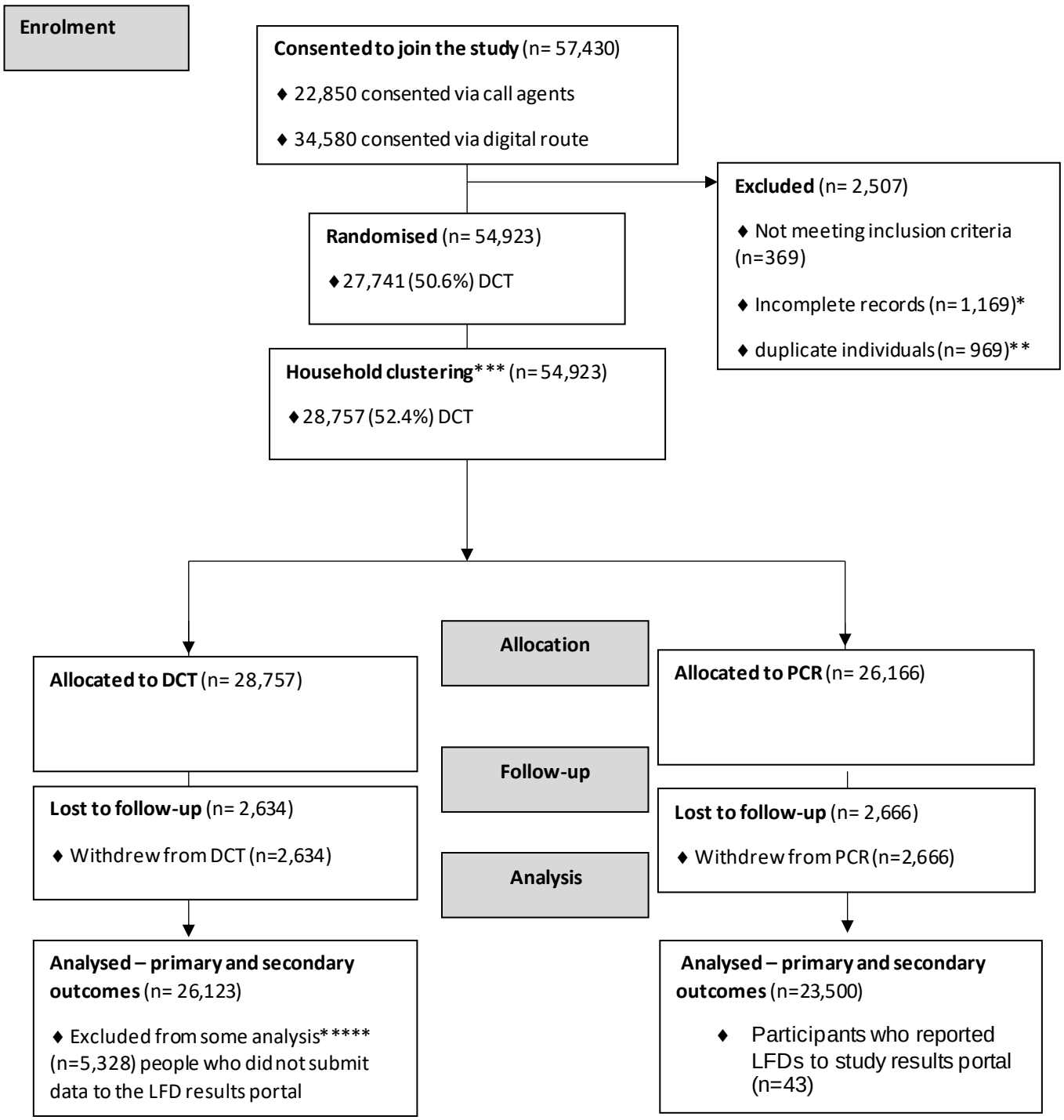
Figure 1 – Flow chart of study participation



* incomplete records were excluded following recruitment as no address or contact information was provided

** If multiple contacts were reported from a single household (concatination of door number and postcode), then all individuals in the household were assigned to the same arm of the study after recruitment, with all individuals assigned to the arm assigned to the first member of the household recruited.

*** If multiple contacts were reported from a single household (concatination of door number and postcode), then all individuals in the household were assigned to the same arm of the study after recruitment, with all individuals assigned to the arm assigned to the first member of the household recruited.

