European AIDS Treatment Group

AVAC Global Advocacy for HIV Prevention

An update on PrEP in Europe

Speakers: Dr Valentina Cambiano of University College London, Daniela Rojas Castro of AIDES and Dr Anastasia Pharris of the European Centre for Disease Prevention and Control (ECDC).

Chaired by Gus Cairns of EATG

PrEP background

Gus Cairns

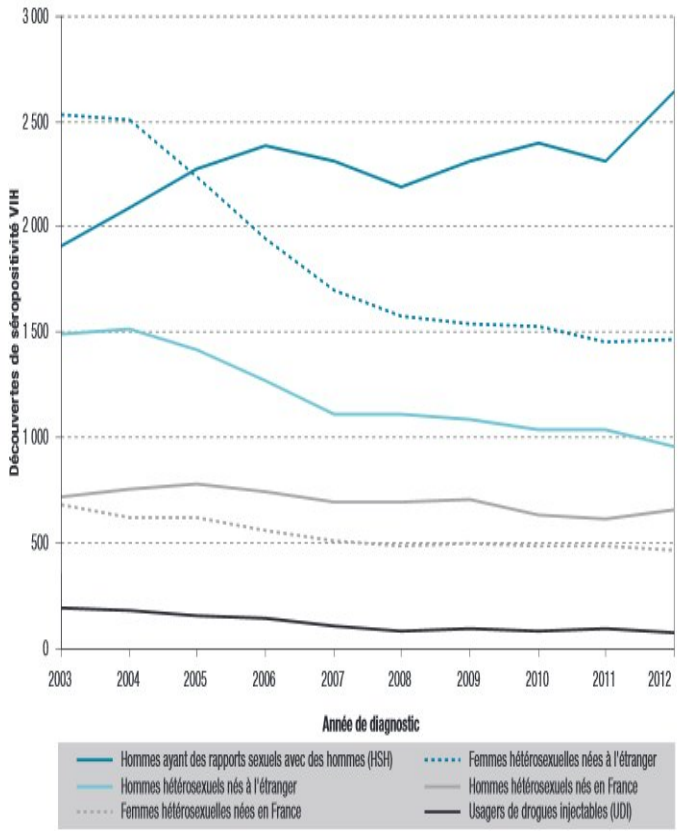
Editor, NAM / www.aidsmap.com

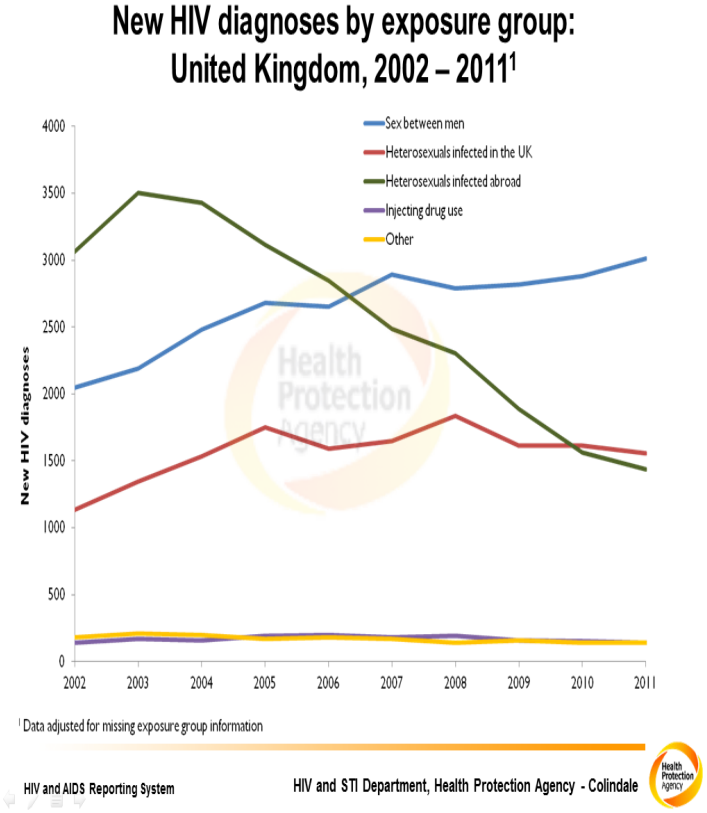
Prevention coordinator, EATG

Co-chair, PROUD Study

HIV is on the increase in at least one group

HIV diagnose in MSM: France 2003-12, UK 2002-11.

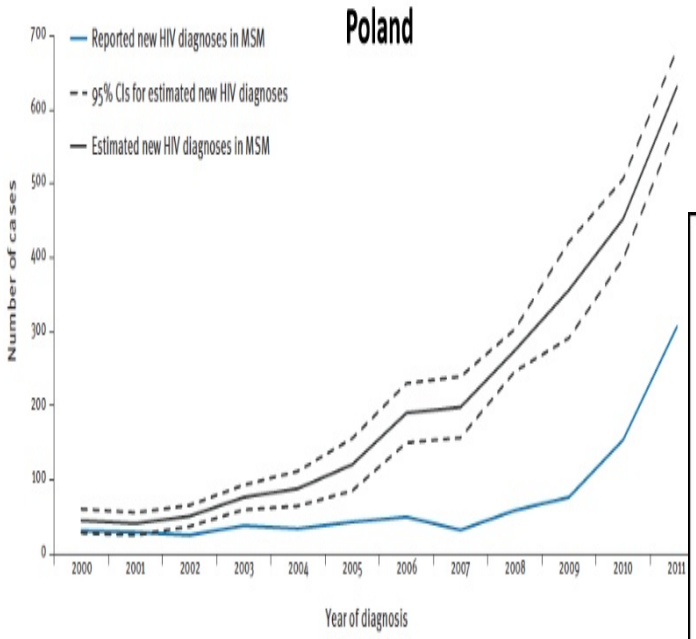


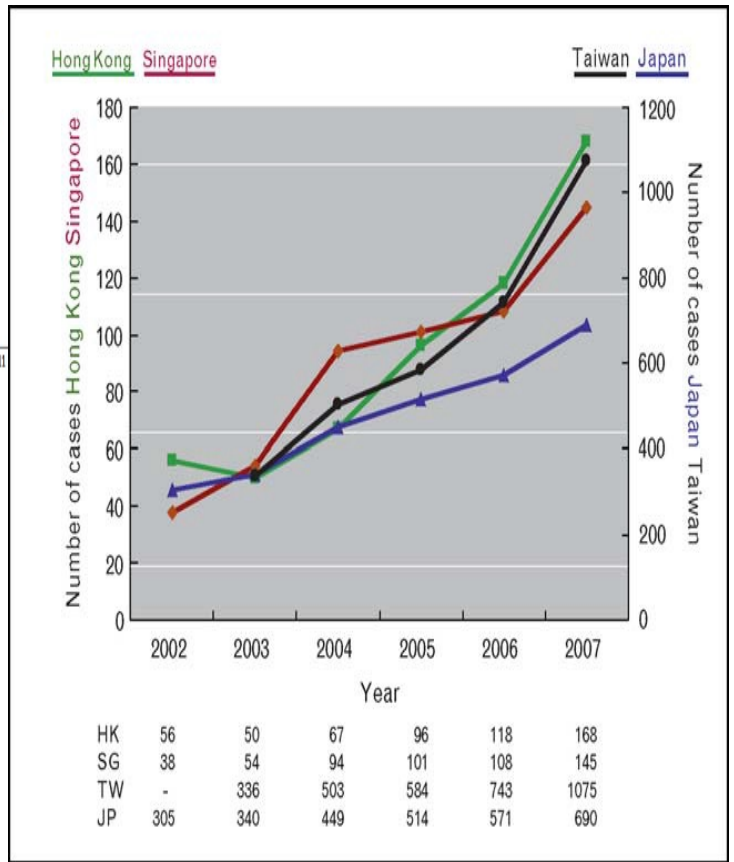


Health Protection Agency.
HIV in the United Kingdom: 2012 Report . HPA, 2012.
Caein F et al.
Découvertes de séropositivité VIH et sida : France, 2003-2012,
Bulletin épidémiologique hebdomadaire 2014; (9-10):154-62.

And more so elsewhere…

HIV MSM diagnoses: Poland 2000-11, east Asia 2002-2007





Ergo: Pre-exposure prophylaxis

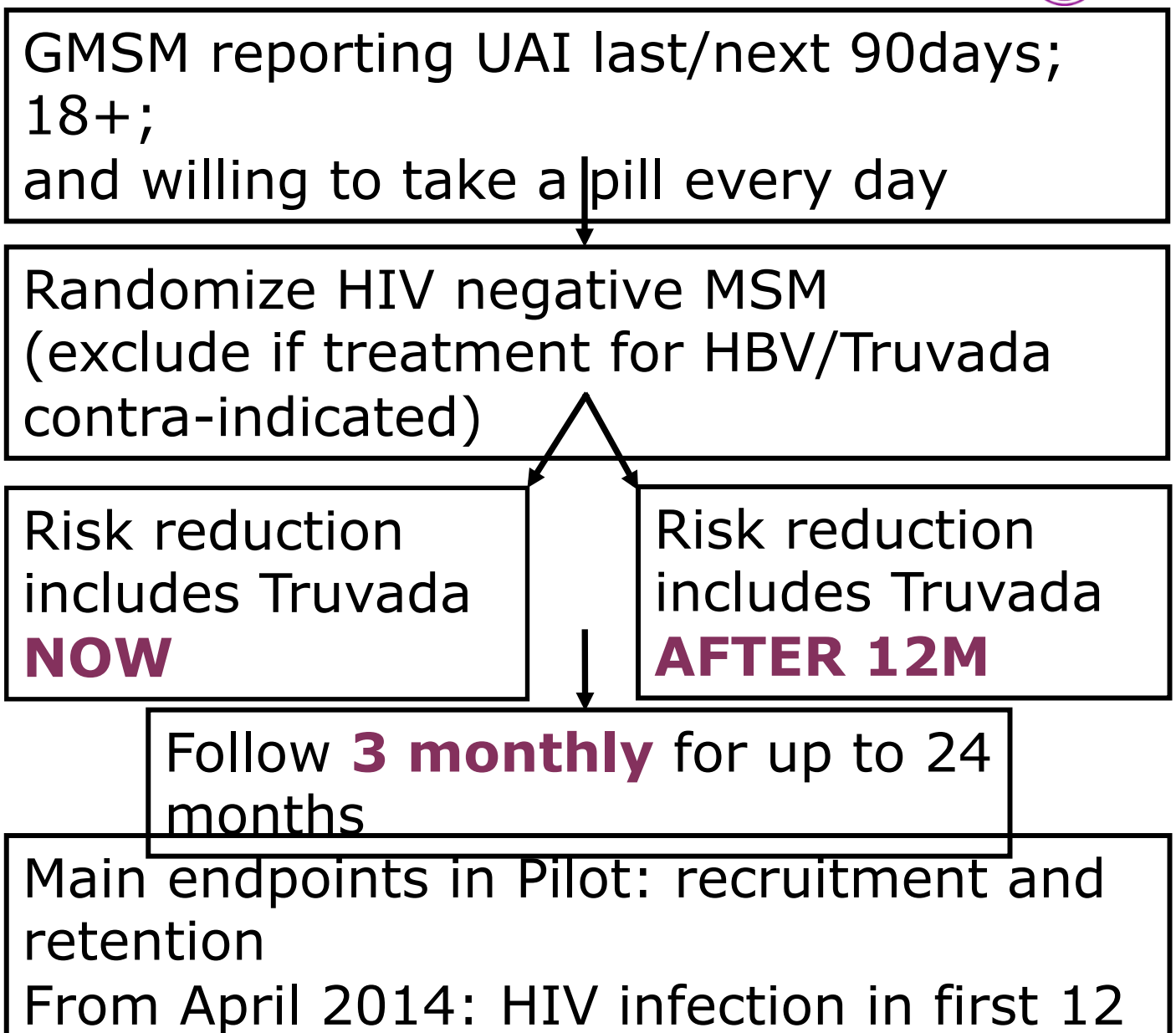
- Idea of medicines to prevent conditions not new:
  - Antimalarial prophylaxis (‘tonic water’)
  - Isoniazid prophylaxis for TB
  - Co-trimoxazole for PJP (PCP)
  - Statins for heart attacks
- And of course:
  - The contraceptive pill

