

Sources of HIV infections today

Ard van Sighem
Stichting HIV Monitoring

8th Italian Conference of AIDS and Antiviral Research (ICAR)
Milan, 6-8 June 2016



Disclosures

- Dr. Ard van Sighem received grants paid to his institution from the European Centre for Disease Prevention and Control, Gilead sciences, and Janssen-Cilag.
- The ATHENA database is maintained by Stichting HIV Monitoring and supported by a grant from the Dutch Ministry of Health, Welfare and Sport through the Centre for Infectious Disease Control of the National Institute for Public Health and the Environment



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.

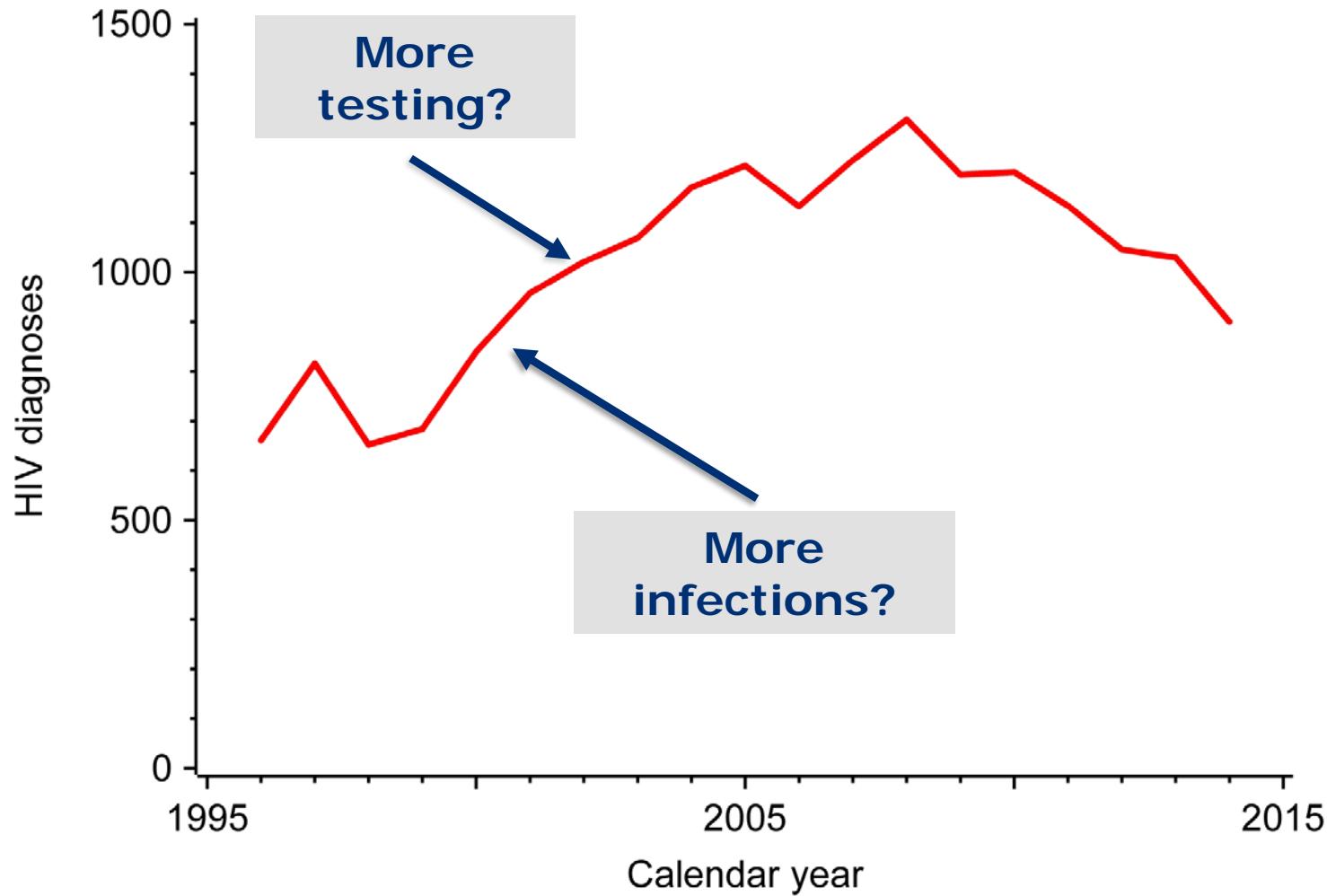


ATHENA cohort

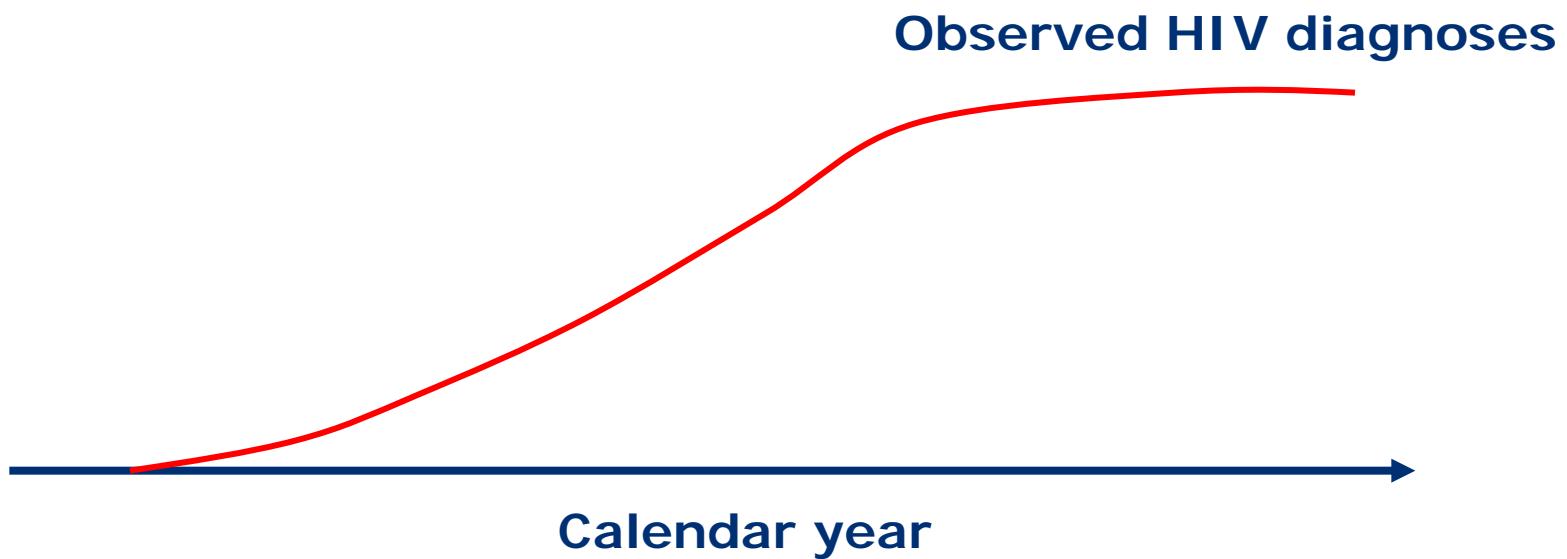
- 27 HIV treatment centres recognised by the Ministry of Health
- collection of anonymous demographic and clinical data done by Stichting HIV Monitoring
- opt-out inclusion
- 23,303 HIV-positive people registered
- 18,355 still in care as of May 2015



