Dr Valerie Delpech

Health Protection Agency, London

COMPETING INTEREST OF FINANCIAL VALUE ≥ £1,000:	
Speaker Name	**Statement**
Valerie Delpech	None
Date	**22 September 2012**

Treatment as prevention (TasP) in the UK: what are the challenges?

Dr Valerie Delpech
Health Protection Agency, London

Outline

- Brief overview
  - Science, models, ecological data, scale up
- UK Experience
  - Epidemiology, access to care, recent modeling work on MSM
- Challenges of scale up
- Conclusions and way forward

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MMWR Weekly

June 5, 1981 / 30(21);1-3

Epidemiologic Notes and Reports

Pneumocystis Pneumonia --- Los Ang

In the period October 1980-May 1981, 5 young men, all active homosexual
biopsy-confirmed *Pneumocystis carinii* pneumonia at 3 different hospitals
California. Two of the patients died. All 5 patients had laboratory-confirm
cytomegalovirus (CMV) infection and candidal mucosal infection. Case
follow.

Patient 1: A previously healthy 33-year-old man developed *P. carinii*
candidiasis in March 1981 after a 2-month history of fever associate
leukopenia, and CMV viruria. The serum complement-fixation CM
in may 1981 it was 32.* The patient's condition deteriorated despi
trimethoprim-sulfamethoxazole (TMP/SMX), pentamidine, and
postmortem examination showed residual *P. carinii* and CMV
neoplasia.

Patient 2: A previously healthy 30-year-old man developed
a 5-month history of fever each day and of elevated liver-fu
documented seroconversion to CMV, i.e., an acute-phase
of 28* in anticomplement immunofluorescence tests. Oth
leukopenia and mucosal candidiasis. His pneumonia res
TMP/.SMX, but, as of the latest reports, he continues t

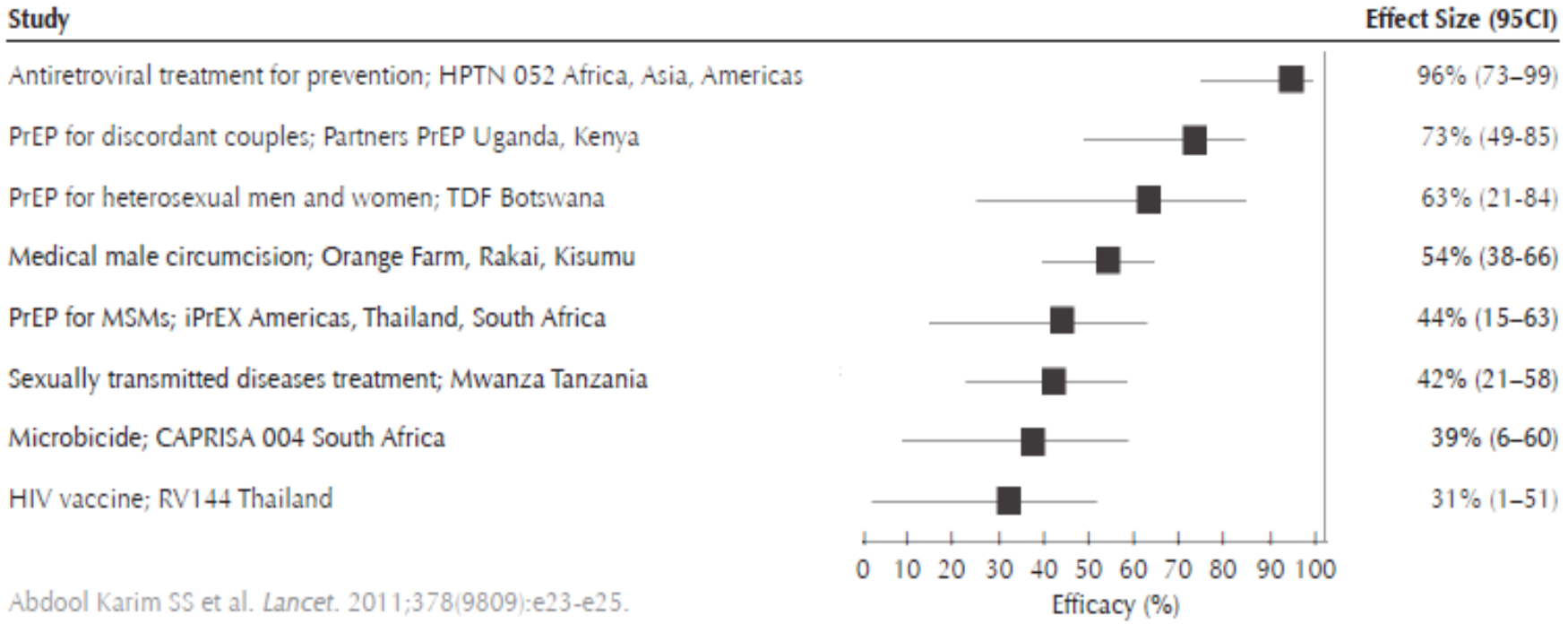
Patient 3: A 30-year-old man was well until January
candidiasis that responded to Amphotericin B treatm
P. carinii pneumonia that responded to TMP/SMX.
pneumonia was diagnosed, and he was again given Amphot
fixation titer in March 1981 was 8. Material from an esophageal bi

Patient 4: A 29-year-old man developed *P. carinii* pneumonia in February 198
Hodgkins disease 3 years earlier, but had been successfully treated with radiation the
did not improve after being given intravenous TMP/SMX and corticosteroids and died in M
Postmortem examination showed no evidence of Hodgkins disease, but *P. carinii* and CMV were
found in lung tissue.

Health Protection Agency

TASP
THE EVIDENCE

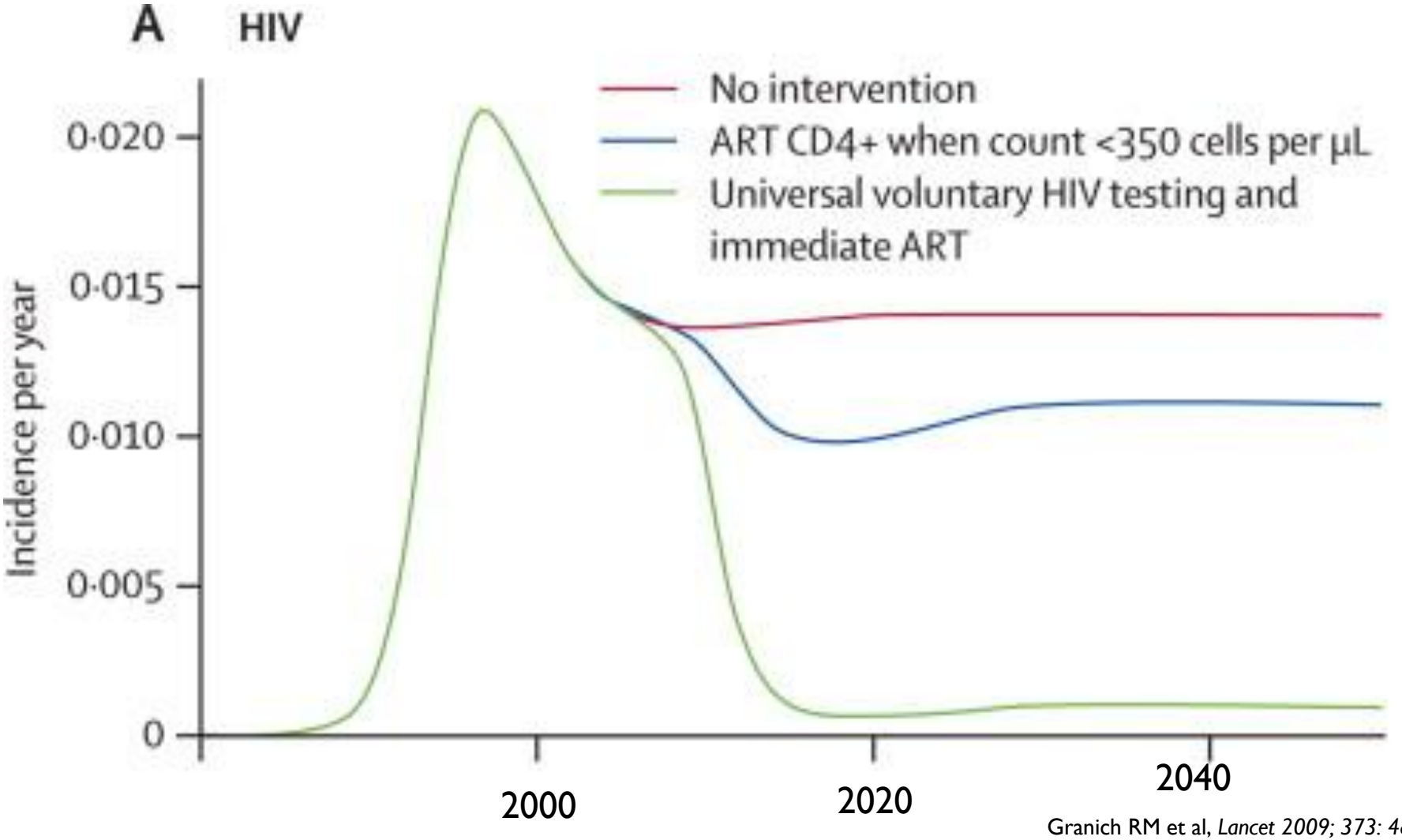
HIV Prevention Technologies Shown to Be Effective in Reducing HIV Incidence in Randomized Clinical Trials



Abdool Karim SS et al. *Lancet*. 2011;378(9809):e23-e25.

