Undiagnosed HIV infections among gay and bisexual men increasingly contribute to new infections in Australia

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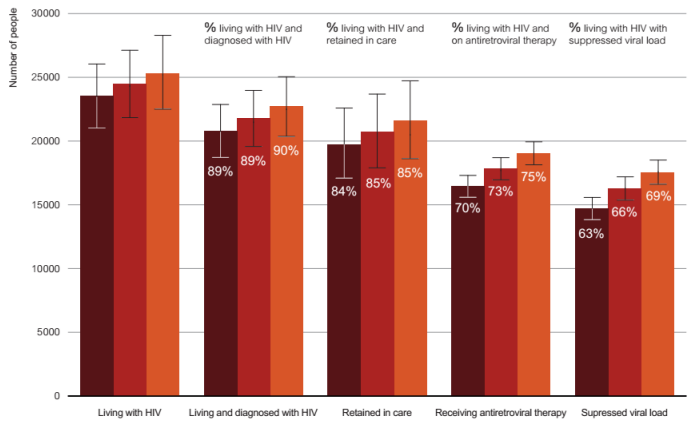
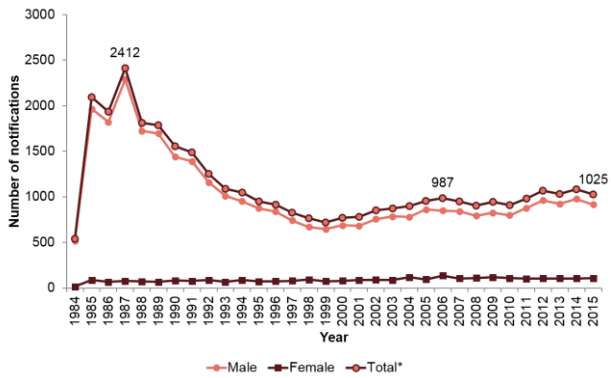
Australian HIV cascade

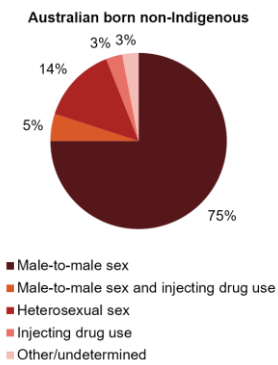
Figure 29 The HIV diagnosis and care cascade, 2013 – 2015



Some PLHIV are: undiagnosed, diagnosed but not on ART, on ART but with detectable VL

Annual HIV notifications





- Closely align with estimates of new infections

- Where do new infections come from?
- What is the contribution of undiagnosed gay and bisexual men?

Methods

Estimating infectivity

Update of approach and estimates presented at ASHM 2015

$$I = \beta_u N_u + \beta_d N_d + \beta_t^u N_t^u + \beta_t^s N_t^s$$

Where:

- I = number of new infections
- N_u = number of people with undiagnosed infection
- N_d = number of people with diagnosed infection but not on ART
- N_t^u= number of people on ART but with unsuppressed virus (> 200 copies/ml)
- N_t^s = number of people on ART but with undetectable viral load (< 200 copies/ml)
- β_u, β_d, β_t^u, and β_t^s are the corresponding annual rates of transmission attributable to each cascade step or **infectivity of people in each step**

From new infections and population sizes we can estimate the β values

Contribution of new infections from undiagnosed: $\beta_u N_u / I$

Number of new infections

Used the European Centre for Disease Prevention (ECDC) HIV modelling tool which uses CD4 count at diagnosis

- http://ecdc.europa.eu/en/healthtopics/aids/pages/hiv-modelling-tool.aspx

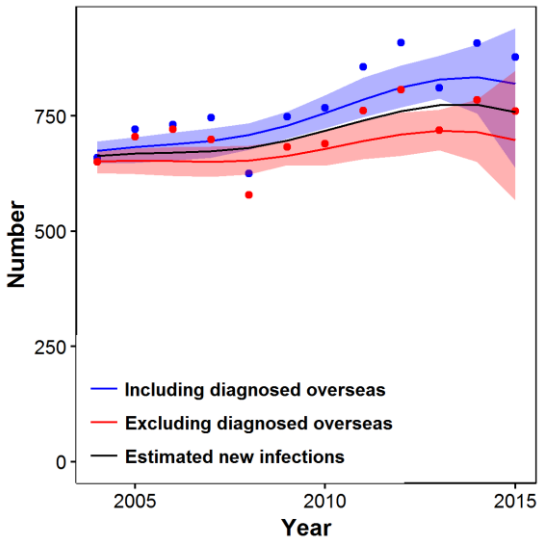
What we use for estimating the proportion undiagnosed in the national HIV cascade (reported in the ASR)

