The HIV prevention revolution

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Queensland Sexual Health Society, 31 May 2012

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The prevention revolution

Tonight's presentation

- Science underlying the prevention revolution
- Actions that are likely to be required to maximise population-level effectiveness
  - HIV testing
  - Treatment as prevention
  - Pre-exposure prophylaxis
- Challenges: how do we make it happen?

Science of the prevention revolution

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Science of the prevention revolution

Revolution, not evolution

- Recent research findings represent an HIV prevention revolution
- This is the prevention equivalent of the 1996 “protease moment”, when AIDS was transformed from a death sentence to a chronic manageable condition
- Business as usual in prevention is not good enough

A revolution (from the Latin revolutio, "a turn around") is a fundamental change in power or organizational structures that takes place in a relatively short period of time

Where were we 3 years ago?

Proven HIV prevention methods, pre-2009

- Condoms
- "Seroadaptive behaviours" in gay men
  - Negotiated safety
  - Strategic positioning
  - Serosorting
- Male circumcision
  - 60% reduction in risk in three RCTs in heterosexuals
  - No population impact in gay men
    - Does offer some protection to the insertive partner

New results
Pre-exposure prophylaxis

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The iPREX study: PrEP in homosexual men

- HIV negative MSM in South/North America, Thailand
  - Randomized TDF/FTC vs Placebo

44% reduction

Subgroup	FTC–TDF	Placebo	FTC–TDF	Placebo	Hazard Ratio (95% CI)	P Value
	no. of patients		*no. of events*			
Analysis						
Intention-to-treat	1251	1248	38	72	0.53 (0.36–0.78)	0.001
Modified intention-to-treat	1251	1248	36	64	0.56 (0.37–0.85)	0.005
As treated						0.48
<50% Pill use	NA	NA	13	17	0.68 (0.33–1.41)	
≥50% Pill use	NA	NA	23	47	0.50 (0.30–0.82)	
Pill use						0.02
<90% Pill use	NA	NA	28	34	0.79 (0.48–1.31)	
≥90% Pill use	NA	NA	8	30	0.27 (0.12–0.59)	

- No-one with detectable drug levels became HIV infected
- Is it really 95% effective?