PrEP history

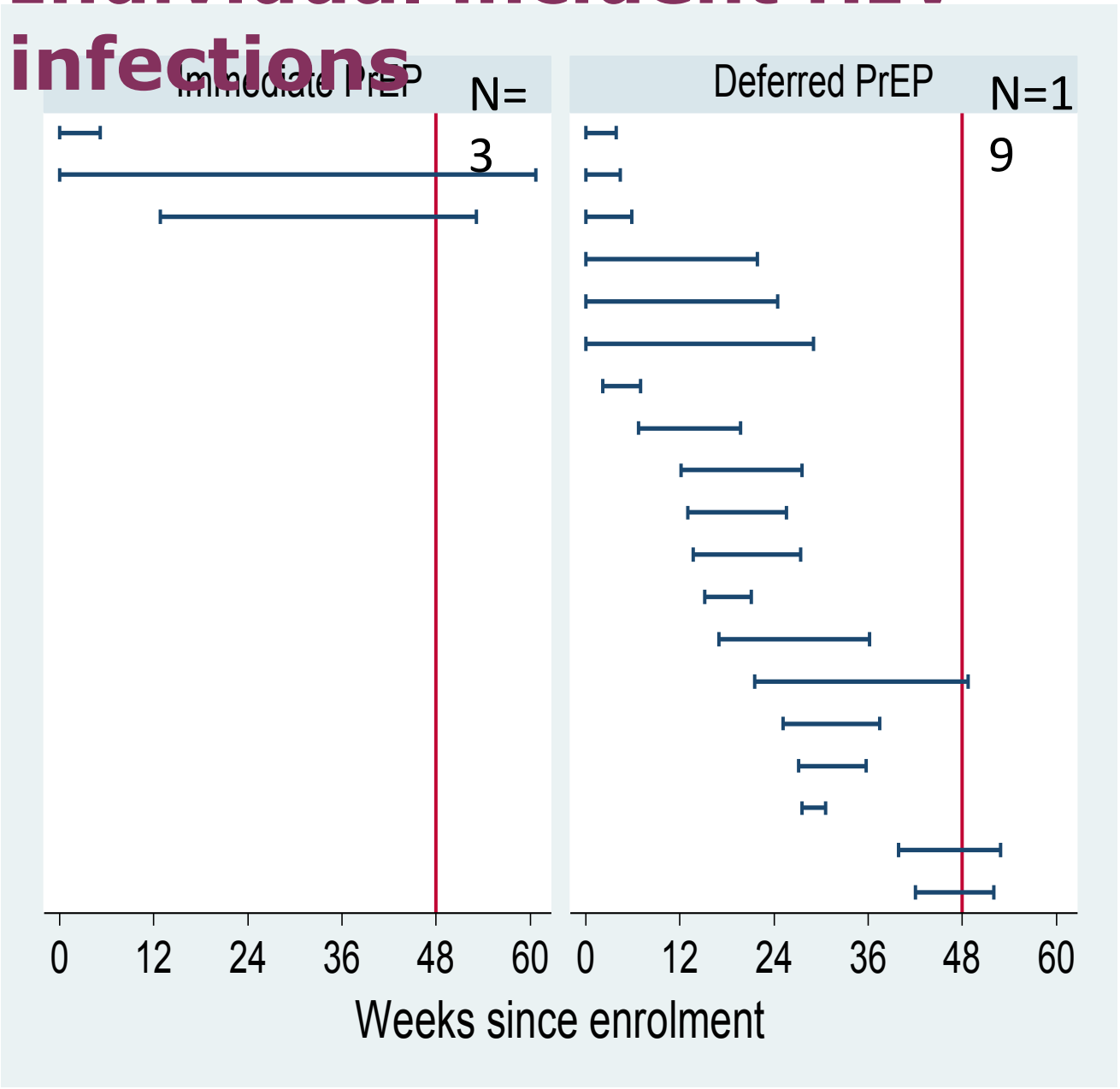
- First animal study: 1995[1]
- First study in infants: 2003[2]
- First adult study (terminated): Cambodia, 2004[3]
- First result (65% reduction in infections, but not significant): Ghana, 2006[4]
- First significant result (44% effectiveness): iPrEx, 2010[5]

1. Tsai CC et al. *Prevention of SIV infection in macaques by (R)-9-(2-phosphonylmethoxypropyl)adenine.* Science 270: 1197-1199, 1995.
2. Vyankandondera J et al. *Reducing risk of HIV-1 transmission from mother to infant through breastfeedingusing antiretroviral prophylaxis in infants (Simba study).* Second International AIDS Society Conference on HIV Pathogenesis and Treatment, Paris, abstract LB7, 2003.
3. Singh JA and Mills EJ. *The Abandoned Trials of Pre-Exposure Prophylaxis for HIV: What Went Wrong?* PLoS Med 2(9): e234. doi: 10.1371/journal.pmed.0020234. 2005.
4. Peterson L et al. *Findings from a double-blind, randomized, placebo-controlled trial of tenofovir disoproxil fumarate (TDF) for prevention of HIV infection in women.* 16th International AIDS Conference, Toronto, abstract ThLb0103, 2006.
5. Grant RM et al. *Preexposure chemoprophylaxis for HIV prevention in men who have*

PROUD Pilot

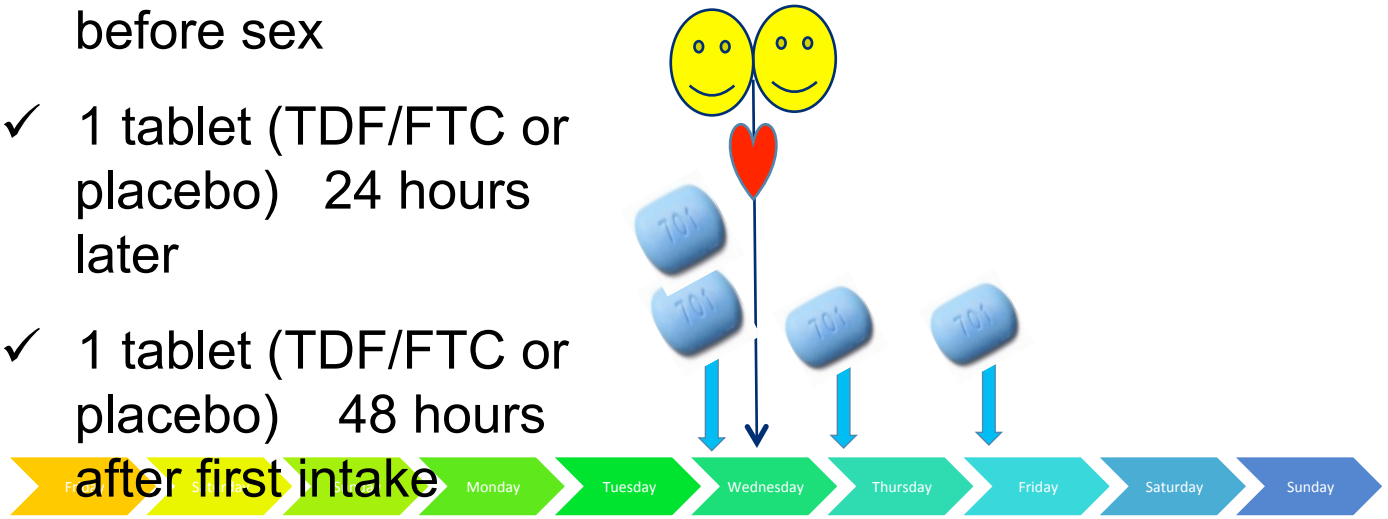

GMSM reporting UAI last/next 90days;
18+;
and willing to take a pill every day
Randomize HIV negative MSM
(exclude if treatment for HBV/Truvada contra-indicated)
Risk reduction includes Truvada NOW
Risk reduction includes Truvada AFTER 12M
Follow 3 monthly for up to 24 months
Main endpoints in Pilot: recruitment and retention
From April 2014: HIV infection in first 12

Individual incident HIV infections

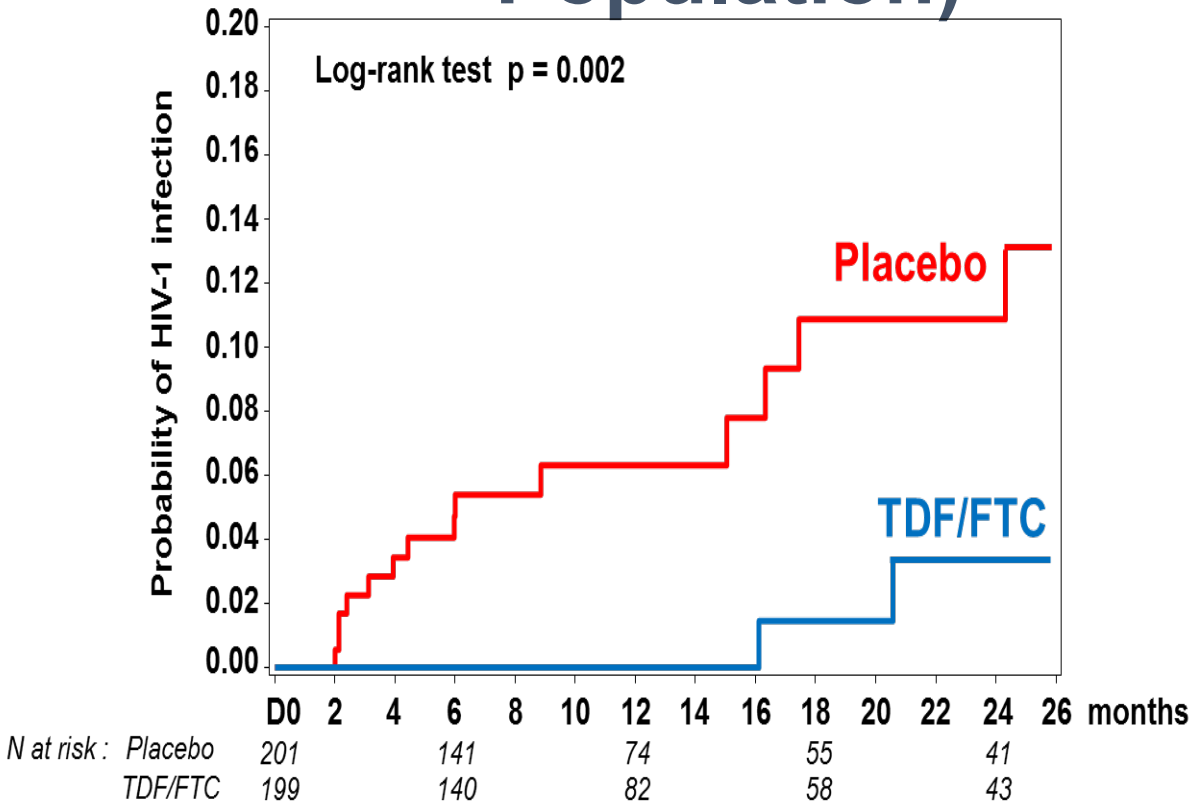


Ipergay : Event-Driven iPrEP

- ✓ 2 tablets (TDF/FTC or placebo) 2-24 hours before sex
- ✓ 1 tablet (TDF/FTC or placebo) 24 hours later
- ✓ 1 tablet (TDF/FTC or placebo) 48 hours after first intake



KM Estimates of Time to HIV-1 Infection (mITT Population)



Mean follow-up of 13 months: 16 subjects infected

14 in placebo arm (incidence: 6.6 per 100 PY), **2 in TDF/FTC arm** (incidence: 0.94 per 100 PY)

86% relative reduction in the incidence of HIV-1 (95% CI: 40-99, p=0.002)

EATG Webinar:
An update on PrEP in Europe,
18th September 2015

Is PrEP for HIV prevention cost-effective in MSM?