HIV diagnoses in the Netherlands

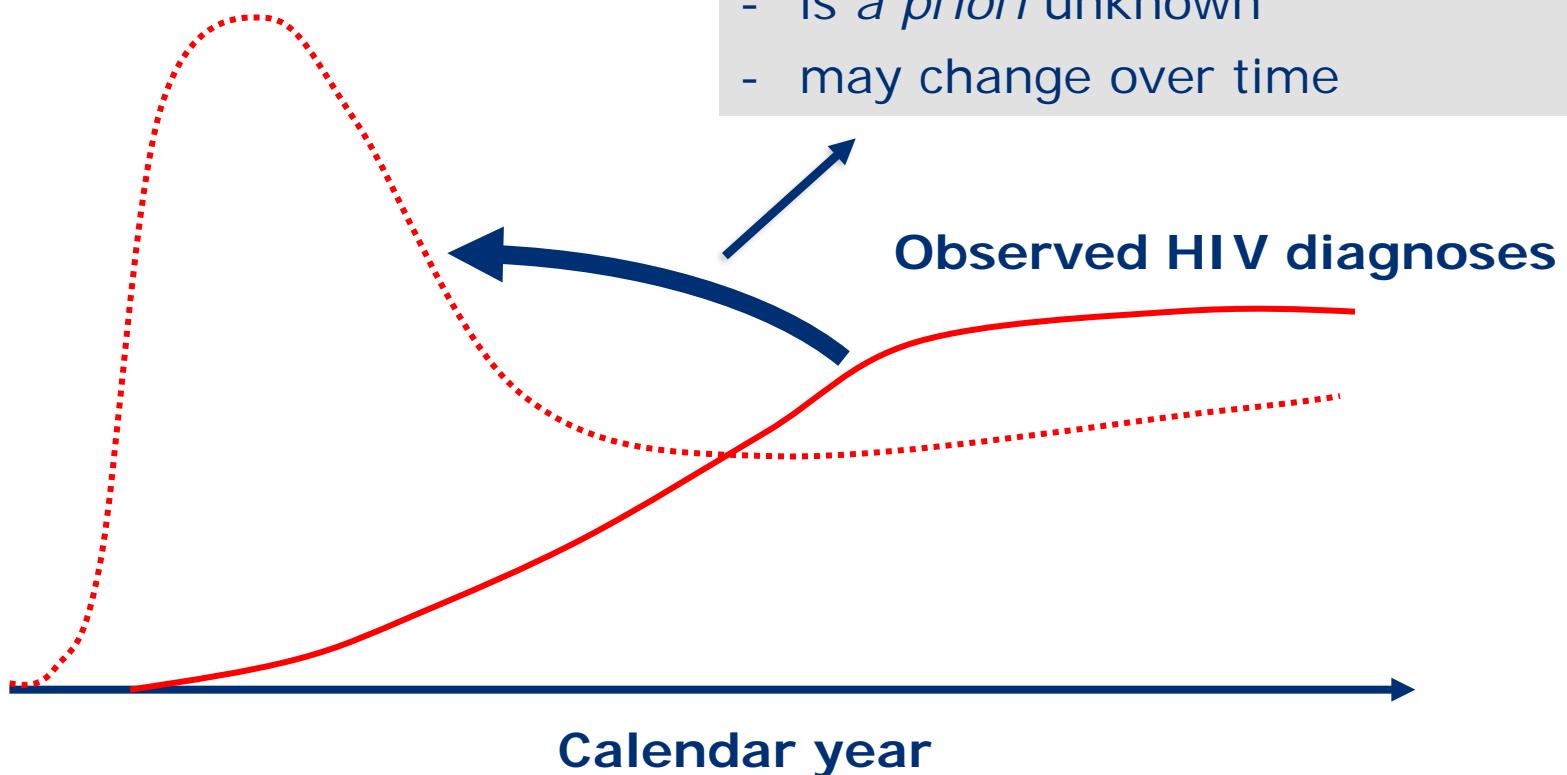


Back-calculation

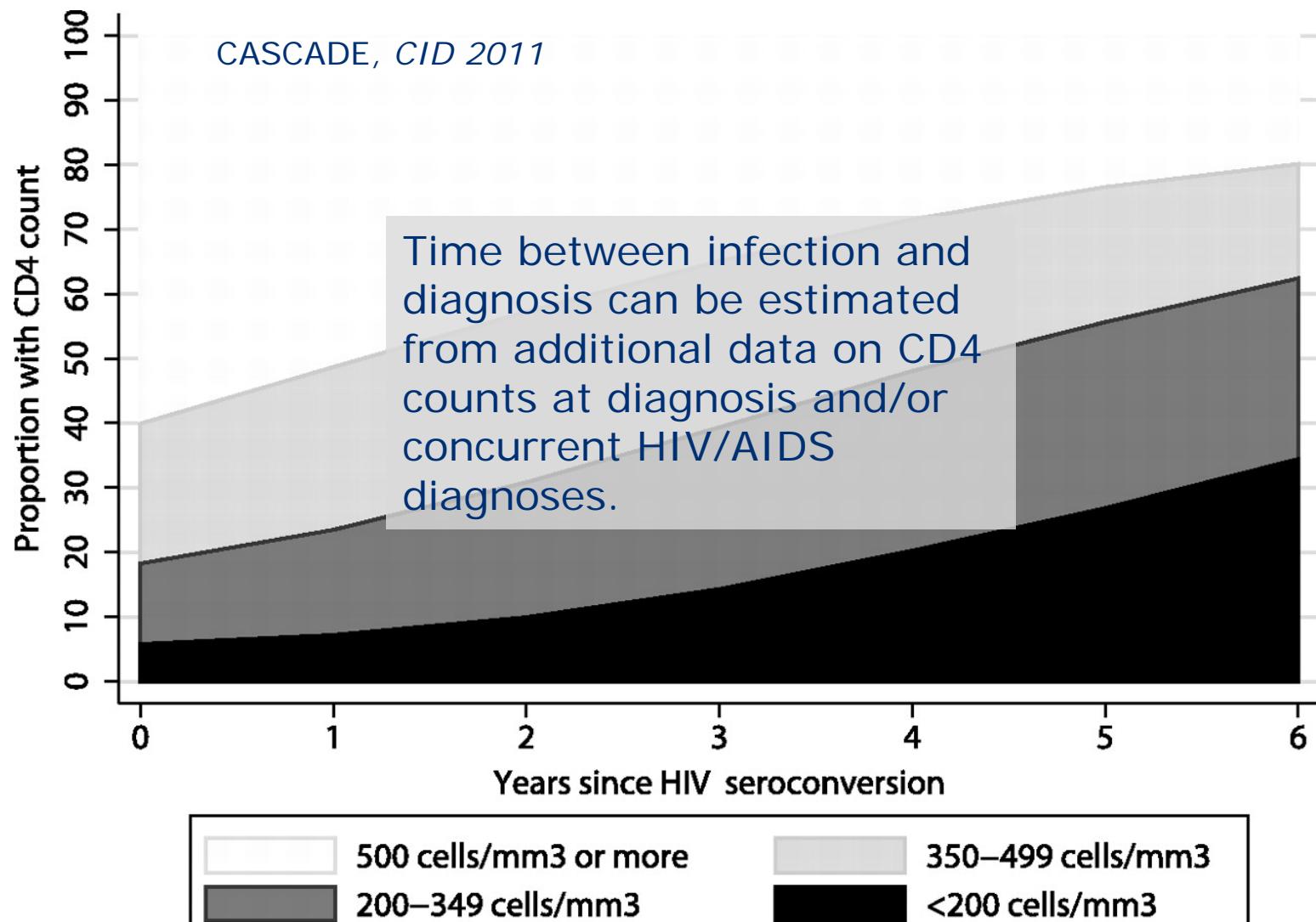


Back-calculation

HIV infections

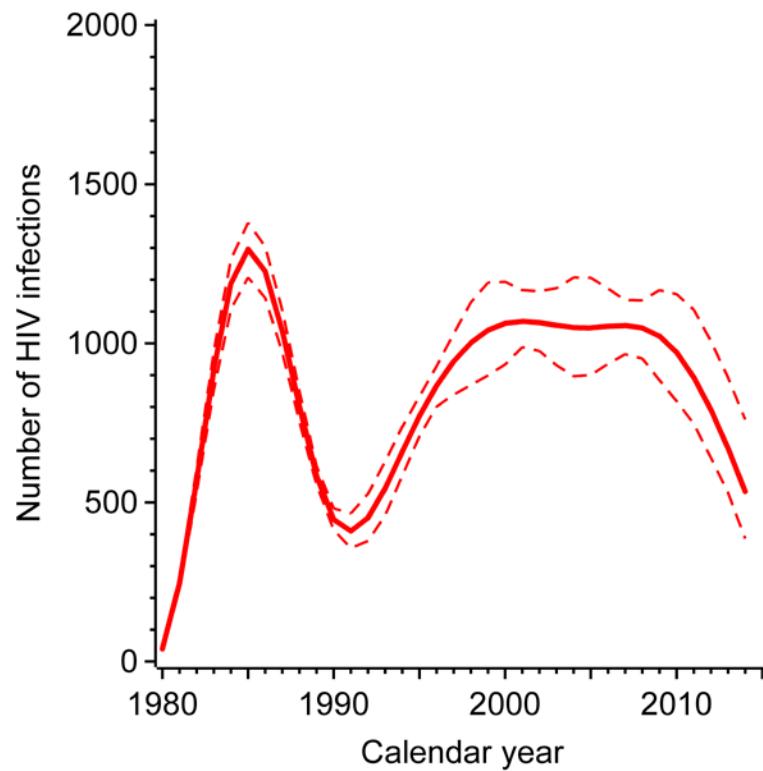


Solution: CD4 counts

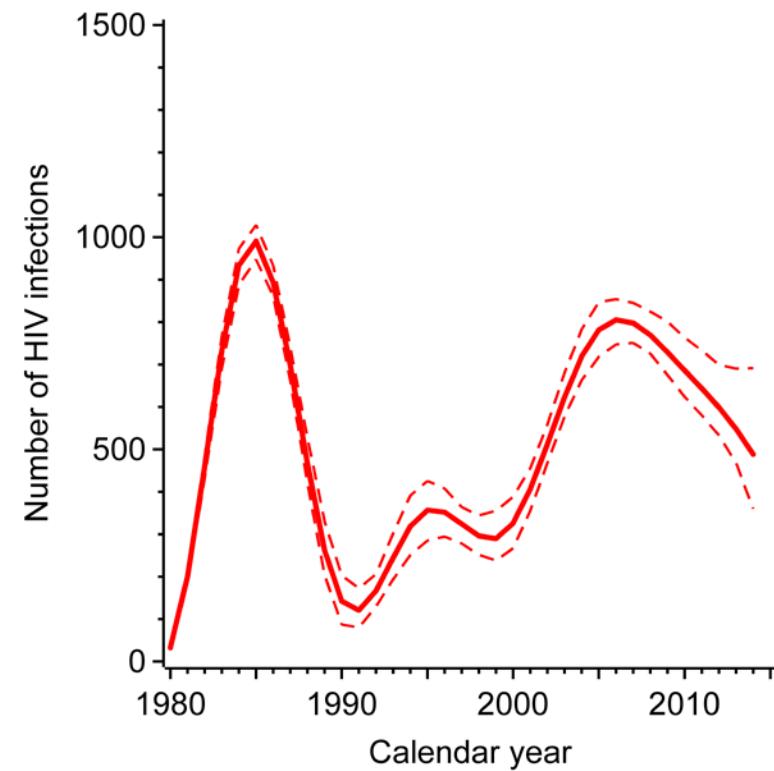


HIV infections in the Netherlands

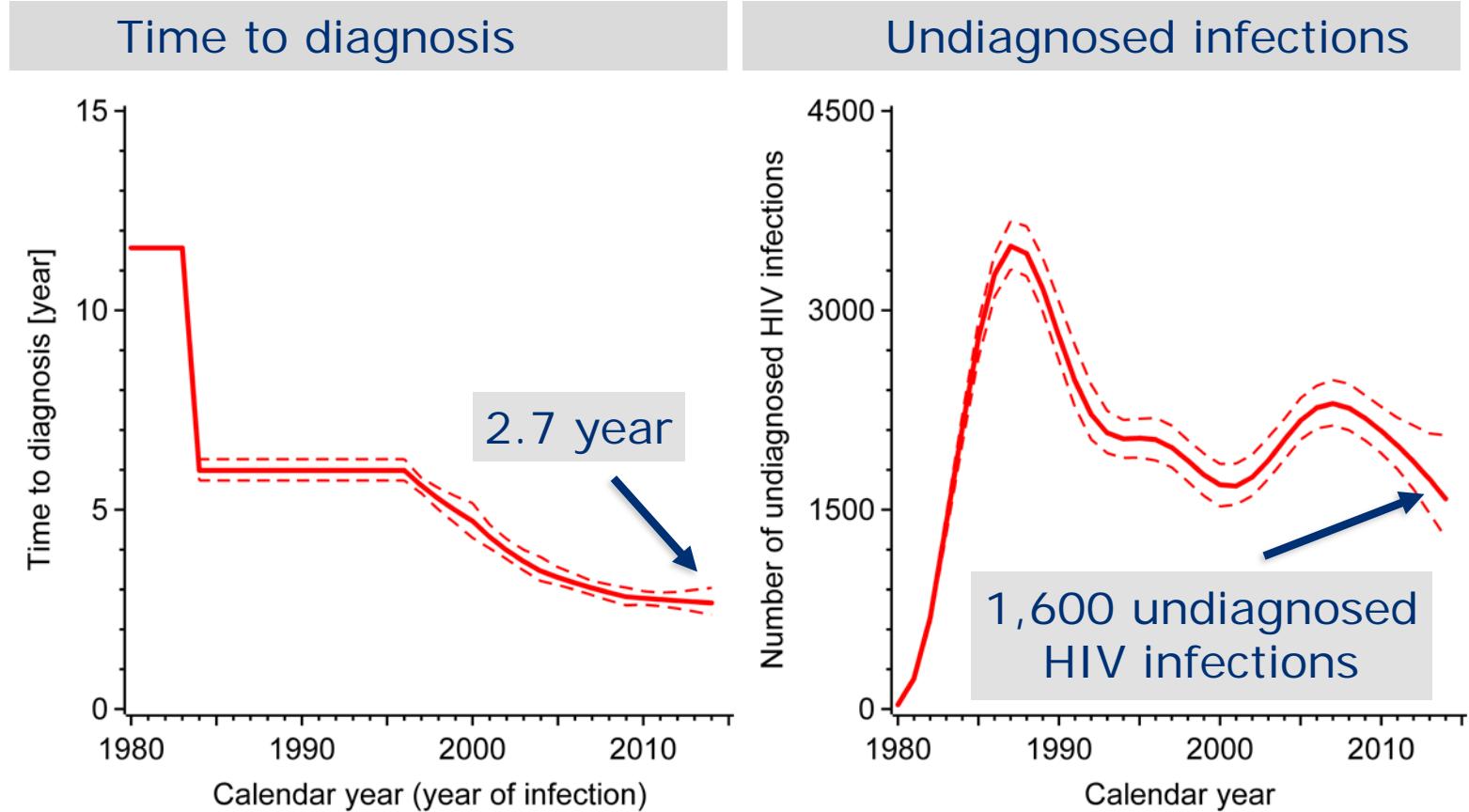
Total population



MSM



Other estimated key outcomes - MSM



ECDC HIV Modelling Tool

Advisory team

Fumiyo Nakagawa

Daniela De Angelis

Matthias Egger