73% reduction

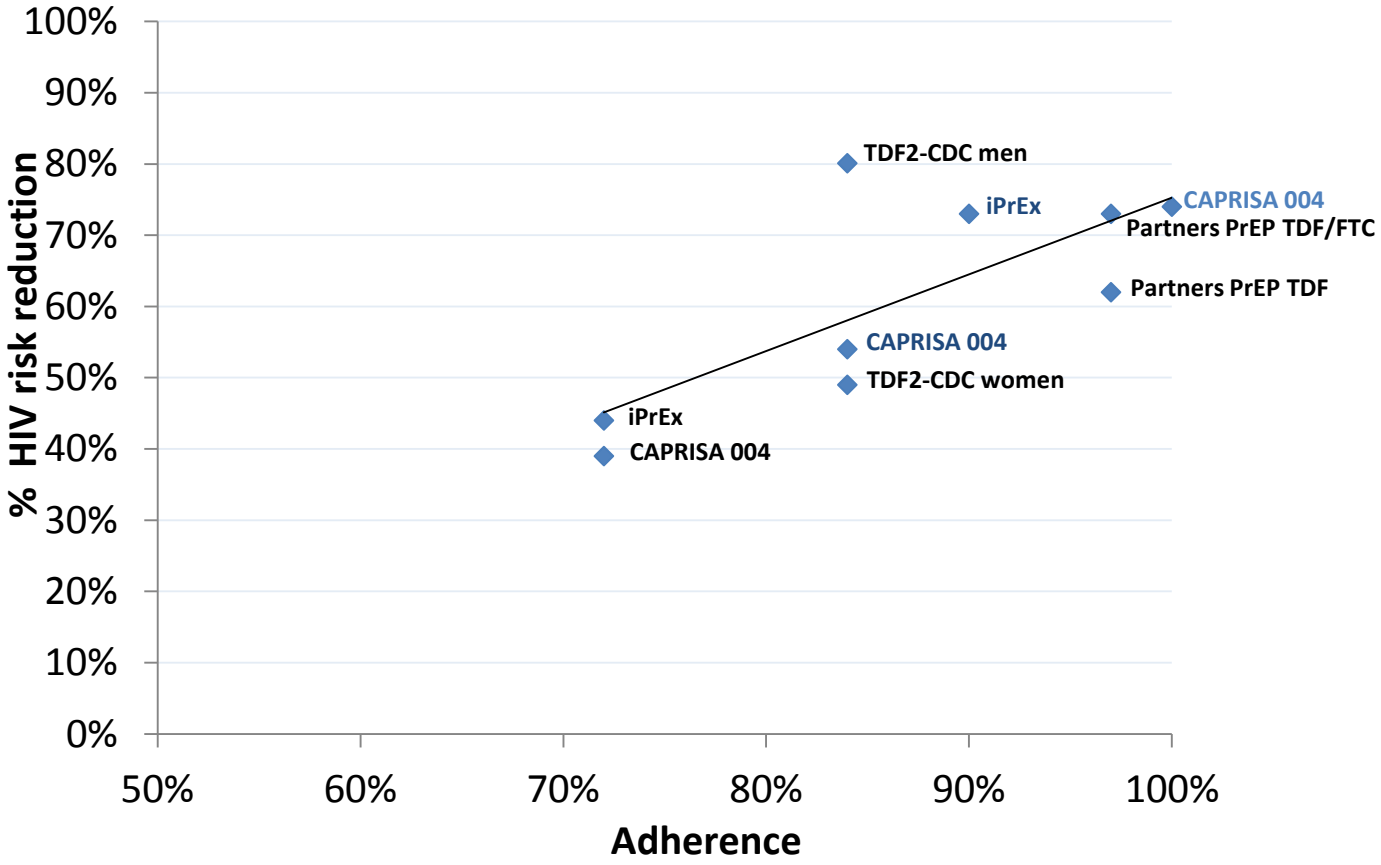
- Should be answered by open-label extension phase, due to report end 2012

RCTs of PREP in heterosexuals

- PARTNERS PrEP (TDF, TDF/FTC; 4,758 heterosexual couples, Africa)
  - Reduction in HIV risk was:
    - TDF 67%
    - TDF/FTC 75%
    - 90% reduction in risk if drug detectable (CROI 2012)
- CDC TDF2 trial (TDF/FTC, 1219 heterosexual men and women in Botswana)
  - 63% reduction in risk
- FEMPREP (TDF/FTC, 1951 African women)
  - RR 0.94, not sig, trial stopped in April 2011. Adherence 30%

