research

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ORIGINAL RESEARCH COMPARE randomised controlled trial

Early surgical reconstruction versus rehabilitation with elective delayed reconstruction for patients with anterior cruciate ligament rupture

Reijman M, Eggerding V, van Es E, et al

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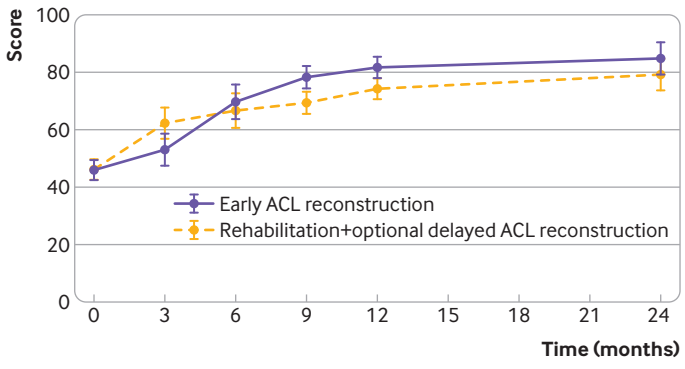
Study question Is there a clinically relevant difference in patients' perceptions of symptoms, knee function, and ability to participate in sports over a period of two years after rupture of the anterior cruciate ligament (ACL) between two commonly used treatment regimens?

Methods Patients aged 18-65 with an acute rupture of the ACL were included in an open labelled, multicentre, parallel randomised controlled trial. Patients were randomised to early reconstruction of the ACL (n=85) or rehabilitation followed by optional delayed ACL reconstruction (n=82, primary non-operative treatment). Patients were evaluated at 3, 6, 9, 12, and 24 months. The primary outcome was patients' perceptions of symptoms, knee function, and ability to participate in sports, assessed with the International Knee Documentation Committee score at each time point over 24 months. A higher score indicates more favourable patient ratings (optimum score 100).

Study answer and limitations In the rehabilitation and optional delayed ACL reconstruction group, 41 (50%) patients underwent reconstruction during follow-up. After 24 months, the early ACL reconstruction group had a significantly better (P=0.026) but not clinically relevant International Knee Documentation Committee score (84.7 *v* 79.4 (difference between groups 5.3, 95% confidence interval 0.6 to 9.9). Early surgical reconstruction of the ACL, compared with rehabilitation followed by elective surgical reconstruction, resulted in improved patients' perceptions of symptoms, knee function, and ability to participate in sports at the two year follow-up. This finding was significant (P=0.026) but the clinical importance is unclear. Interpretation of the results of the study should consider that 50% of the patients randomised to the rehabilitation group did not need surgical reconstruction. Recruitment bias could be present as a third of the eligible patients declined to participate because of a strong preference for one of the treatment options.

What this study adds Recovery was comparable for both treatments for rupture of the ACL. Half of the patients with rupture of the ACL were treated successfully without surgery.

Trial registration Netherlands Trial Register NL 2618.



International Knee Documentation Committee score over 24 months in the early anterior cruciate ligament (ACL) reconstruction group and the rehabilitation and optional delayed ACL reconstruction group. Values are mean (95% confidence intervals). Data were adjusted for sex, body mass index, age, and surgeon

Funding, competing interests, and data sharing The study received funding from ZonMw, a Dutch organisation for health research and care innovation. The authors have no competing interests. Deidentified participant data are available on request.

Covid-19 in Africa

ORIGINAL RESEARCH Prospective systematic postmortem surveillance study **FAST TRACK**

Covid-19 deaths in Africa

Mwananyanda L, Gill CJ, MacLeod W, et al

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Study question What proportion of deaths in an urban African population are associated with covid-19?

Methods Building on an existing postmortem surveillance system being used to track common infections among deceased infants, this study included deceased people of all ages with polymerase chain reaction testing of nasopharyngeal swabs for severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection. The deceased individuals were enrolled at the University Teaching Hospital morgue in Lusaka, Zambia, and molecular testing was conducted on site at a laboratory located minutes away from the morgue.

Study answer and limitations SARS-CoV-2 was detected in at least 16% (58/364) of all deaths during the three month period of surveillance. Deaths occurred across the age spectrum, not just among older people; 76% (53/70) of deaths occurred in people younger than 60 years, and 10% (7/70) were in children. Testing for SARS-CoV-2 was rarely done before death. Only about a third of patients who had died after being admitted to hospital and were included in the study had been tested in life, and no one who had died in the community had been tested. Deaths with covid-19 seemed to be rare only because testing was rarely done, and not because covid-19 was rare. Limitations included the short period of surveillance from a single site and inability to detect deaths occurring as late sequelae of covid-19.