Applied it to notifications attributable to male-to-male sex

Ran two scenarios

- Notifications of those previously diagnosed overseas **included**
- Notifications of those previously diagnosed overseas **excluded**

Number of new infections

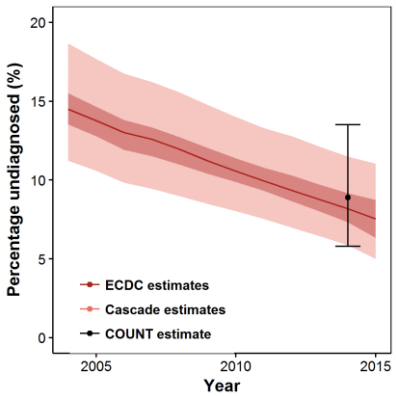


HIV Cascade for GBM

- Used method from 2016 Annual Surveillance Report
- Diagnosed
  - All notifications attributed to male-to-male sex minus duplicates, deaths and emigrants
  - Gives number living with diagnosed HIV over time
- Treated
  - Diagnosed x proportion on treatment from **GCPS**
- Suppressed
  - Treated x proportion with VL < 200 at last test from **AHOD**

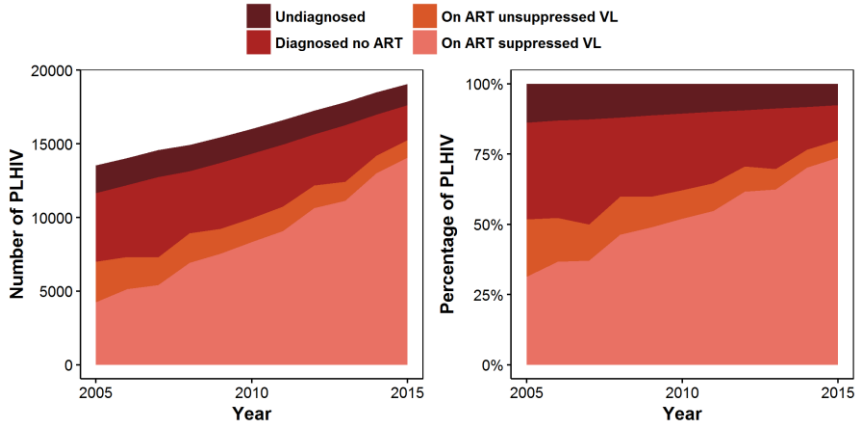
HIV Cascade for GBM - Undiagnosed

- Comes from the ECDC model



- % undiagnosed ↓ from 14.5% in 2004 to 7.5% in 2015

HIV diagnosis and care cascade for GBM



Estimating infectivity - Approach

$$I = \beta_u N_u + \beta_d N_d + \beta_t^u N_t^u + \beta_t^s N_t^s$$

Just like a regression model but the β values are not completely free

- They cannot be less than zero
- They could change over time
- We know people with suppressed virus are much less likely to transmit: HPTN-052, Partner Study, Opposites Attract

Used a **Bayesian methodology** to estimate each infectivity parameter β using estimates for each step of a GBM HIV cascade and estimated number of new infections in GBM over 2004-2015

Assumptions:

- Uncertainty in cascade estimates: $\beta N = \beta' NE$
- β changes linearly over 2004-2015 from β^{start} to β^{end}

Estimating infectivity - Priors

Priors for β_u, β_d, and β_t^u uniform with means satisfying $\beta_u > \beta_d > \beta_t^u$ but with wide ranges so they can overlap