THE MODELS

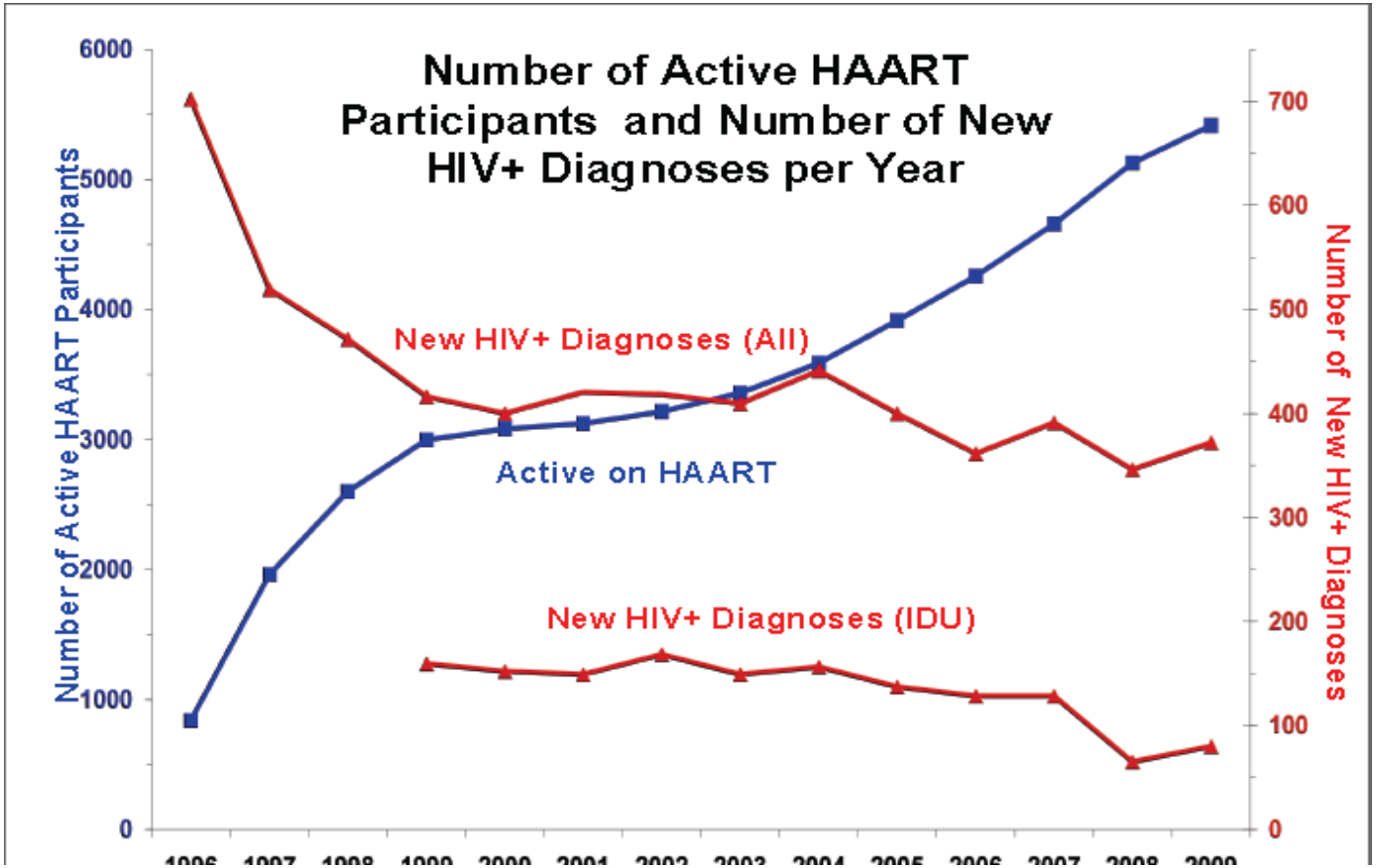
HIV incidence



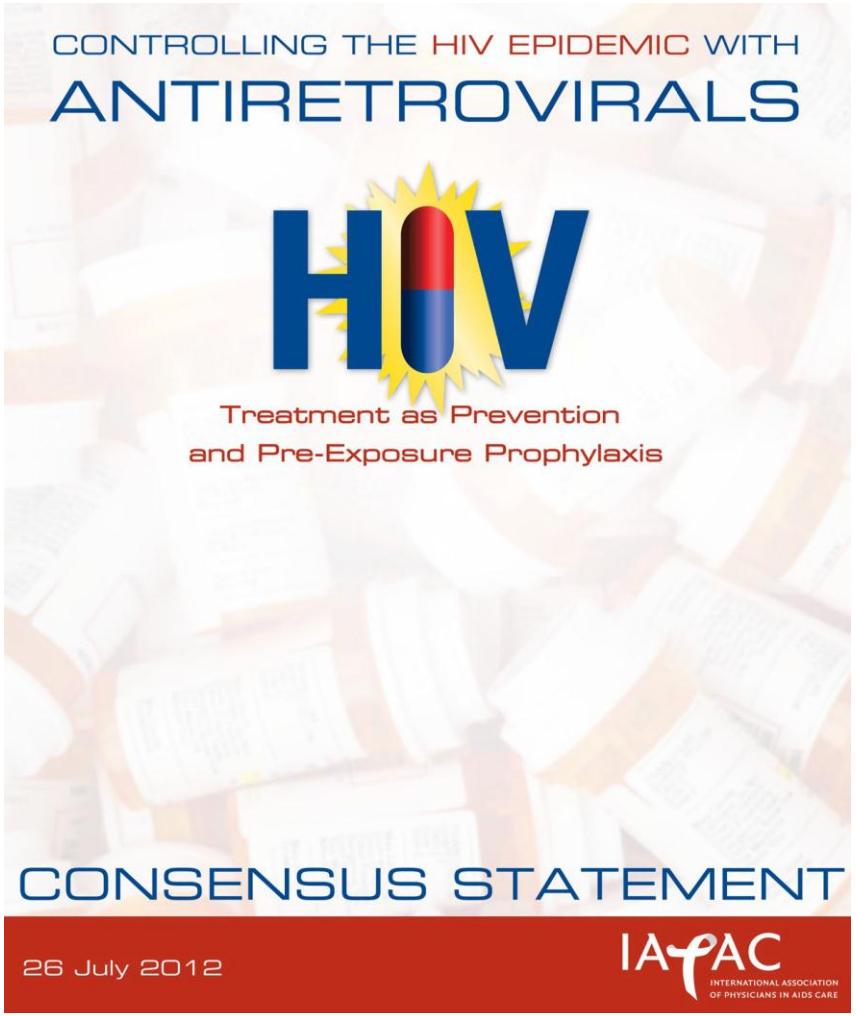
Granich RM et al, *Lancet 2009; 373: 48–57*

ECOLOGICAL STUDIES

British Columbia, Canada: *Montaner et al* (2010)



Position statements 2012



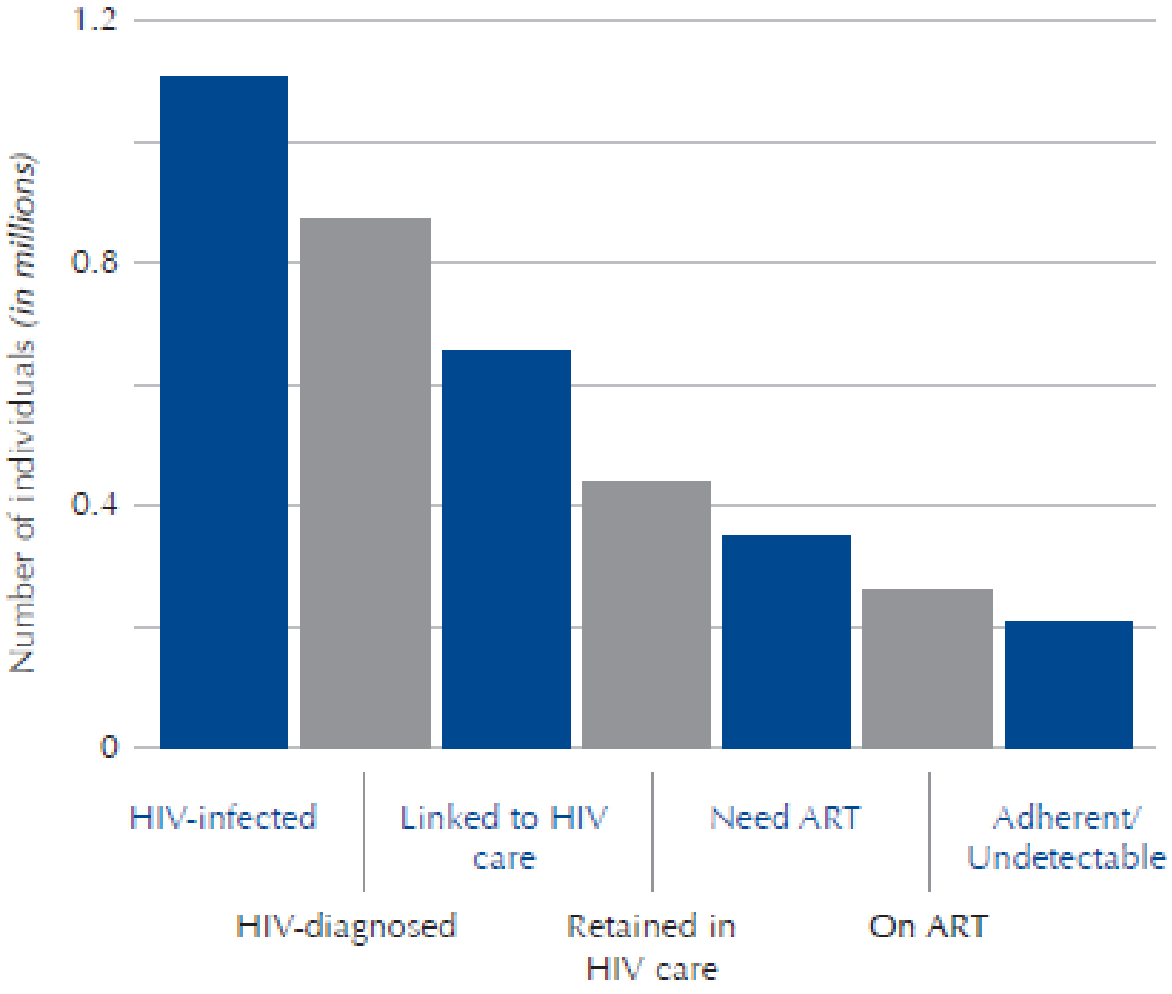
International Association of Physicians in AIDS Care (IAPAC)

CHALLENGES IN SCALE UP

Concerns about "roll-out or scale up" of TasP

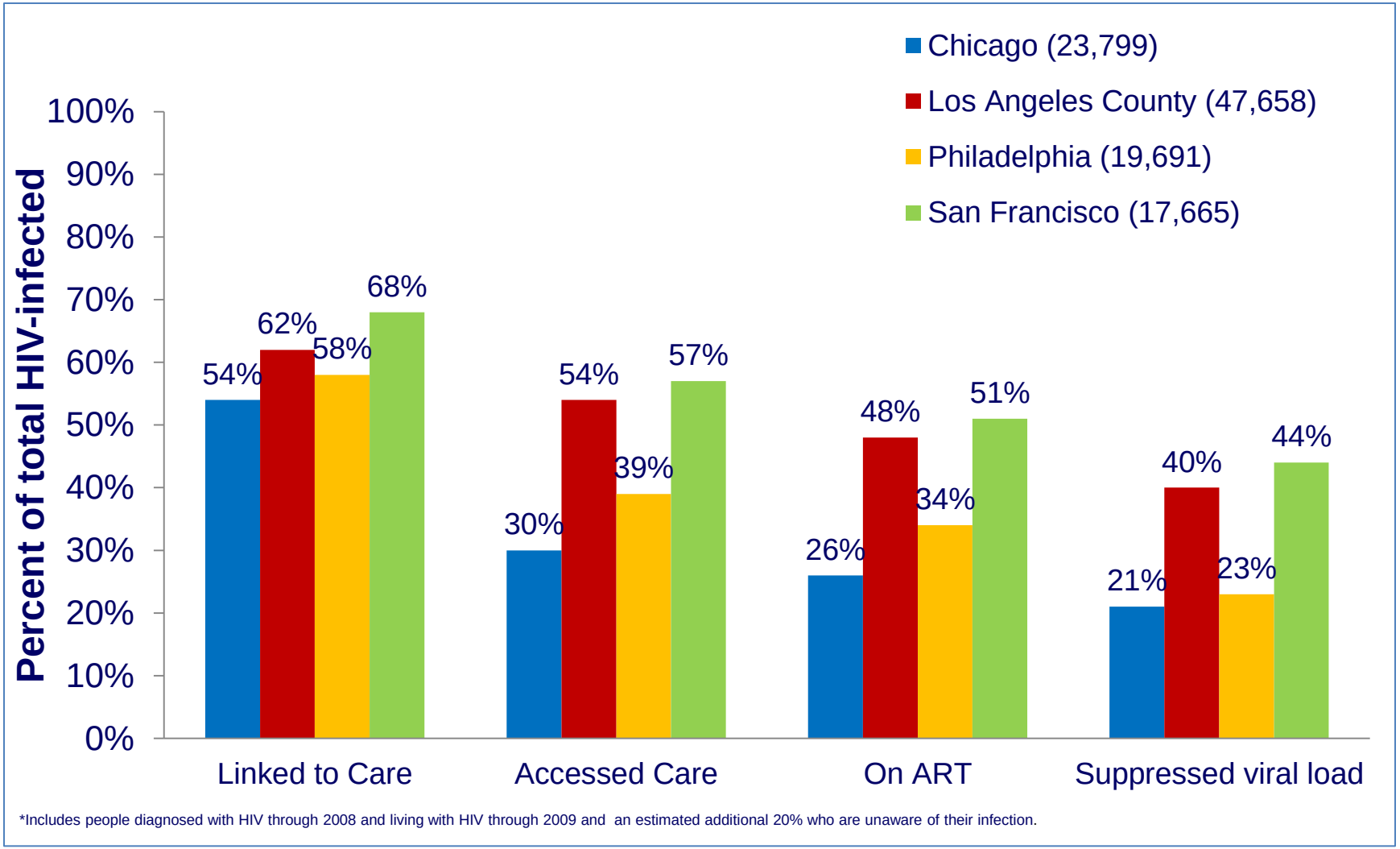
- Efficacy versus effectiveness
  - Individual versus public health benefit
- Feasibility and acceptability
- Ethics
- Resistance and toxicity
- Role of primary HIV infection in transmission
  - MSM versus heterosexual epidemics
- Role of undiagnosed HIV in transmission
- Linkage to care and access to ART

