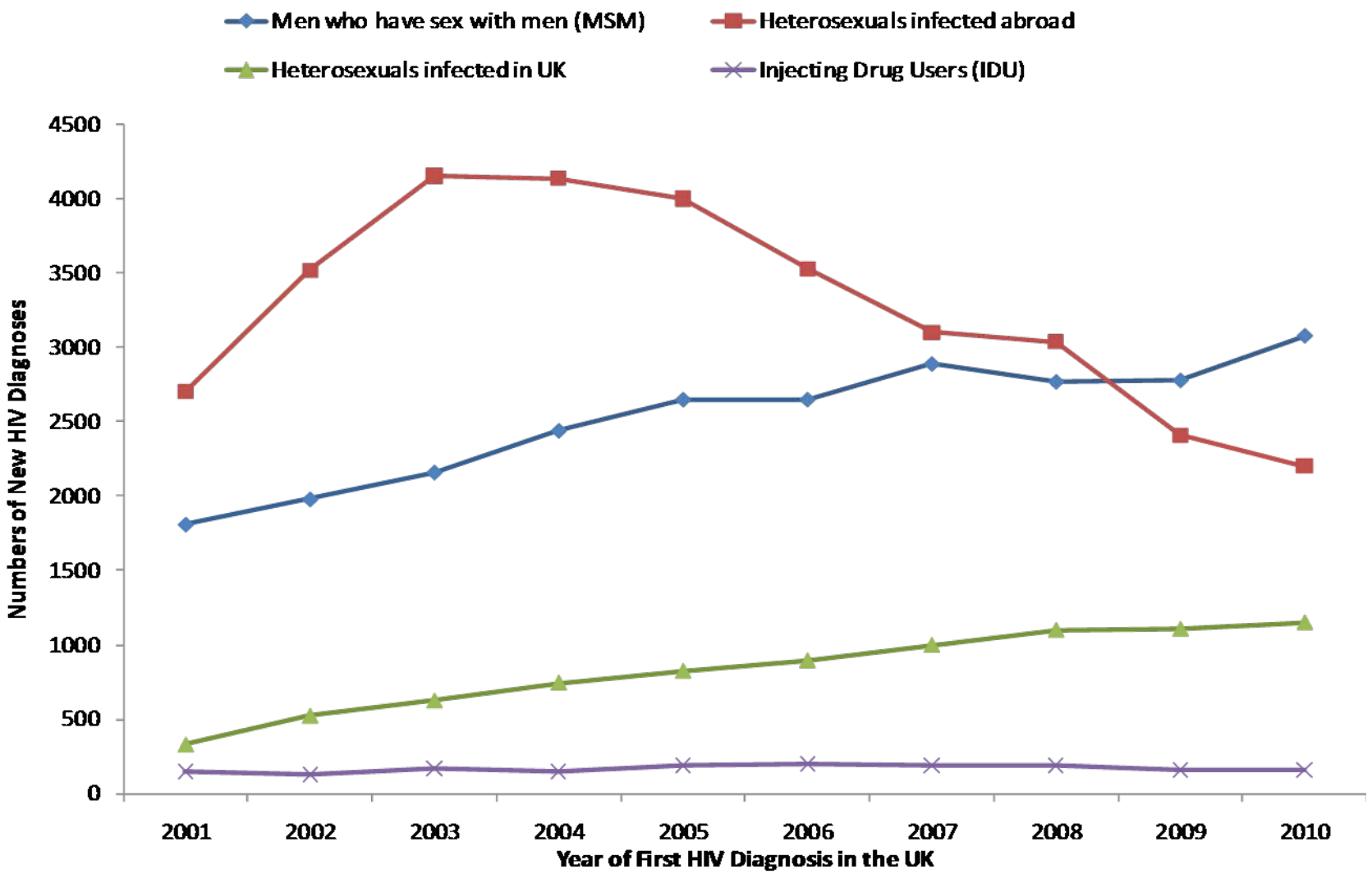
Embedding Open-label PrEP trial in expansion of UK HIV Prevention Programme