What this study adds Other than data from South Africa, this is the first study to present systematic, unbiased data on the impact of covid-19 in an African population. If these results are typical, the impact of covid-19 in Africa has been substantially underestimated.

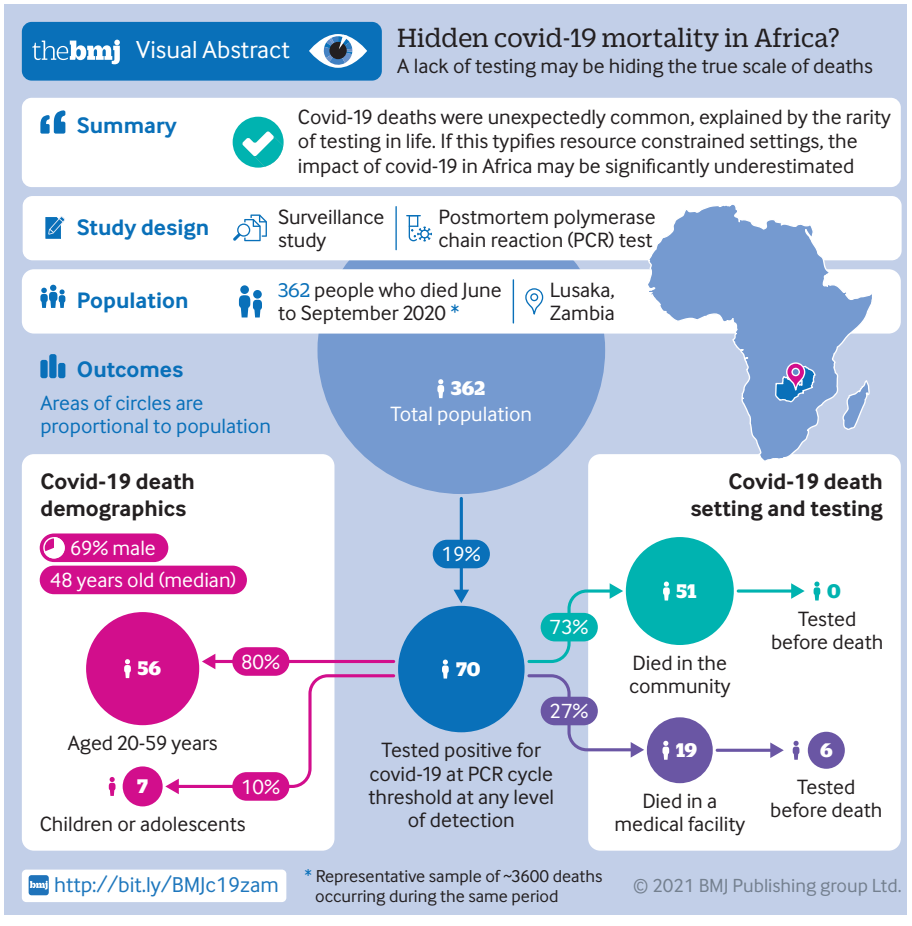
Funding, competing interests, and data sharing
This work was supported by the Bill & Melinda Gates Foundation.

All authors declare no competing interests. The data can be shared through a formal data agreement on reasonable request.

SALIM DAWOOD/AFP VIA GETTY IMAGES

Main findings of study (n=364 deaths). Values are numbers (percentages) unless stated otherwise

Measure	Results
Tested positive for SARS-CoV-2	58 (16) at PCR cycle threshold of <40; 70 (19) at any level of detection
Covid-19 deaths in community outside of medical care	51 (73)
Covid-19 deaths in males	48 (69)
Median (IQR) age of people who died with covid-19 (years)	48 (36-72)
Covid-19 deaths in people aged <60 years	53 (76)
Covid-19 deaths in people aged 20-59 years	46 (66)
Covid-19 deaths among children and adolescents	7 (10)
Tested for SARS-CoV-2 before death with covid-19	6/19 (32) facility deaths; no community deaths tested