Frank de Wolf

Christophe Fraser

Andrew Phillips

ecdc.europa.eu/en/healthtopics/aids/Pages/hiv-modelling-tool.aspx

Tool developer

Daniel Lewandowski

ECDC

Chantal Quinten

Anastasia Pharris

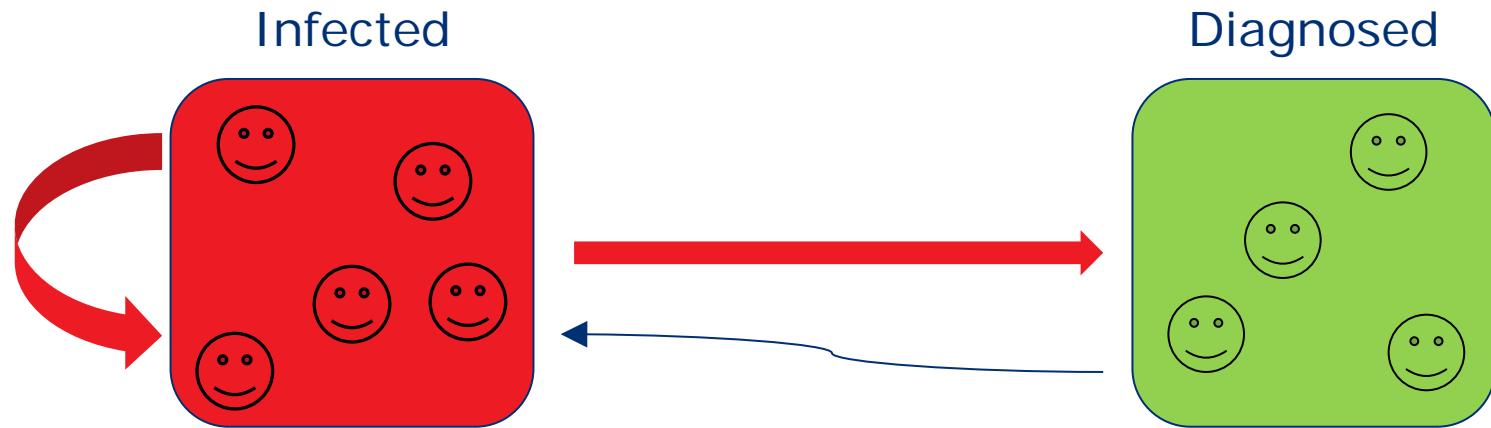
Andrew Amato-Gauci



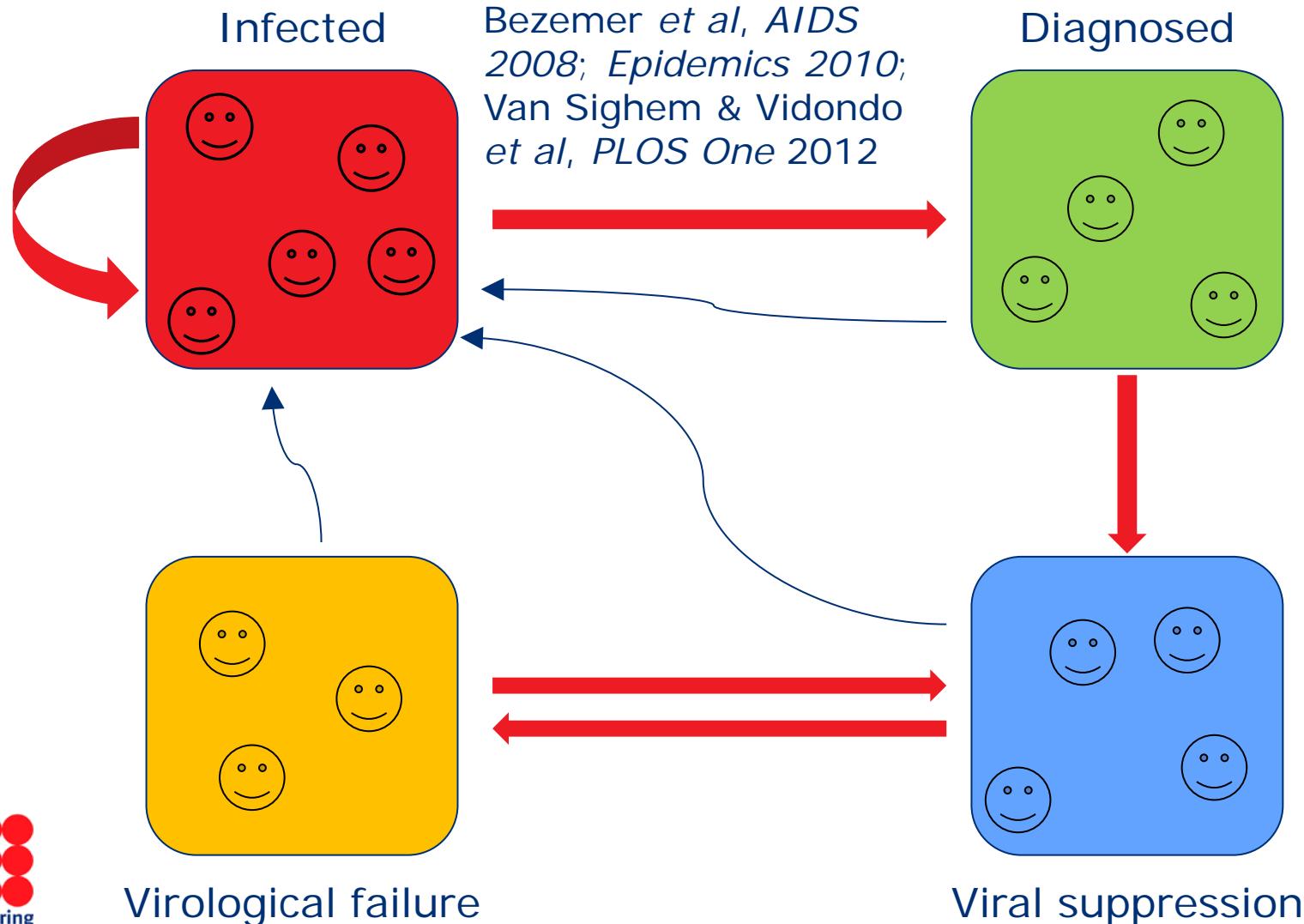
“Static” process



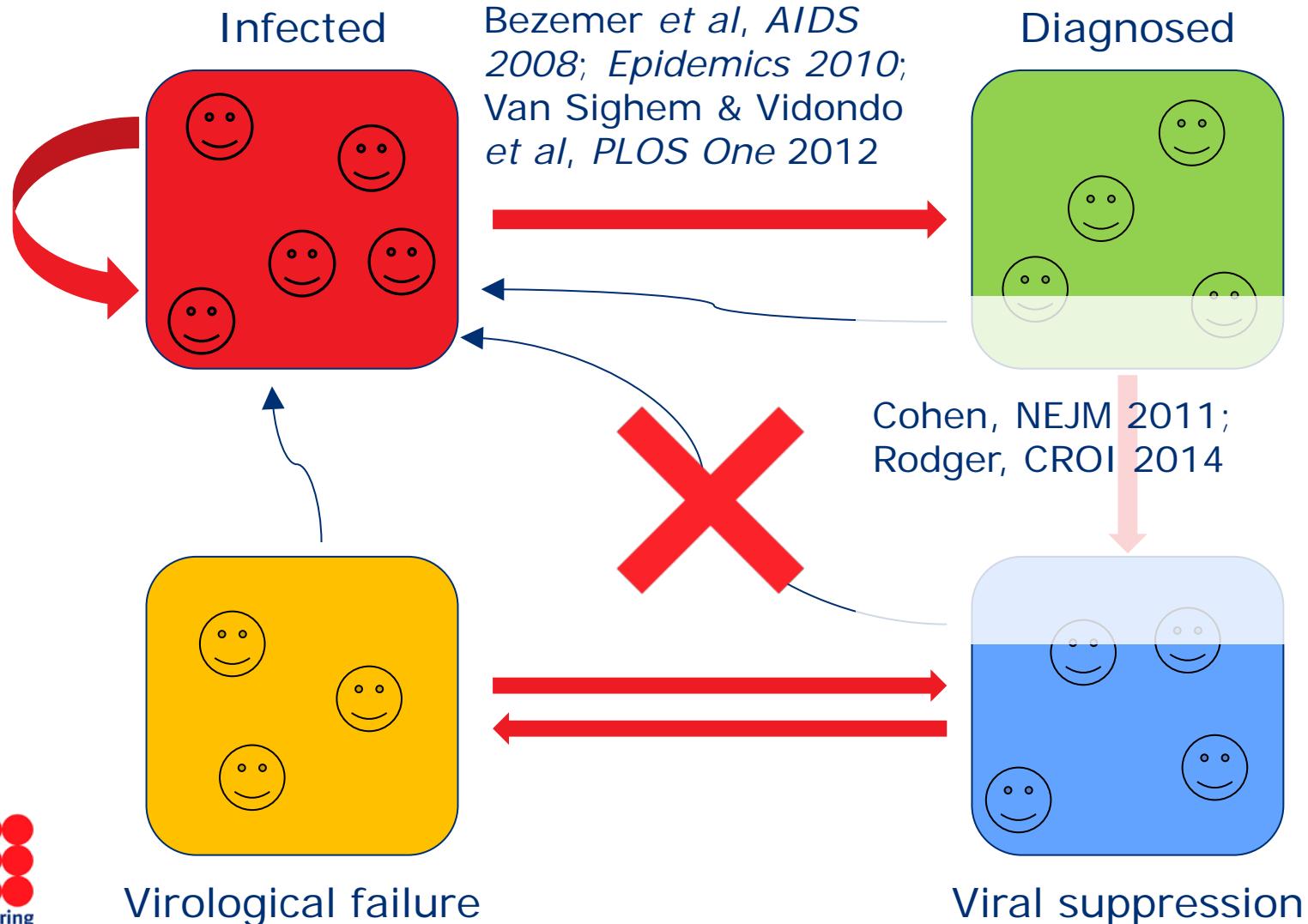
Dynamic transmission model



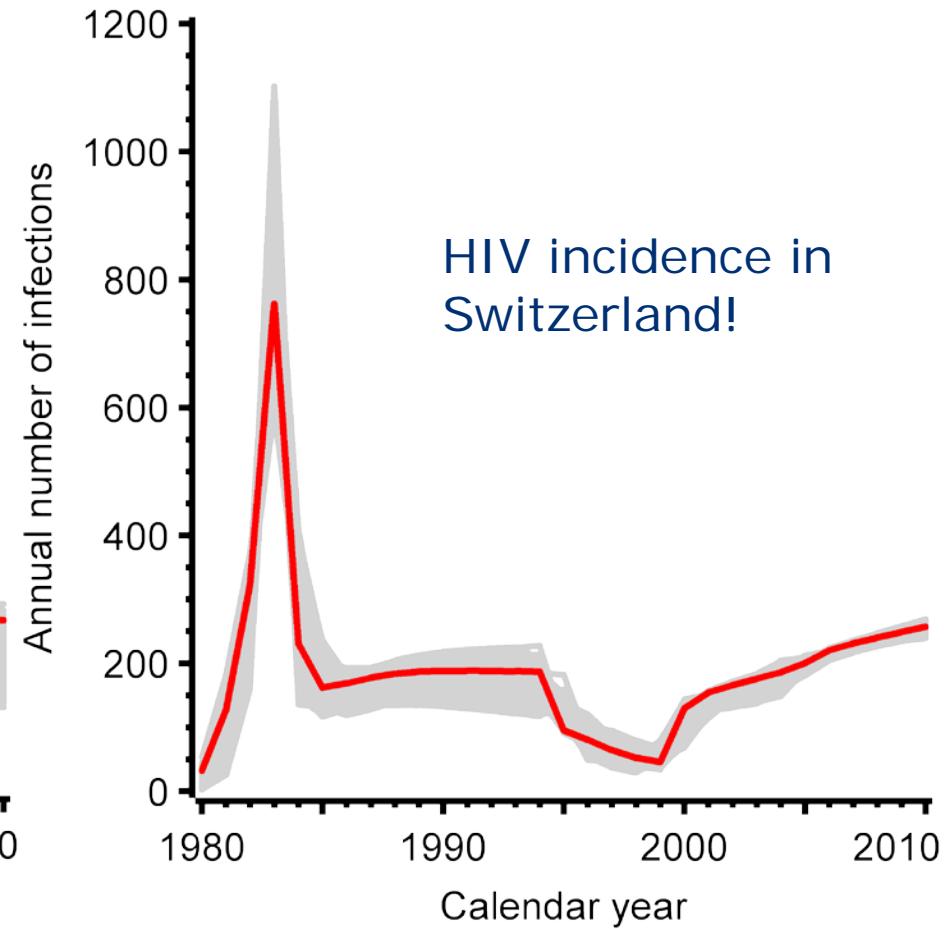
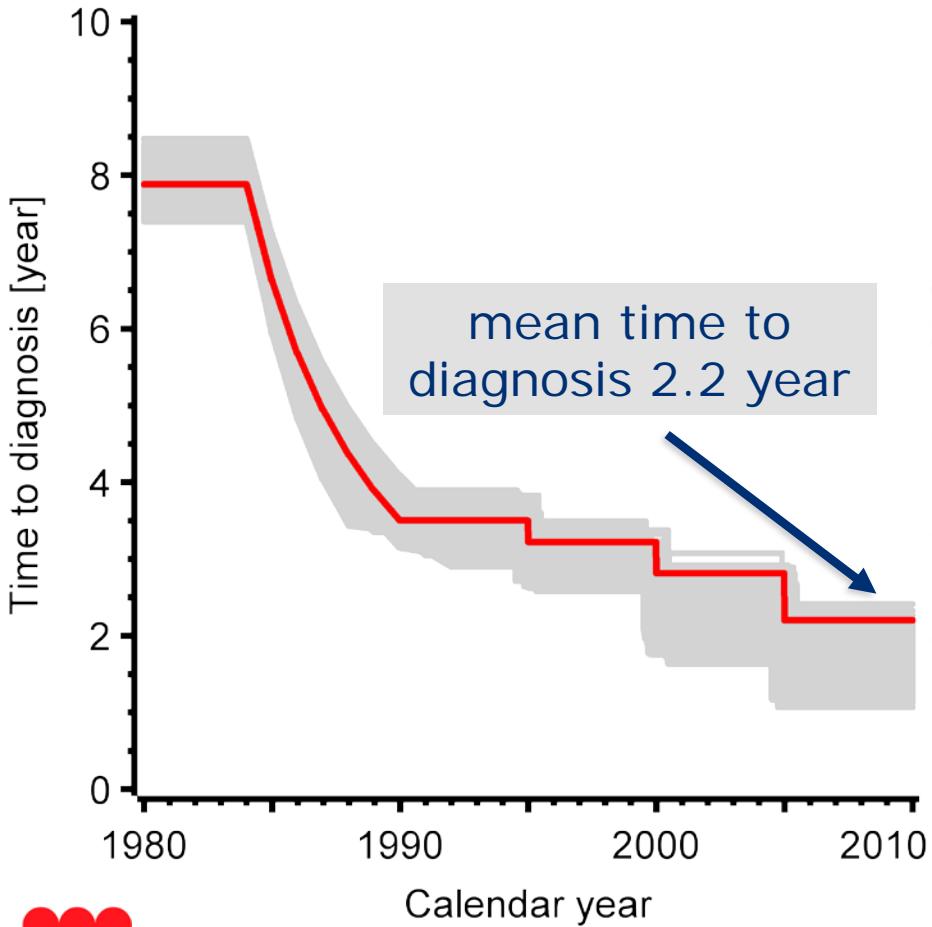
Dynamic transmission model



