Using Surveillance Data to Measure Trial HIV Incidence Outcomes: A Modelling Study

00901

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BACKGROUND

- Using surveillance data on new HIV diagnoses instead of measuring HIV incidence in the trial could reduce costs of conducting expensive cluster-randomized controlled trials (C-RCTs)
- We used a mathematical model to evaluate if and when surveillance data can be used to estimate impact in HIV intervention C-RCTs

METHODS

We used a mathematical model of HIV transmission among men who have sex with men in Baltimore, US[1], parameterised and calibrated to local data, to simulate C-RCTs scaling up:

- Antiretroviral therapy (ART)
- Pre-exposure prophylaxis (PrEP)
- HIV testing

in combination or alone.

We used the model outputs to test whether:

1. Modelled reductions in total cumulative HIV diagnoses reflected cumulative HIV incidence reduction over a simulated 2-year trial.
2. Reductions in diagnoses agree better with incidence reduction over a longer trial duration (3-4 yrs) or when measured in later trial years.
3. Reductions in these other surveillance measures agree better with incidence reduction:
   - Diagnoses with acute infection
   - Diagnoses with early (CD4>500 cells/µl) infection
   - Diagnoses adjusted for testing volume
   - Proportion of diagnosed PLHIV virally unsuppressed

For each surveillance measure, we report:

- **bias** and **variability** of reductions in diagnoses/un-suppression to estimate incidence reductions (median and 95% credible interval of differences)
- **sensitivity** of diagnoses/un-suppression to detect a true incidence reduction

[1] Mitchell KM et al. (2019) J Int AIDS Soc 2:e25246

Surveillance data on new diagnoses or viral suppression cannot reliably be used to estimate HIV incidence reductions in cluster-randomized trials of interventions that include expansion of HIV testing

FIGURE 1. Agreement of reduction in total diagnoses with incidence reduction over a 2 year trial

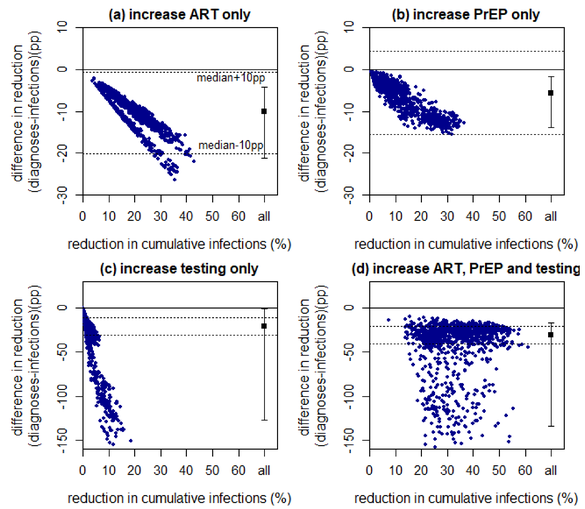
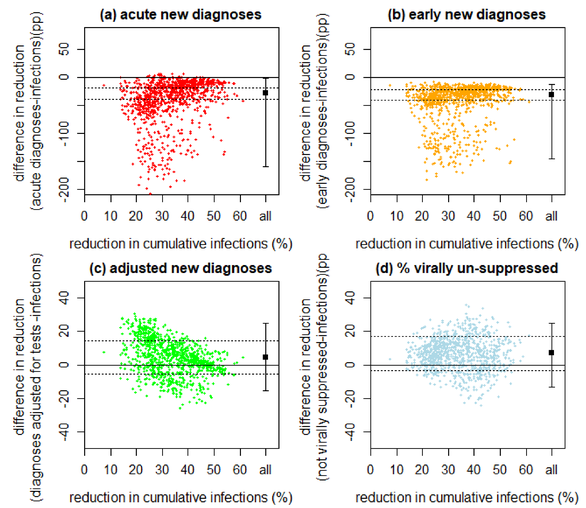


FIGURE 2. Agreement of reduction in different surveillance measures with incidence reduction over a 2 year trial expanding ART+PrEP+testing



RESULTS

Over a 2-year trial expanding ART+PrEP+testing, modelled reductions in total cumulative diagnoses underestimate cumulative incidence reduction by a median 30 percentage points (pp), with considerable variability (95%CrI 16 to 134pp), and have 52% sensitivity (Figure 1d,Table).

Variability and sensitivity were better in trials expanding ART or PrEP alone (Figure 1a,b, Table), but bias remained (-10pp for ART, -6pp for PrEP).

Diagnoses performed worse in trials expanding testing alone as diagnoses increased with decreasing incidence (Figure 1c).

Measuring impact in longer trials or over later years improved sensitivity and reduced bias of total diagnoses reductions, but substantial variability remained (not shown).

For ART+PrEP+testing trials, reductions in acute and early cumulative diagnoses were as biased and had similar sensitivity to total diagnoses reductions (Figure 2, Table).

Reductions in adjusted cumulative diagnoses and the final proportion virally unsuppressed had 100% sensitivity but overestimated incidence reductions (by 4 and 7pp, respectively), and were too variable to be useful markers (Figure 2).

RESULTS (CONT.)

Acceptable variability and sensitivity were only seen for these measures and interventions:

- Diagnoses with acute or early infection when ART alone was expanded (Table)
- Diagnoses adjusted for testing volume when PrEP alone was expanded (Table)

with some bias for early and adjusted diagnoses.

TABLE. Agreement between reductions in different surveillance measures and reductions in HIV incidence over a 2 year trial

Intervention	Outcome measure	Bias (variability); median (95% CrI) difference	Sensitivity
ART+PrEP +HIV testing	Total diagnoses	-30pp (-134,-16pp)	52%
	Acute diagnoses	-28pp (-159,-1pp)	55%
	Early diagnoses	-31pp (-146,-12pp)	53%
	Adjusted diagnoses	4pp (-16,25pp)	**100%**
	% not suppressed	7pp (-13,25pp)	**100%**
ART only	Total diagnoses	-10pp (-21,-4pp)	**100%**
	Acute diagnoses	**-3pp (-6,-1pp)**	**100%**
	Early diagnoses	**-8pp (-16,-3pp)**	**100%**
	Adjusted diagnoses	-10pp (-21,-4pp)	**100%**
	% not suppressed	20pp (9,34pp)	**100%**
PrEP only	Total diagnoses	**-6pp (-14,-2pp)**	88%
	Acute diagnoses	-4pp (-14,15pp)	76%
	Early diagnoses	**-5pp (-11,1pp)**	85%
	Adjusted diagnoses	**10pp (3,18pp)**	**100%**
	% not suppressed	-10pp (-30,-2pp)	88%
HIV testing only	Total diagnoses	-20pp (-128,-1pp)	0%
	Acute diagnoses	-35pp (-194,-1pp)	0%
	Early diagnoses	-25pp (-151,-1pp)	0%
	Adjusted diagnoses	8pp (-6,36pp)	87%
	% not suppressed	-3pp (-18,0pp)	0%

CONCLUSIONS

- Surveillance diagnoses data can only rarely be used to estimate HIV incidence reductions in C-RCTs of HIV interventions
- None of the surveillance markers explored were appropriate for C-RCTs of interventions expanding HIV testing, which is an essential component of any prevention package
- Reductions in acute/early diagnoses or diagnoses adjusted for testing volume may be adequate predictors in C-RCTs expanding ART or PrEP only, and if bias can be adjusted for

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