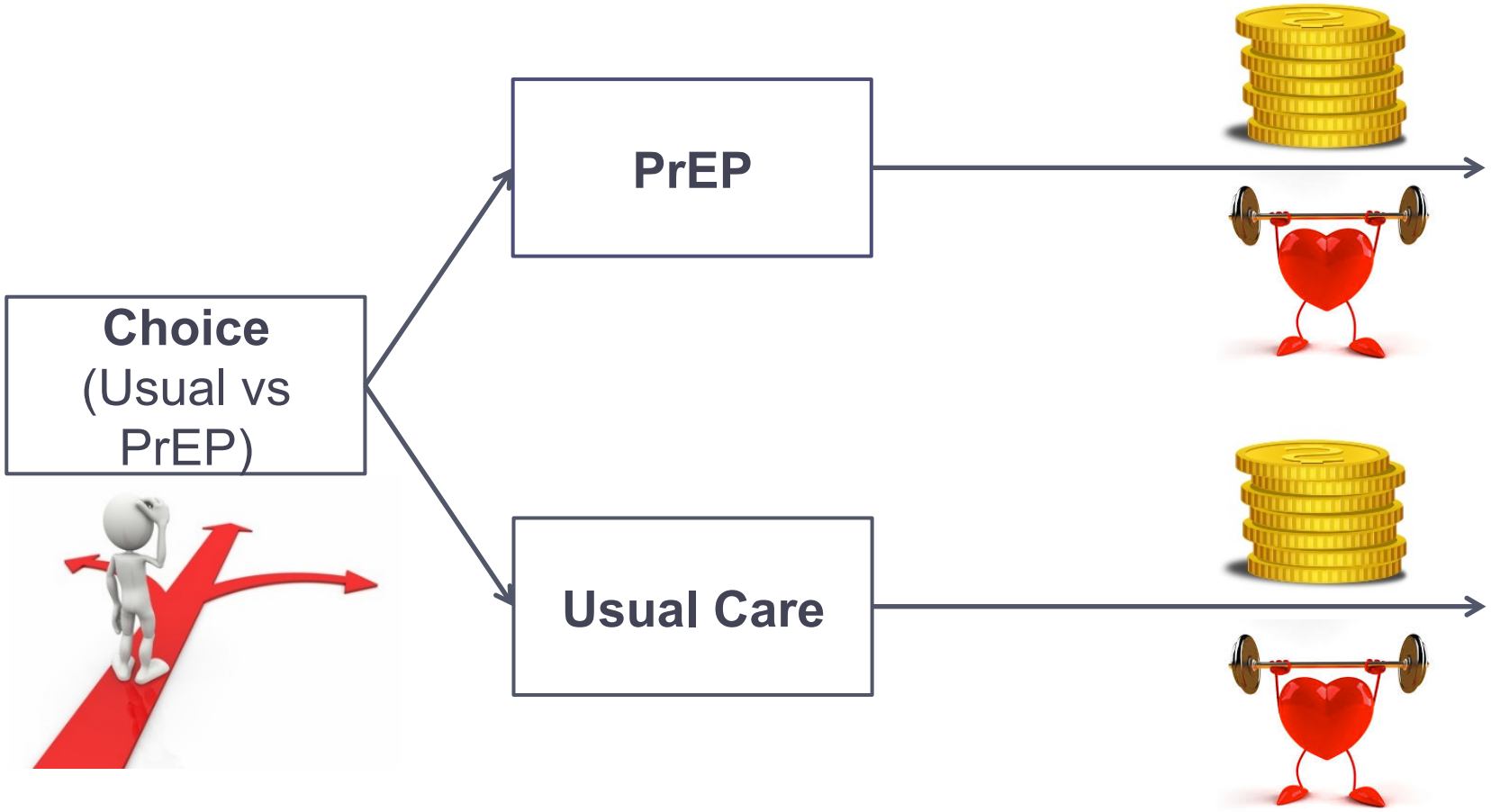
Dr Valentina Cambiano

Summary

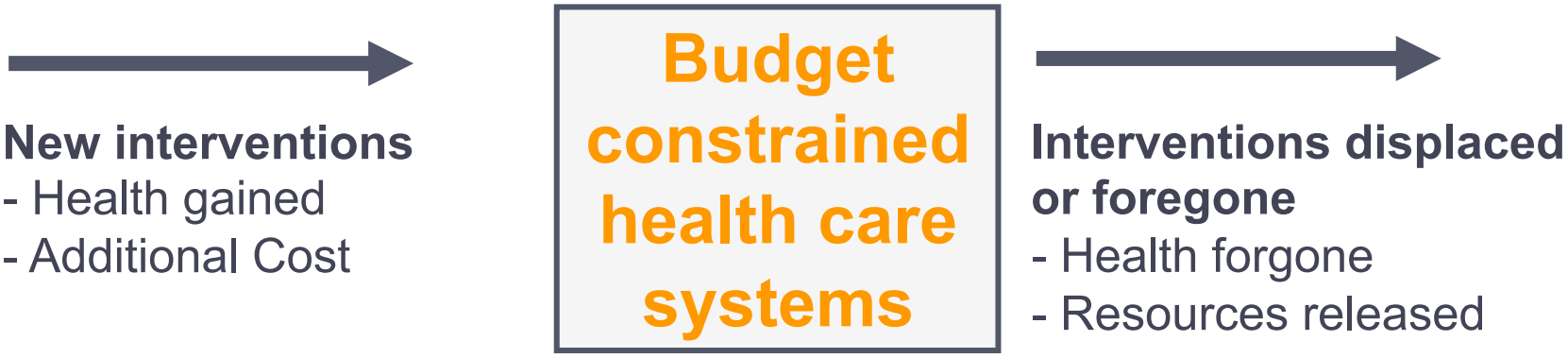
- What is a cost-effectiveness analysis?
- Why are we evaluating whether PrEP is cost-effective?
- How is cost-effectiveness determined?
- Is PrEP cost-effective among MSM in the UK?

Cost-effectiveness analysis (CEA)

- CEA is a form of economic evaluation that informs the choice of healthcare interventions/programmes
- Based upon comparative assessments of costs & health consequences



Why are we evaluating whether PrEP is cost-effective?



Why are we evaluating whether PrEP is cost-effective?

Goal: maximize health of the population

New interventions
- Health gained
- Additional Cost

Budget constrained health care systems

Interventions displaced or foregone
- Health forgone
- Resources released

"Is the new intervention cost-effective?

=

Is the health gain from the new intervention likely to be greater than the health foregone?

Steps 1-2 to determine cost-effectiveness

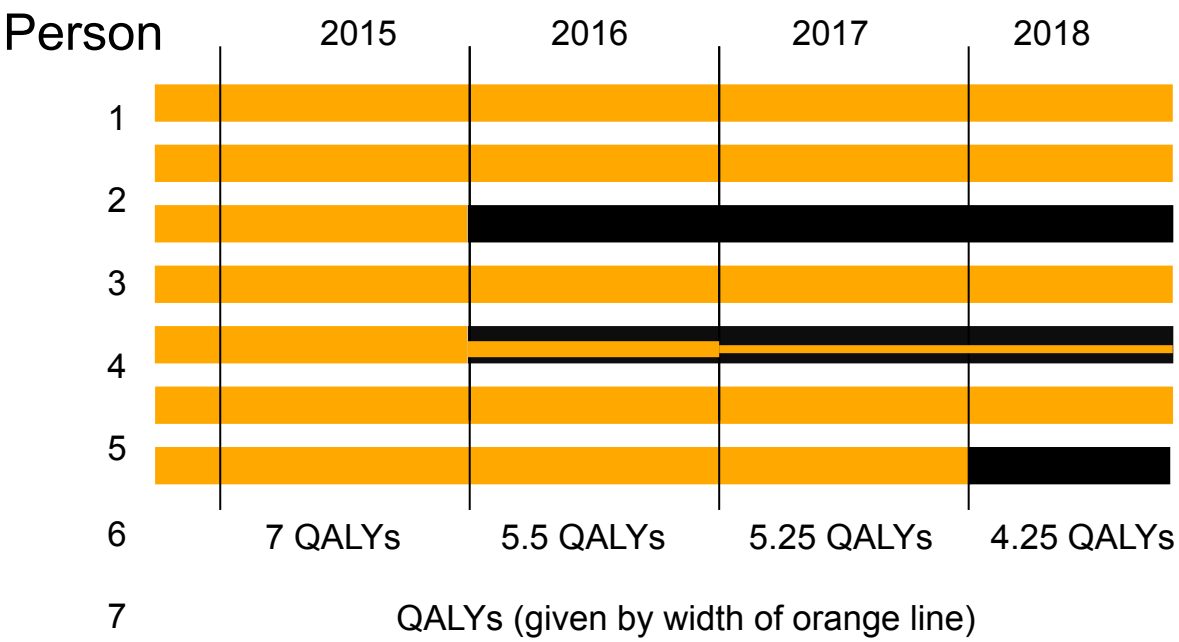
1. Determine the **costs** of alternative interventions
2. Measure and value **health outcomes** (HIV infections, life-years, Quality-adjusted life-years (QALYs)

Quality adjusted life-years (QALYs)

- QALYs measure health on a scale from 0 (representing death) to 1 (full health).

Extent of being healthy given by thickness of orange line

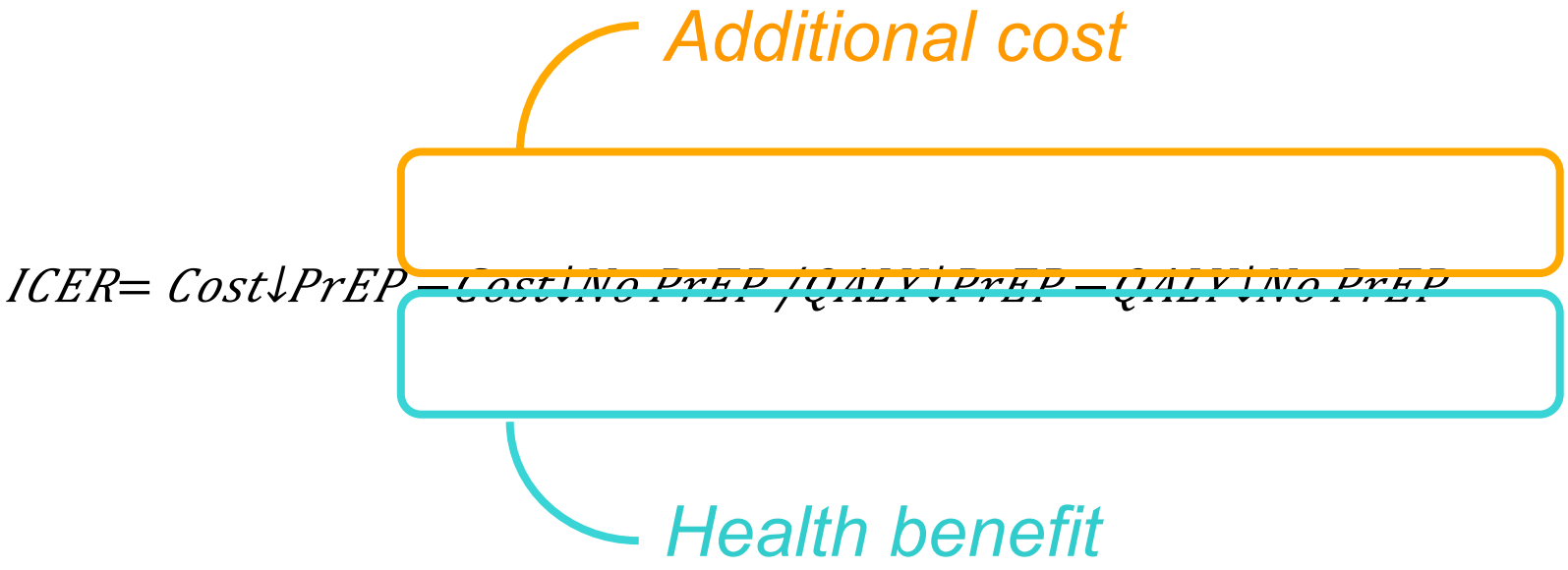
Person is dead



Steps 3-4 to determine cost-effectiveness

3. **Compare** costs and health outcomes (to the reference scenario, usual care)

4. Calculate the 'incremental cost-effectiveness ratio' (ICER): the cost per QALY gained from an alternative.



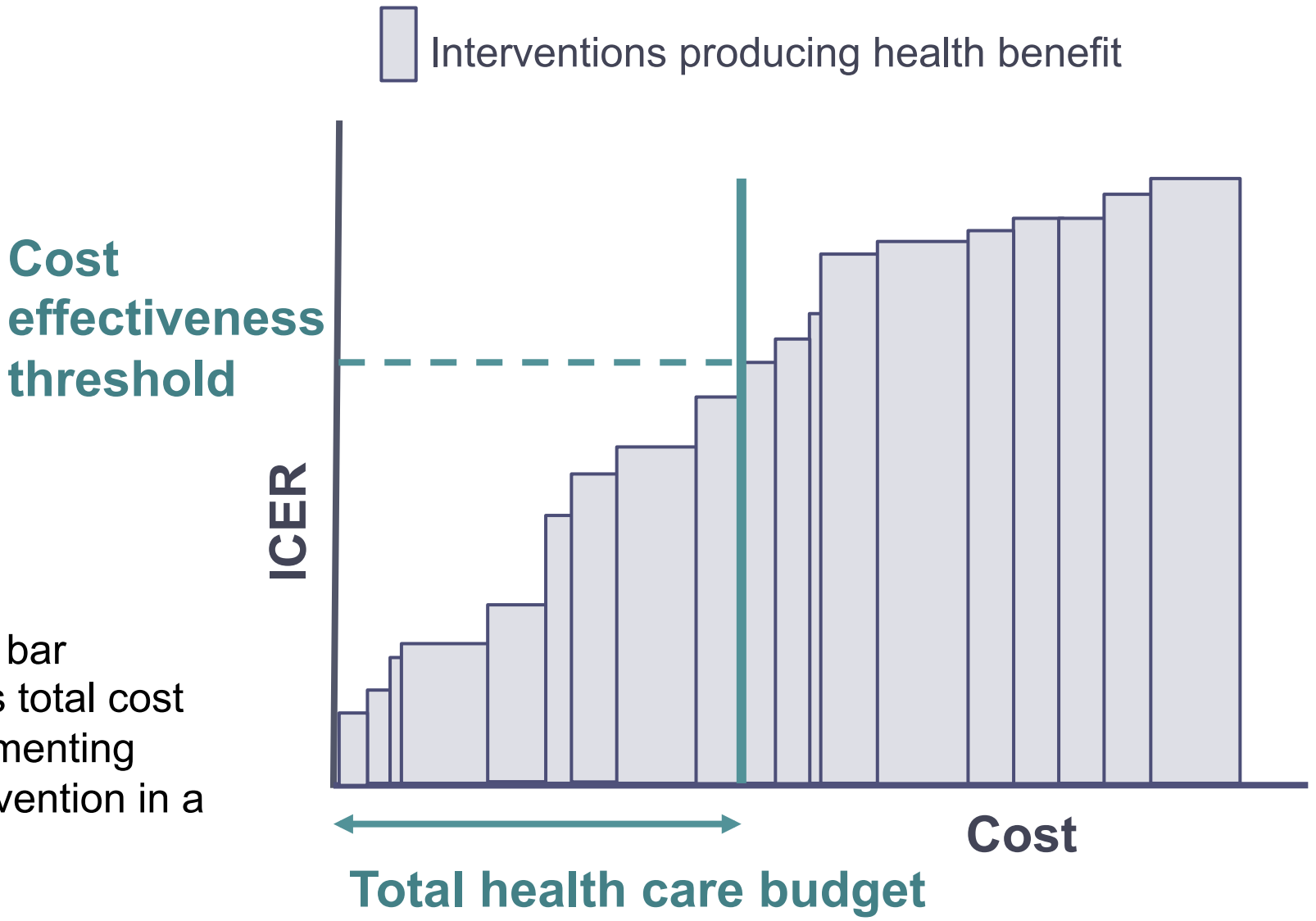
Step 5 to determine cost-effectiveness

5. Compare the ICER to a **threshold ICER** (sometimes called the cost-effectiveness threshold or willingness to pay threshold)

