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Implications of COVID-19 for HIV Research: data sources, indicators, and longitudinal analyses

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1 **Main text**

2

3 *Introduction*

4 Observational research is critical to inform guidelines, policy, and the practice of HIV service
5 delivery.¹ The COVID-19 pandemic has profoundly affected healthcare systems and health behaviors
6 world-wide, including at clinics and research sites that undergird global observational HIV research.²

7 We consider the impact of the COVID-19 pandemic on the capture of relevant HIV data, indicator
8 fidelity, and analytic approaches when investigating effects of COVID-19 itself or accounting for
9 COVID-related changes in service delivery and care-seeking.

10

11 *Data Sources*

12 Observational HIV research relies on robust data sources that accurately reflect the delivery of routine
13 patient care, which is the underlying data-generating mechanism. Due to the COVID-19 pandemic,
14 patient health behaviors and HIV clinical care models have changed. Patients may be unable to attend
15 clinic due to COVID-19 health concerns, reduced transportation, and stay-at-home orders. Clinics
16 globally have responded with increased remote interactions through telehealth, electronic patient
17 portals, social media platforms, and text and email messaging, as well as decentralized antiretroviral
18 treatment (ART) delivery.

19

20 However, new types of care and medication delivery may not be recorded consistently in paper or
21 electronic health record systems and many providers working off-site may not have access to those
22 systems for documentation.^{2,3} Even if these interactions are recorded, data may be inaccessible to
23 researchers if stored in new systems or data fields.⁴ Linked data sources such as pharmacy systems
24 may also experience changes in data quality and content, as prescriptions are dispensed in batches for
25 community delivery or transferred to pharmacies offering reduced-contact dispensing.^{2,3} Mortality
26 and other registries may experience data entry delays due to reporting delays and reduced staffing.
27 These pandemic-related changes are likely to be as heterogeneous across the globe as the pandemic
28 itself, disrupting the data sources researchers have used to assess trends in key HIV-related outcomes,
29 resulting in unreliable and invalid measures of care.²

30

31 *Indicators & Measurement*

32 The HIV care continuum has become the preferred framework for understanding individual
33 movement through various stages of HIV care, from testing and linkage to care, to retention in care,
34 ART receipt, and ultimately, viral suppression. Barriers at various stages of the continuum have been
35 conceptualized as “leaks,” with gaps, delays, and transitions out of care seen as undesirable events
36 that should be mitigated through intervention.^{5,6}

37

38 HIV testing, diagnosis, and linkage to care have been delayed due to suspension or limitation of
39 testing programs during mandatory public quarantine or social distancing measures. Outpatient clinic
40 visits have been shifted to remote encounters when possible, and non-urgent care has been
41 postponed.^{2,7} Individuals that appear to be lost to follow-up at their usual site of care may be seeking
42 care elsewhere and medical records may not travel with them. Delays in ART initiation and refills
43 have occurred due to loss of insurance, limited pharmacy dispensing capabilities, and/or limited
44 outpatient activities. CD4 and viral load monitoring – central to HIV care – may also be delayed due
45 to less available phlebotomy services or co-opting of equipment for COVID-related testing.³

46

47 Both improved data capture and alteration of care continuum metrics may therefore be required to
48 assess the extent of care/service disruptions and reduce measurement error and misclassification.⁸

49 More sensitive definitions of engagement and retention accounting for non-traditional interactions
50 may also be warranted. Many current retention metrics require clinical interactions every 3-6 months,
51 but individuals successfully managed on ART and virally suppressed may need less frequent visits.^{6,9}

52 A conditional retention measure, based on ART receipt and viral suppression prior to clinic service
53 disruption or upon return to clinic, may therefore be more informative about the care continuum than
54 attended or even missed visit counts alone. For example, we could redefine retention status such that
55 an individual would be successfully retained if they were virally suppressed and receiving ART both
56 before local social isolation measures were imposed and after return to the clinic. Such a measure
57 would be a more meaningful indication of the current state of a patient's engagement in the HIV care

58 continuum, even if their recorded HIV care visits were not frequent enough to meet current retention
59 definitions.

60

61 *Analytic Considerations*

62 In addition to changes in data collection and measurement during study design and conduct, we will
63 also need to use analytic approaches that address the potential for artifactual temporal changes in HIV
64 indicators due to COVID-19, selection biases, and measurement errors in the data-generating
65 mechanisms of the care continuum. If patients attending telehealth visits are not representative of the
66 entire cohort, if outcomes are unreliably ascertained among those lost to care, if certain measures are
67 self-reported remotely instead of being collected on-site, or if discontinuities such as disruptions in
68 care persist, appropriate epidemiologic and biostatistical methods such as inverse probability
69 weighting, multiple imputation, double-sampling, and regression calibration should be considered.^{10–}
70 ¹² To facilitate longer-term trend assessments which span the COVID-19 pandemic, analyses should
71 also accommodate maximum flexibility, for example, through the use of restricted cubic splines,
72 piecewise regression, or parametric mixture models.^{13,14} We must continue to assess the local clinical
73 context to obtain more information relevant to HIV care changes induced by the COVID-19 pandemic
74 and inform these approaches.¹⁵

75

76 *Conclusion*

77 Future HIV-related studies and public health goals require a new COVID-19-informed paradigm for
78 the collection and use of observational cohort data. HIV cohorts must capture pandemic-driven
79 changes in data sources, clinic activities, and local policies to inform analyses. Our ability to leverage
80 epidemiologic evidence to inform clinical, programmatic, and public health practice is only as strong
81 as the inferences derived from these analyses are valid and robust to the challenges in HIV care and
82 research that we now face due to the pandemic. Healthcare organizations and public health agencies
83 should revise HIV care continuum measures and analytic strategies. Funding for such work is critical,
84 even in times of economic crisis, so that COVID-19 does not derail the global fight to End the HIV
85 Epidemic.

86 **Competing interests**

87 The authors declare no competing interests.

88

89 **Authors' contributions**

90 PFR, SND, and KNA developed the idea and wrote the initial draft. KKW and DN revised the
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92

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