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COVID-19: could CT provide the best population level biomarker? Incidental COVID-19 in major trauma patients suggests higher than predicted rates of infection in London

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AIM: To evaluate incidental findings in major trauma patients, and to explore whether computed tomography (CT) could be used to assess prevalence and estimate disease spread in the general population.

MATERIALS AND METHODS: The study population included all patients admitted following major trauma between 1 January 2020 and 30 April 2020 with CT including the lungs (n=523). Major trauma patients admitted pre-COVID-19 from 1–31 January and 1–31 March 2019 comprised a control group (n=252). The assessing radiologists, blinded to the time period, used double reading with consensus to determine if the patient had CT signs of COVID-19. Lung appearances were classified as no evidence of COVID-19; minor signs; or major signs. The proportion of patients with incidental COVID-19 changes was recorded over the study period, and the percentage of the population who had been infected by COVID-19 by the end of April 2020 estimated.

RESULTS: CT appearances consistent with COVID-19 began to exceed a background pre-COVID rate in the second week of February and did not decline until 2 weeks after lockdown. By the end of April 2020, approximately 45% of the population had been infected.

CONCLUSIONS: CT of major trauma patients can be used to monitor the spread of COVID-19. This novel technique could be used retrospectively or prospectively anywhere where trauma scans are available, to monitor the disease in the local population.
Introduction

The coronavirus disease 2019 (COVID-19) is caused by the severe acute respiratory syndrome SARS-COV-2 virus.\textsuperscript{1} Chest radiography is generally considered to be the primary imaging method used for clinical management,\textsuperscript{2} but confirmation of disease is usually by reverse-transcription polymerase chain reaction (RT-PCR) testing.\textsuperscript{3} Although the mainstay of diagnosis, RT-PCR testing is not 100% accurate,\textsuperscript{4} and limitations of the test compared with CT have been highlighted.\textsuperscript{5} In addition, its use is frequently restricted to those with symptoms rather than the whole population, with resulting paucity of data on rates of asymptomatic disease, and hence, inadequate knowledge of how many people have had the disease. Furthermore, there is still lack of information on exactly when the disease first affected populations outside China.

Chest computed tomography (CT) is not regarded as the method of choice for the diagnosis of or screening for COVID-19, although CT was used for diagnosis in the early stages of the pandemic in both China and Italy.\textsuperscript{6} Nevertheless, it has been noted that some patients, including those undergoing CT of the chest following major trauma, show CT signs of COVID-19 despite having no other signs or symptoms of the disease. Incidentally discovered COVID-19 has also been reported by other radiologists.\textsuperscript{7,8} Major trauma patients are particularly interesting because trauma can be considered a random event, and this group of patients therefore represents a random, but known sample of the general population. It is now well recognised that many people can have COVID-19 without exhibiting symptoms,\textsuperscript{9} and these people will remain undiagnosed in the absence of whole-population RT-PCR or other testing. The present study used retrospective information from patients who underwent CT for major trauma to evaluate the rates of disease in the general population, on the basis that these patients can be considered to represent an approximation to a random sample of the population. This novel method was used to determine both the start of the disease impacting the population, and how many people have been affected by it. This method, which could be used retrospectively or prospectively, provides insights into the amount of disease in circulation, and population exposure to COVID-19 over time.

Materials and methods

Ethical approval for the study was given by the National NHS Research Ethics Committee (REC) and the combined Health Research Authority (HRA) and Health and Care Research Wales (HCRW) (reference 20/YH/0202).

The study was performed at a major trauma centre within a major trauma network, which comprises seven further acute hospitals, two ambulance services, and two air-ambulance services, serving a population of more than 2.6 million.

Retrospective review of the radiology information system was performed to identify all CT examinations that included the chest referred from the emergency department over the “study” and “control” periods. The study period was 1 January until 30 April 2020 and the control period between 1 and 31 January 2019 and 1 and 31 March 2019. All cases in which the clinical history described major trauma and where the prime clinical indication was to rule out acute traumatic injury were included. All non-traumatic CT chest examinations, including acute chest pain or shortness of breath, were excluded (Fig 1).