At the time of writing, the number of cumulative cases of covid-19 globally stood at 102 million, with 2.2 million deaths. During the first quarter of 2020, Africa was thought to be at high risk of covid-19 mortalities, with the WHO Office for Africa predicting up to 150 078 (best case scenario 82 735; worst case scenario 189 579) covid-19 related deaths in 2020.[2]

More recent figures suggest that 62 504 deaths with covid-19 have occurred in Africa.[1 3] Various reasons for the muted impact of the pandemic in Africa have been postulated, including younger population demographics, rapid early quarantine measures, and pre-existing immunity. The relative contribution of these factors is unknown.[4]

Resource constrained settings need cost effective ways to track the pandemic and monitor the impact of public health interventions. Where clinical management of cases remains unchanged, covid-19 mortality roughly tracks disease incidence over time, so the study by Mwananyanda and colleagues,[5] in which postmortem nasopharyngeal swabs were tested for severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), provides a crude but convenient way to track the progress of the pandemic in Zambia. This study and others like it are important, as they could help us to assess the impact of public health policy decisions.

Mwananyanda and colleagues screened postmortem nasopharyngeal swabs collected from 10% of all deaths reported at the University Teaching Hospital morgue in Lusaka, Zambia, between June and September 2020. They found 19.2% to be positive for SARS-CoV-2 by reverse transcriptase polymerase chain reaction (RT-PCR).[5] Most of the positive samples came from people who had died in the community and were not diagnosed as having covid-19 before death. Furthermore, only 32% (6/19) of those who had died in hospital were tested before they died. A high proportion of positive cases were in children (10%; 7/70).

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Comorbidities

Reported comorbidities among all deaths with covid-19 included tuberculosis (31%), hypertension (27%), HIV/AIDS (23%), alcohol misuse (17%), and diabetes (13%). This echoes findings from other studies, including one from the Western Cape in South Africa that found HIV, tuberculosis, diabetes, hypertension, and chronic kidney disease to be risk factors for death from covid-19.[6] Mwananyanda and colleagues conclude that widespread community transmission of SARS-CoV-2 must be occurring in Zambia, and that many covid-19 cases and deaths are being missed or remain unreported.[5]

Although their findings are compelling, the authors acknowledge that limitations exist as to how far their findings can be generalised, because sampling was done for only three to four months. The RT-PCR assay used was also changed during the study, which might have affected the analytical accuracy of the data, and they did not independently validate the assays before use.

It would be interesting to see how the data presented compare with national autopsy data on SARS-CoV-2 being collected by the Zambia National Public Health Institute (ZNPHI). ZNPHI is the body responsible for coordinating Zambia's pandemic response, and from the start of the pandemic its policy has required postmortem covid-19 testing for all deaths occurring inside or outside health facilities. Its most recent definition of a covid-19 death is any death following a clinically compatible illness, unless a clear alternative and unrelated cause of death can be ascertained.[7 8]

Many covid-19 cases and deaths are being missed

Finally, although the prevalences of important comorbidities are reported, the degree to which these comorbidities might be associated with RT-PCR results remains unclear. The authors are doing further analyses to answer this question.

Mwananyanda and colleagues' findings add to the evidence that the impact of covid-19 in Zambia and elsewhere in Africa might be underestimated. Governments and funding bodies should fund comprehensive autopsy studies to characterise the range of pathologies now associated with covid-19 in Africa and to estimate the true effect of covid-19.[9]

Studies reporting accurate mortality rates in the years leading up to the pandemic are also needed, to help to quantify the number of excess deaths that might be attributable to covid-19 and to create a more accurate picture of the impact of this disease on the whole continent.

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SOPA/GETTY IMAGES

Excess mortality in Wuhan city and other parts of China during the three months of the covid-19 outbreak