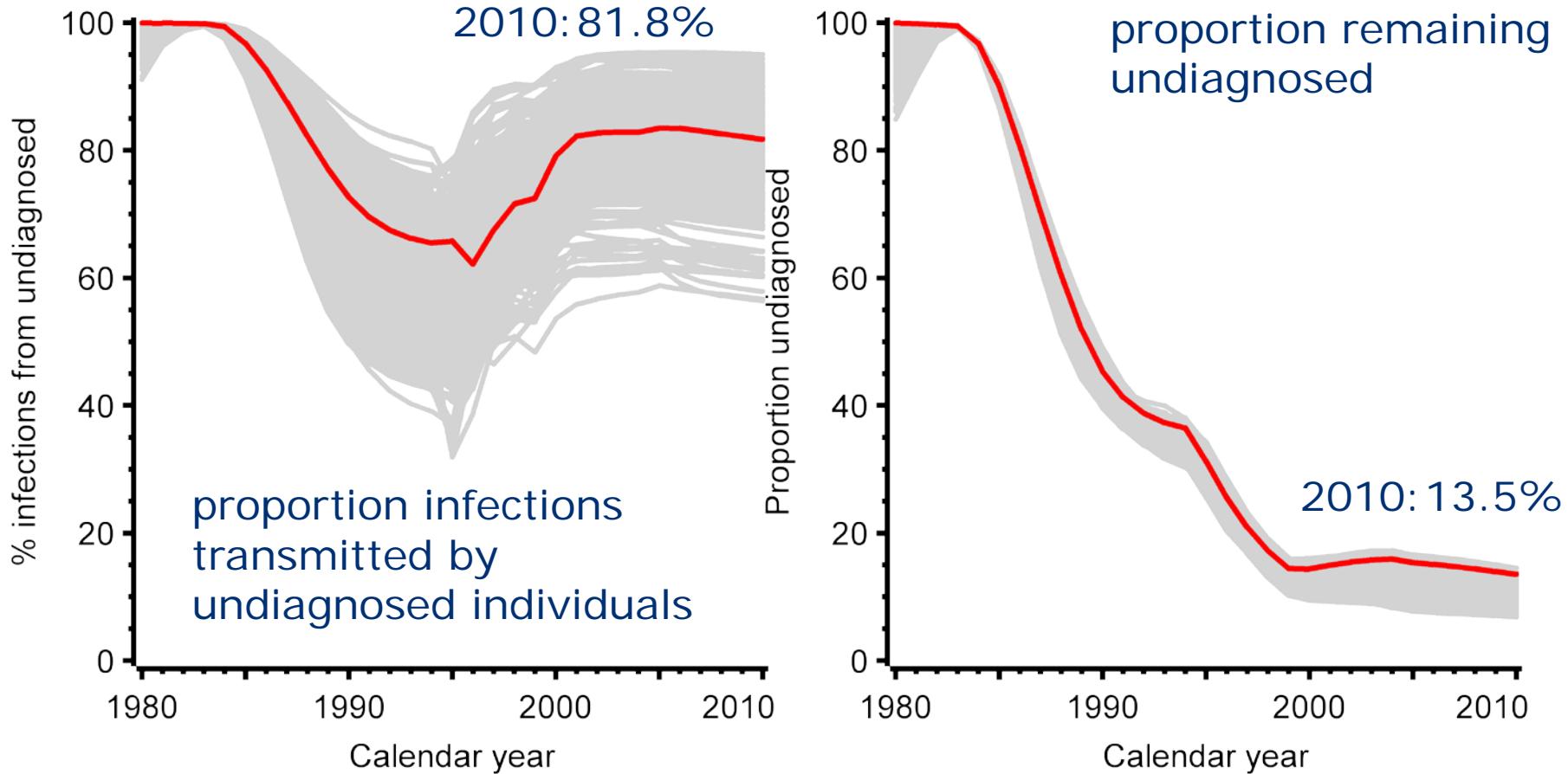
Dynamic transmission model



Time to diagnosis and HIV incidence

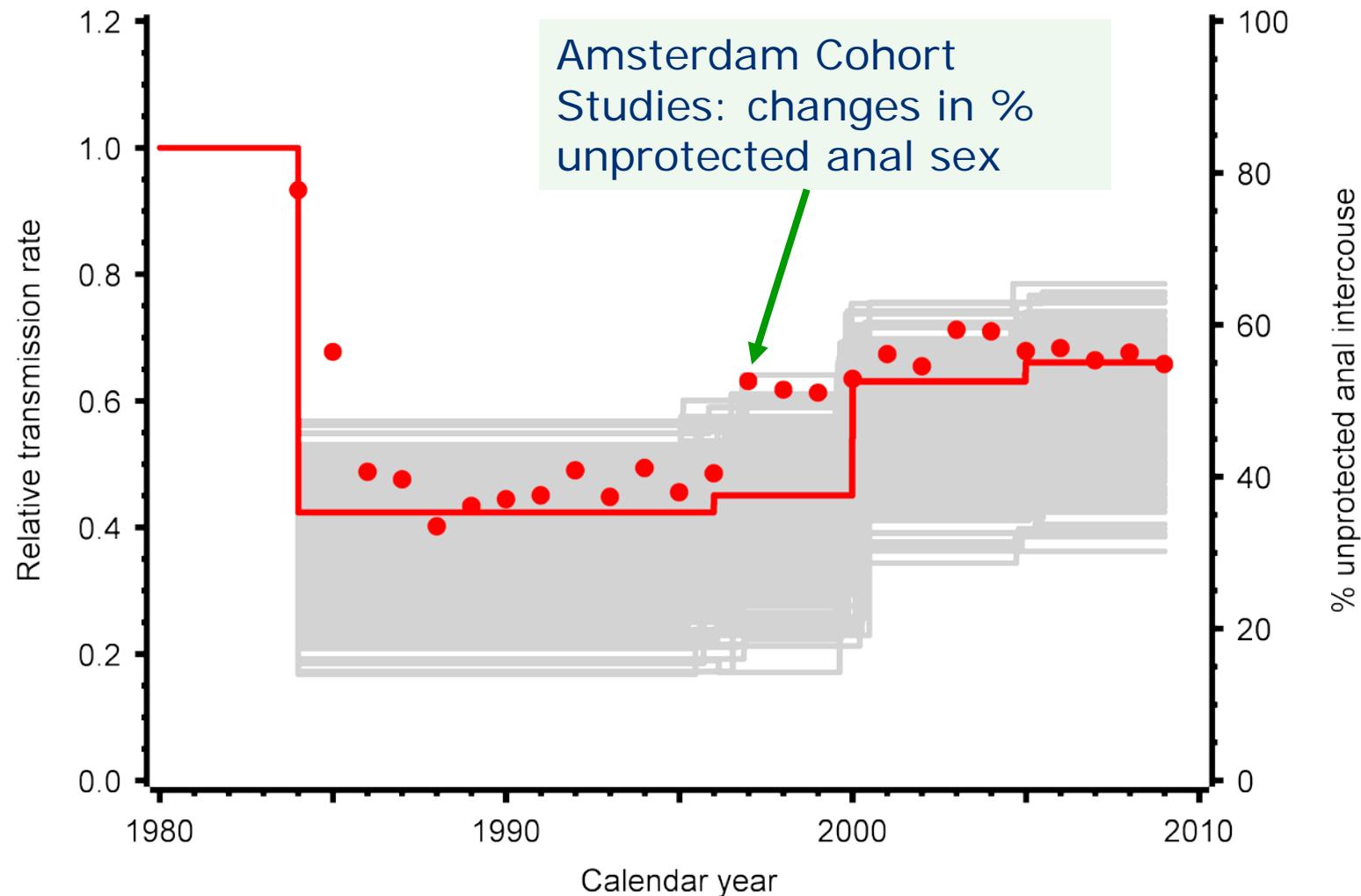


Undiagnosed infections

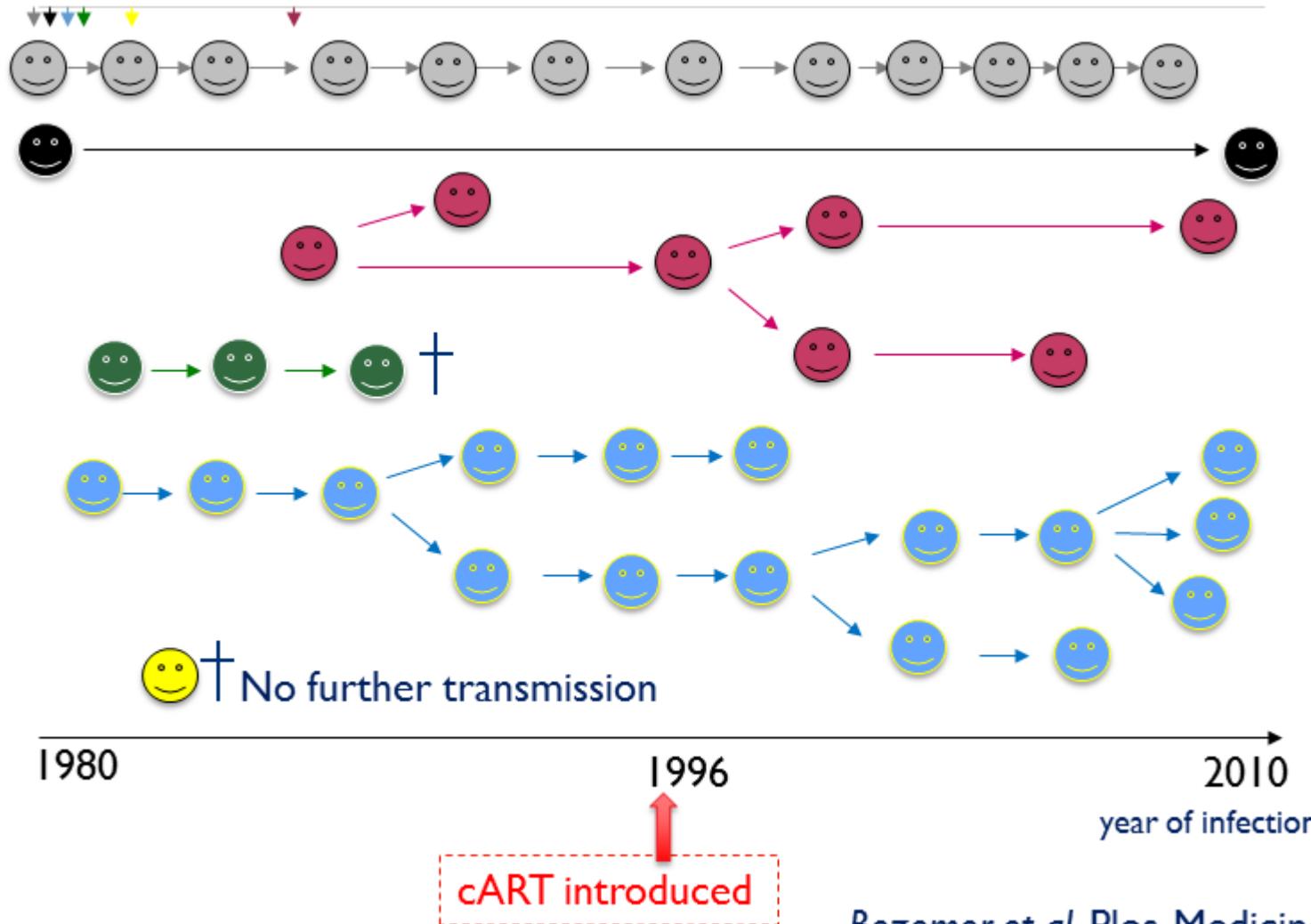


Bezemer *et al*, AIDS 2008; Epidemics 2010; Van Sighem & Vidondo *et al*, PLOS One 2012