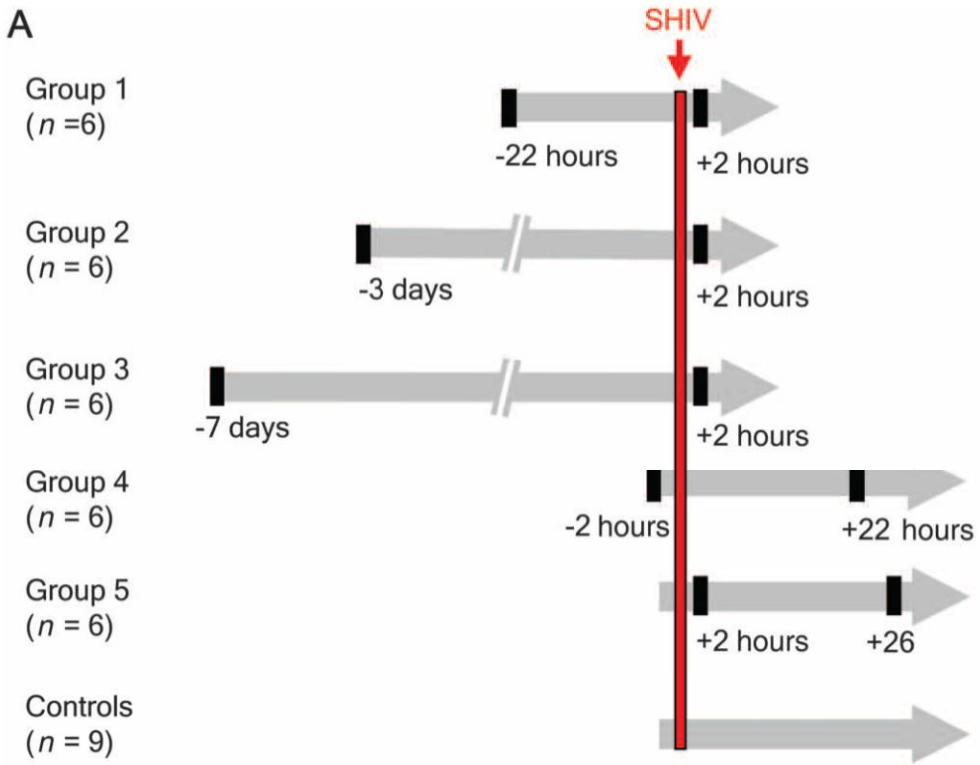
If you take the drug regularly, it protects you

Drug adherence and HIV risk