Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

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robust data for pandemic preparedness, reporting, and response.

Crit Care Africa, funded by UK Research and Innovation, and a sibling of the ten-country Wellcome-funded Asia network,[5] is one such initiative that has built a federated network of high-quality registries of intensive care units across the continent. The network uses a setting-adapted data platform and a Common Data Model, enabling local research priorities and seamless data sharing with the WHO–International Severe Acute Respiratory and Emerging Infection Consortium pandemic protocol (appendix). Informed by this model, a similar network has been implemented across nine African countries: Kenya, Uganda, South Africa, Namibia, Mozambique, Ethiopia, Ghana, Sierra Leone, and Cameroon.

See **Online** for appendix

Functionality, rather than limitation of resources, was raised by the ACCCOS findings. Critical care registries in LMICs have the potential to provide quality data in resource-limited environments, overcoming some of the limitations faced by the ACCCOS.

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For more on the **ACCCOS risk stratification calculator** see https://www.asos.org.za/index.php

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Authors' reply

Luigi Pisani and colleagues highlight the potential and needed role of critical care registries in the COVID-19 pandemic response in low-income and middle-income countries (LMICs). Registry data are a powerful tool when operationalised at scale.[1] However, despite funded collaborative efforts, the existing registries in LMICs alone have been insufficient in providing an adequate pandemic response, lamented as recently as May, 2021.[2] In contrast, the African Perioperative Research Group (APORG), an unfunded network, pivoted to respond to the pandemic in Africa. By April, 2020, the African COVID-19 Critical Care Outcomes Study (ACCCOS) was established, and through funding of the Critical Care Society of southern Africa, the data management of the study was supported. Simple pragmatic research with a clear question and few datapoints generated data documenting outcomes with explanatory variables. These data can now be used for risk stratification during the third wave[3] with the ACCCOS risk stratification calculator available on the APORG website. Early ACCCOS findings were available in October, 2020,[4] and these findings were the largest peer reviewed cohort of COVID-19 outcomes from LMICs at the time of the meta-analysis, exceeding the published data from all other LMICs.[3]

ACCCOS acknowledged and highlighted various challenges facing critical care research in Africa.[3] The true burden of disease is often poorly measured, as shown by the 3027 (44·7%) patients referred for critical care support but not admitted in ACCCOS.[3] A single data source cannot determine the relative importance of functionality or resource limitation on the mortality reported in ACCCOS. This is partly because the true denominator is not easily gauged during a pandemic when the normal baselines are disrupted, because the availability and definitions of a critical care bed change due to demand. Pragmatic research is agile to respond to some of these challenges, which might be more difficult for a registry response, especially where registry penetration is poor.

Going forward, initiatives such as the Critical Care Africa network provide a well thought out technological platform for centres in Africa to collect data relevant to their critical care practice to inform clinical research and quality improvement. Data harmonising efforts will allow more informed study of results within their context. Collaboration between networks is necessary to leverage the differing strengths of these networks, to provide a rapid, comprehensive understanding of drivers of outcomes, especially during a pandemic.

We declare no competing interests.

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Targeted radioactive therapy for prostate cancer

Progressive metastatic castration-resistant prostate cancer is a highly lethal disorder. In the randomised trial reported by Michael Hofman and colleagues,[1] lutetium-177 [^{177}Lu]Lu-PSMA-617, a small molecule delivering targeted radiation by binding to prostate-specific membrane antigen (PSMA), led to a higher proportion of patients having a 50% or more decrease in prostate-specific antigen (PSA) compared with cabazitaxel (66% *vs* 37% by intention to treat; p<0·0001) and fewer grade 3 or 4 adverse events.[1] Remarkably, some patients did not receive all six planned [^{177}Lu]Lu-PSMA-617 courses due to excellent response.[1] Also, in a previous trial, a 96% or more decrease in PSA, with minor or no residual foci on PSMA imaging, led to a decision to suspend treatment in 20% of patients.[2] In both trials, however, disease ultimately progressed. Some patients responded to additional [^{177}Lu]Lu-PSMA-617 cycles offered at progression.[1,2] To explain disease resurgence after "exceptional response", the authors postulate that ^{177}Lu is less effective in targeting microscopic deposits.[2] Radiation-absorbed doses to small metastases can be boosted using radionuclides emitting alpha particles or low energy Auger electrons.[3] Terbium-161 (^{161}Tb) is of particular interest as it has similar chemical properties and decay characteristics as ^{177}Lu, except for additional emissions of Auger electrons.[3–5] Monte Carlo simulations showed a 2-fold to 4-fold higher radiation dose deposit with ^{161}Tb over ^{177}Lu in micrometastases and single tumour cells.[3] In-vivo studies in mice bearing tumour xenografts documented superior efficacy of ^{161}Tb-PSMA-617 compared with [^{177}Lu]Lu-PSMA-617 with similar, excellent, tolerance.[4] The opinion of Hofman and colleagues, on whether novel radionuclides could be used to deepen response, would be appreciated.

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Michael Hofman and colleagues[1] report more frequent prostate-specific antigen response and prolonged progression-free survival with lutetium-177 [^{177}Lu]Lu-PSMA-617, compared with cabazitaxel, in patients with metastatic castration-resistant prostate cancer with high prostate-specific membrane antigen (PSMA) expression. Nevertheless, the median progression-free survival was 5·1 months in both arms, but a subpopulation of 19% of patients had a 1-year progression-free survival with [^{177}Lu]Lu-PSMA-617 versus 3% with cabazitaxel. The authors deliberately excluded 30% of patients who were unlikely to benefit from [^{177}Lu]Lu-PSMA-617 therapy according to baseline imaging, recognising a direct cause-and-effect mechanism of visualising target expression in the theranostic framework. However, it would be interesting to verify if patients with 1-year progression-free survival benefit were associated with higher uptake on pretherapeutic imaging.

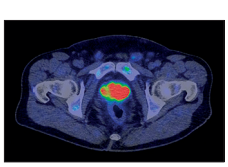
In a phase 2 study on [^{177}Lu]Lu-PSMA-617 in patients with metastatic castration-resistant prostate cancer, we showed better progression-free and overall survival in 25 patients with normal circulating *AR* versus 15 patients with *AR* gene amplification.[2] Interestingly, circulating *AR* status seems to be associated with before treatment PSMA uptake.

In a retrospective analysis, whole-exome sequencing data on 25 patients with metastatic castration-resistant prostate cancer treated with [^{177}Lu]Lu-PSMA-617 showed that *BRCA2* mutations can predict favourable progression-free and overall survival.[3] *BRCA2* and DNA damage repair aberrations present in 15–20% of metastatic castration-resistant prostate cancers are associated with higher PSMA expression.[4]

Testing for *BRCA2* is currently recommended in all patients with metastatic castration-resistant prostate cancer in international guidelines.[5]

In this scenario, is it conceivable to select patients for [^{177}Lu]Lu-PSMA-617 according to gallium-68-PSMA-11 and fluorine-18-fluorodeoxyglucose PET-CT or evaluate the molecular stratification to personalise the approach to these patients?

We declare no competing interests.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