Recognised CT features of COVID-19 were used to determine whether there were major or minor signs indicating COVID-19 lung disease on the emergency scans.\textsuperscript{10} Major signs of COVID-19 on CT were defined as multifocal, bilateral, ground-glass opacities with or without consolidation, in a peripheral, mixed (peripheral and central), or perilobular distribution. Minor signs were defined as non-peripheral, ground-glass opacities, or unilateral changes.

As these signs are not unique to COVID-19, a control time period before the virus was circulating, but at a corresponding time of year, was required to capture the rate of background seasonal, non-COVID-19 viral lung infections. The prevalence of signs in this time period was assumed to represent the baseline of expected lung changes related to non-COVID-19 infections, and this (the “noise”) was subtracted from the prevalence of signs in the study period (the “signal”) to calculate the true disease prevalence of COVID-19.\textsuperscript{11}

All CT examinations were read by two experienced radiologists (experience ranging from 7 to 27 years) by double reading with consensus and blinded to the time period. Given the study population, particular regard was made to ensure that the changes were not due to pulmonary contusion or aspiration (by excluding signs of significant

\begin{figure}[h]
\centering
\includegraphics[width=\textwidth]{methodology.png}
\caption{Methodology for identification of study and control groups.}
\end{figure}
The incidence rate times the average duration. Finally, the month is rare, and therefore, the point prevalence equals simple formula in any month as the prevalence (P) divided by 0.5 using the simple formula \( I = P / D \) where we assume the disease in any month is rare, and therefore, the point prevalence equals the incidence rate times the average duration. Finally, the percentage of the population who have had COVID-19 equates to the cumulative incidence.

All tests of significance and statistical analysis used STATA version 14 (Stata Corporation, TX, USA). The main statistical analysis was a test of two proportions, with \( p < 0.05 \) considered as indicating significance.

**Results**

Patient characteristics in the control and study groups show similar characteristics between the two groups (Table 1). Fig 2 shows a histogram of the age distribution of patients in the study and control group combined, showing a broad range of ages from 1 to 100 years. Approximately 67% are male in both groups. As a random sample there are slightly more males than would be expected for the population. Nevertheless, the results confirm trauma patients are a reasonable sample of the general population.

Table 2 shows the overall test results by age (<50 years and ≥50 years) for the study and control groups. The proportion of signs that were major rather than minor increased with age, suggesting greater disease severity.

The prevalence within each month of the control and study periods is summarised in Table 3. The prevalence of lung signs in the pre-COVID-19 control group was 2.4%. In February, March, and April 2020 there was a steady increase in the prevalence due to COVID-19 from 3.8% to 8.3%–10.6% respectively. Overall, the study group prevalence of 7.6% was three-times higher than the control group prevalence of 2.4% \( (p=0.004 \text{ using a test of two proportions}) \). When considering just March 2020 to March 2019 this increased to six-times higher \( (10.7 \text{ versus } 1.7, p=0.005) \). The significance level changed to \( p<0.001 \) if just the study group from February to April 2020 is considered where there is evidence that the virus had affected the population compared to the control group. To estimate the incidence rate, the control prevalence is subtracted and divided by 0.5 to obtain the incidence rate per 100 per month. The cumulative incidence then gives the proportion of the population who have had the disease. This increases from 0% by the end of January, to 7.6% by the end of February, 24.2% by the end of March, and 45.4% by the end of April.

Table 4 shows the percentage of patients with COVID-19 signs weekly from 1 January 2020 week by week and the three-week moving average. Up to the week ending 4 February, the proportion with signs was similar to the control group proportion of 2.4%, suggesting that the virus had minimal impact during that time; however, from 5 February, there was a large and sustained increase indicating that COVID-19 infection had started to impact on the population.

Fig 3 shows a graph of the percentage of patients with COVID-19 signs in the study group by weeks starting on 1 January 2020. The graph includes a 3-week moving average to smooth the data points. The graph also shows the control group prevalence of 2.4% as a straight line and marks the points in time of the start of the impact of COVID-19 on the population (estimated as 5–11 February) and the date of lockdown on 23 March. The data points suggest a downturn in the prevalence rate occurred about 2 weeks after the start of lockdown, and Table 4 and Fig 3 show that the peak prevalence was between 25 March and 7 April. During the month of April, the estimated population who had experienced COVID-19 infection increased from 24.2% to 45.4%.