**** 5,328 were excluded from the LFD arm as they had not submitted results to the LFD portal and it was not possible to verify that they had participated in the study. Specific exclusion from supplementary attack rate analysis, LFD and PCR concordance.

515 **Table 1 – Socio-demographic characteristics of study participants by study arm**

516

		DCT arm (n=26,123)			PCR arm (n=23,500)			p-value
		Percentage	[95% CI]	(Number)	Percentage	[95% CI]	(Number)	
Sex	Female	53.6%	[53 - 54.2%]	(14,000)	54.2%	[53.6 - 54.8%]	(12,734)	0.18
	Male	46.4%	[45.8 - 47%]	(12,113)	45.8%	[45.2 - 46.4%]	(10,756)	
Age	Mean	41.8 years			42 years			0.38
	95% CI	[41.7 – 42.0]			[41.8 - 42.2]			
	Range	18 – 87			18 – 89			
Geography	East Midlands	7.0%	[6.7 - 7.3%]	(1,822)	7.0%	[6.6 - 7.3%]	(1,635)	0.26
	East of England	8.3%	[7.9 - 8.6%]	(2,158)	8.9%	[8.5 - 9.2%]	(2,086)	
	London	11.3%	[10.9 - 11.7%]	(2,947)	11.2%	[10.8 - 11.6%]	(2,627)	
	North East	8.7%	[8.4 - 9.1%]	(2,282)	8.5%	[8.1 - 8.8%]	(1,992)	
	North West	18.8%	[18.4 - 19.3%]	(4,917)	19.3%	[18.8 - 19.8%]	(4,524)	
	South East	14.6%	[14.2 - 15%]	(3,813)	14.2%	[13.7 - 14.6%]	(3,331)	
	South West	10.7%	[10.3 - 11%]	(2,782)	10.4%	[10 - 10.8%]	(2,446)	
	West Midlands	8.4%	[8.1 - 8.8%]	(2,199)	8.5%	[8.1 - 8.8%]	(1,995)	
	Yorkshire & Humber	12.2%	[11.8 - 12.6%]	(3,176)	12.2%	[11.7 - 12.6%]	(2,856)	
Index of multiple deprivation	1 - Most deprived	5.8%	[5.5 - 6%]	(1,493)	6.0%	[5.7 - 6.3%]	(1,403)	0.04
	2	6.3%	[6 - 6.6%]	(1,630)	6.8%	[6.5 - 7.1%]	(1,589)	
	3	7.4%	[7 - 7.7%]	(1,912)	7.7%	[7.3 - 8%]	(1,788)	
	4	8.4%	[8.1 - 8.8%]	(2,194)	8.4%	[8.1 - 8.8%]	(1,972)	
	5	9.7%	[9.3 - 10.1%]	(2,521)	9.3%	[8.9 - 9.7%]	(2,168)	
	6	10.3%	[9.9 - 10.7%]	(2,672)	10.4%	[10 - 10.7%]	(2,418)	
	7	11.7%	[11.3 - 12.1%]	(3,032)	11.8%	[11.3 - 12.2%]	(2,745)	
	8	12.3%	[11.8 - 12.6%]	(3,182)	12.5%	[12.1 - 12.9%]	(2,922)	
	9	12.9%	[12.5 - 13.3%]	(3,357)	12.6%	[12.2 - 13.1%]	(2,952)	
	10 - Least deprived	15.4%	[14.9 - 15.8%]	(3,993)	14.6%	[14.1 - 15%]	(3,399)	
Ethnicity	Asian	3.3%	[3.1 - 3.5%]	(856)	3.6%	[3.3 - 3.8%]	(826)	0.12
	Black	1.0%	[0.9 - 1.1%]	(264)	1.0%	[0.9 - 1.2%]	(241)	
	Mixed	2.7%	[2.5 - 2.9%]	(707)	2.5%	[2.3 - 2.6%]	(569)	
	White	91.8%	[91.4 - 92.1%]	(304)	91.9%	[0.9 - 1.2%]	(250)	