reduction in clinical trials of ARV based oral/topical PrEP



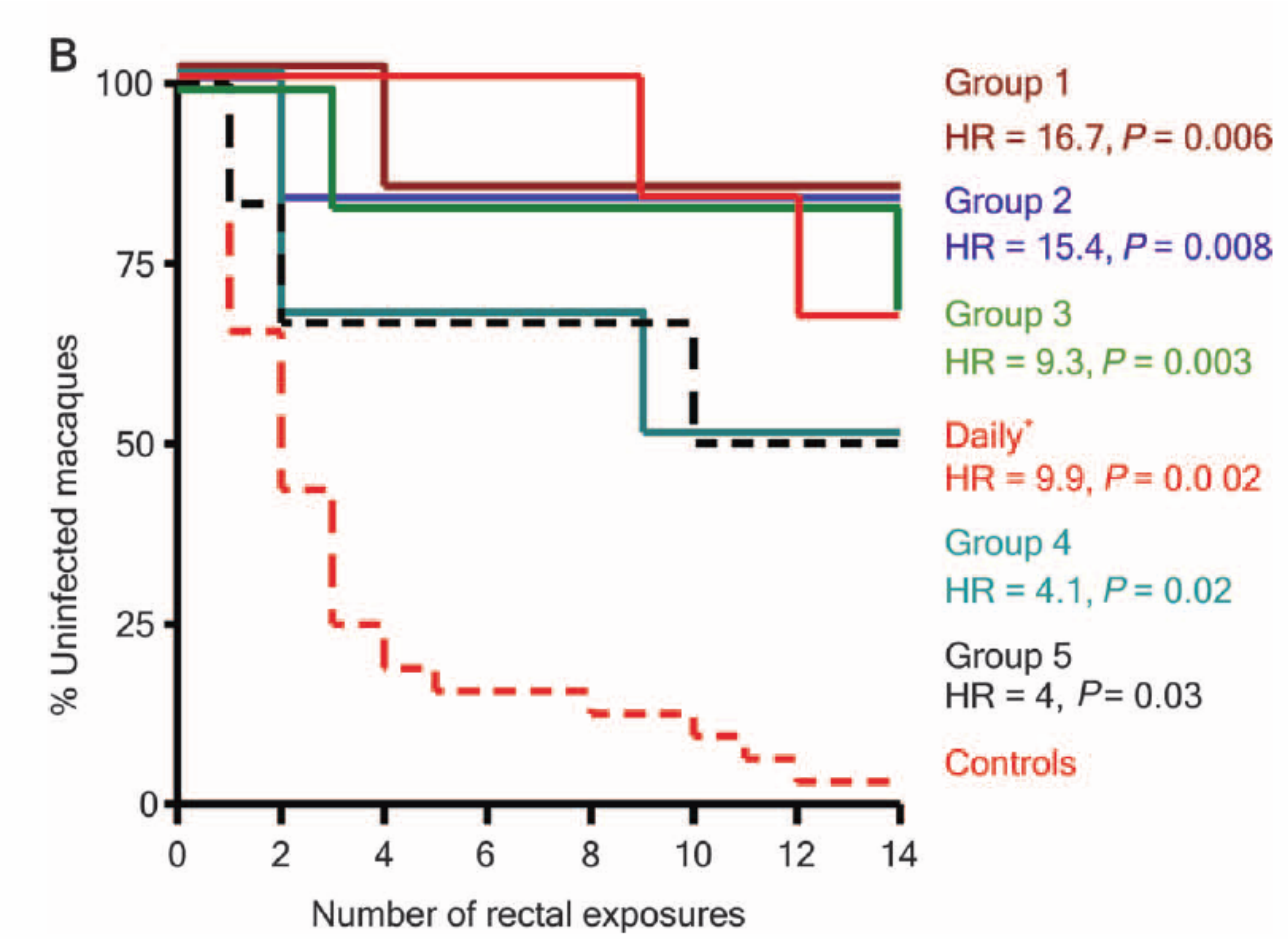
Intermittent PrEP?