Number of HIV-Infected Persons Engaged in Selected Stages of the Continuum of HIV Care – United States



Gardner EM et al. *Clin Infect Dis*. 2011;52(6):793-800.

Percentage of estimated number of HIV-infected persons* in stages of continuum of HIV care in four large United States cities through December 2009



*Includes people diagnosed with HIV through 2008 and living with HIV through 2009 and an estimated additional 20% who are unaware of their infection.

THE UK EXPERIENCE

BHIVA guidelines, 2012
Treatment to reduce transmission

Recommendations (4.4)

- We recommend the evidence that treatment with ART lowers the risk of transmission is discussed with all patients, and an assessment of the current risk of trans- mission to others is made at the time of this discussion

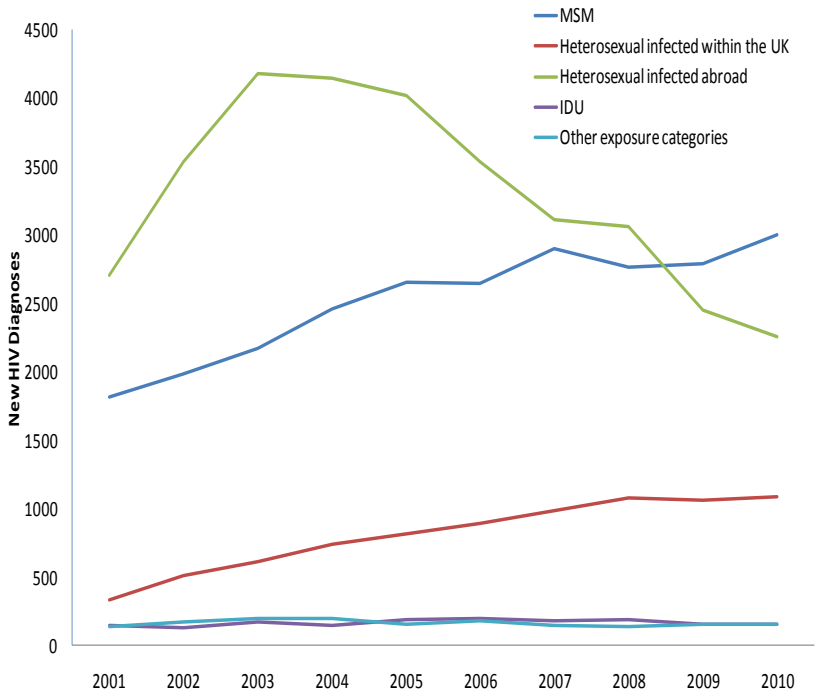
- We recommend following discussion, if a patient with a CD4 cell count >350 cells/mL wishes to start ART to reduce the risk of transmission to partners, this decision is respected and ART is started

UK HIV Epidemic

- 100,000 living with HIV in 2012, 26% undiagnosed
- Overall prevalence is low 1.6/1,000 prevalence
- Epidemic concentrated in MSM, Africans communities & persons who inject drugs

- Recent decline heterosexual infections acquired abroad & Increases in MSM

New HIV diagnoses by exposure group



Average Profile: Man with HIV in 2011

Probable route of infection:	Sex with other men
Ethnicity:	White
Place of birth:	UK
Probable place of infection:	UK
Median age at diagnosis:	34
Median CD4 at diagnosis:	398
Place of diagnosis:	STI clinic
Most likely accessing care in:	London

For illustration purposes only, does not imply HIV Status

MSM with HIV in the UK

Probable route of infection:

Ethnicity:

Place of birth:

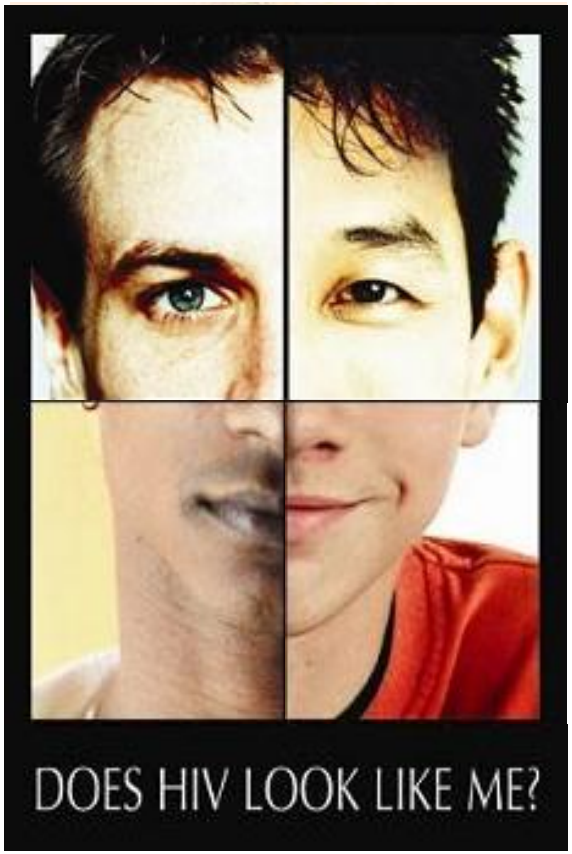
Probable place of infection:

Median age at diagnosis:

Median CD4 at diagnosis:

Place of diagnosis:

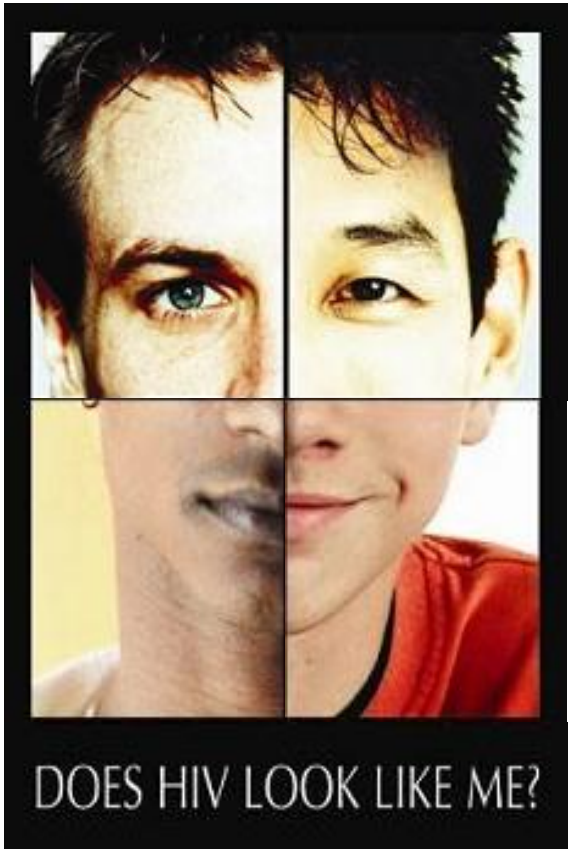
Mostly accessing care in:



For illustration purposes only, does not imply HIV Status

MSM with HIV in the UK

Probable route of infection:	MSM & IDU (2%) ?het misclass
Ethnicity:	Non-white (15%)
Place of birth:	Born in EU (12%)
Probable place of infection	Europe (8%), North America (6%)
Median age at diagnosis:	Over 50 (9%)
Median CD4 at diagnosis:	Diagnosed late (<350) (42%)
Place of diagnosis:	GP (5%), inpatient (5%)
Mostly accessing care in:	Outside London (44%)



Average Profile: Woman with HIV in 2011

Probable route of infection:	Heterosexual
Ethnicity:	Black African
Place of birth:	Africa
Probable place of infection:	Africa
Median age at diagnosis:	31
Median CD4 at diagnosis:	277
Place of diagnosis:	STI clinic
Mostly accessing care in:	Outside London

For illustration purposes only, does not imply HIV Status

Women with HIV in the UK

Probable route of infection:	Heterosexual
Ethnicity:	Black African
Place of birth:	Africa
Probable place of infection:	Africa
Median age at diagnosis:	31
Median CD4 at diagnosis:	277
Place of diagnosis:	STI clinic
Mostly accessing care in:	Outside London

For illustration purposes only, does not imply HIV Status

Women with HIV in the UK

Probable route of infection:	Heterosexual
Ethnicity:	White (19%)
Place of birth:	UK (15%)
Probable place of infection:	UK (21%)
Median age at diagnosis:	Over 50 (6%)
CD4 at diagnosis:	Diagnosed late (<350) (42%)
Place of diagnosis:	Antenatal clinic (25%)
Mostly accessing care in:	London (46%)

A new method to assign country of HIV infection among heterosexuals born abroad and diagnosed with HIV in the UK

Brian D. Rice[a,b,*], Jonathan Elford[b], Zheng Yin[a] and Valerie C. Delpech[a]

Objective: To apply a new method to ascertain likely place of HIV infection among persons born abroad and diagnosed with HIV in the United Kingdom (UK).