	Other	1.2%	[1 - 1.3%]	(23,718)	1.1%	[91.5 - 92.2%]	(21,346)	
Self-reported vaccination*	Unvaccinated	13.1%	[12.7 - 13.5%]	(3,390)	13.0%	[12.5 - 13.4%]	(3,022)	0.02
	1 dose	24.6%	[24 - 25.1%]	(6,343)	25.7%	[25.1 - 26.2%]	(5,978)	
	2 doses	62.3%	[61.7 - 62.9%]	(16,103)	61.4%	[60.7 - 62%]	(14,291)	
Case in household**	No	39.3%	[38.7 – 39.9%]	(10,134)	40.3%	[39.7 – 41%]	(9,376)	0.02
	Yes	60.7%	[60.1 – 61.3%]	(15,666)	59.7%	[59 – 60.3%]	(13,877)	
Homeworker***	No	40.1%	[39.5 - 40.7%]	(10,324)	43.2%	[42.6 - 43.9%]	(10,035)	<0.001
	Yes	59.9%	[59.3 - 60.5%]	(15,424)	56.8%	[56.1 - 57.4%]	(13,175)	
Household multiple****	No	58.3%	[57.7 - 58.9%]	(15,239)	63.9%	[63.2 - 64.5%]	(15,006)	<0.001
	Yes	41.7%	[41.1 - 42.3%]	(10,884)	36.1%	[35.5 - 36.8%]	(8,494)	

* Self-reported vaccination status. Question: 'Have you received a vaccination for COVID-19'. Options; Yes – 2 doses, Yes – 1 dose, No.

** Self-reported. Question: 'Does the person with COVID-19 that you were exposed to live in your household?'. Options; Yes, No.

*** Self-reported. Question: 'Are you able to work from home?'. Single choice options; Yes, No.

****Derived from house number and postcode given at recruitment. Participants with same postcode and house number grouped as household members. Includes individuals registered more than once if more than 3 days from first registration.

[1] Data completeness for sex n=23,490 PCR (100%) and 26,113 DCT (100%). Pearson Chi^2 =1.77

Data completeness for age n=23,153 PCR (98.5%) and 25,749 DCT (98.6%). Mann-Whitney

Data completeness for geography (PHE region) n=23,492 PCR (100 %) and 26,096 DCT (99.9%). Pearson Chi^2 =10.04

Data completeness for index of multiple deprivation (IMD) n=23,356 in PCR (99.4%) and 25,986 DCT (99.5%). Pearson Chi^2 =10.04

Data completeness for ethnicity n=23,232 PCR (98.9%) and 25,849 DCT (99.0%). Pearson Chi^2 =8.69

Data completeness for self-reported vaccination status n=23,291 PCR (99.1%) and 25,836 DCT (98.9%). Pearson Chi^2 =8.14

Data completeness for index case being in household n=23,253 PCR (98.9%) and 25,800 DCT (98.8%). Pearson Chi^2 =5.55

Data completeness for self-reported ability to work from home n=23,210 in PCR (98.8%) and 25,748 DCT (98.6%). Pearson Chi^2 =49.52

Data completeness for having more than one household member/an individual being registered more than once in the study n=23,500 PCR (100%) and 26,123 DCT (100%). Pearson Chi^2 =158.36

Table 2 – Number of COVID-19 PCR positive participants (secondary cases), their contacts (secondary contacts) and the number of tertiary cases identified in CTAS records

	DCT	SI	Total
Number of PCR positive cases among study participants (secondary cases)	2,202	2,359	4,561
Number of PCR positive cases among study participants (secondary cases) identified in CTAS	2,230	2,385	4,615
Number of secondary cases with CTAS secondary contacts	1,762	1,948	3,710
Number of secondary cases with CTAS household secondary contacts	1,727	1,922	3,649
Number of secondary cases with CTAS non-household secondary contacts	219	214	433
Number of secondary contacts	4,909	5,206	10,115
Number of household secondary contacts	4,305	4,638	8,943
Number of non-household secondary contacts	604	568	1,172
Number of tertiary cases	314	390	704
Number of tertiary cases from household contacts	296	370	666
Number of tertiary cases from non-household contacts	18	20	38
Number of secondary contacts per participant case (all cases)	2.2	2.2	2.2
Number of secondary contacts per participant case (cases with contacts)	2.8	2.7	2.7
Number of household secondary contacts per participant case (all cases)	1.9	1.9	1.9
Number of household secondary contacts per participant case (cases with household contacts)	2.5	2.4	2.5
Number of non-household secondary contacts per participant case (all cases)	0.3	0.2	0.3
Number of non-household secondary contacts per participant case (cases with non-household secondary contacts)	2.8	2.7	2.7
Number of tertiary cases per CTAS secondary case	0.1	0.2	0.2
Number of tertiary cases per secondary case via household secondary contact	0.1	0.2	0.1
Number of tertiary cases per secondary case via non-household secondary contact	0.01	0.01	0.01