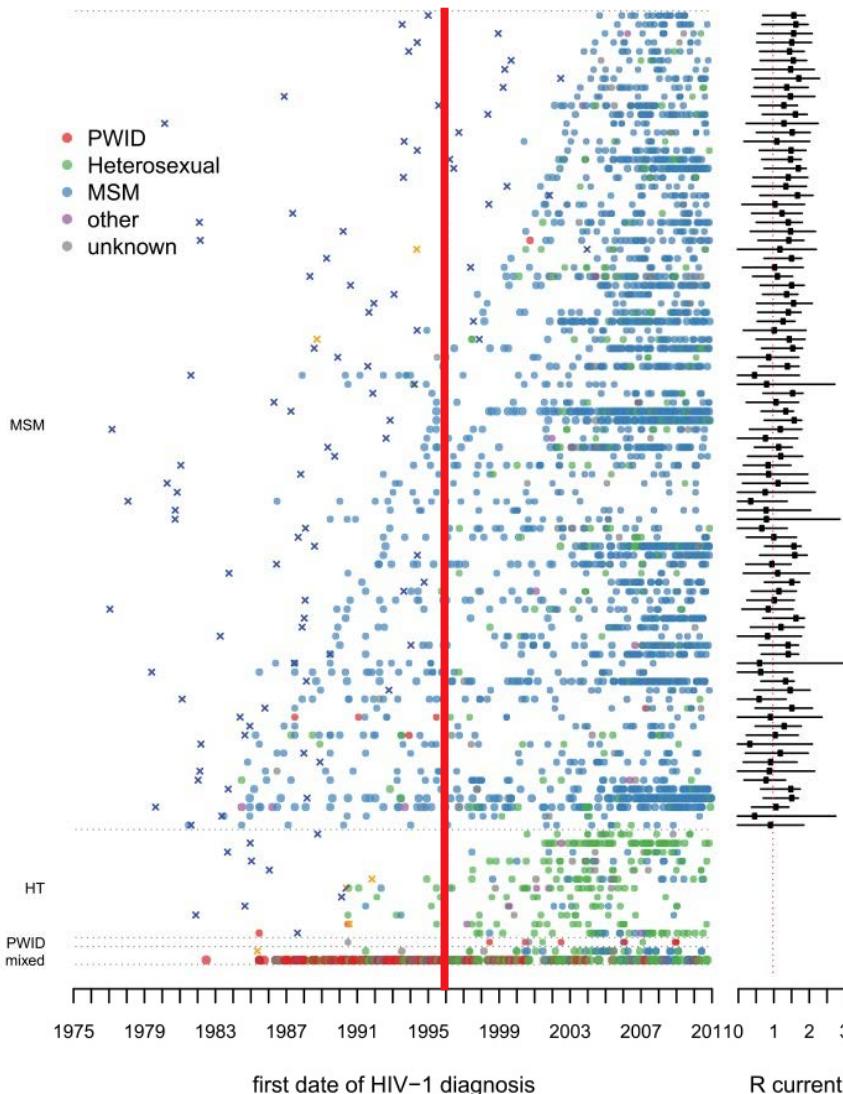
“Risk behaviour”



Transmission network dynamics



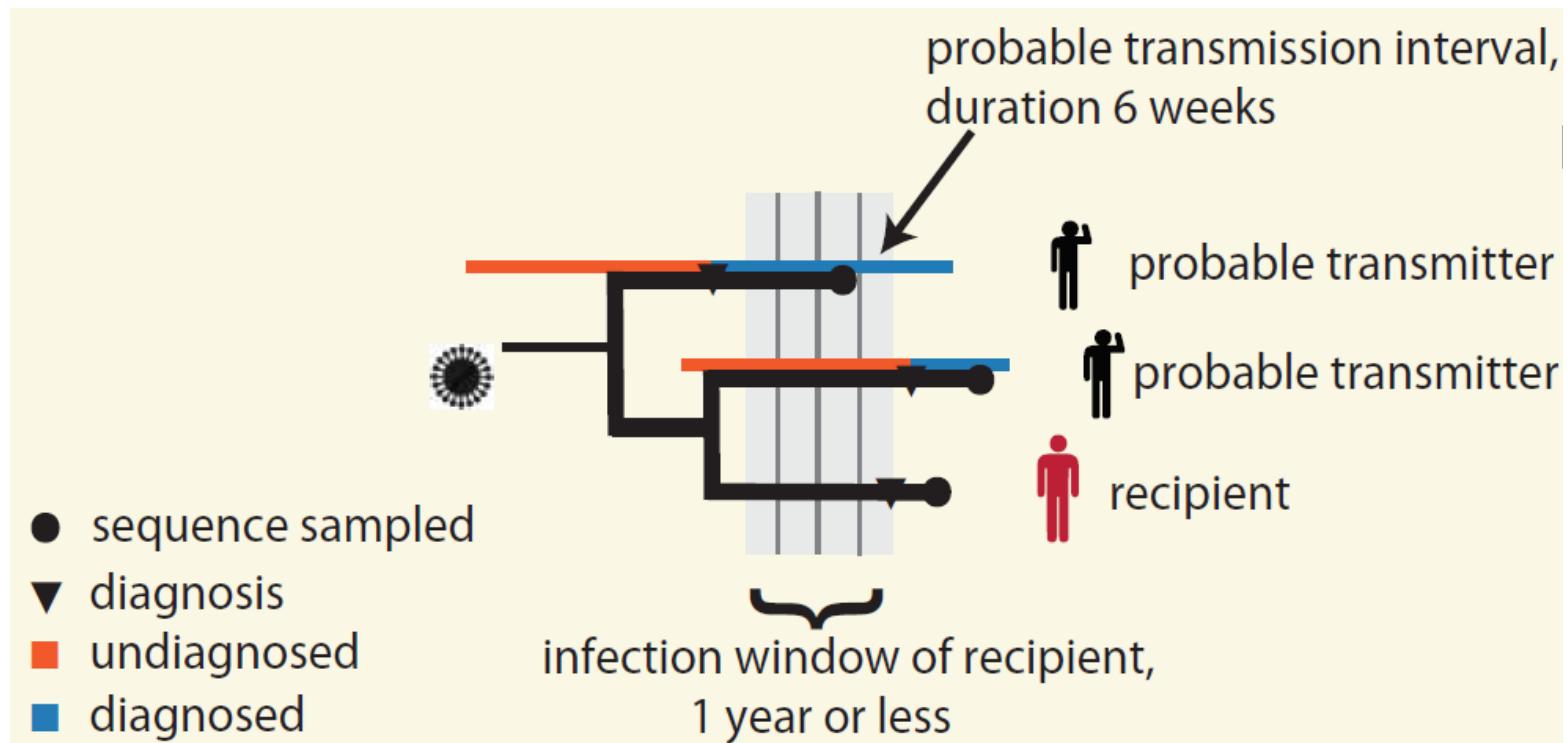
Transmission clusters among MSM



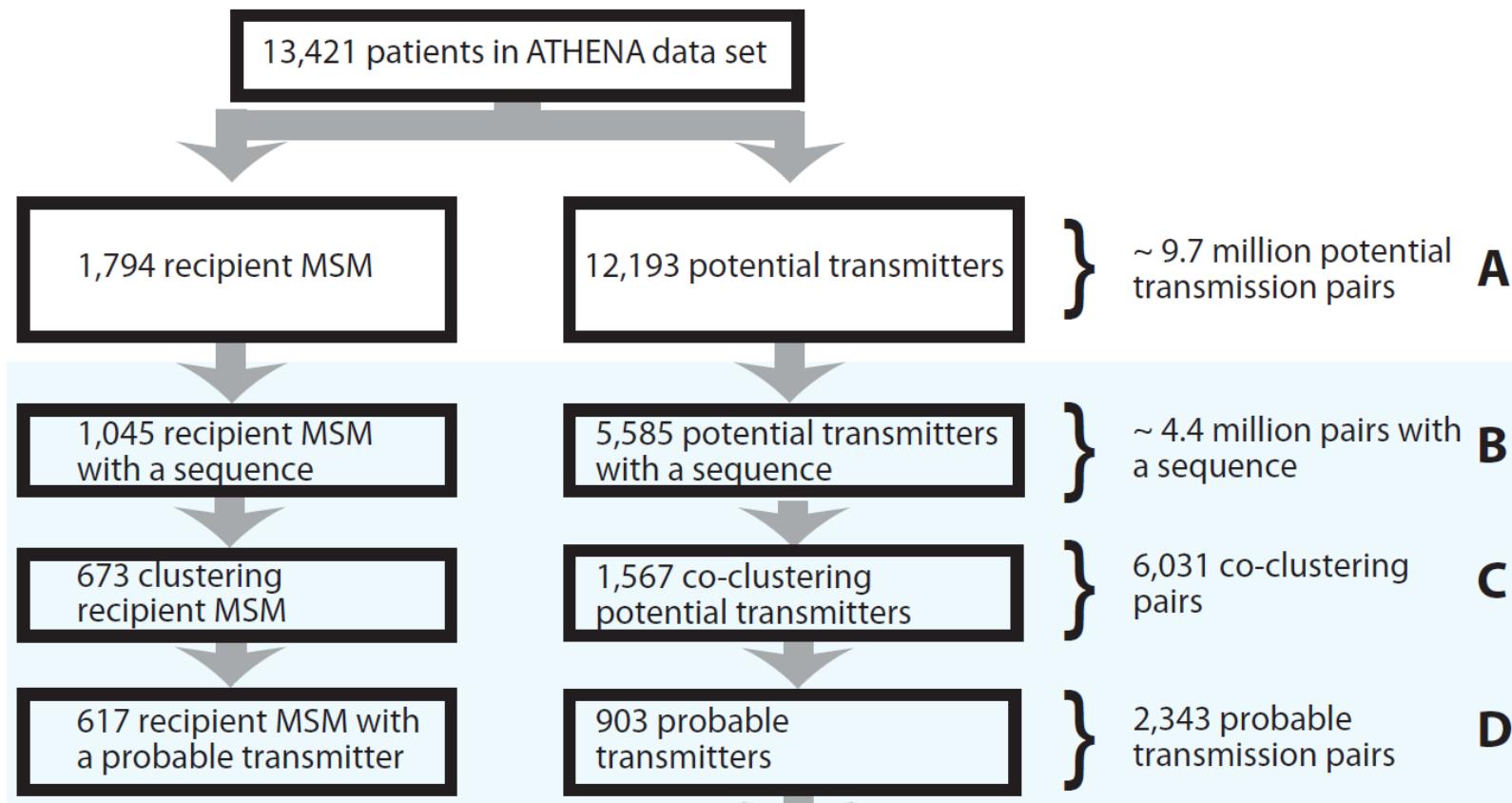
- 106 networks
- include 3061 (52%) of 5852 individuals with subtype B infection
- 91 majority MSM
- 54 (59%) present before 1996
- networks don't stop!