**Table 1**

| Group  | Total | Men | Women | Mean age (SD) | Proportion men |
|--------|-------|-----|-------|---------------|---------------|
| Control | 252   | 171 | 81    | 49.9 (23.2)   | 67.8          |
| Study  | 523   | 346 | 176   | 54.9 (23.9)   | 66.2          |
| Total  | 775   | 517 | 257   | 53.3 (23.8)   | 66.7          |

Male/female not recorded for one patient in the study group.

**Figure 2** Histogram of ages of patients in study and control groups. Study: \( n=523 \), mean 54.9 (SD 23.9); median 56, range 1–100; control: \( n=252 \), mean 49.9 (SD 23.2) median 47, range 16–99.

**Table 2**

| Result | Study <50 years | ≥50 years | Control <50 years | ≥50 years | Total <50 years | ≥50 years | Total |
|--------|-----------------|-----------|-------------------|-----------|-----------------|-----------|-------|
| Negative | 214             | 269       | 483               | 134       | 112             | 246       |       |
| Minor   | 10              | 20        | 30                | 1         | 4               | 5         |       |
| Major   | 1               | 9         | 10                | 0         | 1               | 1         |       |
| Total   | 225             | 298       | 523               | 135       | 117             | 252       |       |

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Figs 4 and 5 show selected images from the study. Fig 4a,b is from a man aged 84 years with major signs of COVID-19. These are multifocal, rounded, ground-glass opacities in a peripheral distribution within both lungs. There were 10 people with this level of disease in the study group. Fig 4c shows a woman aged 86 years and Fig 4d shows a younger person, a man aged 19 years, both with minor signs of COVID-19. In both cases, the changes were morphologically consistent with COVID-19, but they were unilateral. In the study group, of those aged 15–34 years there were 7.5% (11/146) with signs, between 35–54 years there were 0% (0/107) and aged >55 years there were 10.9% (29/266). Fig 5 shows the only case of major signs to occur in the control group prior to COVID-19 in March 2019. Given its very close resemblance to COVID-19 lung disease, it is surmised that this was probably a less severe coronavirus type of viral pneumonia.

### Discussion

One of the difficulties in tracking COVID-19 infection is the major variation in symptoms, from none at all to life threatening. In the absence of mass RT-PCR testing, a test which itself has limitations, the true incidence in the population at any one time is not known. CT is generally not recommended as the primary method for screening for COVID-19 for three major reasons. Firstly, the CT signs of COVID-19 may overlap with other respiratory conditions. Secondly, some patients with COVID-19 have normal chest CT early in the course of disease, and thirdly COVID-19 is highly contagious, and using imaging equipment on the population is not recommended because of the risk the virus may remain on the surface of a CT scanner. Asymptomatic disease is a public health issue because asymptomatic individuals who are nevertheless infectious to

### Table 3

Prevalence within each month and estimated percentage population who have had COVID-19 signs for the control and study groups.

| Date    | Total | With any COVID-19 signs on imaging (major signs) | Prevalence | Prevalence (P) minus baseline | Estimated incidence rate (I=P/0.5) per month | Estimated percent of the population who have had disease |
|---------|-------|-------------------------------------------------|------------|-------------------------------|---------------------------------------------|-----------------------------------------------------|
| **Control** |       |                                                 |            |                               |                                             |                                                     |
| Jan 2019 | 137   | 4 (0)                                           | 2.9%       |                               |                                             |                                                     |
| Mar 2019 | 115   | 2 (1)                                           | 1.7%       |                               |                                             |                                                     |
| **Study** |       |                                                 |            |                               |                                             |                                                     |
| Jan 2020 | 130   | 3                                               | 2.3%       | NC                            | NC                                          | 0.0                                                 |
| Feb 2020 | 167   | 11 (5)                                          | 6.2%       | 3.8%                          | 7.6 per 100                                 | 7.6                                                 |
| Mar 2020 | 131   | 14 (5)                                          | 10.7%      | 8.3%                          | 16.6 per 100                                | 24.2                                                |
| Apr 2020 | 100   | 13 (5)                                          | 13.0%      | 10.6%                         | 21.2 per 100                                | 45.4b                                               |
| **Total** | 523   | 40 (10)                                         | 7.6%       |                               |                                             |                                                     |

NC, not calculated as prevalence the same as the control group prevalence and estimated effect of virus on population is zero.