***** where a case had multiple records, all were included

552 **Table 3 – Attack rates in secondary contacts and difference in percentages amongst secondary contacts**

553

Attack rates in secondary contacts		Percent positive	95% Confidence interval	Percent positive	95% Confidence interval
		Unadjusted (n = 10,115)		**Adjusted (n = 9,962)**	
DCT arm		6.40%	(5.67%, 7.13%)	6.40%	(5.67%, 7.12%)
SI arm		7.49%	(6.71%, 8.27%)	7.44%	(6.67%, 8.22%)
Difference in percentage	DCT vs SI arms	-1.09%	(-2.16%, -0.03%)	-1.04%	(-2.11%, 0.02%)
		Unadjusted (n = 10,115)		**Adjusted (n = 9,962)**	
DCT arm: household secondary contacts		6.88%	(6.08%, 7.67%)	6.88%	(6.07%, 7.68%)
SI arm: household secondary contacts		7.98%	(7.13%, 8.82%)	7.96%	(7.11%, 8.81%)
DCT arm: non-household secondary contacts		2.98%	(1.52%, 4.44%)	2.79%	(1.37%, 4.21%)
SI arm: non-household secondary contacts		3.52%	(1.90%, 5.14%)	3.55%	(1.92%, 5.18%)
Difference in percentage	DCT vs SI: household secondary contacts	-1.10%	(-2.26%, 0.06%)	-1.08%	(-2.25%, 0.09%)
	DCT vs SI: non-household secondary contacts	-0.54%	(-2.72%, 1.64%)	-0.77%	(-2.95%, 1.41%)
		Unadjusted (n = 10,077)		**Adjusted (n = 9,962)**	
DCT arm: 0 or 1 dose vaccine		6.93%	(5.88%, 7.98%)	7.07%	(6.03%, 8.11%)
SI arm: 0 or 1 dose vaccine		7.78%	(6.72%, 8.85%)	7.81%	(6.75%, 8.88%)
DCT arm: 2 doses vaccine		5.72%	(4.71%, 6.73%)	5.62%	(4.63%, 6.62%)
SI arm: 2 doses vaccine		7.06%	(5.94%, 8.17%)	7.01%	(5.90%, 8.13%)
Difference in percentage	DCT vs SI: 0 or 1 dose vaccine	-0.85%	(-2.34%, 0.64%)	-0.74%	(-2.23%, 0.74%)
	DCT vs SI: 2 doses vaccine	-1.33%	(-2.84%, 0.17%)	-1.40%	(-2.91%, 0.11%)

554

555 'Unadjusted' models include named variables (arm, arm and household exposure, and arm and vaccination status)
556 as covariates. 'Adjusted' versions of these models were obtained by adding all others from household exposure,
557 vaccine status and ability to work from home. SI was used as a baseline against which DCT was compared. Model
558 testing for significance of arm and household exposure interaction and arm and vaccination status interaction were
559 not significant (Unadjusted model arm and household exposure: p=0.97, adjusted model arm and household
560 exposure: p=0.81 and unadjusted model arm and vaccination status: p=0.56, adjusted model arm and vaccination
561 status: p=0.46 respectively).

562

563

564 **Table 4 - PCR results by test and by participant**

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		PCR arm	DCT arm	Total
		Results by test		
Result	Negative	23,388	33,090	56,478
	Positive	2,790	2,203	4,993
	Void	316	403	719
	Total	26,494	35,696	62,190
		Results by participant		
Result	Negative and/or void only	14,985	15,967	30,952
	Positive	2,359	1,647	4,006
	Total	17,344	17,614	34,958
	Proportion positive	13.6%	9.4%	11.5%