Probable transmitters to MSM

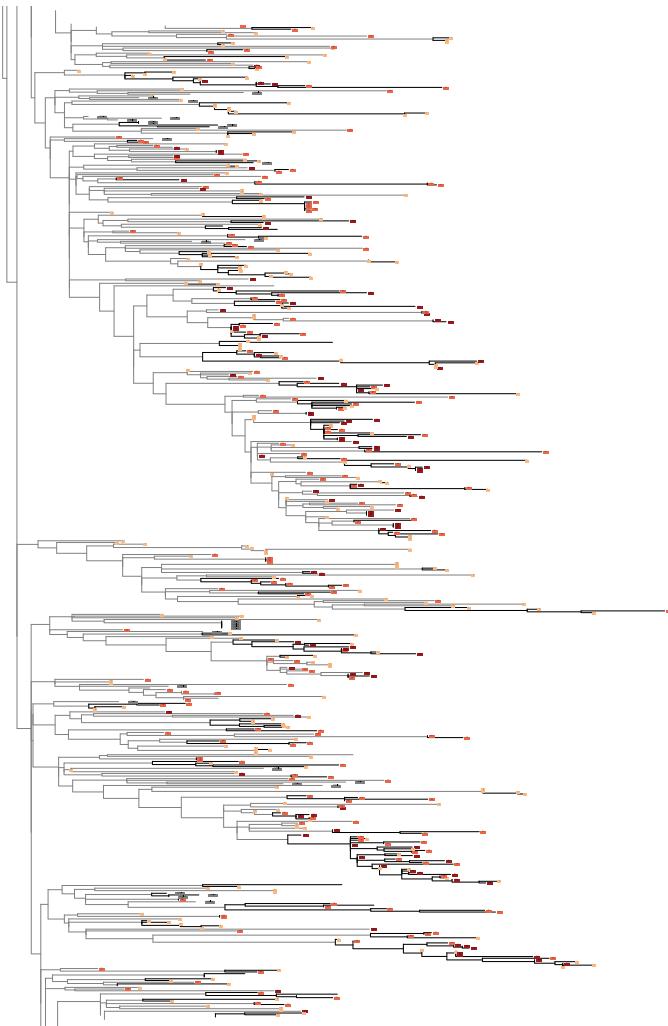
- 1,794 MSM confirmed to have been infected at most 12 months before diagnosis



Probable transmitters

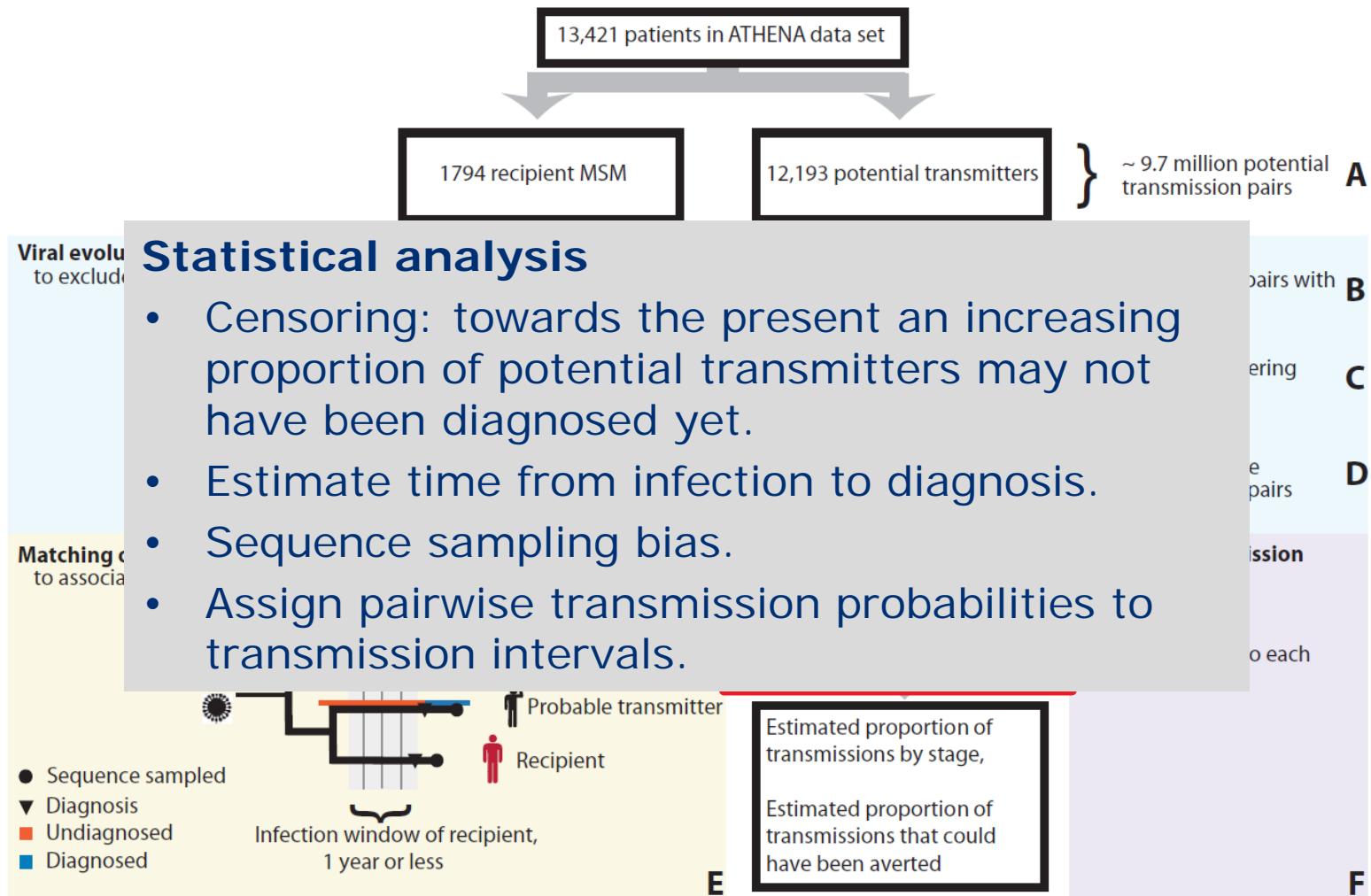


Phylogenetic analysis

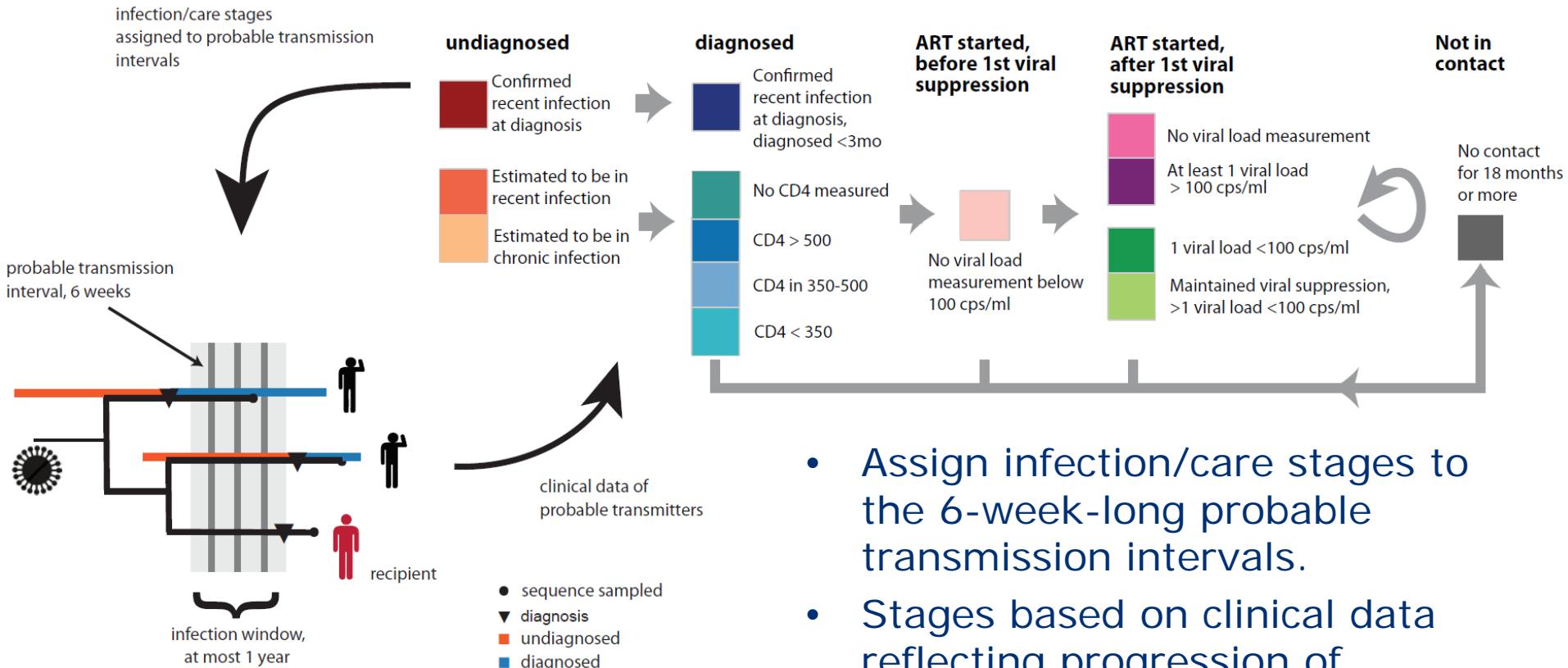


- Exclude potential transmission pairs who are not in the same cluster.
- Exclude pairs incompatible with direct transmission:
 - low probability that the lineages from the potential transmitter and the recipient coalesce after the transmitter was infected and before the recipient was diagnosed.

Probable transmitters

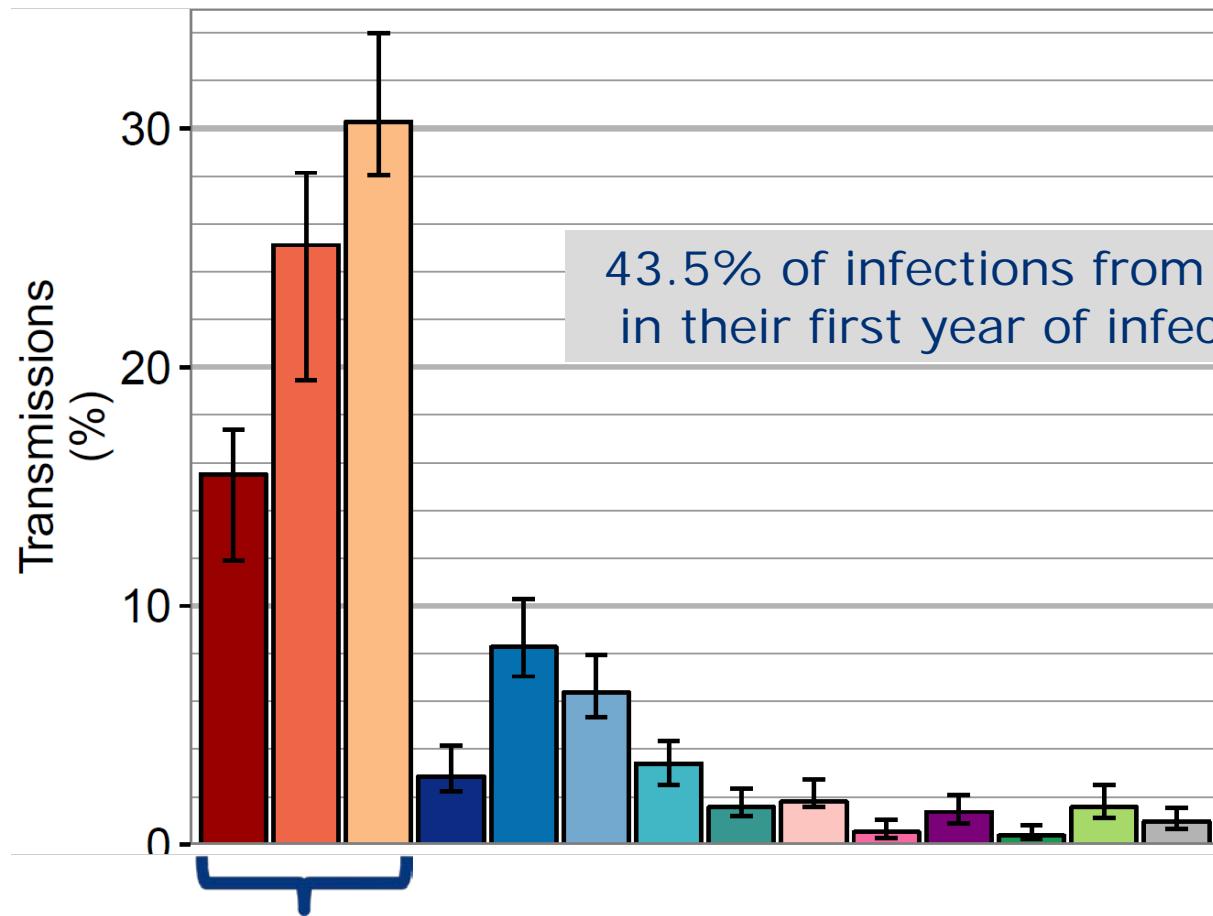


Linking to HIV infection and care stages



- 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.