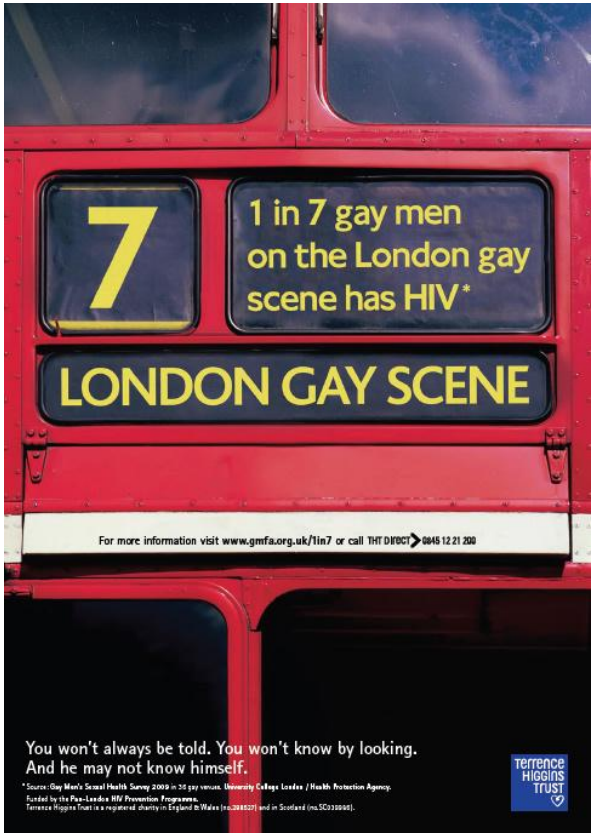
Design: Analyses of heterosexual adults born abroad, diagnosed with HIV in the UK between 2004 and 2010, and reported to the national HIV diagnoses database.

Methods: Year of infection was ascertained by applying an estimated rate of CD4-cell count decline between an individual's CD4-cell count at diagnosis and estimates of CD4-cell count at infection. A person was classified as having probably acquired HIV while living in the UK if estimated year of infection was later than reported year of arrival in the UK.

Results: Of 10,612 heterosexual adults born abroad included in the analyses, 85% (9065) were of black-African ethnicity. We estimate that 33% (26%-39%) of persons acquired HIV whilst living in the UK. This percentage increased from 24% (16%-39%) in 2004 to 46% (31%-50%) in 2010 ($p < 0.01$). The estimate of 33% is three times higher than national estimates of HIV acquired in the UK based on clinic reports (11%) ($p < 0.01$).

Conclusions: Assigning place of HIV infection using routinely available clinical and demographic data and estimated rates of CD4-cell decline is feasible. We report a high and increasing proportion of persons born abroad who appear to have acquired their HIV infection whilst living in the UK These findings highlight the need for continued targeted HIV prevention efforts, particularly among black-African communities.

AIDS 2012, **26**:000–000



THE UK EXPERIENCE: THE MSM EPIDEMIC

HIV epidemic in MSM, UK

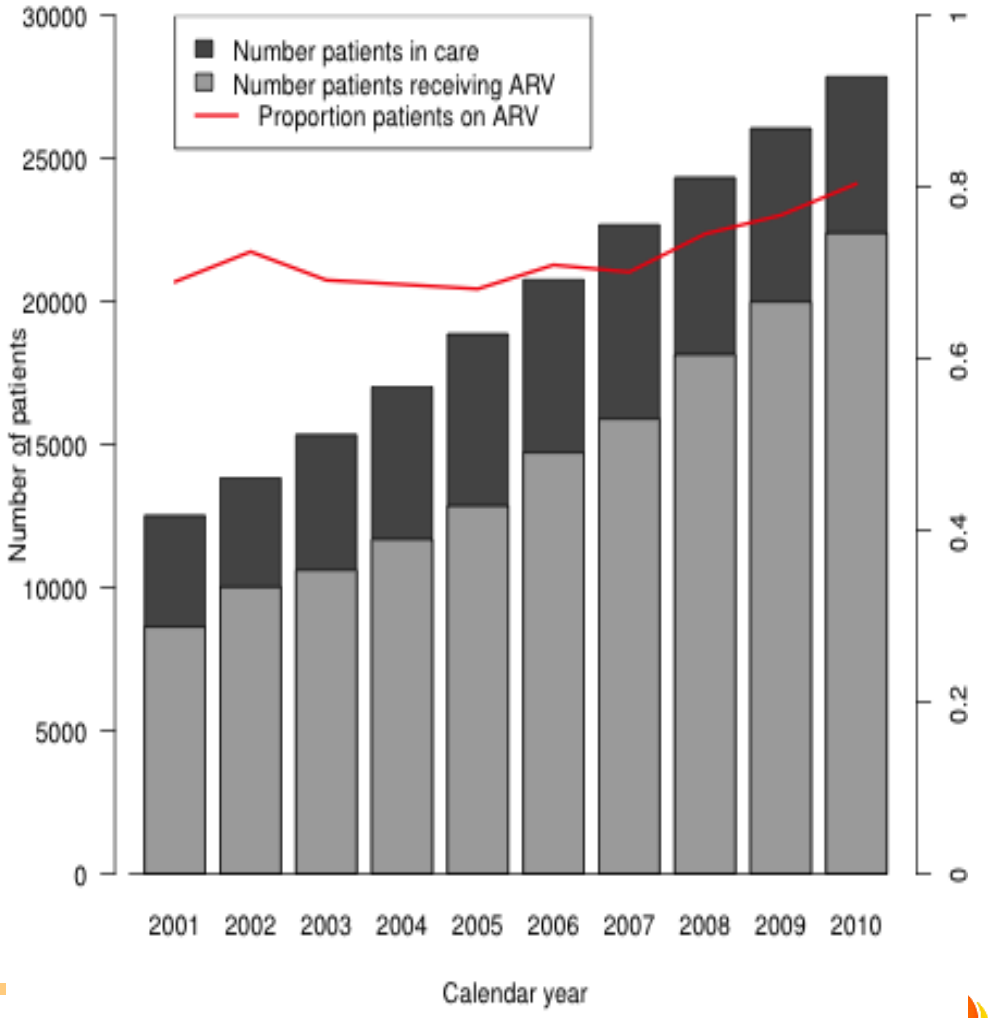
- 500,000+ MSM

(3.4% of the adult male population aged 15-44)

- 40 000 MSM living with HIV, 26% undiagnosed
  - 9% prevalence in London,
  - 3% outside

- 80% of diagnosed MSM on ART,
- (84% of MSM with CD4<350)

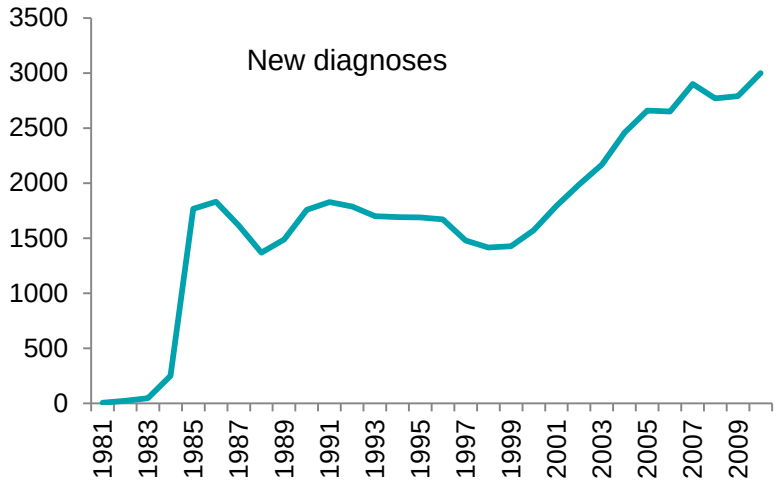
- Access to & retention in care >95% throughout period



HIV epidemic in MSM, UK

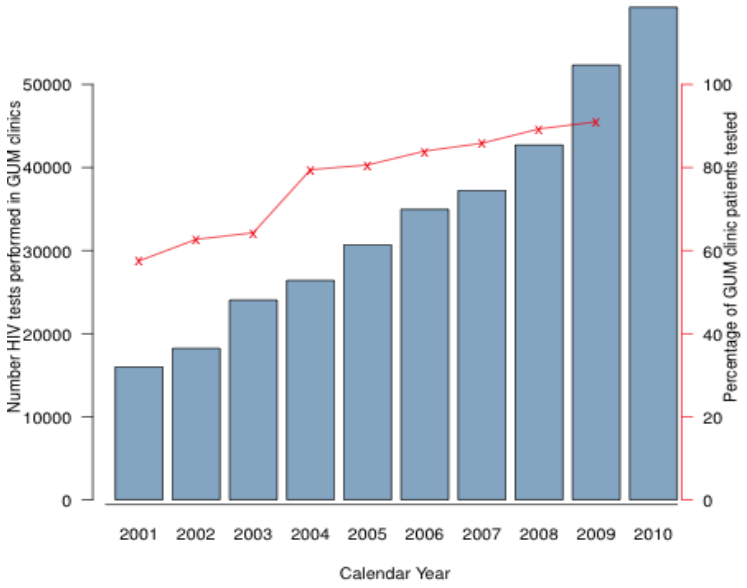
Despite high ARV coverage and retention in care

- Year on year increase in new diagnoses
- >3,000 in 2010, >25% are recently acquired (RITA)



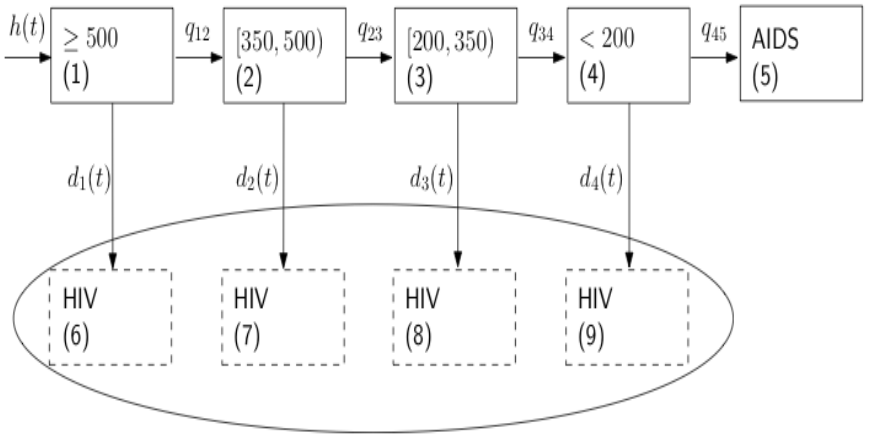
Impact of testing??