- Assume start and end priors are the same

Prior for β_t^s based on the results of clinical studies

- Assume no change over time

Study	Prior	Notes
Partner study	Exponential mean: 1/2.8 per 1000 GBM with suppressed virus.	Zero transmissions but upper 95% confidence interval was 8.4 transmissions per 1000 couple-years
HPTN-052	Lognormal distribution: mean 0.04 (95% CI: 0.01-0.27) relative to β_d	$\beta_t^s = \text{prior x } \beta_d$
Partner, Opposites Attract	$\beta_t^s = 0$	Zero transmission from suppressed

Estimating infectivity – Fitting Procedure

To fit the model to the estimates for new infections and each cascade step we used a **Bayesian melding** procedure

- Sampling-Importance-Resampling Procedure
- Took 5 million samples of the priors
- For each sample ran the model and calculated a weight based on the fit

To generate the posterior distributions for each β we resampled 100,000 times based on the weights

- This set used to generate all the results

Sensitivity scenarios

Focus on 2015 cascade estimates with uncertainty ranges and Partner study prior

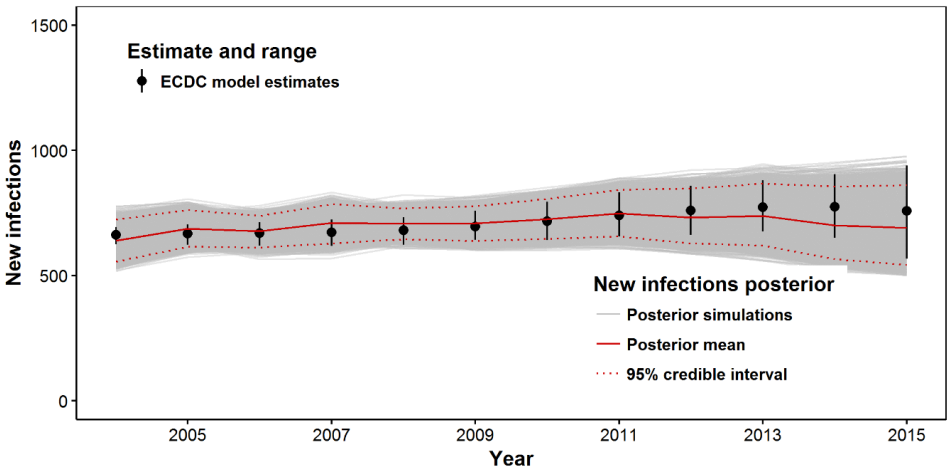
Also ran scenarios:

- 2015 cascade and HPTN-052 prior
- 2015 cascade and zero transmission from suppressed
- 2015 cascade with best estimates only and Partner prior
- HIV cascade over 2004-2014 using 2015 ASR methodology (higher estimates for diagnosed due to lower emigration) and Partner study prior

Contribution of undiagnosed HIV infections to new infections

Results

Fit to new infections



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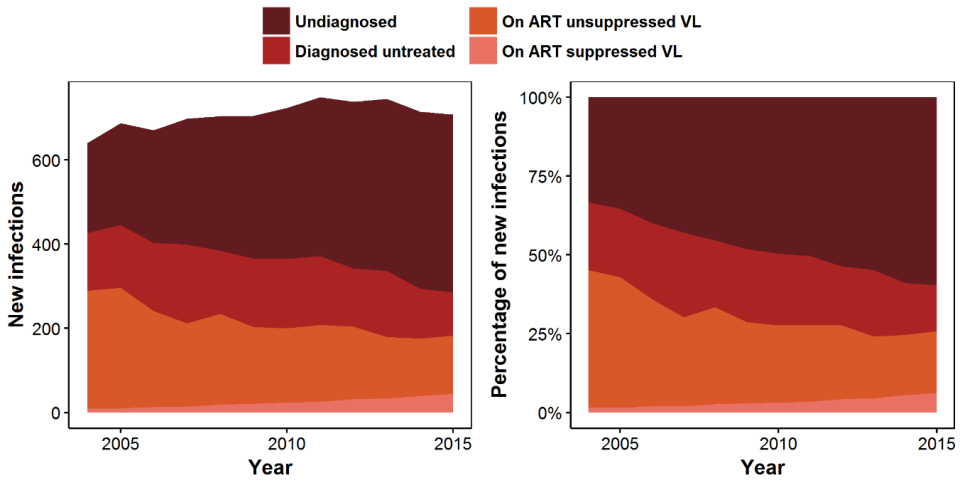
New infections attributable to each cascade step