- The threshold represents the **opportunity cost,** the value of the alternative that is foregone
- In the UK the threshold is around £20,000/QALY gained

IF we adopt an intervention with ICER > £20,000/QALY gained
---> more health lost/forgone from the commitment of resources to that intervention than results from its provision

Concept of cost-effectiveness threshold – ideal scenario



Width of bar indicates total cost of implementing the intervention in a country

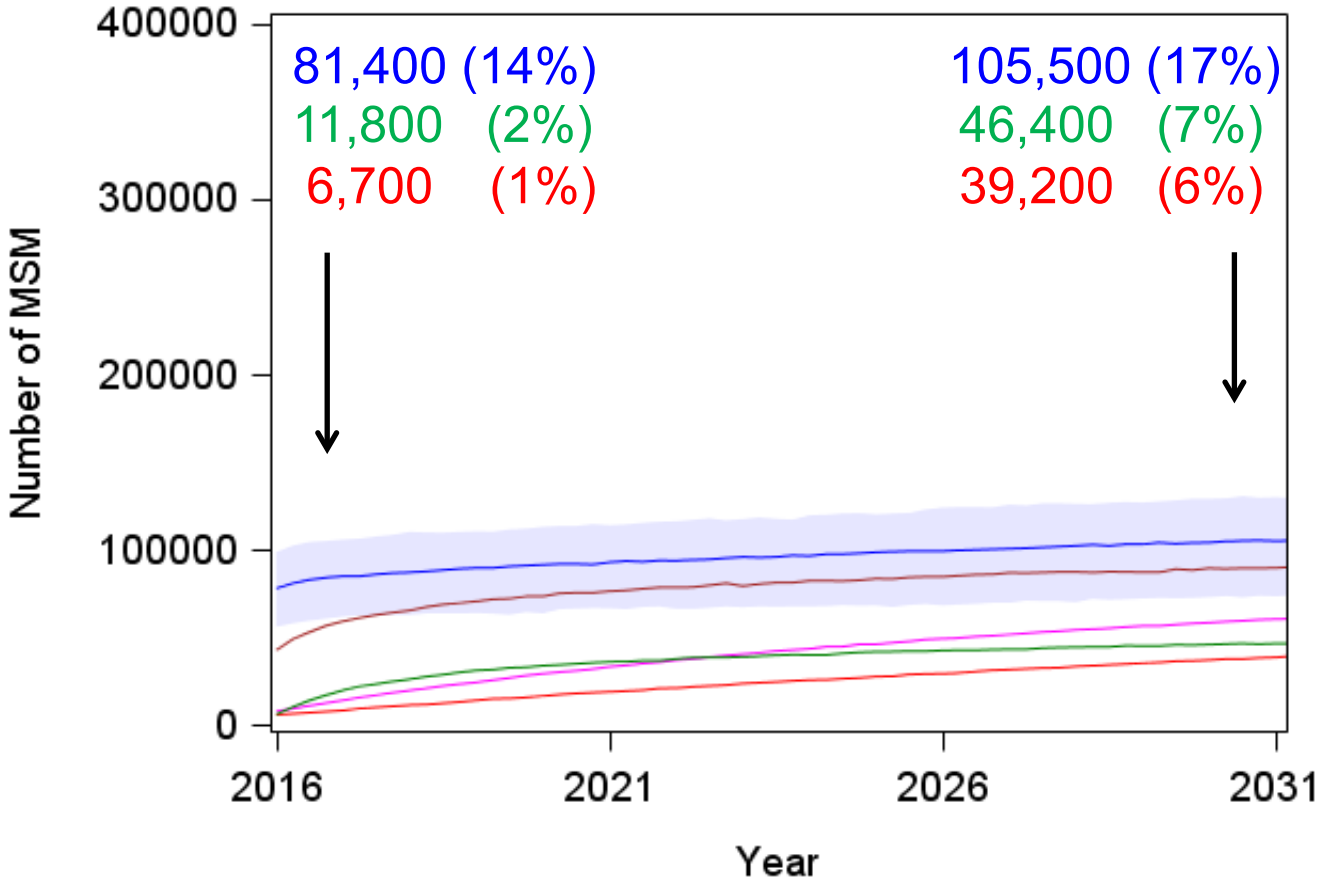
Is PrEP for HIV prevention cost-effective in MSM in the UK?

		Publich Health England	UCL
Type of model		Static	Dynamic
Intervention		PrEP for 1 year	PrEP when having CLS once initiated
Population		MSM presenting with bacterial STI	Different MSM groups
Timeframe		Life-time	
	Population	Eligibility criteria as in PROUD (CLS in the last 3 months and tested in the last year)	
	Cost	Considering cost obtained a from Freedom of information Act request (lower, possibly closer to reality)	

PHE model

- PrEP in high risk MSM is unlikely to be cost-effective at 64% effectiveness *plus* risk compensation, given to a population with 3.3% Year 1 HIV incidence (ICER £34,000/QALY gained) → ICER becomes less favourable if target population's Year 1 incidence is lower.
- Estimated cost-effectiveness of PrEP is very sensitive to:
  - target population's Year 1 HIV incidence;
  - patient adherence (much uncertainty, especially with programme scale-up) → affects effectiveness;
  - PrEP drug cost
- **Conclusions: Substantial price reductions of anti-retroviral drugs used for PrEP is needed to give necessary assurance of cost-effectiveness, & for an affordable public health programme of sufficient size.**

Number (%) of MSM projected to be on PrEP



Men who tested for HIV and had

- CLS
- CLS with ≥1 STP
- CLS with ≥5 STP
- CLS with STIs
- CLS (no increase in CLS or testing)

90% range

By 2096:
128,300 (20%) on PrEP

Overall cost of ART and of PrEP

1 year **<u>on ART</u>**
(CD4>200 cells/mm^3):

£6,488 Atripla (BNF 2015)
£4,063 Healthcare
£ 164 (£41x4) CD4 measurements
£ 276 (£69x4) VL measurements
[£ 238 resistance test at ART initiation]

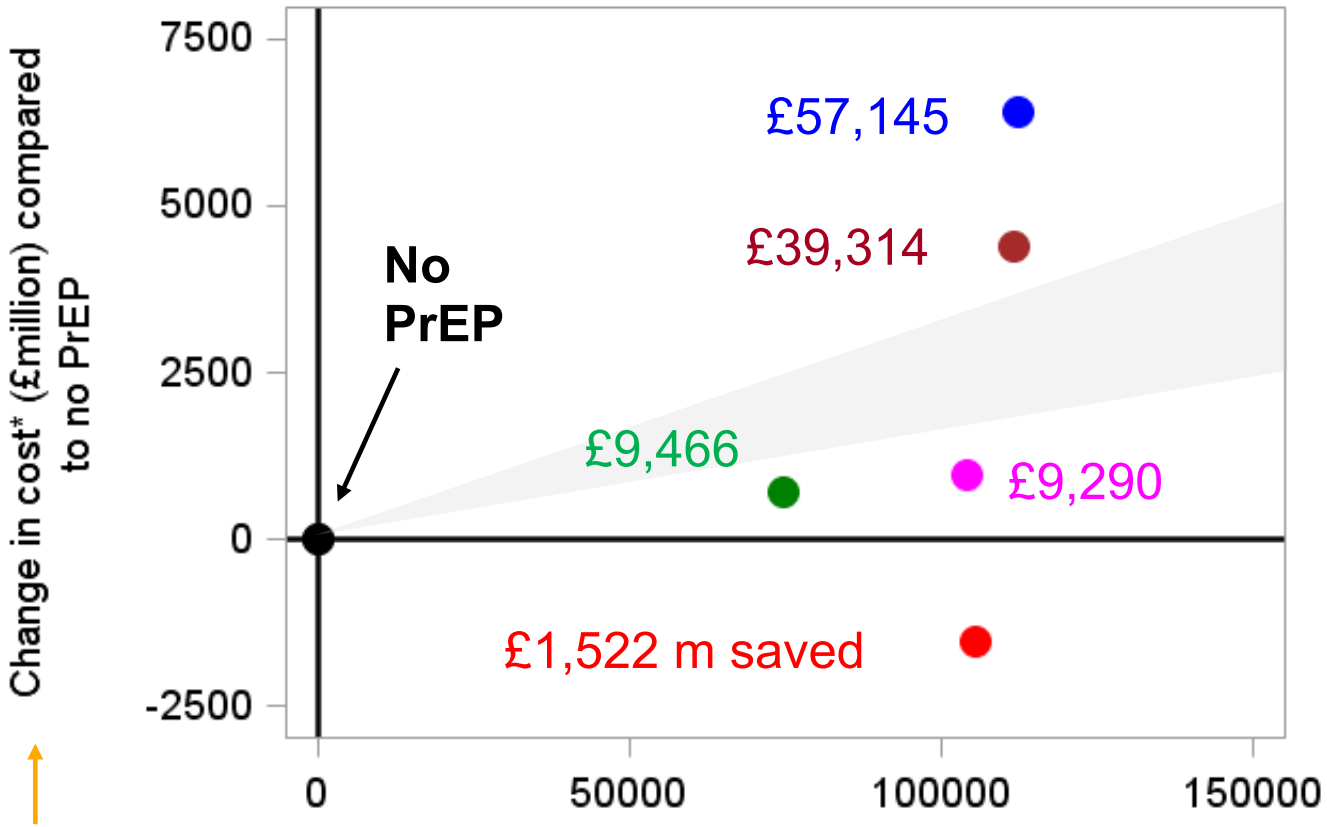
~£11,000

£4,331 Truvada (BNF 2015)
£ 234 First visit for PrEP
£ 232 (£58x4) HIV tests
£ 284 Additional cost of monitoring people on PrEP compared to people at similar risk not on PrEP

~£5,000

1 year **<u>on PrEP</u>**:

Health benefits and costs over 80 years



PrEP in men having:

- CLS
- CLS with ≥1 STP
- CLS with ≥5 STP
- CLS with STIs
- CLS (no increase in CLS or testing)

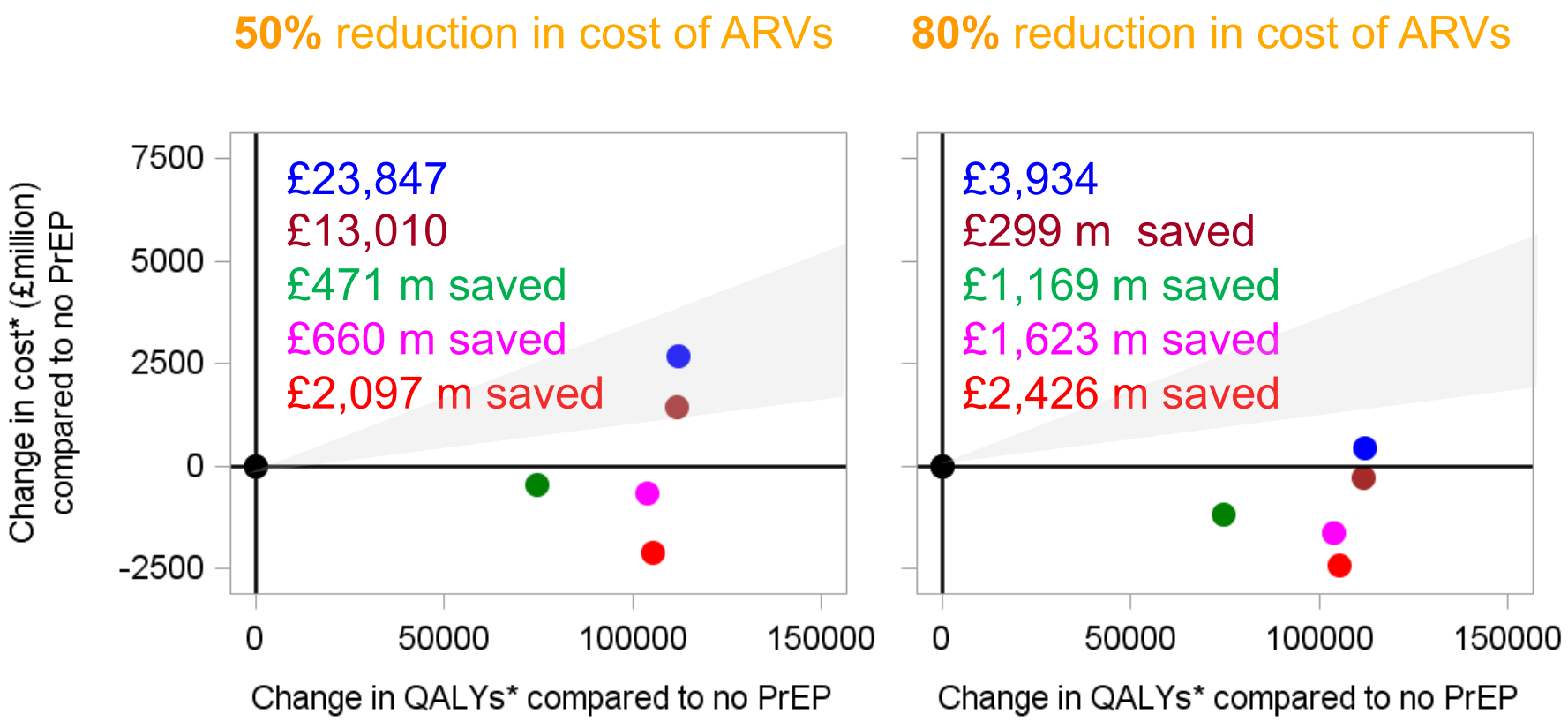
Cost-effectiveness threshold range

Additional cost (vs No PrEP)

