Sources of HIV infections today

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Introduction

• Combination antiretroviral treatment (cART) has transformed HIV into a lifelong disease.

• cART is also one of the most effective strategies for preventing new infections.

• However, among MSM, cART has so far not resulted in appreciable reductions in new HIV infections.

• Impact of interventions – earlier diagnosis, immediate treatment, PrEP – relies crucially on how many HIV transmissions originate from different stages in the entire HIV infection and care continuum.
ATHENA cohort

• 27 HIV treatment centres recognised by the Ministry of Health

• collection of anonymous demographic and clinical data done by Stichting HIV Monitoring

• opt-out inclusion

• 23,303 HIV-positive people registered

• 18,355 still in care as of May 2015
HIV diagnoses in the Netherlands

More testing?

More infections?

SHM Monitoring Report 2015
Back-calculation

Observed HIV diagnoses

Calendar year
Back-calculation

Need to know the time between infection and diagnosis, which
- is *a priori* unknown
- may change over time

HIV infections

Observed HIV diagnoses

Calendar year
Time between infection and diagnosis can be estimated from additional data on CD4 counts at diagnosis and/or concurrent HIV/AIDS diagnoses.
HIV infections in the Netherlands

Other estimated key outcomes - MSM

Time to diagnosis

- 2.7 year

Undiagnosed infections

- 1,600 undiagnosed HIV infections

Van Sighem et al, Epidemiology 2015 (updated)
ECDC HIV Modelling Tool

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“Static” process

Infected → Diagnosed
Dynamic transmission model

Infected

Diagnosed
Dynamic transmission model

- Infected

- Diagnosed

- Virological failure

- Viral suppression
Dynamic transmission model

Infected → Bezemer *et al*, *AIDS* 2008; *Epidemics* 2010; Van Sighem & Vidondo *et al*, *PLOS One* 2012 → Diagnosed

Virological failure → Cohen, *NEJM* 2011; Rodger, CROI 2014

Viral suppression
Time to diagnosis and HIV incidence


HIV incidence in Switzerland!

mean time to diagnosis 2.2 year
Undiagnosed infections

- **2010: 81.8%**
- **2010: 13.5%**

Proportion remaining undiagnosed

Proportion infections transmitted by undiagnosed individuals

``Risk behaviour``

Amsterdam Cohort Studies: changes in % unprotected anal sex

Transmission network dynamics

1980 1996 2010
year of infection

cART introduced

No further transmission

Bezemer et al, Plos Medicine, 2015
Transmission clusters among MSM

- 106 networks
- include 3061 (52%) of 5852 individuals with subtype B infection
- 91 majority MSM
- 54 (59%) present before 1996
- networks don’t stop!

Bezemer et al, PLOS Med 2015
Probable transmitters to MSM

- 1,794 MSM confirmed to have been infected at most 12 months before diagnosis

Ratmann et al, Science TM 2016
Probable transmitters

13,421 patients in ATHENA data set

1,794 recipient MSM

1,045 recipient MSM with a sequence

673 clustering recipient MSM

617 recipient MSM with a probable transmitter

12,193 potential transmitters

5,585 potential transmitters with a sequence

1,567 co-clustering potential transmitters

903 probable transmitters

\{ \}
\sim 9.7\ million potential transmission pairs

\{ \}
\sim 4.4\ million pairs with a sequence

\{ \}
6,031 co-clustering pairs

\{ \}
2,343 probable transmission pairs

Ratmann et al, Science TM 2016
Phylogenetic analysis

- Exclude potential transmission pairs who are not in the same cluster.

- Exclude pairs incompatible with direct transmission:
  - low probability that the lineages from the potential transmitter and the recipient coalesce after the transmitter was infected and before the recipient was diagnosed.
Probable transmitters

Statistical analysis

- Censoring: towards the present an increasing proportion of potential transmitters may not have been diagnosed yet.
- Estimate time from infection to diagnosis.
- Sequence sampling bias.
- Assign pairwise transmission probabilities to transmission intervals.

13,421 patients in ATHENA data set
1794 recipient MSM
12,193 potential transmitters
~ 9.7 million potential transmission pairs

Ratmann et al, Science TM 2016
Linking to HIV infection and care stages

- Assign infection/care stages to the 6-week-long probable transmission intervals.
- Stages based on clinical data reflecting progression of transmitters through the infection/care continuum.

Contribution from infection/care stages

Undiagnosed: 70.9% (95% CI, 65.8-72.5)

Ratmann et al, Science TM 2016

43.5% of infections from men in their first year of infection
Contribution from infection/care stages

Diagnosed and untreated:
22.4% (95% CI, 20.7-26.2)

Ratmann et al, Science TM 2016
Contribution from infection/care stages

Treated: 5.7% (95% CI, 5.2-2.7)

RR viral suppression vs. untreated 0.04 (95% CI, 0.02-0.1)

before first suppression
no viral suppression

Ratmann et al, Science TM 2016
Contribution from infection/care stages

Lost to follow-up: 1.0% (95% CI, 0.7-1.6)

Ratmann et al, Science TM 2016
Transmission between age groups

Ratmann et al, CROI 2016

13% transmissions (%) undiagnosed

27% transmissions (%) diagnosed
Conclusions

• Mathematical modelling and phylogenetic analysis give similar results.

• ~71% of infections among MSM are from undiagnosed men

• cART is highly effective in preventing transmissions.

• Very few transmissions are attributable to temporary or permanent loss to follow-up.

• Increasing proportion of new infections from young MSM.

• The number of new HIV infections among MSM appears to be in a convincing decline.
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