566

567 **Table 5 - Final survey behavioural responses, by group**

568

	Responses	PCR (N=8,807)		DCT – tested positive (N=754)		DCT - no positive test (N=10,443)		*p*-value^
		n	%**	n	%**	n	%**	
1. Last 24-hour activities *	**Work, college, university**	72	25%	24	20%	2,462	29%	0.028
	Other indoor place	105	37%	42	35%	3,813	45%	0.001
	Outdoors with friends/family	72	25%	21	17%	2,349	28%	0.023
	Indoors with friends/family	54	19%	9	7%	1,146	14%	0.005
	Any other reason	110	39%	67	55%	2,984	35%	<0.001
	None of these*	487	63%	631	84%	2,029	20%	<0.001
2. 7 days close contacts during study period	**Much more**	209	2%	9	1%	374	4%	
	Slightly more	289	3%	20	3%	742	7%	
	About the same	699	8%	67	9%	1,801	17%	<0.001
	Slightly less	415	5%	28	4%	1,563	15%	
	Much less	7,180	82%	626	84%	5,946	57%	
3. Confidence in test accuracy	**Completely**	3,590	43%	255	40%	4,638	44%	
	Very	2,997	36%	156	24%	4,025	39%	
	Fairly	1,510	18%	121	19%	1,617	16%	<0.001
	Not very	180	2%	68	11%	127	1%	
	Not at all	69	1%	44	7%	33	0%	
4. Activities whilst self-isolating	**Work, college, university**	713	19%	29	13%	-	-	0.055
	Other indoor place	1,264	33%	107	48%	-	-	<0.001
	Outdoors with friends/family	918	24%	49	22%	-	-	0.638
	Indoors with friends/family	684	18%	29	13%	-	-	0.096
	Left home for any other reason	3,122	81%	168	76%	-	-	0.088
5. Reasons for leaving home when isolating⁺	**Earn money**	74	2%	4	2%	-	-	0.992
	Keep my job	59	1%	4	2%	-	-	0.609
	Practical reasons (shopping, caring etc)	393	8%	13	6%	-	-	0.328
	Mental health	668	14%	15	7%	-	-	0.005
	Other important things	265	6%	18	9%	-	-	0.100

Probably not infectious	152	3%	8	4%	-	-	0.787
I didn't leave home+	4,099	47%	532	73%	-	-	<0.001
To take a coronvirus test	4,084	87%	182	87%	-	-	1.000

Items are as follows:

1. Thinking about yesterday, please tick all the things you did (Data completeness: 8.7% (769/8,807) in PCR arm, 99.7% (752 /754) in DCT – tested positive group , 99.9% (10,431/10,443) in DCT – no positive test group provided at least one response to items 1-6)
2. Compared to the week before, in the last 7 days did you have more or less close contact with people you don't live with, indoors and for more than 15 minutes? (Data completeness: 99.8% (8,792/8,807) in PCR arm, 99.5% (750/754) in DCT –tested positive group , 99.8% (10,426/10,443) in DCT –no positive test group responded to this question)
3. [If yes to: In the past 7 days, did you take any tests for coronavirus] How confident are you that your test results were accurate? (Data completeness: 94.8% (8,346/8,807) in PCR arm, 85.4% (644/754) in DCT – tested positive group , 100.0% (10,440/10,443) in DCT –no positive test group responded to this question)
4. Thinking about the last 7 days, how often have you done each of these things [since getting your first positive test result] (note: these were recoded as binary never vs once or more, options were: never, once or twice, three or four times, five times or more) (Data completeness: 43.8% (3,858/8.807) in PCR arm, 29.3% (221/754) in DCT - tested positive group provided at least one response to items 1-5)
5. Did you leave home [following a positive test result / during your self-isolation period] for any of the following reasons? (Please tick all that apply) (Data completeness: 98.5% (8,678/8.807) in PCR arm, 97.2% (733/754) in DCT - tested positive group provided at least one response to items 1-8)

* Percentages for responses 1-5 are calculated from those who reported leaving home; for response 6 (none of these) the proportion is calculated among those who responded to any of items 1-6.

** Except where noted, percentages are calculated from those who responded to each question

+ Percentages for responses 1-6 are calculated from those who reported at least one reason for leaving home, this includes people who left home to take a coronavirus test [data not presented here]; for response 7 (I didn't leave home) the proportion is calculated among those who provided at least one reponse to this question.

^ For items where respondents were asked to tick all responses that applied to them, p-values were calculated for each 2x2 comparison. For items where respondents were asked to select a single response, an overall p-value was calculated for that item.