* Based on estimated duration of signs visible on CT for 2 weeks (0.5 months) and incidence = prevalence/duration, and basic unit of time is months. Estimates could be refined using the prevalence odds where \( P(1−P) = ID \) rather than \( P=ID \). Given the potential error in the estimation in the time that the disease is visible on imaging \( D \), more sophisticated measures may only serve to suggest false accuracy and have been avoided in the present study.

** Ninety-five percent confidence interval (33.3–61.9%). Test of two proportions between study group prevalence of 7.6% and control group of 2.4% \( p=0.004 \).

### Table 4

Percentage of patients in the study group with COVID-19 signs by weeks from 1 January 2020, 3-week moving percentage, and the prevalence in study group after subtracting the control group prevalence.

| Week    | Patients | COVID-19 signs (major) | Percentage | 3 week moving percentage (P) | \( P−\text{control (2.4%)} \) |
|---------|----------|------------------------|------------|-------------------------------|--------------------------------|
| 1–7 Jan | 30       | 0                      | 0%         | NC                            | NC                             |
| 8–14 Jan| 33       | 0                      | 0%         | 2.4                           | 0.0                            |
| 15–21 Jan| 22     | 2                      | 9.1%       | 2.4                           | 0.0                            |
| 22–28 Jan| 27     | 0                      | 0%         | 4.2                           | 1.8                            |
| 29–4 Feb| 46       | 2                      | 4.3%       | 2.6                           | 0.2                            |
| 5–11 Feb| 42       | 1                      | 2.4%       | 6.2                           | 3.8                            |
| 12–18 Feb| 41      | 5                      | 12.7%      | 7.0                           | 4.6                            |
| 19–25 Feb| 31      | 2                      | 6.5%       | 7.3                           | 4.9                            |
| 26–3 Mar| 38       | 1                      | 2.6%       | 6.4                           | 4.0                            |
| 4–10 Mar| 40       | 4 (1)                  | 10.0%      | 7.3                           | 4.9                            |
| 11–17 Mar| 32     | 3                      | 9.4%       | 9.9                           | 7.5                            |
| 18–24 Mar| 19      | 2 (1)                  | 10.5%      | 13.7                          | 11.3                           |
| 25–31 Mar| 22      | 5 (3)                  | 22.7%      | 20.0                          | 17.6                           |
| 1–7 Apr| 24       | 6 (3)                  | 25.0%      | 20.0                          | 17.6                           |
| 8–14 Apr| 19       | 2 (1)                  | 10.5%      | 15.5                          | 13.1                           |
| 15–21 Apr| 28    | 3 (0)                  | 10.7%      | 9.7                           | 7.3                            |
| 22–28 Apr| 25     | 2 (1)                  | 8.0%       | NC                            | NC                             |

NC, not calculated: 3-week moving percentage cannot be calculated.

* Estimated start of the effect of COVID-19 on population.
others will unknowingly be circulating in the general population.\textsuperscript{17}

Trauma can be considered a random event, and therefore, people presenting with major trauma represent a randomly selected sample of the local population. Major trauma describes serious and often multiple injuries that may require lifesaving interventions. It is recognised that trauma can have a bi-modal distribution with a first peak at younger ages and a second peak at older ages.\textsuperscript{18} The present distribution is more uniform, but with a larger dataset any studies with such a distribution could be statistically adjusted to a uniform distribution. The incidence of unsuspected COVID-19 CT lung changes found on scans carried out for trauma in southwest London in early 2020 indicate a clear pattern of previously unsuspected disease in this population, with a control pre-COVID trauma population for comparison. This incidence increased very rapidly over time, indicative of the spread of COVID-19 in London. It is likely, based on the present radiological evidence that the spread of infection in the catchment area of southwest London started earlier and was higher than originally thought. The present study estimates that the virus started to impact on the London population in the second week of February 2020. By the start of Lockdown on 23 March, approximately 20% were affected, but this increased to about 45% by the end of April, and that the peak disease prevalence occurred between 25 March and 7 April. It was only from 8 April, over 2 weeks after lockdown that the prevalence declined. The data before lockdown fit well with an exponential model where cumulative incidence = \(0.52 \times (1.37)^{\text{week}}\). Such a model suggests that the date of lockdown in critical. The model suggests that without lockdown 100% of the population would have been infected by week 17 (before the end of April); a week before or a week after makes a huge difference and provides additional evidence of the importance of the timing of lockdown.