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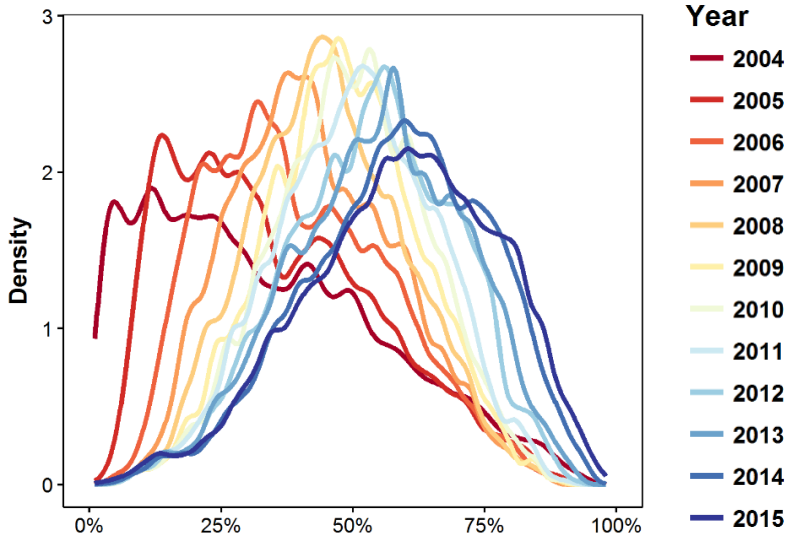
New infections attributable to each cascade step

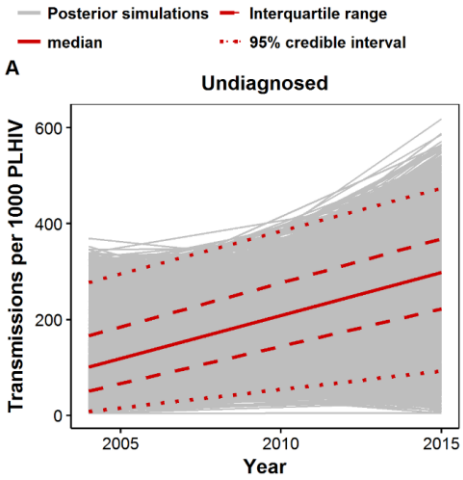
Cascade step	New infections 2015	Percentage 2015
Undiagnosed	423 (132-680)	59% (20.8-89.8%)
Diagnosed untreated	103 (8-221)	15% (1.2-34.4%)
Treated but unsuppressed	138 (6-307)	19.8% (0.9-45.3%)
Suppressed	44 (1-159)	6.2% (0.2-21.4%)

New infections attributable to undiagnosed



Rate of transmission for undiagnosed PLHIV

Increased from 110 per 1000 PLHIV in 2004 to 290 per 1000 PLHIV in 2015



Realistic?

- Increase in condomless anal intercourse
- Serosorting amongst HIV-negative
- Reduction in time between infection and diagnosis means larger proportion of time with high VL

Effect of variations in suppressed prior

Changing the prior for β_t^S did not change the estimated contribution of undiagnosed infections to new infections substantially (57-65%)

- 65% if suppressed have zero transmission

Using the best estimates for the cascade without uncertainty pushes the contribution of undiagnosed infections to 74% (with much tighter posterior distribution)

Conclusions

Using this approach

- In 2015 around 59% of new infections in GBM are attributed to undiagnosed men
- Rate of HIV transmission from undiagnosed GBM increased substantially over 2004-2015
- Minimizing number of undiagnosed men and maximizing effective ART coverage would likely have a substantial impact on HIV incidence
- Also highlights the potential of PrEP but will need a more complex model to assess the contribution of PrEP

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