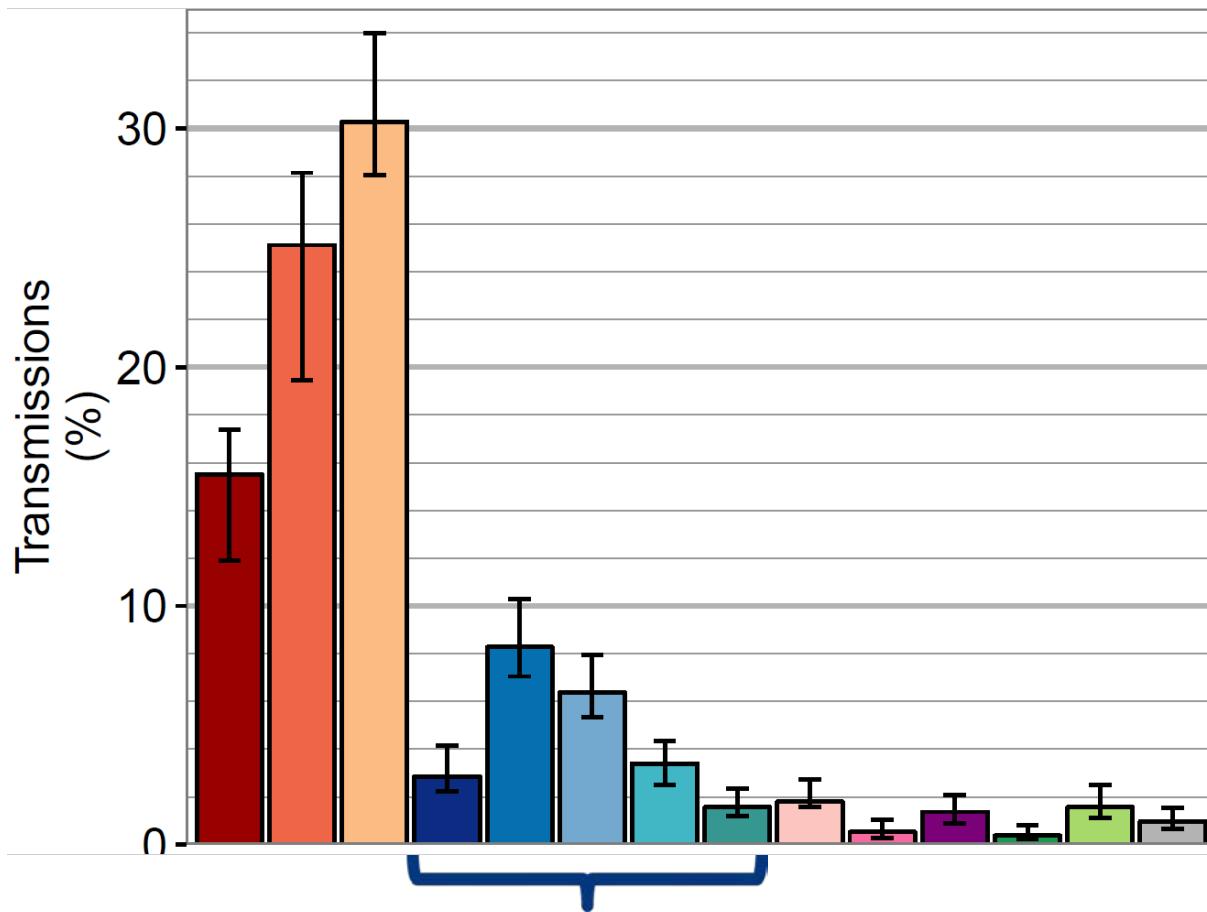
Contribution from infection/care stages



43.5% of infections from men
in their first year of infection

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

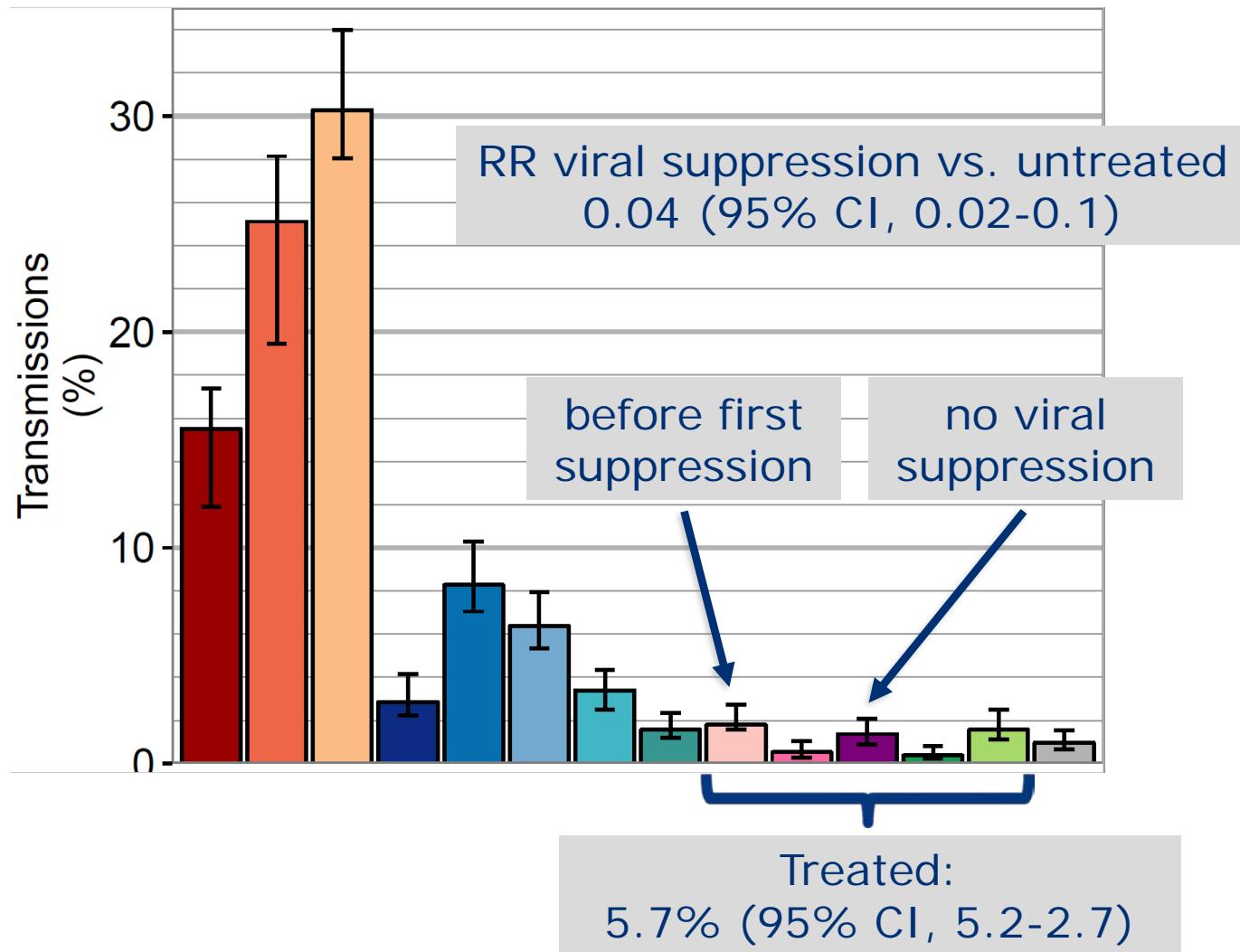
Contribution from infection/care stages



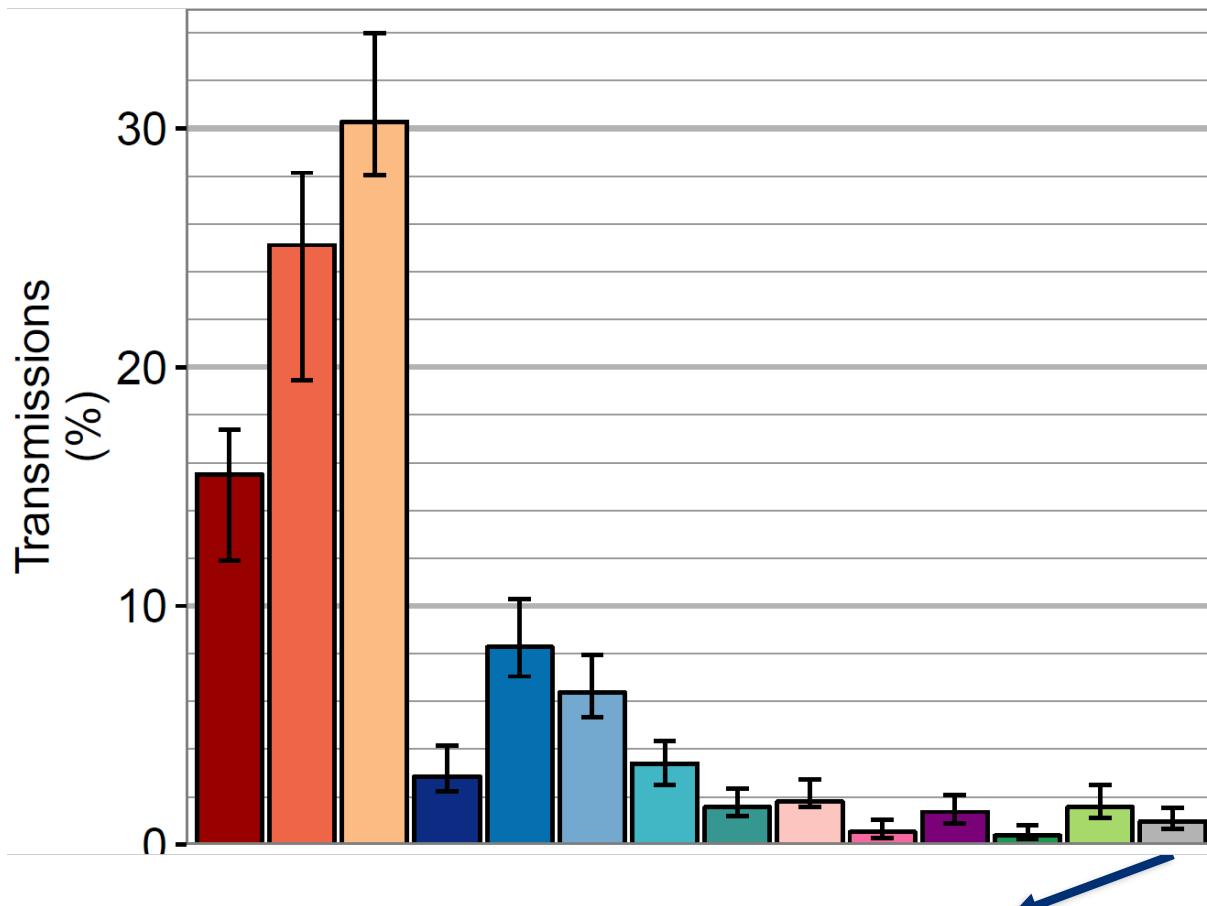
Diagnosed and untreated:
22.4% (95% CI, 20.7-26.2)