Health benefit

*discounted at 3.5% rate

Health benefits and costs over 80 years



PrEP in men having: ● CLS ● CLS with ≥1 STP ● CLS with ≥5 STP ● CLS with STIs ● CLS (no increase in CLS or testing)

Cost-effectiveness threshold range;

*discounted at 3.5% rate

Preliminary Conclusions

This analysis suggests that the use of PrEP among MSM in the UK is cost-effective when:

- it is targeted to men who had 5 STP or more in the last year without using condom or present with an STI

or

- the cost of ARVs is assumed at least 50% lower than current full list prices, once patents expire (which seems realistic based on past experience and may well be an under-estimate)

or

- when there is no increase in CLS and not an increase in HIV test, as a consequence of PrEP becoming available

Thank you very much to:

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PHE team
KohJun Ong
Sarika Desai
Monica Desai
Anthony Nardone
Albert Jan van Hoek
Noel Gill

…and you for your attention!

Questions

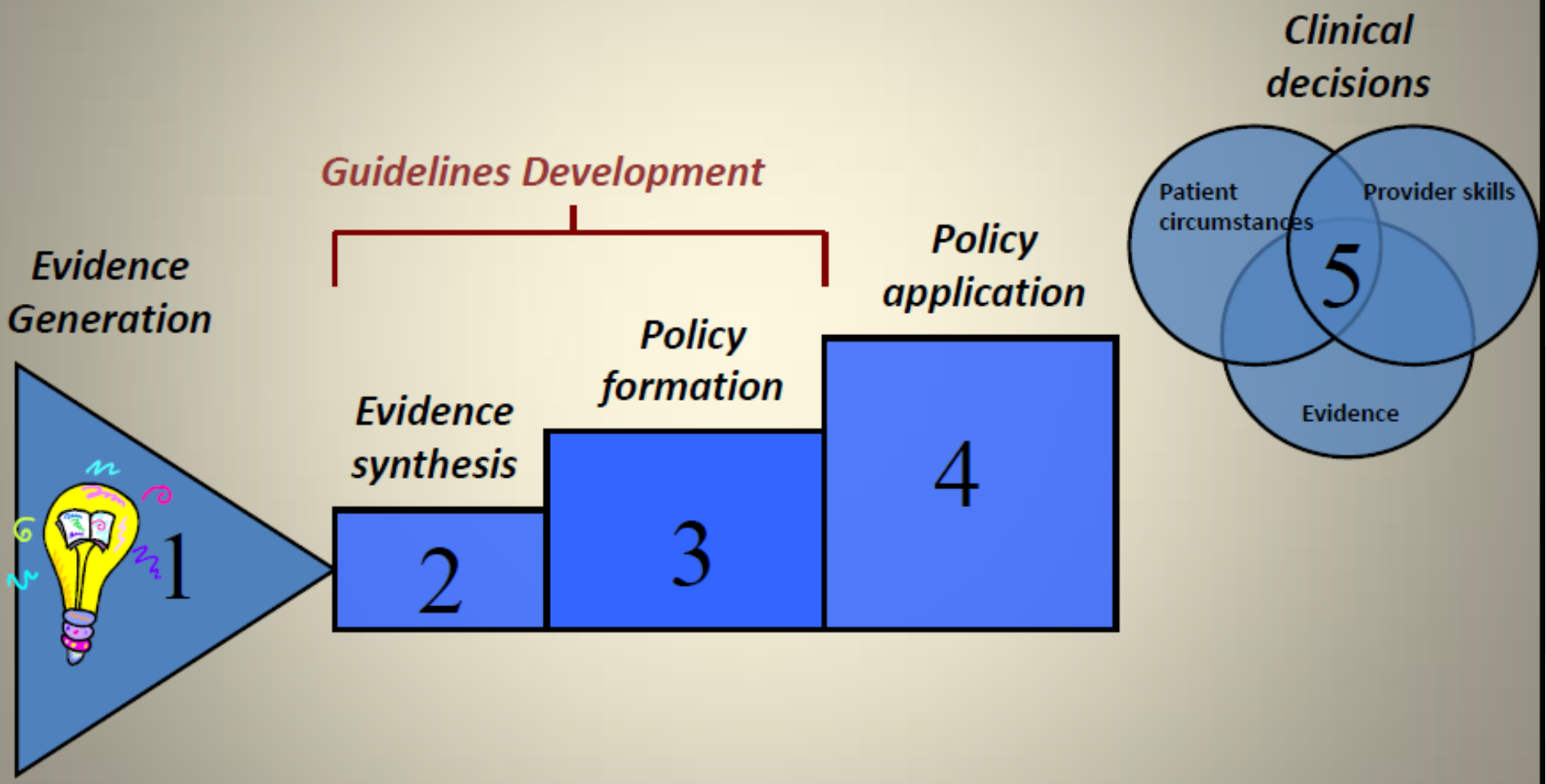
Is it cost-effective among MSM in other resource rich settings?

- high-risk MSM in New York ✓ (ICER $32,000). Desai et al 2008
- high-risk MSM in the US **unlikely**, unless price reductions and/or increases in efficacy. Possibly cost-effective in younger populations or populations at higher risk of infection (ICER $298,000). Paltiel et al 2009
- high-risk MSM in the US ✓ (ICER>$40,000), but annual PrEP expenditures of more than $4 billion. Juusola et al 2012
- MSM in a discordant regular partnership in Australia ✓ (ICER > $110,000), but not large population level impact, other scenarios **unlikely**. Schneider et al 2014
- MSM in Canada (using on demand PrEP) ranges from cost-saving to highly cost-effective. Ouellet 2015

Challenges to the implementation of PrEP in Europe

Anastasia Pharris
ECDC Programme on HIV, STI and viral hepatitis

Steps from evidence generation to clinical application



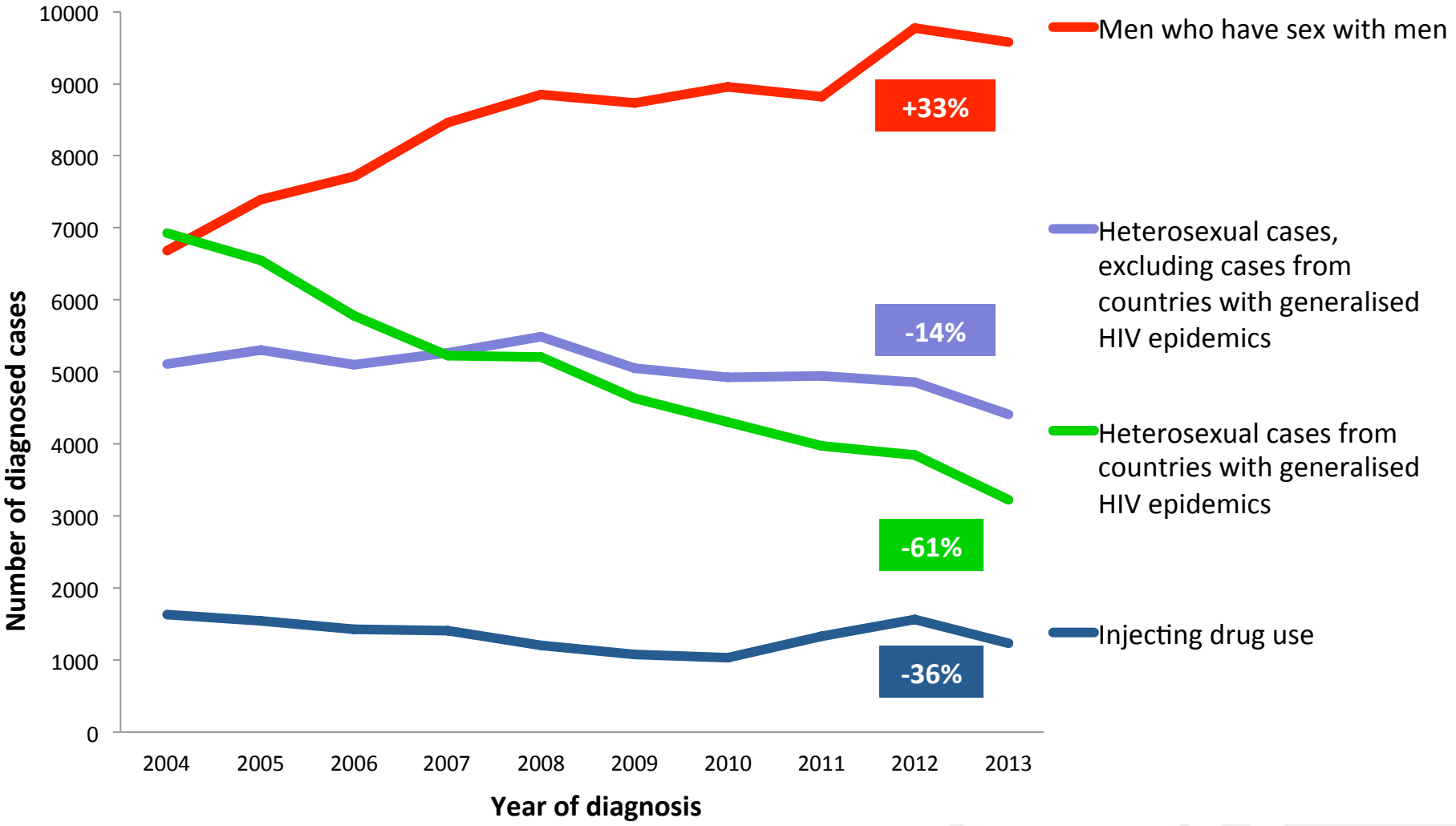
Research funding

Slide courtesy of Dawn K. Smith, CDC

Issues influencing policy formation and application

- Efficacy of the intervention
- Public and individual health rationale

HIV infections diagnosed among MSM in Europe have increased during the last decade



Source: ECDC/WHO (2014). HIV/AIDS Surveillance in Europe, 2013. Data from Estonia and Poland excluded due to incomplete reporting on transmission mode during the period; cases from Italy and Spain excluded due to increasing national coverage over the period.

Issues influencing policy formation and application

- Efficacy of the intervention
- Public and individual health rationale
- Regulatory issues
- Guidelines (regional, national and local)

Diverse health systems in Europe which affect the organisation and delivery of health care

- National health systems
- Mixed health insurance
- Private insurance
- Out-of-pocket payment

In Europe, health provision tends to be state-provided and financed and the decision to provide PrEP is done by public bodies considering cost constraints.

How health care is organised and financed will affect decisions on the payment threshold for PrEP

PrEP as a medicine and a prevention method

NGOs and public health bodies

HIV prevention often occurs via NGOs and public health authorities

Hospitals and clinical bodies

HIV medicines procurement and provision for treatment has occurred via clinical bodies, hospitals

The provision of PrEP is a comprehensive package which necessitating collaboration and task-sharing

Where to target PrEP?

Risk group approach?

MSM, people who inject drugs, sex workers

Risk assessment approach?