- 3.7 fold increase in STI clinics last 10 years BUT only 60,000 in 2010
- So in 2010, estimated 15 - 25% of all MSM aged 15-59 tested



Birrell et al, Model of HIV epidemic among MSM England & Wales (2012)

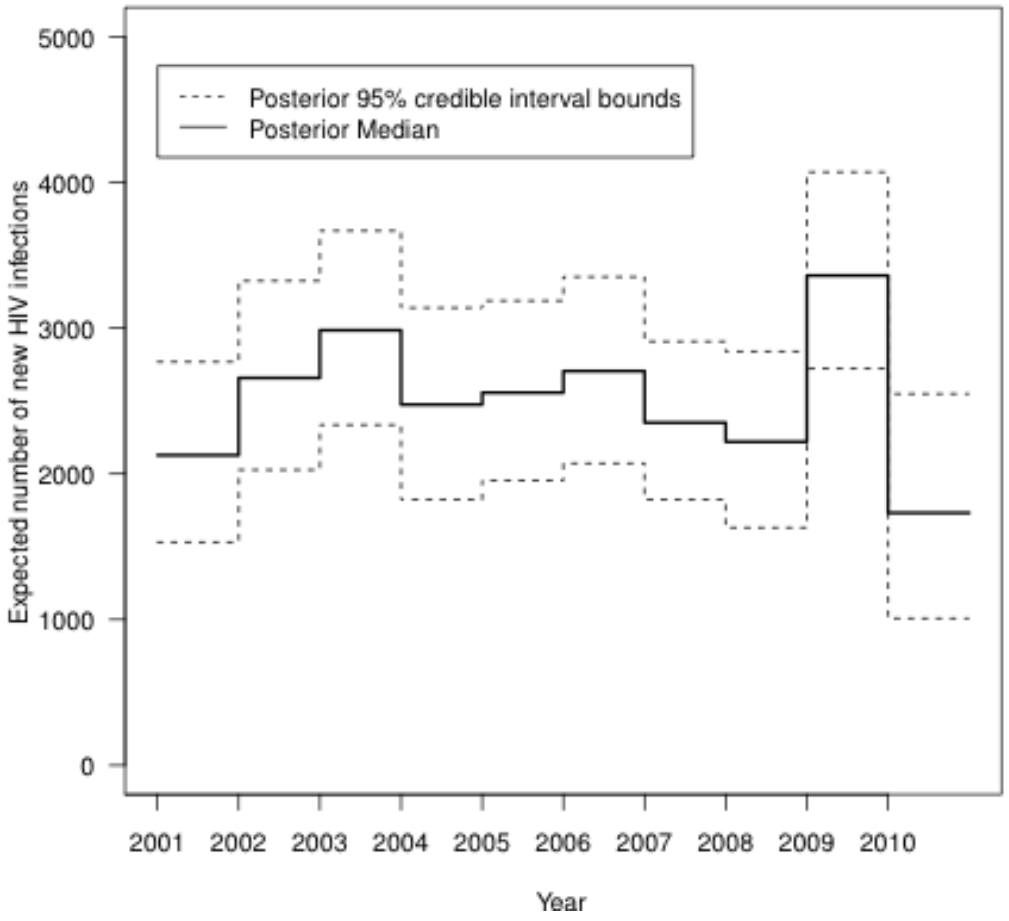
- MSM epidemic 1981-2010
- Multi-state model using surveillance data (new diagnoses)
- Back calculation approach based on CD4 count at diagnosis (>80% complete)



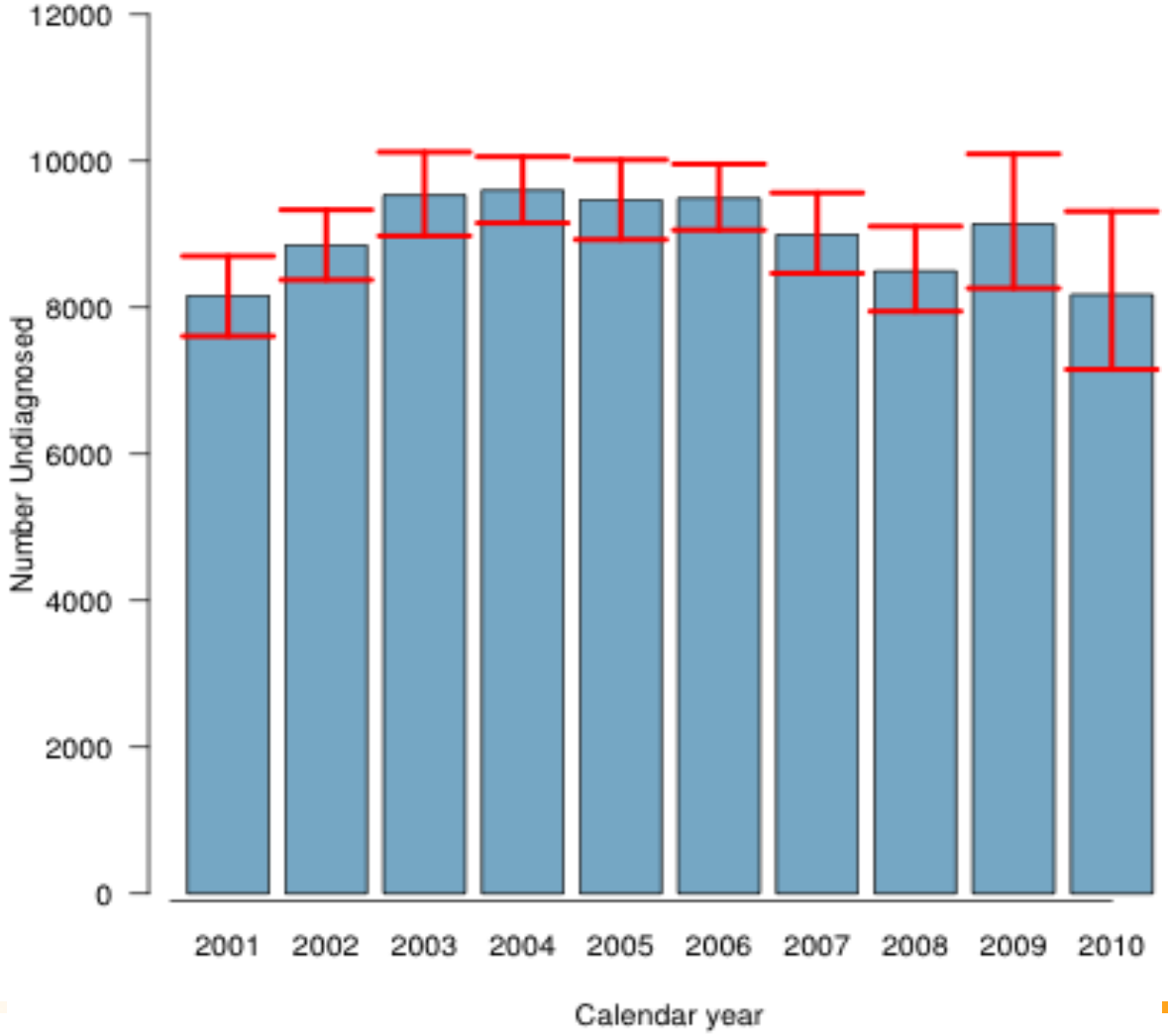
- Outputs
  - Estimates on incident cases
  - Diagnosis rates
  - Undiagnosed

No evidence of a decline in HIV incidence
Birrell et al

Annual HIV incidence in MSM, 2001- 2010, England & Wales



Sustained high level of undiagnosed infections in MSM; Birrell et al

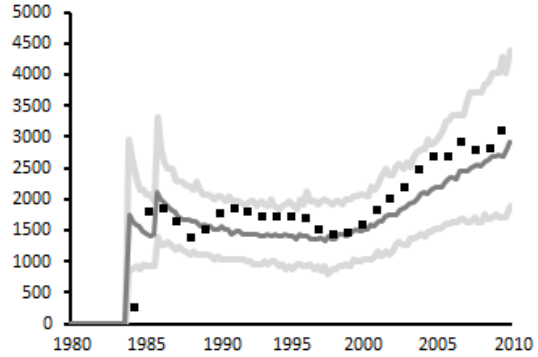


A.Phillips et al – Modelling of HIV epidemic among MSM (2012)

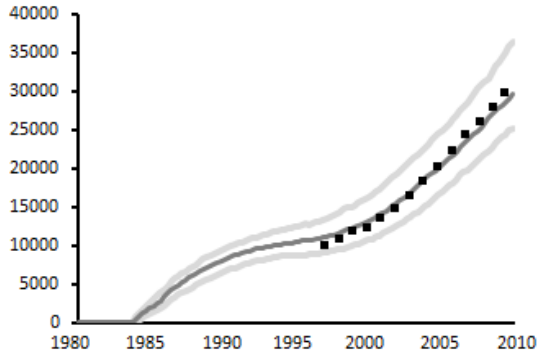
- Stochastic computer simulation model
- Individual based simulation of transmission, progression and effect of ART
- Large range of surveillance data (1981-2010), Natsal and other behaviour data from variety of sources
- Individual-based Assumes all transmission take place via condomless anal sex with an infective partner
- Sexual behaviour modelled as the number of short (3 months) vs long-term partners

Phillips et al – model fits

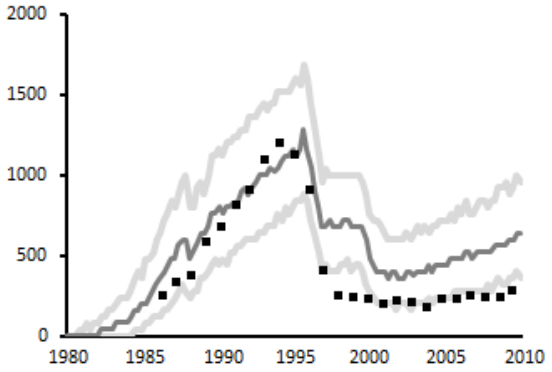
Number diagnosed per year



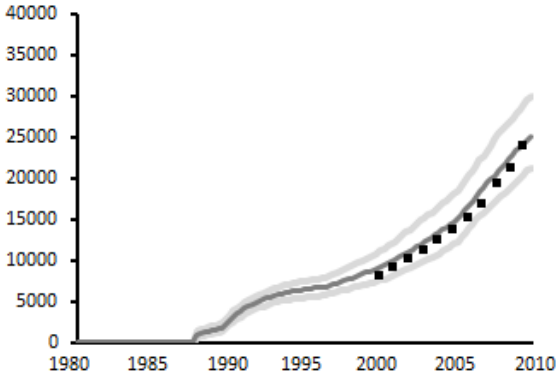
Number seen for care per year



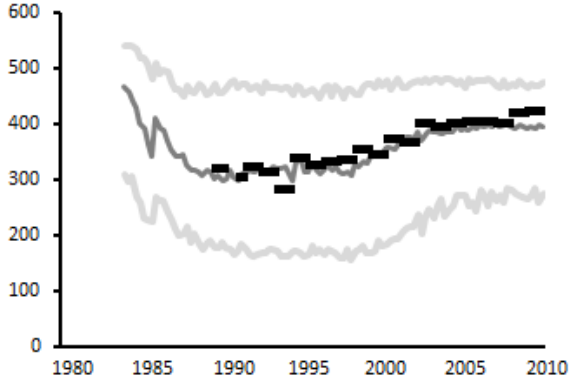
Number of deaths per year



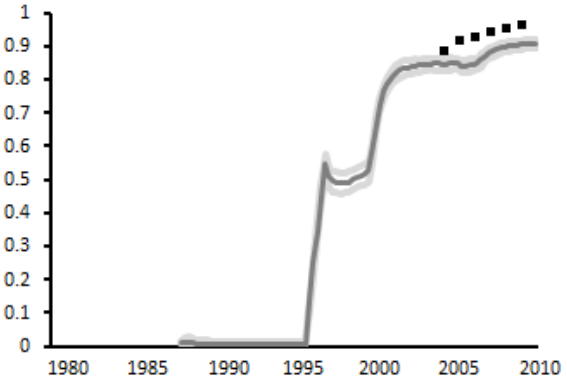
Number on ART per year



Median CD4 count at diagnosis



Proportion of men on ART with viral load <500



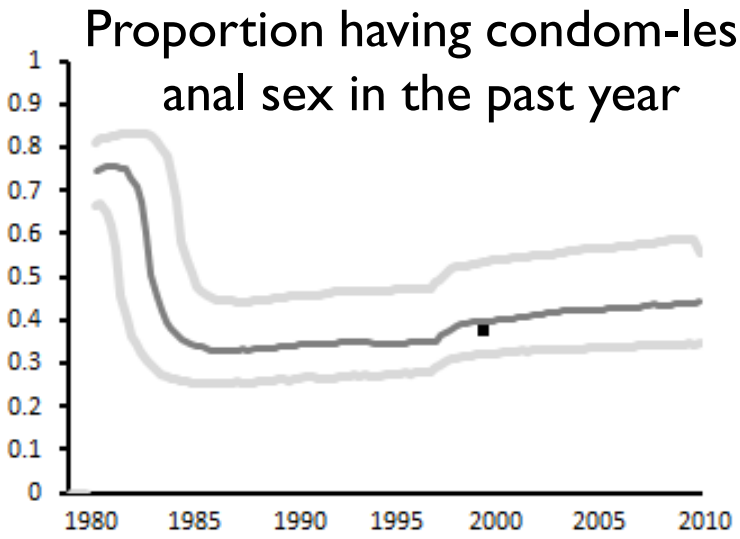
Incidence of HIV in MSM, *Phillips* et al (2012)