Efficacy of intermittent PrEP with TDF/FTC in the repeat low-dose macaque rectal challenge model: design



J. Gerardo García-Lerma, *et al.* *Sci Transl Med* **2**, 14ra4 (2010);

Intermittent PrEP?



New results
Treatment as prevention

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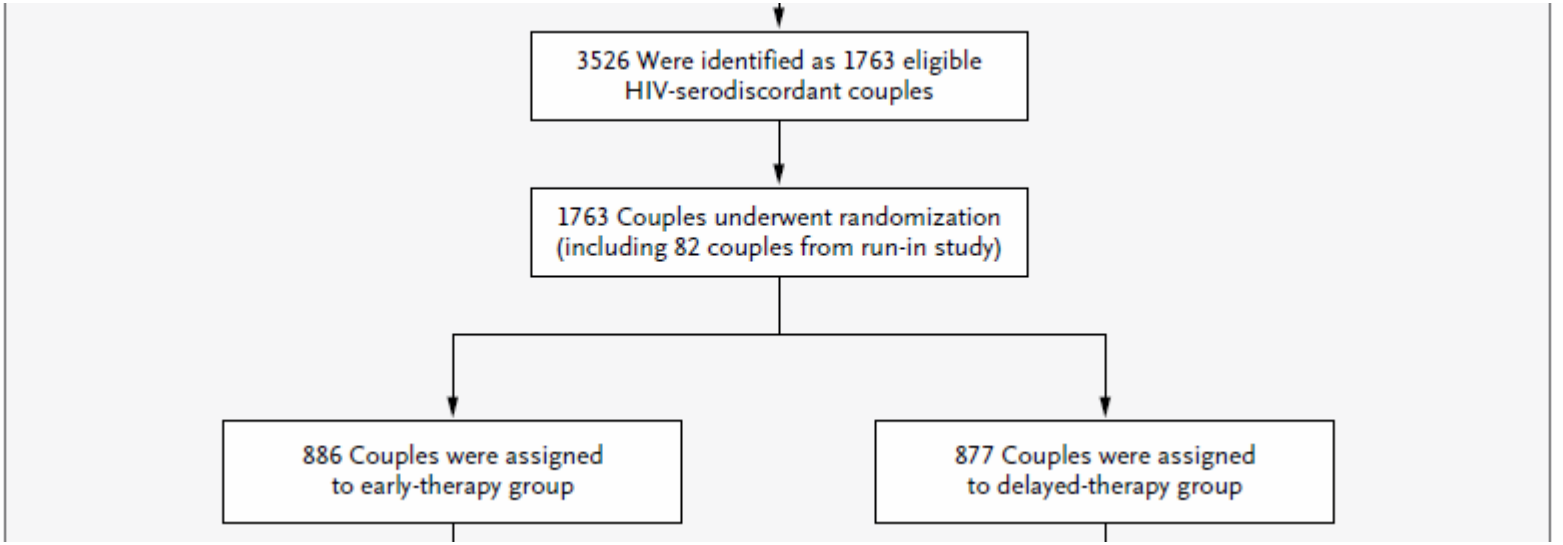
HPTN 052: Does early HIV treatment reduce transmission?