Contribution from infection/care stages

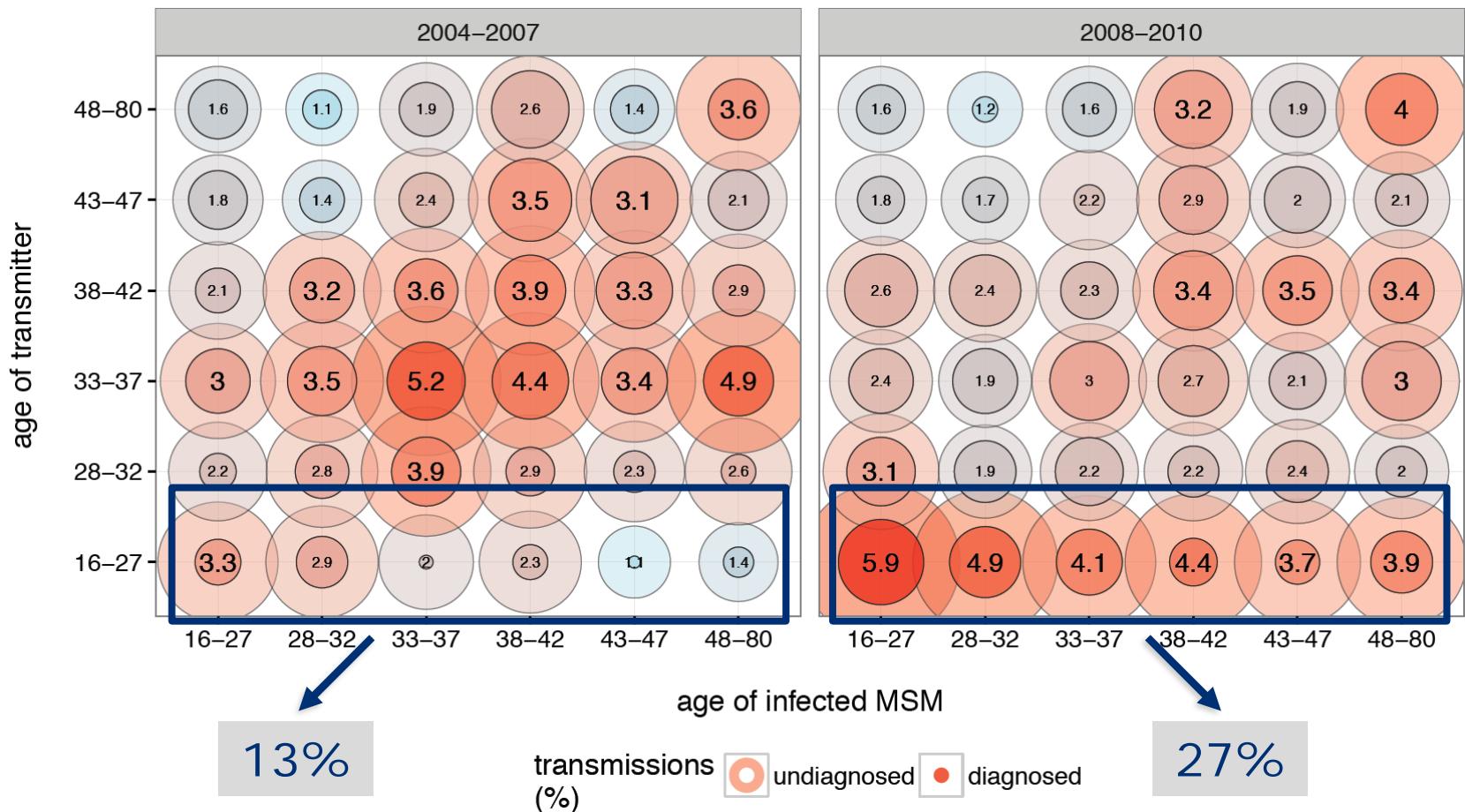


Contribution from infection/care stages



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

Transmission between age groups



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.



Acknowledgements



Daniela Bezemer



Oliver Ratmann

Alexandra Gavryushkina
Suzanne Jurriaans
Annemarie Wensing
Frank de Wolf
Peter Reiss
Christophe Fraser

Anne Cori
Hillegonda Hermanides
Bas Dutilh
Luuk Gras
Nuno Rodrigues Faria
Rob van den Hengel
Ashley Duits

Acknowledgements

Academic Medical Centre of the University of Amsterdam: J.M. Prins, T.W. Kuijpers, H.J. Scherbvier, J.T.M. van der Meer, F.W.M.N. Wit, M.H. Godfried, P. Reiss, T. van der Poll, F.J.B. Nellen, S.E. Geerlings, M. van Vugt, D. Pajkrt, J.C. Bos, W.J. Wiersinga, M. van der Valk, A. Goorhuis, J.W. Hovius, A.M. Weijzenfeld, J. van Eden, A. Henderiks, A.M.H. van Hes, M. Mutschelknauss, H.E. Nobel, F.J.J. Pijnappel, S. Jurriaans, N.K.T. Back, H.L. Zaaijer, B. Berkhout, M.T.E. Cornelissen, C.J. Schinkel, X.V. Thomas. **Admiraal De Ruyter Ziekenhuis, Goes:** M. van den Berge, A. Stegeman, S. Baas, L. Hage de Looff,: D. Versteeg. **Catharina Ziekenhuis, Eindhoven:** M.J.H. Pronk, H.S.M. Ammerlaan , E.S. de Munnik. A.R. Jansz, J. Tjhie, M.C.A. Wegdam, B. Deiman, V. Scharnhorst. **Emma Kinderziekenhuis:** A. van der Plas, A.M. Weijzenfeld. **Erasmus Medisch Centrum, Rotterdam:** M.E. van der Ende, T.E.M.S. de Vries-Sluijs, E.C.M. van Gorp, C.A.M. Schurink, J.L. Nouwen, A. Verbon, B.J.A. Rijnders, H.I. Bax, M. van der Feltz, N. Bassant, J.E.A. van Beek, M. Vriesde, L.M. van Zonneveld., A. de Oude-Lubbers, H.J. van den Berg-Cameron, F.B. Bruinsma-Broekman, J. de Groot, M. de Zeeuw- de Man, C.A.B. Boucher, M.P.G Koopmans, J.J.A van Kampen. **Erasmus Medisch Centrum—Sophia, Rotterdam:** G.J.A. Driessen, A.M.C. van Rossum, L.C. van der Knaap, E. Visser. **Flevoziekenhuis, Almere:** J. Branger, A. Rijkeboer-Mes, C.J.H.M. Duijf-van de Ven. **HagaZiekenhuis, Den Haag:** E.F. Schippers, C. van Nieuwkoop, J.M. van IJperen, J. Geulings, G. van der Hut, P.F.H. Franck. **HIV Focus Centrum (DC Klinieken):** A. van Eeden, W. Brokking, M. Groot, L.J.M. Elsenburg, M. Damen, I.S. Kwa. **Isala, Zwolle:** P.H.P. Groeneveld, J.W. Bouwhuis, J.F. van den Berg, A.G.W. van Hulzen, G.L. van der Bliek, P.C.J. Bor, P. Bloembergen, M.J.H.M. Wolfhagen, G.J.H.M. Ruijs. **Leids Universitair Medisch Centrum, Leiden:** F.P. Kroon, M.G.J. de Boer, M.P. Bauer, H. Jolink, A.M. Vollaard. W. Dorama, N. van Holten, E.C.J. Claas, E. Wessels. **Maastrad Ziekenhuis, Rotterdam:** J.G. den Hollander, K. Pogany, A. Roukens, M. Kastelijns, J.V. Smit, E. Smit, D. Struik-Kalkman, C. Tearno, M. Bezemer, T. van Niekerk, O. Pontesilli. **Maastricht UMC+, Maastricht:** S.H. Lowe, A.M.L. Oude Lashof, D. Posthouwer, R.P. Ackens, J. Schippers, R. Vergoossen, B. Weijenberg-Maes, I.H.M. van Loo, T.R.A. Havenith. **MC Slotervaart, Amsterdam:** J.W. Mulder, S.M.E. Vrouwenraets, F.N. Lauw, M.C. van Broekhuizen, H. Paap, D.J. Vlasblom, P.H.M. Smits. **MC Zuiderzee, Lelystad:** S. Weijer, R. El Moussaoui, A.S. Bosma. **Medisch Centrum Alkmaar:** W. Kortmann, G. van Twillert, J.W.T. Cohen Stuart, B.M.W. Diederden, D. Pronk, F.A. van Truijen-Oud, W. A. van der Reijden, R. Jansen. **Medisch Centrum Haaglanden, Den Haag:** E.M.S. Leyten, L.B.S. Gelinck, A. van Hartingsveld, C. Meerkerk, G.S. Wildenbeest, J.A.E.M. Mutsaers, C.L. Jansen. **Medisch Centrum Leeuwarden, Leeuwarden:** M.G.A.van Vonderen, D.P.F. van Houte, L.M. Kampschreur, K. Dijkstra, S. Faber, J Weel. **Medisch Spectrum Twente, Enschede:** G.J. Kootstra, C.E. Delsing, M. van der Burg-van de Plas, H. Heins, E. Lucas. **Onze Lieve Vrouwe Gasthuis, Amsterdam:** K. Brinkman, P.H.J. Frissen, W.L. Blok, W.E.M. Schouten, G.E.L. van den Berk, C.J. Brouwer, G.F. Geerders, K. Hoeksema, M.J. Kleene, I.B. van der Meché, A.J.M. Toonen, S. Wijnands, M. Damen, D. Kwa. **Radboudumc, Nijmegen:** P.P. Koopmans, M. Keuter, A.J.A.M. van der Ven, H.J.M. ter Hofstede, A.S.M. Dofferhoff, R. van Crevel, M. Albers, M.E.W. Bosch, K.J.T. Grintjes-Huisman, B.J. Zomer, F.F. Stelma, J. Rahamat-Langendoen, D. Burger. **Rijnstate, Arnhem:** C. Richter, E.H. Gisolf, R.J. Hassing, G. ter Beest, P.H.M. van Bentum, N. Langebeek, R. Tiemessen, C.M.A. Swanink. **Sint Lucas Andreas Ziekenhuis, Amsterdam:** J. Veenstra, K.D. Lettinga, M. Spelbrink, H. Sulman, M. Spelbrink, E. Witte, M. Damen, S.Q. van Veen. **Spaarne Gasthuis, Haarlem:** S.F.L. van Lelyveld, R. Soetekouw, N. Hulshoff, L.M.M. van der Prijt, J. van der Swaluw, N. Bermon, W.A. van der Reijden, R. Jansen, B.L. Herpers, D.Veenendaal. **Stichting Medisch Centrum Jan van Goyen, Amsterdam:** D.W.M. Verhagen, M. van Wijk. **St Elisabeth Ziekenhuis, Tilburg:** M.E.E. van Kasteren, A.E. Brouwe, B.A.F.M. de Kruif-van de Wiel, M. Kuipers, R.M.W.J. Santegoets, B. van der Ven, J.H. Marcelis, A.G.M. Buiting, P.J. Kabel. **Universitair Medisch Centrum Groningen, Groningen:** W.F.W. Bierman, H. Scholvinck, K.R. Wilting, Y. Stienstra, H. de Groot-de Jonge, P.A. van der Meulen, D.A. de Weerd, J. Ludwig-Roukema, H.G.M. Niesters, A. Riezebos-Brilman, C.C. van Leer-Buter, M. Knoester. **Universitair Medisch Centrum Utrecht, Utrecht:** A.I.M. Hoepelman, M.M.E. Schneider, T. Mudrikova, P.M. Ellerbroek, J.J. Oosterheert, J.E. Arends, R.E. Barth, M.W.M. Wassenberg, E.M. Schadd, D.H.M. van Elst-Laurijssen, E.E.B. van Oers-Hazelzet, J. Patist, S. Vervoort, M. van Berkelaer, R. Schuurman, F. Verduyn-Lunel, A.M.J. Wensing. **VU medisch centrum, Amsterdam:** E.J.G. Peters, M.A. van Agtmael, M. Bomers, J. de Vocht, M. Heitmuller, L.M. Laan, A.M. Pettersson, C.M.J.E. Vandebroucke-Grauls, C.W. Ang. **Wilhelmina Kinderziekenhuis, UMCU, Utrecht:** S.P.M. Geelen, T.F.W. Wolfs, L.J. Bont, N. Nauta. **Coordinating centre:** P. Reiss, D.O. Bezemer, A.I. van Sighem, C. Smit, F.W.M.N. Wit, S. Zaheri, M. Hillebregt, A. de Jong, D. Bergsma, P. Hoekstra, A. de Lang, S. Grivell, A. Jansen, M.J. Rademaker, M. Raethke, L. de Groot, M. van den Akker, Y. Bakker, M. Broekhoven, E. Claessen, A. El Berkaoui, J. Koops, E. Kruijne, C. Lodewijk, R. Meijering, L. Munjishvili, B. Peeck, C. Ree, R. Regtop, Y. Ruijs, T. Rutkens, L. van de Sande, M. Schoorl, S. Schnörr, E. Tuijn, L. Veenenberg, S. van der Vliet, T. Woudstra, B. Tuk.