Persons having condomless receptive anal intercourse

STI diagnosis or PEP use during last six months

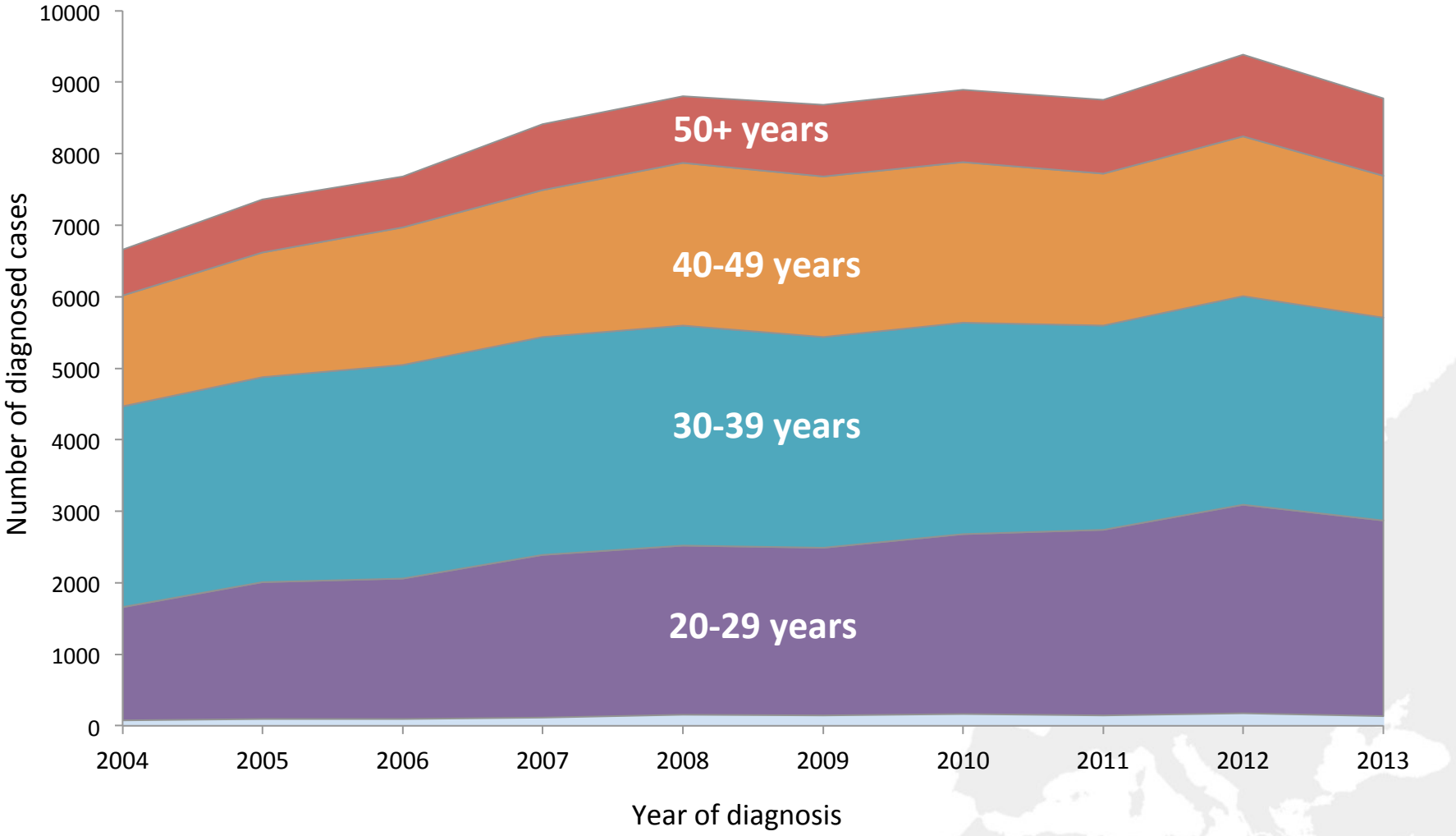
Situations heralding 'seasons of risk'

Self-referral approach?

Those who ask for PrEP

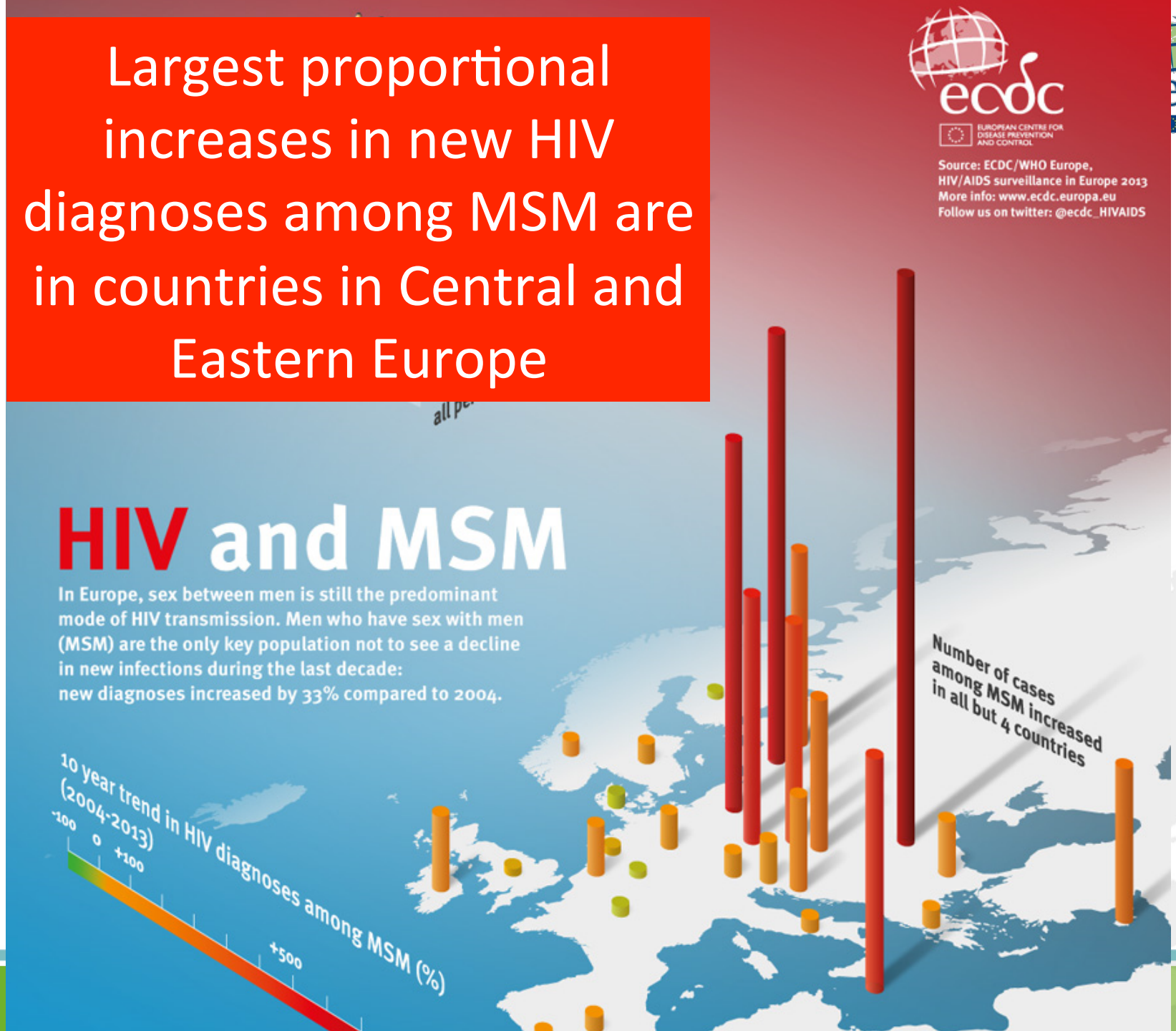
Groups to target are likely to differ depending on the national/sub-national epidemiological situation

One-third of new HIV diagnoses among MSM are among men <30 years



Source: Adapted from Pharris, Eurosurveillance (2014). Excludes data from countries with changed coverage over the period (Bulgaria, Italy, Spain) and incomplete data on transmission mode (Estonia, Poland)

Largest proportional increases in new HIV diagnoses among MSM are in countries in Central and Eastern Europe



Care models

Infectious disease clinics

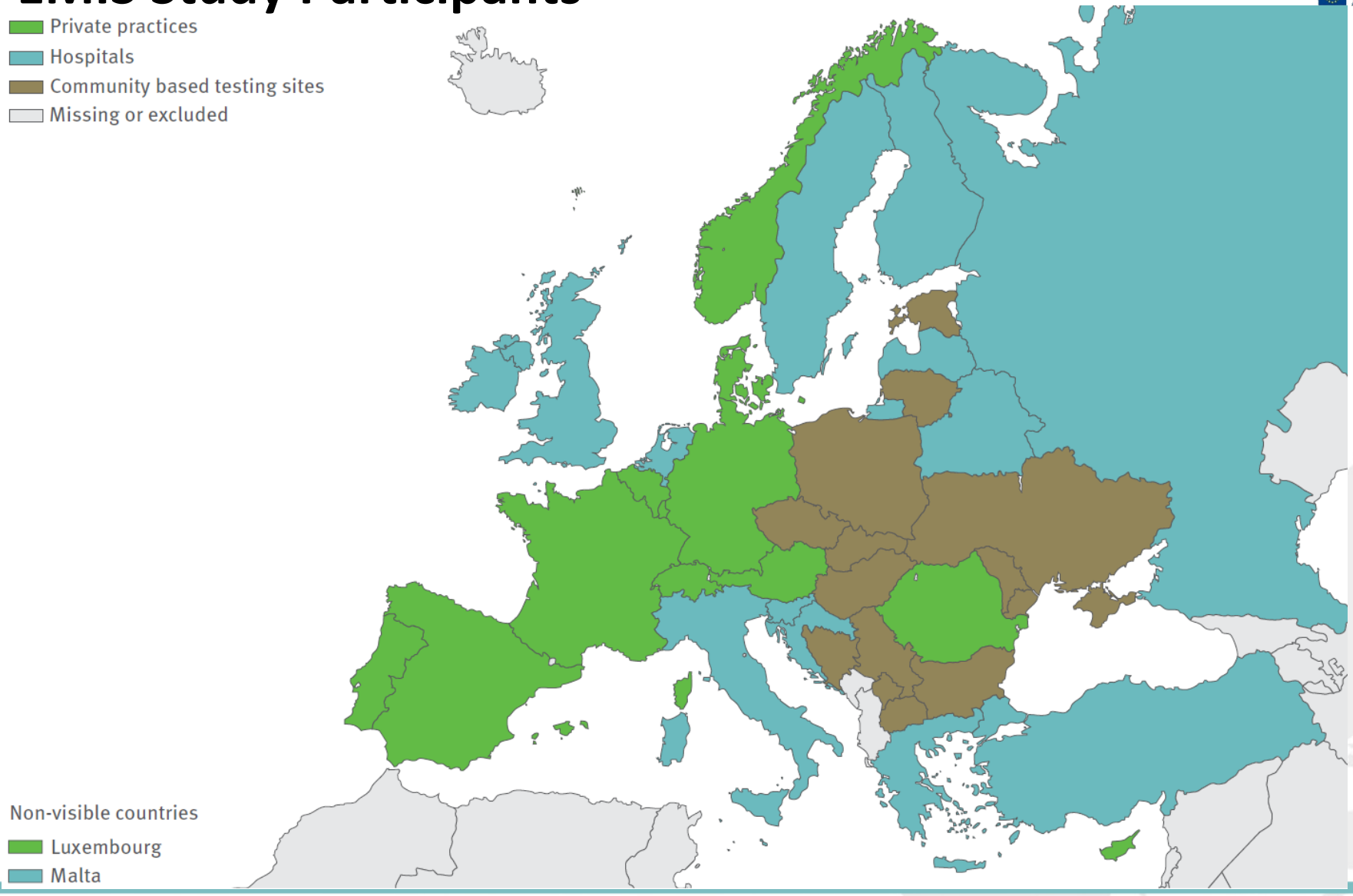
STI/GUM clinics

Primary care settings

Drug treatment centres

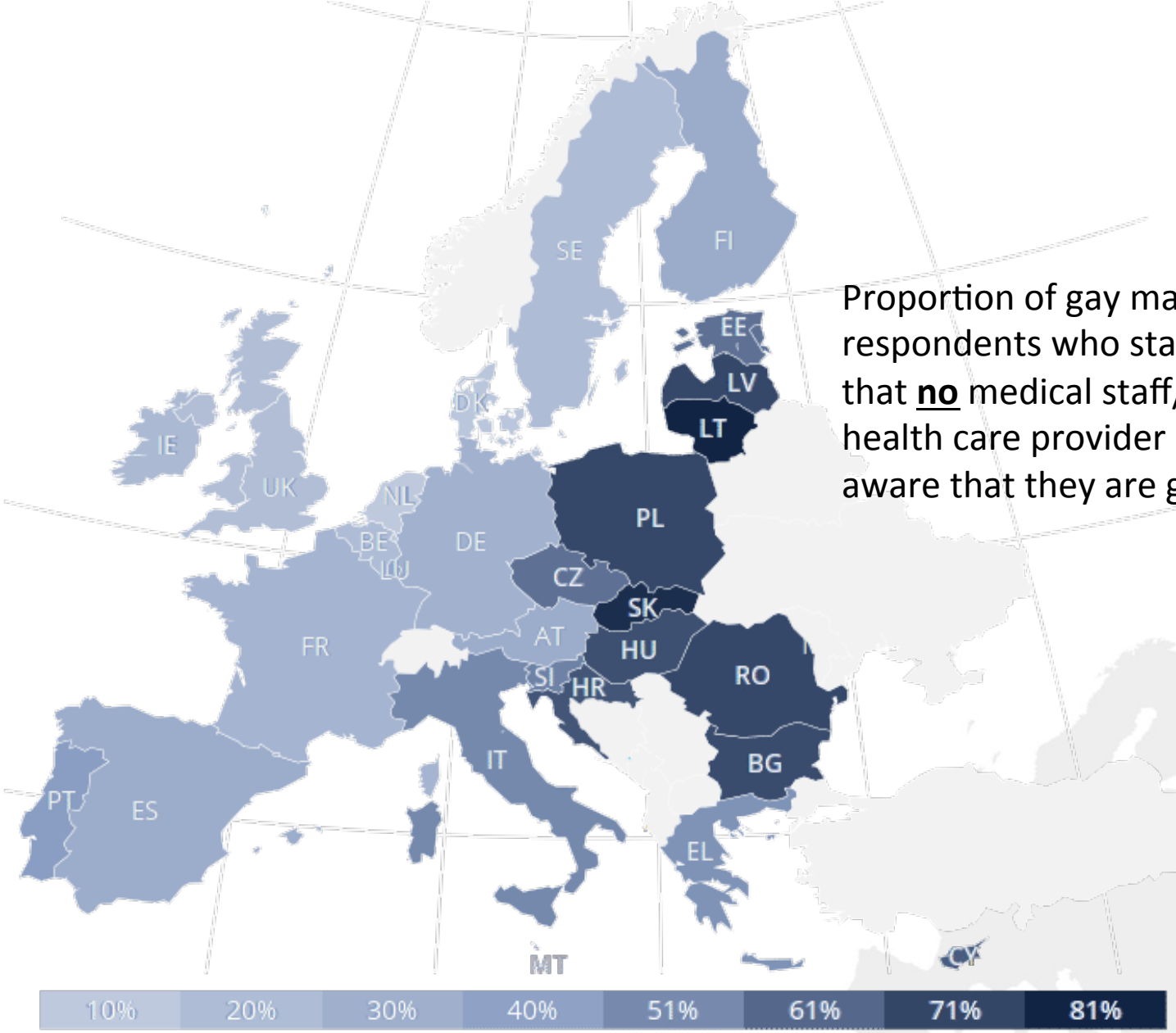
Community settings?