A RCT in HIV serodiscordant heterosexual couples



Cohen, MS et al, 2011

This article (10.1056/NEJMoa1105243) was published on July 18, 2011, at NEJM.org.

A 96% reduction in HIV transmission risk

The NEW ENGLAND JOURNAL of MEDICINE

Table 2. Incidence of Partner-Linked and Any HIV-1 Transmission and Clinical and Composite Events.

Variable	Early Therapy			Delayed Therapy			Hazard or Rate Ratio (95% CI)*
	Events	Person-yr	Rate (95% CI)	Events	Person-yr	Rate (95% CI)	
		no.	%		*no.*	%	
Linked transmission							
Total	1	1585.3	0.1 (0.0–0.4)	27	1567.3	1.7 (1.1–2.5)	0.04 (0.01–0.27)
1 yr	1	819.0	0.1 (0.0–0.7)	16	813.3	2.0 (1.1–3.2)	0.06 (0.00–0.40)
2–3 yr	0	686.5	0.0 (0.0–0.5)	9	682.8	1.3 (0.6–2.5)	0.00 (0.00–0.50)
>3 yr	0	79.9	0.0 (0.0–4.6)	2	71.2	2.8 (0.3–10.1)	0.00 (0.00–4.75)

96% reduction

Science magazine's advance of the year 2011

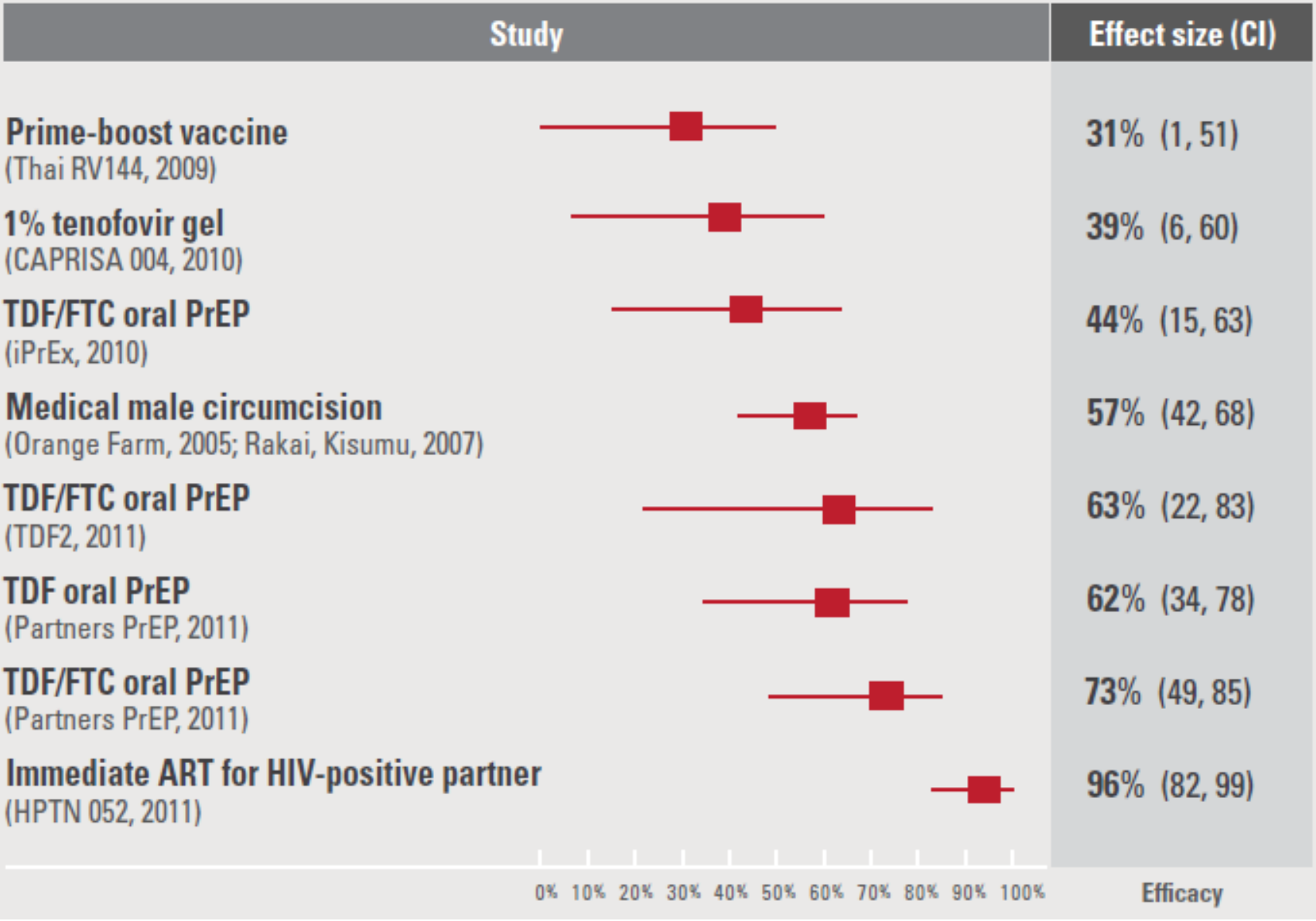
Cohen, MS et al, 2011