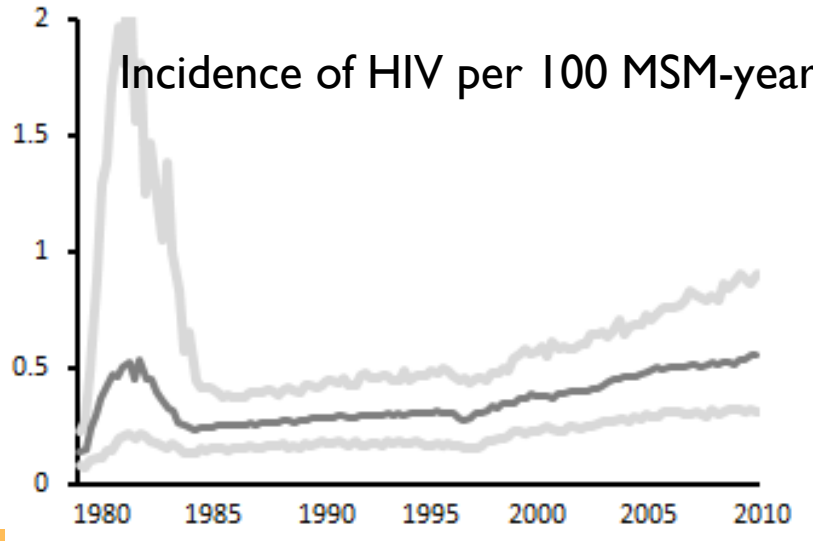
- High incidence in early 1980s with a decline in response to condom use

- Incidence increased after the introduction of ART due to a modest rise in 'condomless' sex (26%)

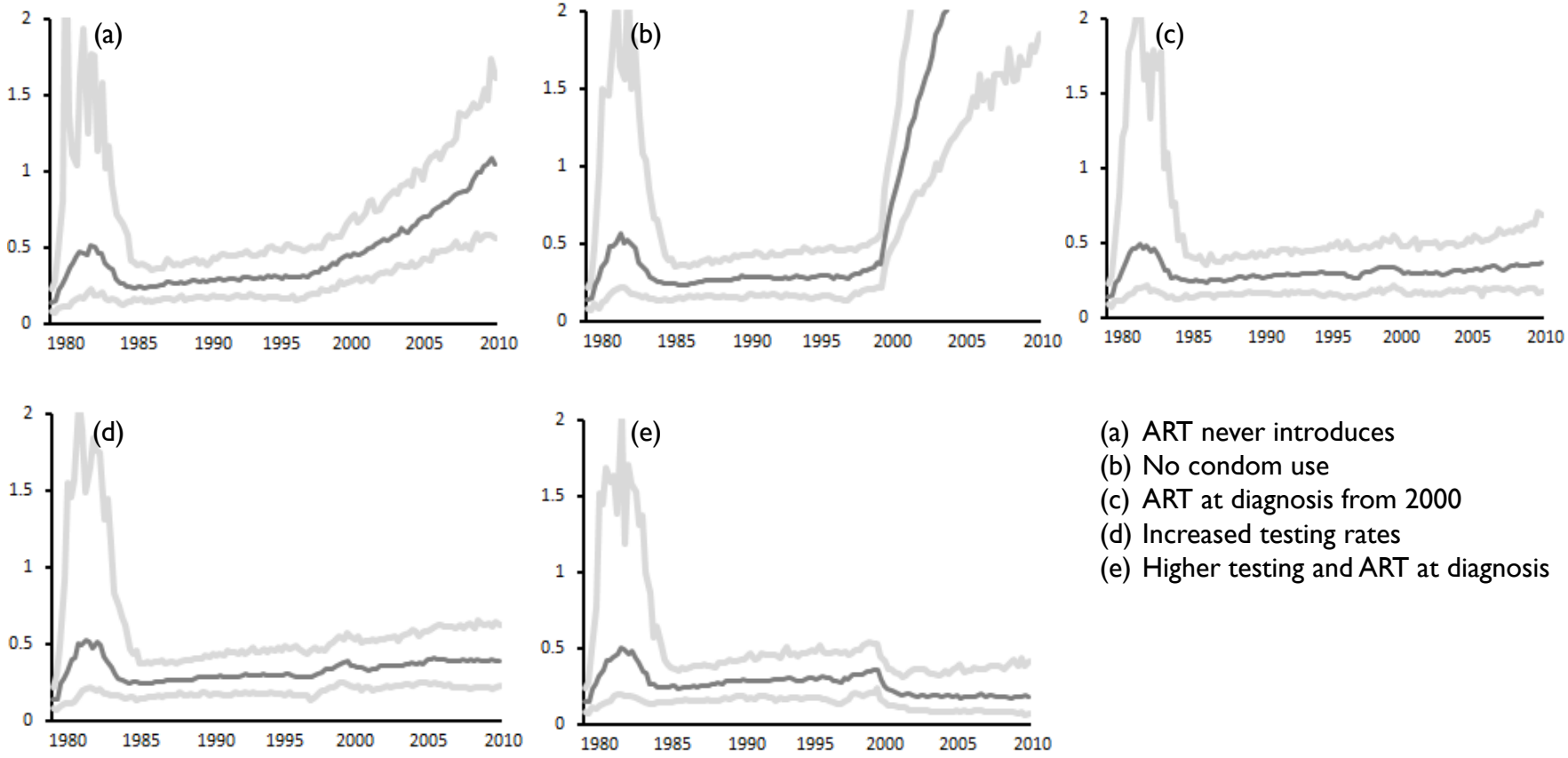
In 2010:

- 48% (34-64) of new infections were acquired from undiagnosed men in primary infection,
- 34% other undiagnosed,
- 10% diagnosed ART naïve,
- 7% ART experienced





Counter – factual scenarios



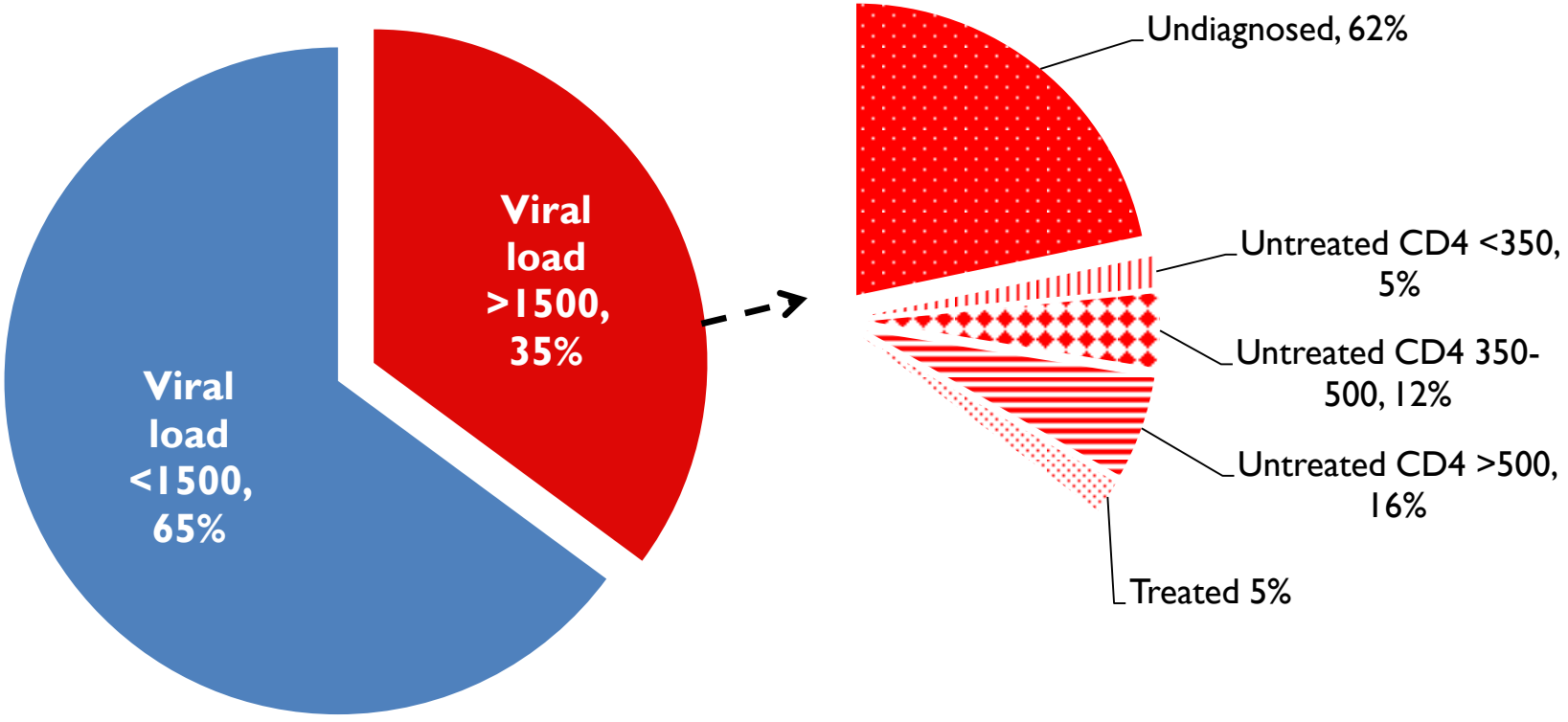
(a) ART never introduces
(b) No condom use
(c) ART at diagnosis from 2000
(d) Increased testing rates
(e) Higher testing and ART at diagnosis