Recent pilot antibody testing has suggested that 17% of the general London population have antibodies to the disease,\textsuperscript{19} although this may vary across the city, and the accuracy or false-negative rate of antibody tests themselves is not established in COVID-19. It is possible some people have only T-cell or poor or transient antibody responses, and therefore, the antibody tests may be an underestimate.\textsuperscript{20,21} The present method uses CT examinations, which were already available and have the advantage of being a random sample of the local population. If these data are collected prospectively, it could provide a continuous method of disease monitoring, and provide an opportunity for an early warning of future surges. The present study population is small, and it is acknowledged that there is some margin of error in the best estimate. Further sources of error could occur if the average disease duration on CT is much less or more than 2 weeks. Two weeks is considered to be a reasonable estimate, but if it were lower than this, the percentage of the population affected would be even higher; further analysis shows that 12 days, 2 weeks, or 3 weeks results in estimates that are 56.8%, 45.4% and 30.3% respectively. All these estimates are higher than the antibody test result of 17%, but highly dependent on the exact disease duration period. Although 2 weeks is the best estimate, further studies would be required to refine this. The method could be improved if a number of hospitals in an area combined to increase the numbers of patients and events. The method could potentially be applied by
designated small clusters of hospitals to give estimates of start dates as well as relative and absolute disease prevalence around the country.

Using a control group at the same time of year, but pre-COVID-19, allowed for the problem that signs of the disease on CT are not specific to COVID-19. The other major issue cited by the American College of Radiologists is that some patients with COVID-19 have normal chest CT, although there may be some issues related to how a definitive diagnosis is defined as all tests have problems associated with sensitivity and specificity. In response to this, a further improvement to the study design might be obtained by focusing only on men aged >50 years, who are the most likely group to consistently show signs of the disease if exposed. All patients in the study group described as showing major signs of COVID-19 were in this demographic and major signs were not seen until March. The number of events is smaller if this restriction is applied, but the overall estimate of the percentage of the population affected by the disease at the end of March 2020 does not appear to be dissimilar to the results using the whole study group. Although examination of the data shows that patients between the ages of 15–34 and >55 years are the mostly likely groups to show signs of COVID-19, further studies are required to look at this more closely. This could be chance or a genuine finding. If genuine, it may suggest that the lifestyle of younger people in London may increase the risk of infection, possibly as the result of multiple exposures related to socialising. In contrast, older men, in particular, may have a much lower tolerance to the disease, and hence, show more severe symptoms from lower levels of exposure.

Could the present results be explained by confounding? The present study looked at age and sex and adjusted for these factors and they are not confounders. The possibility of contusions mimicking COVID-19 was also considered, but contusions would not be expected to increase exponentially in February and March and then decline after lockdown; therefore, the results are consistent with SARS-COV-2 infection rather than any other explanation related to confounding factors; however, it is acknowledged that, in any prospective application of this methodology, it would be helpful to collect additional information and that the method will require some level of prospective validation.

In summary, the present results suggest that imaging of major trauma patients has great potential to provide insight into the spread and population prevalence of COVID-19 using already available evidence, and by making a further assumption on duration of the CT signs, the incidence, cumulative incidence, and the percentage population who have had the disease can be estimated. The method could be further developed by a working group of radiologists and epidemiologists and could then be applied to any population, retrospectively and prospectively, to follow the disease trajectory over time. If used in a real-time setting and with increasing radiologists’ awareness, both individuals and their contacts could benefit from the diagnosis of unsuspected disease, but it could also serve as an early warning of further local surges.

Conflict of interest

The authors declare no conflict of interest.

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