This article (10.1056/NEJMoa1105243) was published on July 18, 2011, at NEJM.org.

Treatment as prevention in homosexual men

- A RCT is no longer possible
- Observational studies of treatment and transmission
  - PARTNER study
    - Europe, recruiting currently
  - Opposites Attract
    - NHMRC funded 2011-2015, recruiting in Sydney, Melbourne, Adelaide, Brisbane
- These observational studies will not report back for several years

What Works in HIV Prevention – November 2011



The evidence revolution has happened:

what action is required?

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Required elements of the prevention revolution

- Increase HIV testing in people at risk

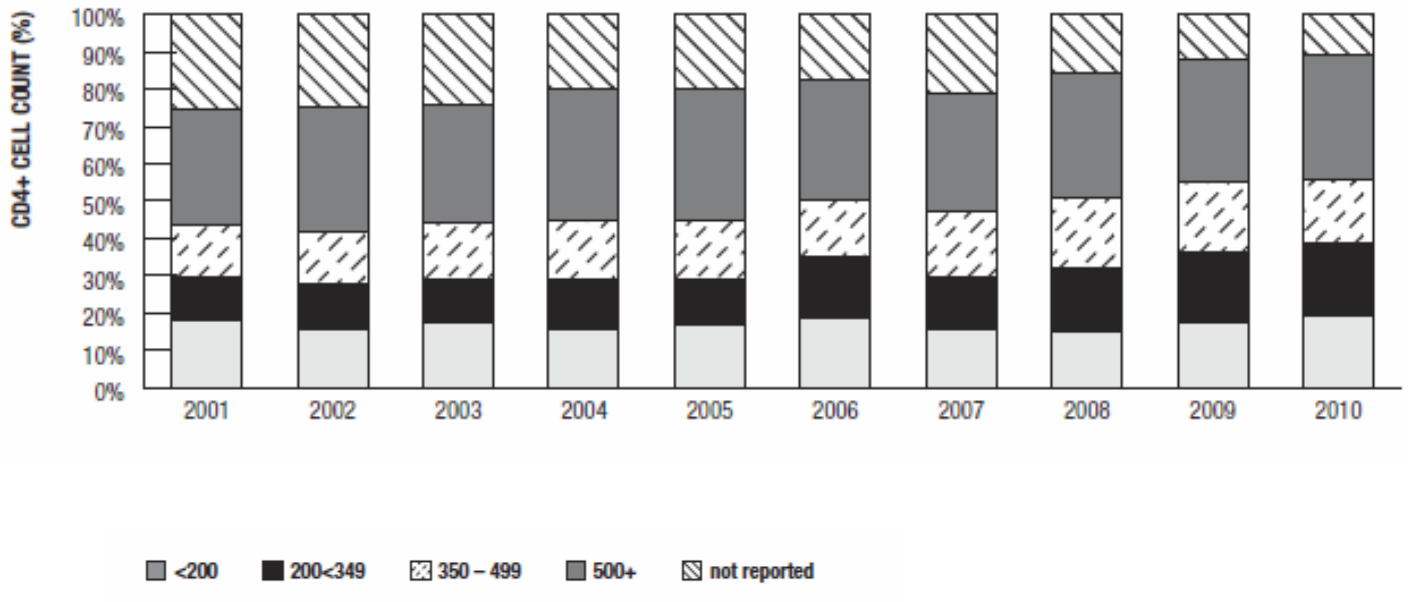
- Treatment as prevention
  - Earlier diagnosis of HIV
  - Increased proportion of those diagnosed with HIV on treatment, ie start treatment early
  - Decreased viral load in the community
  - Decreased new HIV transmissions