NOTE

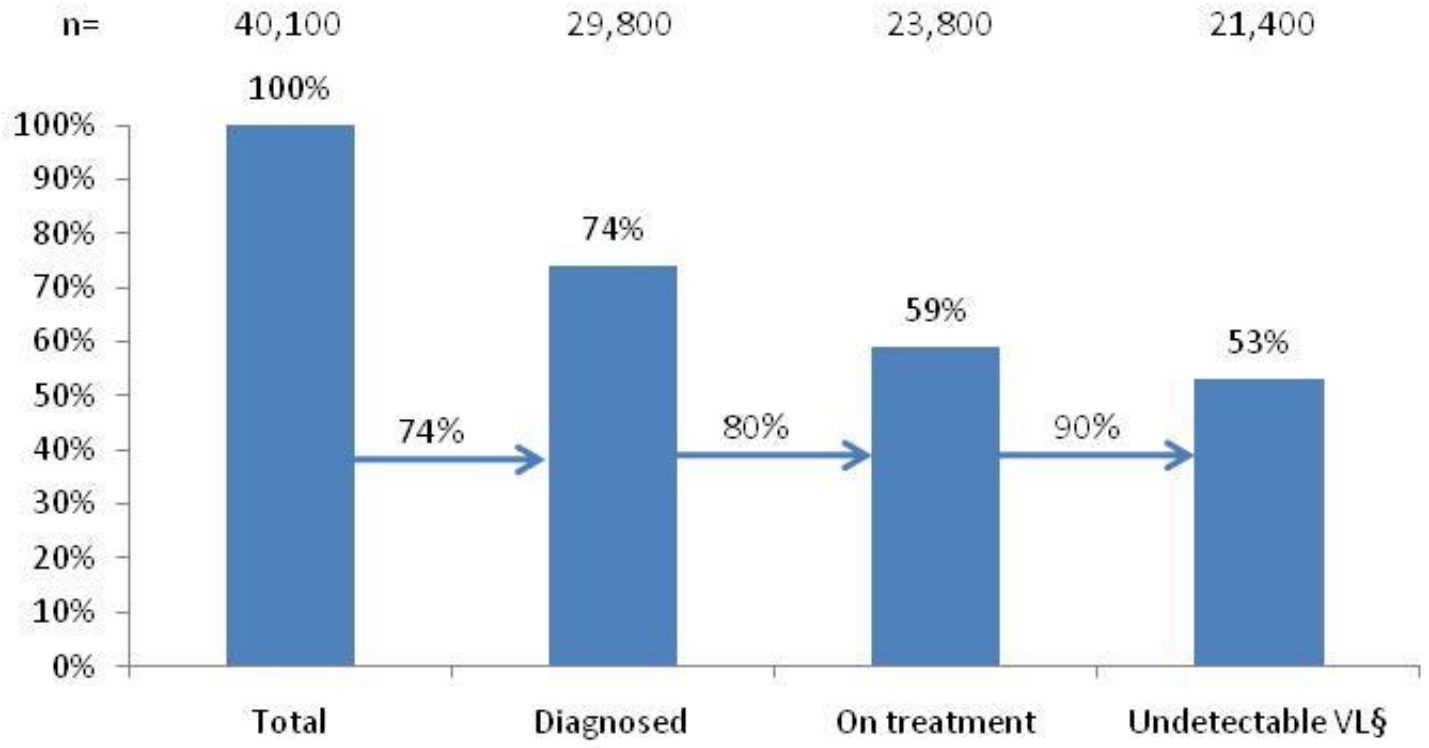
(b) Cessation of all condoms in 2000 would have resulted in a 400% increase in incidence

(e) A policy of higher (68% testing yearly) testing and immediate ART would have resulted in a 62% lower incidence

Distribution of HIV infected MSM with a viral load >1500 copies/mL, UK: 2010 *Brown et al*



MSM living with HIV by diagnosis, treatment and viral load status: UK, 2010



* Numbers were adjusted by missing information and rounded to the nearest 100.
§ Viral load <50 copies/ml after HIV treatment initiation in the year of initiation.

Failure of TasP among MSM in the UK?

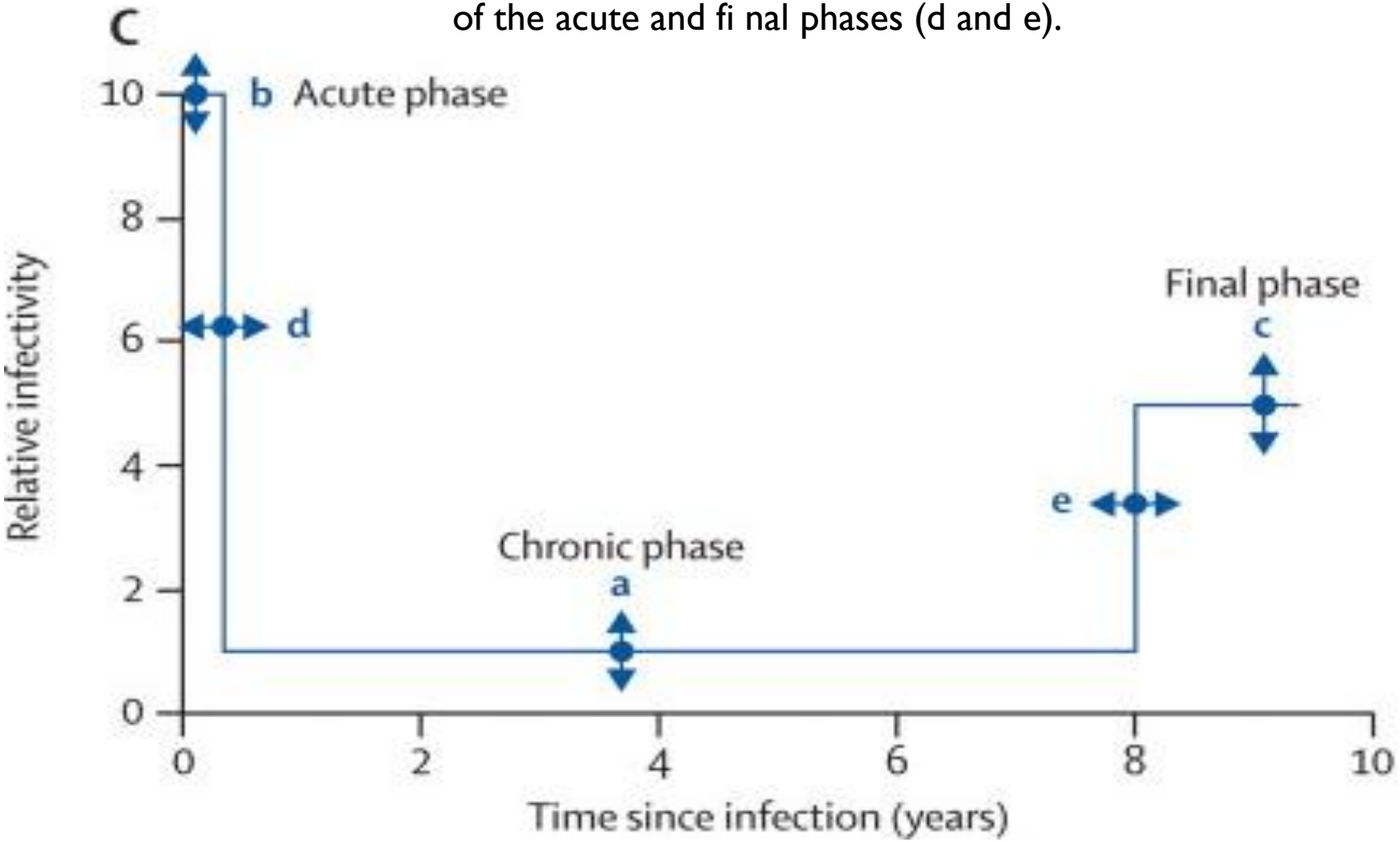
- Despite substantial progress of 'test and treat' prevention policies over the past decade in the UK, there is no evidence of a reduction in the incidence of HIV infection in MSM

Reasons

- Declines in safer sex with the introduction of ART
- Continued high rates of undiagnosed
- Low testing rates
- ?High rates of STIs

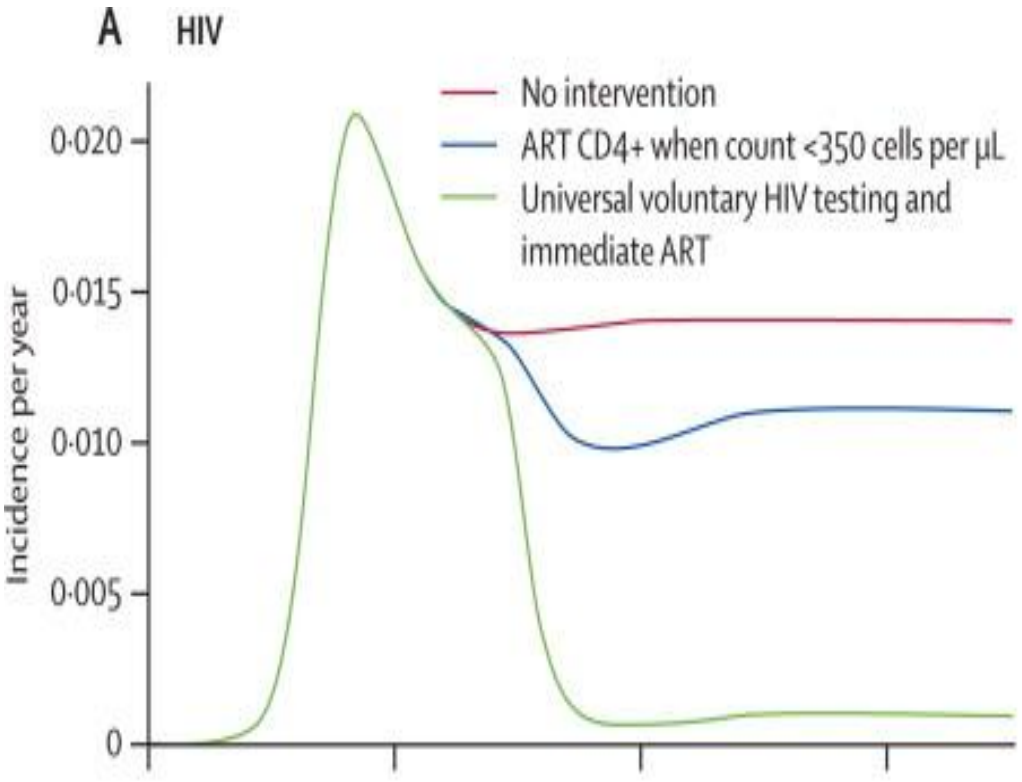
Theoretical basis for the stochastic and deterministic transmission models -

Schematic diagram of the change in infectivity with time in a person who survives for 10 years. The infectivity during all three phases (a–c) can be varied, as can the duration of the acute and final phases (d and e).