Liu J, Zhang L, Yan Y, et al

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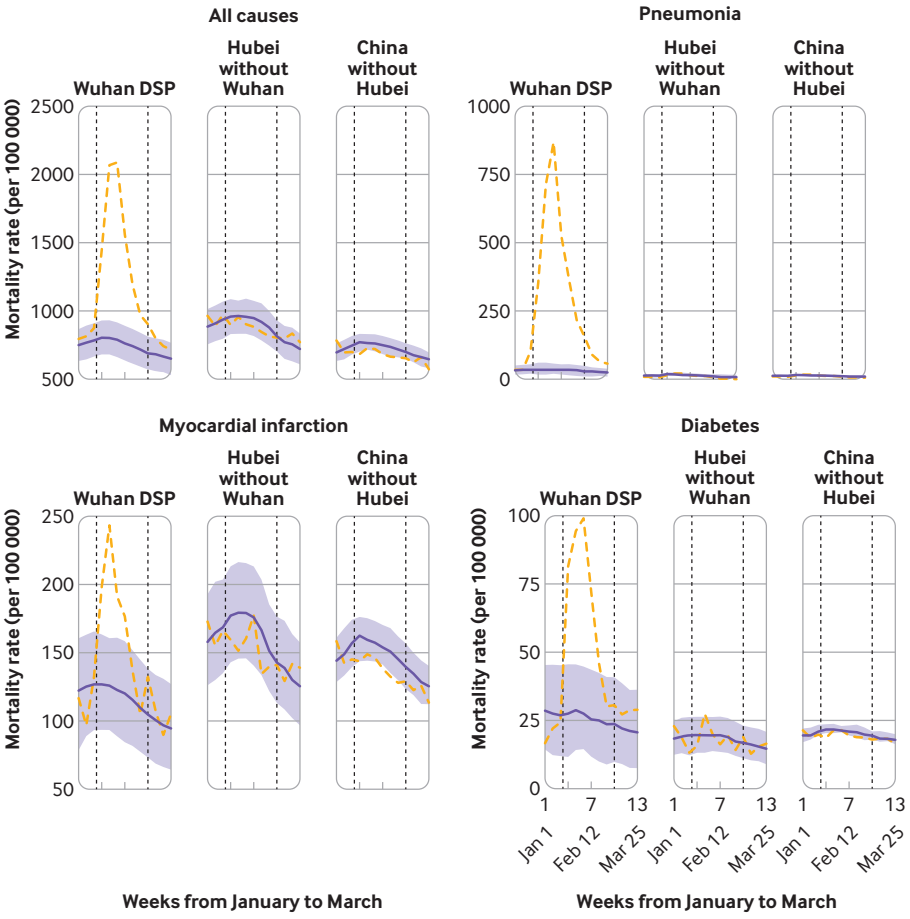
Study question What were the excess all cause and cause specific mortality rates in Wuhan city and elsewhere in China during the three months of the covid-19 outbreak?

Methods The nationally representative Disease Surveillance Point (DSP) system collected cause specific mortality from 605 urban districts and rural counties, covering more than 300 million people. The overall and weekly mortality rates during January-March 2020 (n=580 819 deaths) were estimated and compared with the predicted (or mean 2015-19) rates in different areas of China to obtain the rate ratios.

Study answer and limitations In three Wuhan DSP districts, the observed total mortality rate was 56% (rate ratio 1.56, 95% confidence interval 1.33 to 1.87) higher than the predicted rate (1147 *v* 735 per 100 000), chiefly as a result of an eightfold increase in pneumonia mortality (n=1682; 275 *v* 33 per 100 000; 8.32, 5.19 to 17.02), mainly covid-19 related, but a more modest increase in deaths from certain other diseases, including cardiovascular disease (n=2347; 1.29, 1.05 to 1.65) and diabetes (n=262; 1.83, 1.08 to 4.37). In Wuhan city (13 districts), 5954 additional (4573 pneumonia) deaths occurred in 2020 compared with 2019, with excess risks greater in central than in suburban districts (50% *v* 15%). In other parts of Hubei province or China, the small excess mortality from covid-19 was outweighed by reductions in death rates from non-covid-19 related pneumonia, chronic respiratory diseases, and road traffic incidents. This study could not assess the impact of the covid-19 outbreak on hospital admissions, clinical procedures, and case fatality rates after infection with severe acute respiratory syndrome coronavirus 2, responsible for covid-19.

What this study adds Except in Wuhan city, no increase was found in overall mortality in other parts of China during the three months of the covid-19 outbreak.



Trends in weekly observed (dashed orange lines) versus predicted (blue solid lines) mortality rates for selected major diseases between 1 January and 31 March 2020 in China across different Disease Surveillance Point areas. First vertical dotted line indicates the time when lockdown was implemented in Wuhan. Second vertical dotted line indicates when temporary makeshift hospitals were closed in Wuhan that provided central quarantines for all people who tested positive for severe acute respiratory syndrome coronavirus 2 during the covid-19 outbreak. For different diseases, the ranges of mortality rates vary in y axis. The shaded areas indicate 95% confidence intervals for predicted mortality rates

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