Predominant types of HIV testing site reported by EMIS Study Participants



Addressing the needs of PrEP providers

- Many potential PrEP providers do not yet know that it exists
- Some potential providers may not be experienced with antiretroviral treatment, sexual health counselling/risk assessment
- Implementing appropriate systems for follow-up and monitoring of PrEP users (STI testing, laboratory screening)
- Partnering with clinical societies, training, setting-specific guidelines, sharing of implementation practices, other support (hotlines, etc)



Proportion of gay male respondents who state that **no** medical staff/ health care provider is aware that they are gay.

EU LGBT Survey; European Union Agency for Fundamental Rights (FRA); 2013

Ongoing and planned European demonstrations projects important to address remaining questions

- Who will request and take PrEP?
- How often (intermittent and/or regular dosing) and for how long?
- What are the optimal care models and referral pathways?
- Longer term effects on the users of PrEP?
    - Adherence
    - Uptake in the intended target group
    - STI rates
    - Quality of life and sexual health

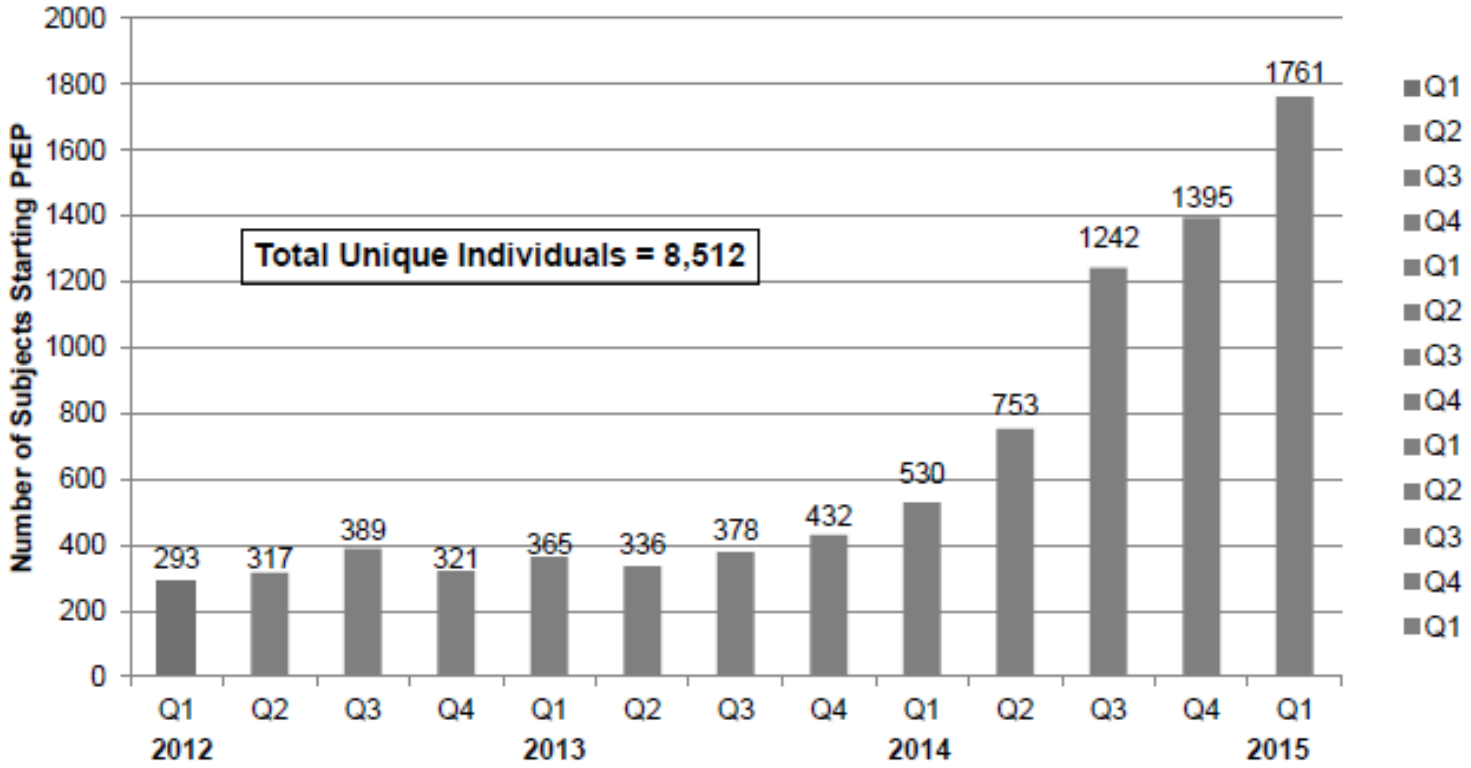
Addressing the needs of PrEP users

- Many potential PrEP users are not yet aware that it exists

- Information provision
  - Is PrEP right for me?
  - Where can I access it?
  - Is it effective?
  - Is it dangerous?
  - PrEP-related stigma

- Adherence support

Scale-up takes time: new persons started on PrEP per quarter in the United States



IMS National Prescription Database accounts for approx. 39% of all TVD prescriptions

Bush, S. et al; IAPAC Prevention 2015; #74

Summary

- Momentum is growing in Europe with regard to the use of PrEP as part of a comprehensive approach to HIV prevention among some populations

- Some factors related to European health systems make decision on funding and implementing PrEP complex

- Actors in Europe have the opportunity to collectively address and document solutions to implementation challenges at policy, care provision, provider and patient levels

The role of community **involvement** in IPERGAY and other PrEP studies

Daniela Rojas Castro

September 18th 2015

AIDES
Membre de la Coalition Internationale Sida PLUS

Introduction

- AIDES (1984) – Social Transformation
- Working **with** PLWH or exposed to HIV
- Informing, involving…and empowering the community/the communities
- PrEP, but also…access to treatment, health rights for migrants, educational intervention targeting injecting drug users, etc

AIDES
Membre de la Coalition Internationale Sida PLUS

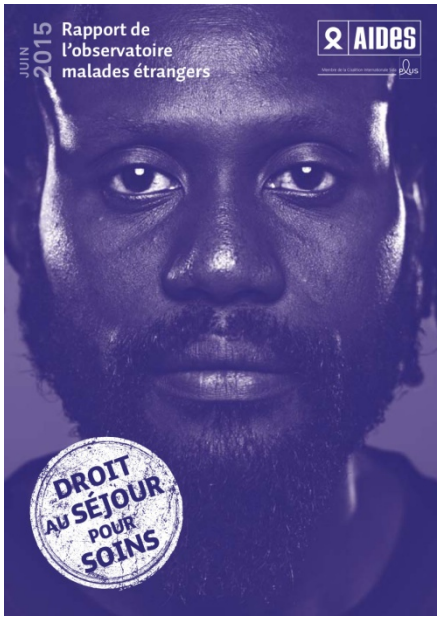
Targets & Partners Strategy

AIDES
Membre de la Coalition Internationale Sida PLUS

ACTION
75 sites and the net

serOnet

Gay Bareback Zone.com
For Cum Addicts!!!!



AIDES
Membre de la Coalition Internationale Sida

ADVOCACY

ANSM (French FDA) - Independent working group for a Temporary Authorisation (TU) 2014

- AIDES asked for a “TU” for PrEP to the ANSM
- ANSM decides to create an independent group to analyze the possibility to open “TU” (of Truvada for PrEP)
- 2 commissions
  - Risk and benefits of PrEP
  - Deliverance framework (medical advice, reimbursement by the healthcare system,….)
  - What about the role of peers providing information and counseling ?

ADVOCACY

Minister of Health June 2015

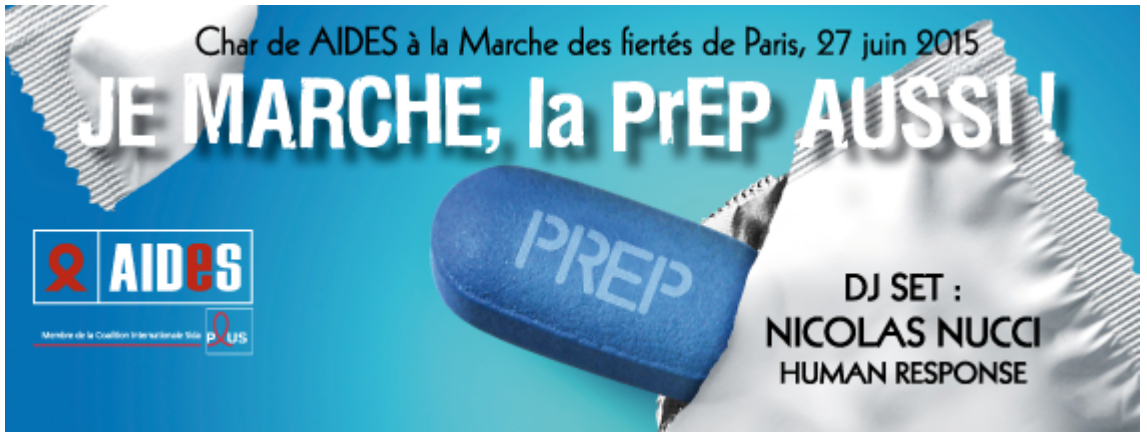
- She asked to ANSM and CNS to produce reports on PrEP to define the role of this tool in the global strategy of prevention
  - Results by the end of the year?

- Synergy with the Morla expert's report

AIDES
Membre de la Coalition Internationale Sida PLUS

ADVOCACY

Pride 2015



ADVOCACY EUROPE

EATG

Network of European Associations asking for PrEP

Fear no more!