Granich RM et al, *Lancet 2009; 373: 48–57*

WHO deterministic transmission model

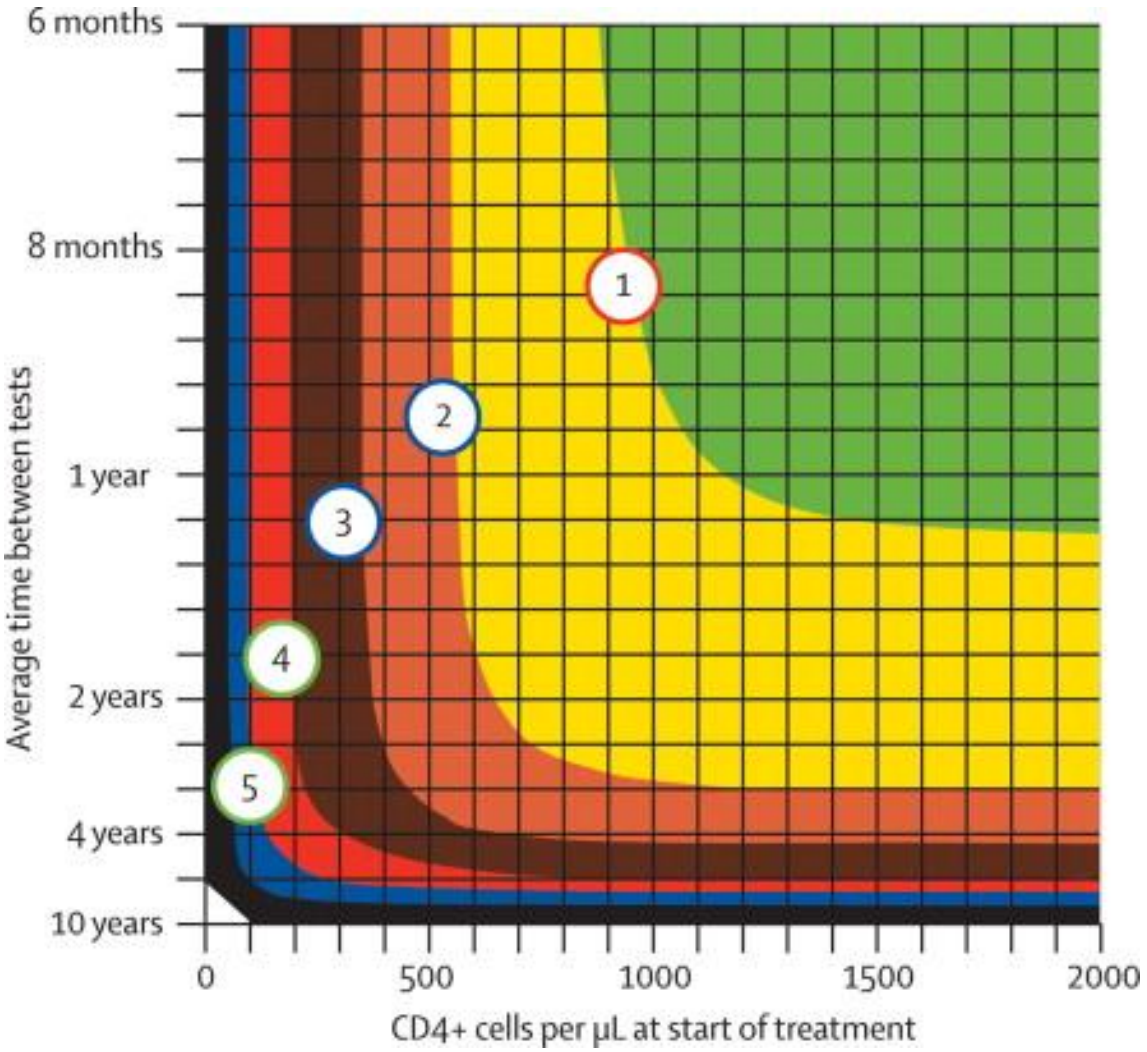


Granich RM et al, *Lancet 2009; 373: 48–57*

Assumptions

- Based on South Africa
- Test whole population every year
- Immediate ART treatment
- Irrespective of CD4 count
- High retention & adherence
- Eliminate incidence within(<1/1,000 persons per year)

Relation between HIV testing frequency, CD4+ cell count, and R0



Granich RM et al, *Lancet 2009; 373: 48–57*

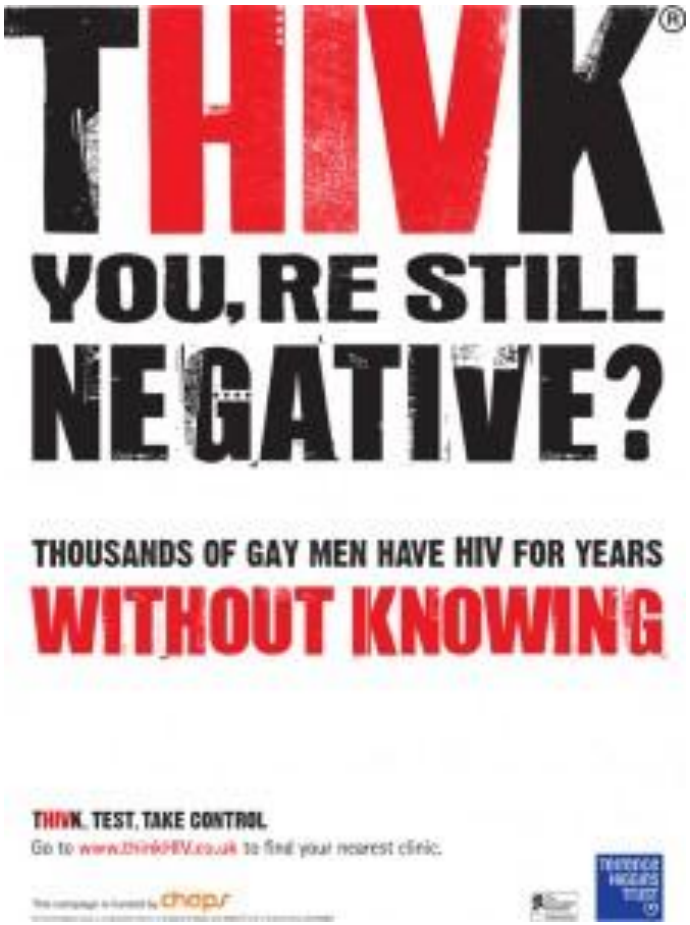
Models of ART and transmission

San Francisco	Katz, Am J Pub Health, 2002	Increase in risk behaviour in MSM will outweigh benefit of ART
Australia	Clements, JAIDS, 2004	ART benefits outweighed by increased risk in MSM
South Africa	Bertran, JAIDS, 2004	WHO guidelines: 12% reduction in incidence US guidelines: 72%
Amsterdam	Bezemer, AIDS, 2008	Benefits of ART outweighed by increased risk behaviour in MSM
British Columbia	Lima, JID, 2008	67% reduction in incidence if 100% treated at CD4 <350
Australia	Wilson, Lancet, 2008	ART rather than condoms may increase incidence 4 fold
WHO	Granich, Lancet, 2009	Annual testing and universal ART could reduce prevalence of HIV to <1%

Conclusions

- Despite this, high access to treatment and care in the UK, no evidence of a decline in incidence among MSM

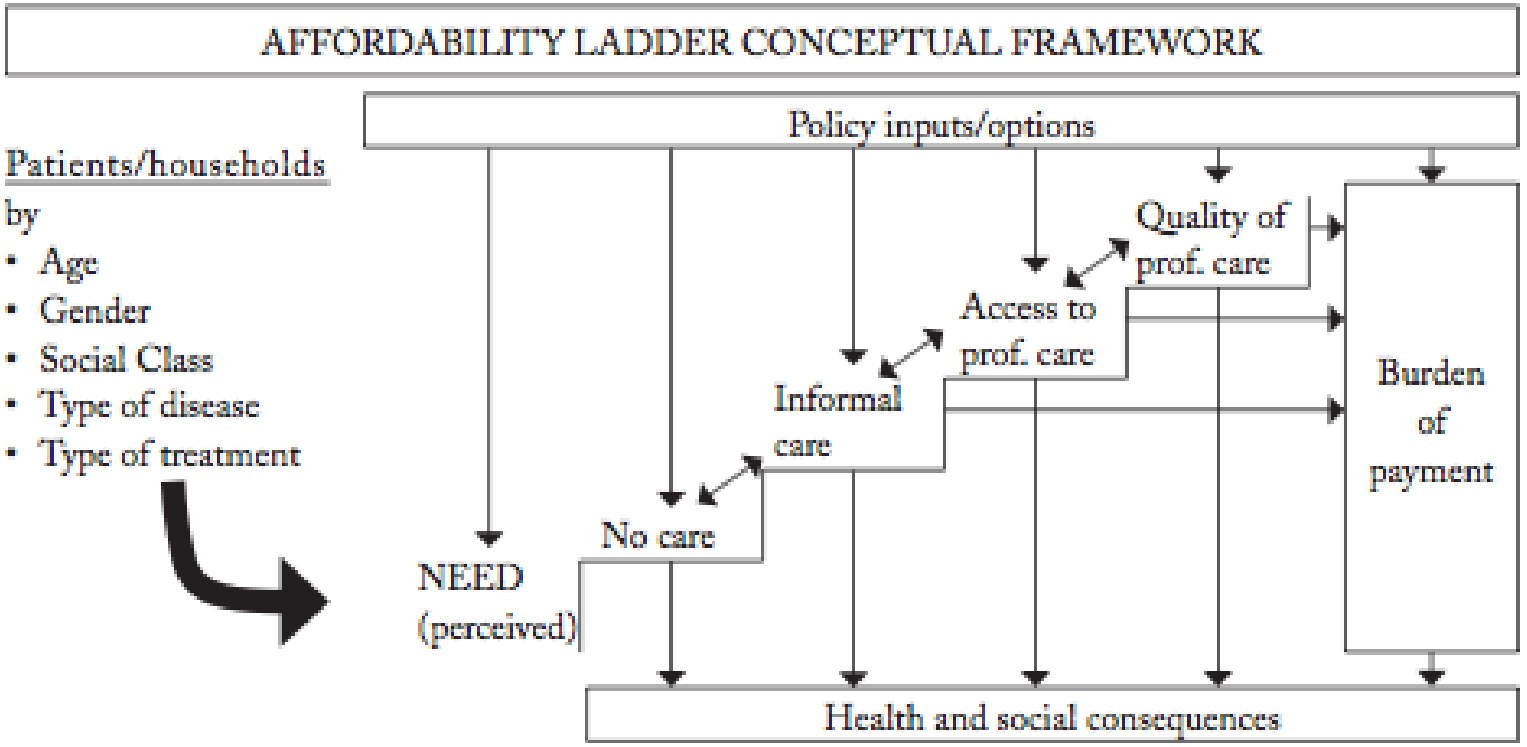
- Undiagnosed remain source of 60%-80% transmissions and half of these during primary infection
- Much high rates of testing are required
- Health promotion and prevention remains key
- Need for close monitoring of our public health efforts (Public Health Outcome Framework only has Late diagnosis)



WHO Levelling up

a discussion paper on concepts and principles for tackling social inequities in health

Fig. 3. The ALPS approach to assessing equity and health systems



Source: Dahlgren (2004)

Conclusions from IAPAC tasp Statement, 2012

No further trials are considered necessary to demonstrate TasP's efficacy… BUT

'…more research into its effectiveness on the population level as well significant will, new resources, community involvement, provider support and individual commitment to provide the increased levels of HIV testing, linkage to and retention in care, access to quality treatment and adherence – all of which are critical to achieving TasP's promise'

Acknowledgements

- Andrew Phillips, Paul Birrell, Paul Ward & Martin Fisher
- HIV & GUM physicians and all those who contribute to HIV & STI surveillance
- Colleagues at the HIV &STI Department, HPA
- Conference organisers

Thank-you

www.hpa.org.uk