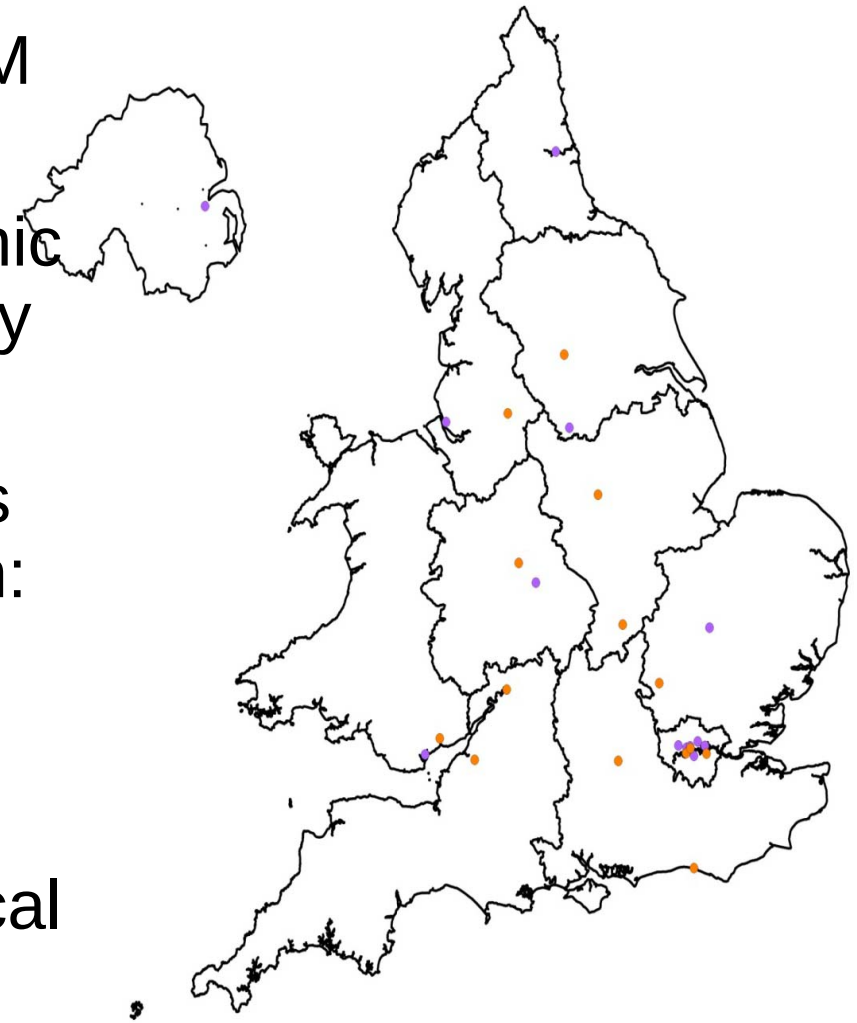
New HIV diagnoses (Adjusted) - UK



Health Protection Agency

UK clinic network

- 204 STI clinics in England
  - ~38,000 HIV^{-}/Unknown MSM attend each year
- 50% MSM attended an STI clinic in past year (London bar survey 2008)
- Two professional organisations working together on prevention: BHIVA and BASHH
- Position statement on PrEP (prelude to guidelines) recommends prescribe in clinical research programme



Incidence of HIV among MSM (GUMCAD)

- Preliminary analysis of data on MSM of HIV negative or unknown status attending GUMNet clinics in 2009
- ~21,000 MSM attended clinic and were HIV-ve at first visit
- ~7,000 MSM re-attended and had an HIV test at a subsequent visit
- 149 sero-converters identified (2.4 per 100 person-years)

UK PrEP Working Group

- Established for Position Statement
- Followed presentation of PrEP proposal by the public health team for England at BHIVA conference
- Two conference calls early on to collect views
  - Concern that behavioural interventions had not been given a proper chance
  - Concern about practical issues, and in particular who would pay for sustained roll-out (budget cuts the norm)
  - Desire to avoid PEPSE scenario of patchy implementation
- Several small meetings, one large, one further call to define the clinical research programme
  - Need to make efficiencies through synergy of funded work
  - Need to strengthen evaluation of change in behaviour

Why a trial?

- We want to offer more than daily, and to achieve universal access so need to address cost and negative impact on condom use

- This means we need ‘real-life’ efficacy
  - When individuals know they are using an effective alternative to condoms
  - Placebo controls behaviour, so need ***non-placebo*** control group

- Propose randomise to immediate offer vs deferred to 12m
  - Mimic clinic routine as much as possible
  - Measure ***net benefit***, ie cannot reliably separate behaviour and biology

Design (1)

- Eligibility
  - MSM
  - reporting unprotected anal intercourse or consider themselves at risk of HIV infection
  - willing to consider PrEP as an option to reduce their risk
- Point of entry is negative HIV test
  - complete behavioural data questions
  - given information about trial
  - if interested, given appointment to re-attend in ~4 weeks time when a clinician available (may be longer depending on local clinical practice)

Design (2)

- Joint decision between participant/clinician
  - that PrEP is an appropriate option (no suggestion of seroconversion illness)
- Randomise to Truvada (a) prescribed immediately or (b) deferred for 12 months
- Decide regimen to start using individual's reported risk behaviour

Design (3)

- Follow ***all participants*** at
  - Months 1, 6, 12, 18, 24
- In between these visits complete behavioural data through web-entry and HIV testing
  - Months 3, 9, 15, 21
- Keep follow-up procedures ***as simple as possible*** to minimise burden on clinics
- Everyone receives
  - additional behavioural support
  - STI screening at 3m intervals

Analyses

- Primary
  - acquisition of HIV infection during first 12m in FU (main randomised comparison)
- Secondary analyses
  - acquisition of HIV infection during 12-24m FU (randomised comparison)
  - before/after comparison of reported behaviour and markers of unprotected anal sex in deferred arm
  - effectiveness by reported adherence (2 or 3 groups)
  - sub-study of adherence using detectable drug

Sample size

- Assuming incidence of
  - 2 per 100 person-years with no intervention
  - 1 per 100 person-years with PrEP
- Total of 4000 person-years gives power of
  - 83% to demonstrate statistical significance
  - 63% to exclude rate difference of <0.25
  - 36% to exclude rate difference of <0.50
- Need to inflate to allow for loss to follow-up
- Aim to enrol 5000

Integral initiative: Pilot Study

- Planning for a pilot study while outline funding application being assessed to:
  - assess level of ***real*** interest among MSM in taking PrEP
  - assess acceptability of randomisation and visit schedule
  - validate web-entry records of core behavioural and adherence data
  - ensure procedures to fit in with routine clinical practice in 4 or more of the larger GUMNet clinics (N~50 in each)
  - ***optimise links to community organisations***
- Piggy-back on other initiatives (underway or planned)

Opportunity

- Recent Government review of HIV likely to emphasise importance of prevention
- Clinic initiatives have started and are proliferating – more frequent testing, introduction of behavioural interventions
- Community initiatives are there and open to unified strategic approach – online support, 1 to 1 peer and group support
- Funding systems also in process of change
  - but will still rest within a national framework
  - informed by guidelines drafted by BHIVA and BASHH
- ARVs only prescribed within the clinic network

Conclusion

- PrEP is only one chapter in the book of behaviour
- We can use it to change the story

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