Catalysing the empowerment of gay men for
HIV prevention, treatment and stigma reduction in Europe

Activist consultation organised jointly by the European AIDS Treatment Group and UNAIDS

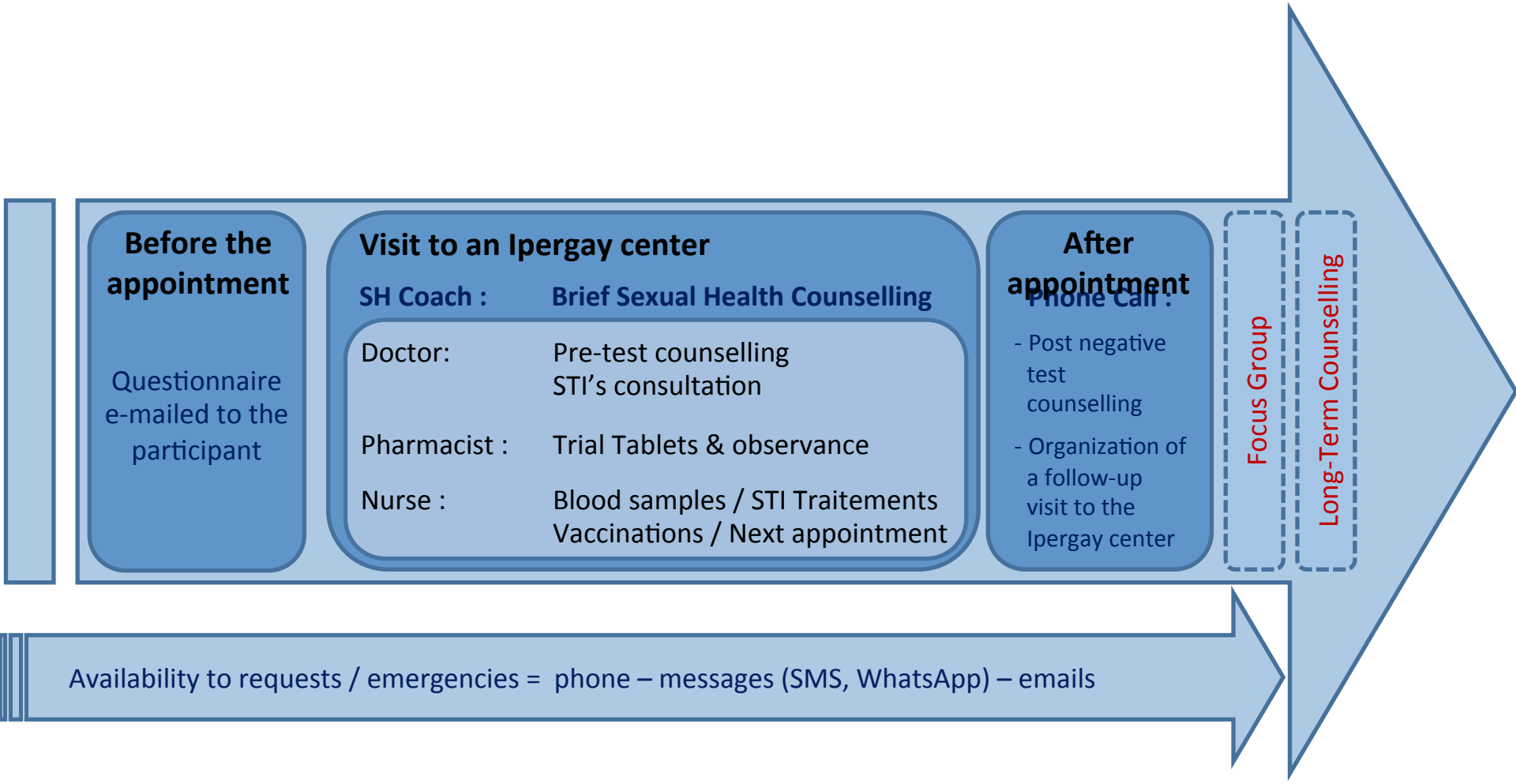
Brussels, 22-24 June 2015

AIDES
Membre de la Coalition Internationale Sida PLUS

COMMUNITY-BASED RESEARCH

- An opportunity to fulfill a **need** (survey 2009)
- A possibility to include and ensure counseling and **personal coaching** regarding sexual health
- Integration of a **psychosocial** approach in the biomedical project
- Social transformation
- Potential benefits of intermittent PrEP
  - Higher adherence: more convenient dosing regimen
  - Less health risks because of a lower drug exposure (kidneys, bones)
  - Cost-effectiveness

What else happens in Ipergay in addition to medical monitoring?



Thanks to Stéphane Morel for this slide

ipergay
ANRS
Intervention Préventive de l'Exposition aux Risques avec et pour les Gays

COMMUNITY-BASED SUPPORT IN THE ANRS IPERGAY TRIAL:
IMPROVING ADHERENCE TO THE TRIAL AND ACCESS TO OVERALL HEALTH

Issue

The ANRS-IPERGAY double-blind randomised trial, initiated in 2012, focuses on the use of "on demand" pre-exposure prophylaxis (PrEP) among gay men, bisexuals and transgender people who do not consistently use condoms for anal sex. The involvement of community-based sexual health coaches in this experimental research to reduce the risks of HIV and STI infection aims to implement global support strategies and to encourage reflection on health and sexual well-being among participants.

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1. The tools proposed by the community-based sexual health coach

In each centre, a community-based sexual health coach was part of the medical research team. Their chosen support model was inspired from the RESPECT model and the community-based practices and know-how which the CBO AIDES has built up since 1984. Each sexual health coach is a reference point and privileged contact for about one hundred participants.

They build a long-term relationship with participants based on a non-judgmental and confidential attitude. At their disposal, they have an innovative toolkit of:

- **brief counselling sessions** which are systematically offered to the participants at each visit (during the follow-up, the announcement of the negative test result) on top of medical consultations;
- **more in-depth counselling sessions** on demand and a personalised follow-up proposal in case of a positive STI test result;
- **monthly self-support focus groups** for the trial participants: a time for information and appropriation, renewal and collective development and for sharing experiences;
- **implementation of an on-line forum** for sharing experiences and point of views, restricted to the trial participants;
- **large availability of the sexual health coaches** (can be reached by phone, text message or apps) to adjust preventive responses and solutions in real time according to the needs of the participants.

This community-based offer was intensified, at the request of participants, when the placebo arm stopped in October 2014 (all participants accessed Truvada®), in order to help participants to better understand the implication of this sensitive and rapid transition.

2. The trial, the placebo pill and I: how to enhance clinical trial adherence and comfort?

- **Peer exchanges** at inclusion (between the participant and the sexual health coach) aimed at clarifying – in non-medical terms – the trial design, the choice of Truvada® instead of others ARVs strategies and previous results of PrEP trials. This was also the opportunity for an **initial appraisal of individual needs**, especially concerning risk assessment.
- **A trusting relationship** was set up, ensuring participants had privileged access to a referent, able to provide relevant information, listen and relay their needs.
- **The community-based support fostered a better appropriation of the trial** by the participant trough individual counselling and self-support focus groups. The sexual health coach ensured the correct understanding of regarding the dosing regimen and worked on a personalised and targeted prevention strategy.
- **In the open phase, community-based support was crucial for individual and collective appropriation of the trial's results.** Emerging needs were answered (e.g. questions about observance with Truvada®). Coaching times were also opportunities to share concerns about the end of the trial and the future framework for accessing PrEP in France.

3. My PrEP, my sexuality: how to embrace the sexual health field, how do I think "global"?

- **Throughout the trial, time for support has increased awareness concerning STIs' prevalence and allowed a better assessment of sexual risk according to sexual practices.** The trial offered a privileged moment to talk about combined prevention on a regular basis: what is the place for condom, placebo, Truvada® (at the time of open phase)? The aim was to focus on experience to promote a personalised harm reduction strategy corresponding to participants needs.
- **In the open phase, self-support focus groups were** an opportunity to question the feeling of safety (and its consequences), disinhibition (and how to deal with it) and the possibility of increasing the quality of sexual life.
- Community-based support lays the foundations for an increasingly autonomous **multidisciplinary health path** and focused on specific and clearly identified needs (referral to other health professionals: psychologist, addiction specialist, sexologist, dermatologist, proctologist).

Lesson learned

- The offer provided by community-based sexual-health coaching has been the heart to promote a good understanding of the trial through peer exchanges and enable the adherence of participants.
- It has also raised the participant awareness of a global health approach.
- The present experiment is as such a major innovation. It seems essential to include community-based support in therapeutic trials and prevention policies in the future.

AIDS IMPACT 2015 - AMSTERDAM

COMMUNITY-BASED RESEARCH

- **To describe HIV negative people's awareness of PrEP, their willingness and intention to use it**
  - What populations are informed? What populations are willing to take PrEP? And what proportion of them intend to take PrEP?
  - What are the reasons for interested/intention of taking PrEP and vice versa?

- **To describe informal PrEP use**

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COMMUNITY-BASED RESEARCH

- 3024 respondents
- Internet and paper survey
- Only 33.6% of respondents were aware of PrEP before answering the questionnaire
- Intention to use PrEP if available : mostly migrants and heterosexual men
- People at high or very high risk for HIV infection
- **4.5 % informal use of PrEP**

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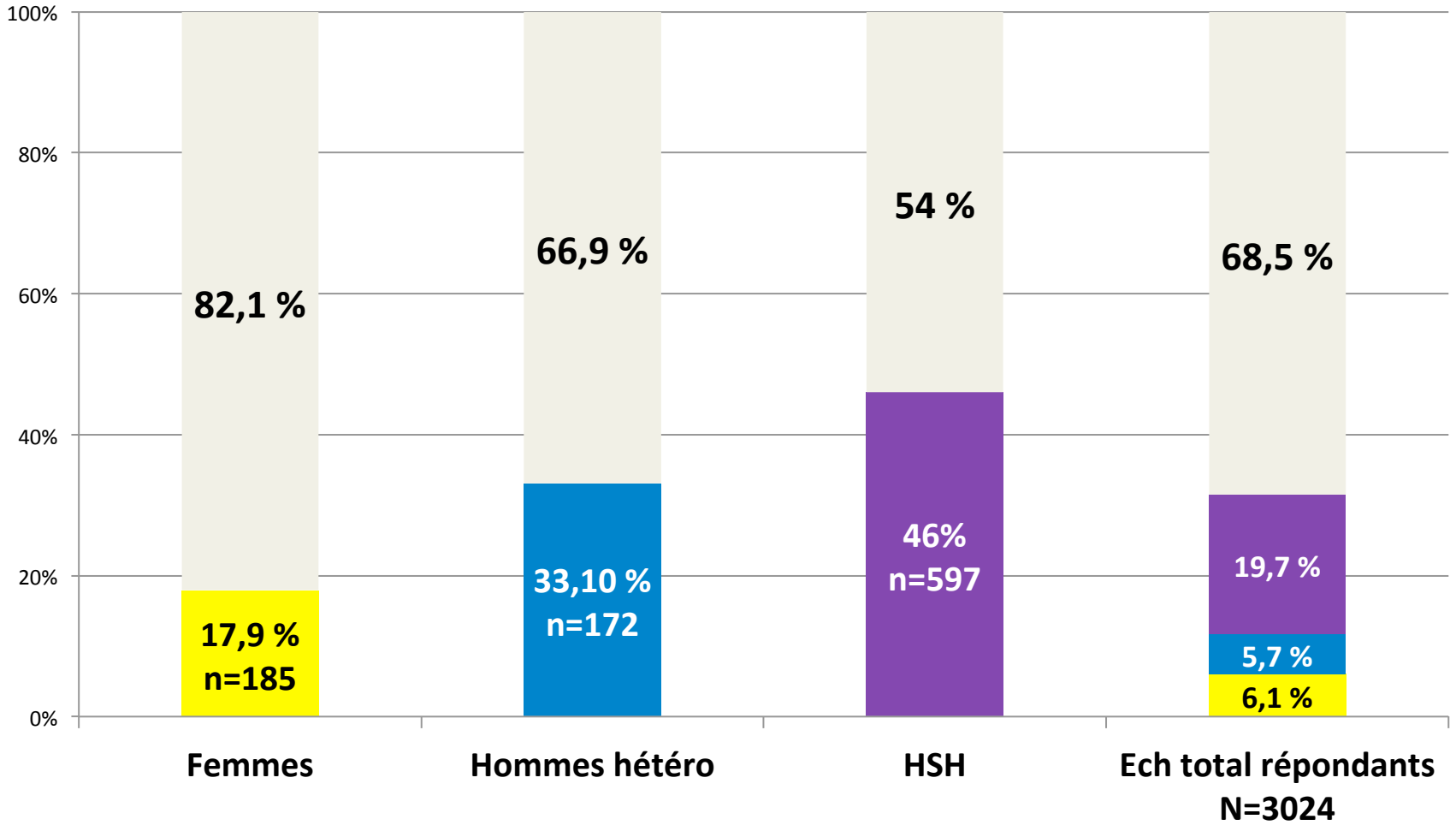
PrEP Knowledge

(N=2853)



520 Heterosexuel men
1 036 Women
1 297 MSM
Statistically significance

COMMUNITY-BASED RESEARCH

4,5% (n=136) **of respondents have already used PrEP** at least once.

74.2% are MSM (n=98)
11.4 % are heterosexual men (n=15)
14.4 % are women (heterosexual and WSW) (n=19)

Informal PrEP use	YES
Women	1.8 %
Heterosexual men	2.9%
MSM	7.6%

MSM are significantly more likely to informally use PrEP (7,6% vs. 2,9% of heterosexual men, p<0,001)

Those reporting to be at high or very high risk for HIV infection are significantly more likely to report informal PrEP use (35.9% vs. 10.3% of people not using PrEP; p<0,001)

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COMMUNITY-BASED RESEARCH

Prepage Study

30 interviews

Get information on :

- The experience and the needs of people who use " informal PrEP”
- The experiences and expectations of informal PrEP users in order to design an appropriate delivery framework

Partners:

AIDES
ANRS(Agence de recherche ANRS (France Recherche Nord&Sud Sida-HIV Hépatites)
INSERM (Institut national de la santé et de la recherche médicale)
Groupe Hospitalier Hôtel Dieu

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Next Steps

- **National advocacy strategy:**
  - Open-label PrEP in France
  - Medical working group to establish guidelines/recommendations concerning informal PrEP use (Société Française de Lutte contre le SIDA)
  - Showcasing the coaching/support provided by peers
  - AIDES has decided (12/13 September 2015) to deliver PrEP and to refer informal PrEP users for follow-up (in partnership with medical staff)
- **European advocacy strategy:**
  - ECDC - guidelines
  - EATG
  - European Medicine Agency
  - Gilead (Marketing authorization for prevention use of Truvada…) but also other pharmas developing new PrEP drugs (Jensen, VIIV)
- Scientific valorisation: Ipergay, FlashPrEP, Prepage…
- Develop a **Flash PrEP EUROPE**

Informing, involving, empowering, is **more than** just recruiting…

The time for debate on the effectiveness of PrEP is over.

Merci…

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