- PrEP: a small proportion of high risk HIV negative men

Why increased testing?

Distribution of CD4 at diagnosis, Australia

Figure 40 CD4+ cell count at HIV diagnosis, 2001 – 2010, by year



Median CD4 count at diagnosis: 458
Estimated average time: of 4.6 years between infection and diagnosis

Why aren't gay men getting tested more often?

PASH study (2300 gay men, on line survey)

"I should get tested on a regular basis. However, due to how busy I normally am, it is difficult to find time and make an appointment and organise."

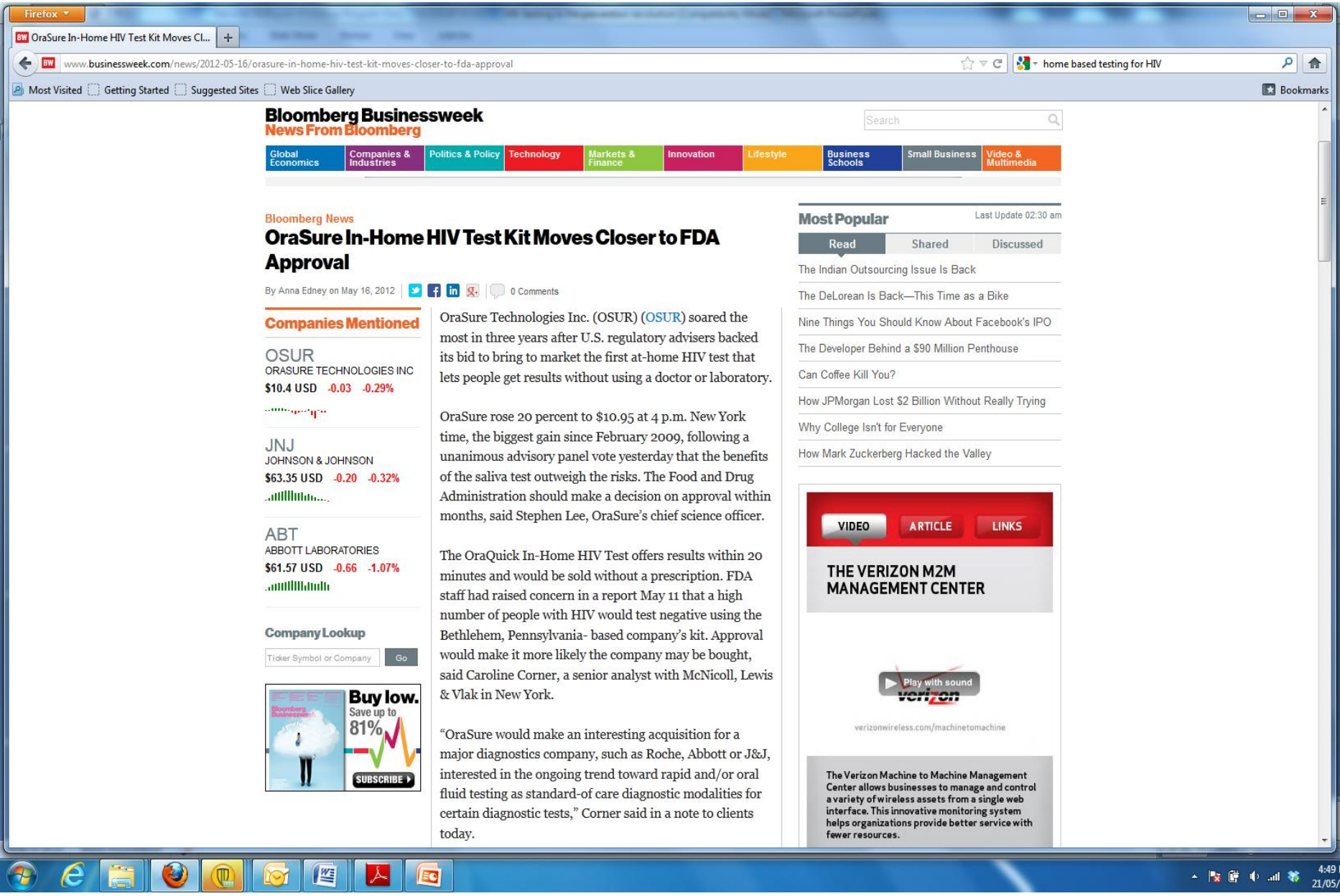
(Adelaide, 22, HIV status unknown)

"If you've already got that obstacle 'I've gotta go out of my way to be tested and now I've got to go out of my way twice a year to be tested' then that's kind of not gonna work. So it's gotta be easier to get tested."

(Sydney, age unknown, HIV-negative)

What might the new testing landscape look like?

- How do we achieve increased HIV testing?
  - "community-based" (shop front) rapid testing;
  - "one-stop" traditional testing with result returned by text or email
    - No follow up visit to see doctor required
  - easier access to free testing;
  - nurse-led testing; results by phone
  - home testing



Bloomberg News

OraSure In-Home HIV Test Kit Moves Closer to FDA Approval

By Anna Edney on May 16, 2012 | 0 Comments

OraSure Technologies Inc. (OSUR) (OSUR) soared the most in three years after U.S. regulatory advisers backed its bid to bring to market the first at-home HIV test that lets people get results without using a doctor or laboratory.

OraSure rose 20 percent to $10.95 at 4 p.m. New York time, the biggest gain since February 2009, following a unanimous advisory panel vote yesterday that the benefits of the saliva test outweigh the risks. The Food and Drug Administration should make a decision on approval within months, said Stephen Lee, OraSure's chief science officer.

The OraQuick In-Home HIV Test offers results within 20 minutes and would be sold without a prescription. FDA staff had raised concern in a report May 11 that a high number of people with HIV would test negative using the Bethlehem, Pennsylvania- based company's kit. Approval would make it more likely the company may be bought, said Caroline Corner, a senior analyst with McNicoll, Lewis & Vlak in New York.

"OraSure would make an interesting acquisition for a major diagnostics company, such as Roche, Abbott or J&J, interested in the ongoing trend toward rapid and/or oral fluid testing as standard-of care diagnostic modalities for certain diagnostic tests," Corner said in a note to clients today.

Companies Mentioned

OSUR
ORASURE TECHNOLOGIES INC
$10.4 USD -0.03 -0.29%

JNJ
JOHNSON & JOHNSON
$63.35 USD -0.20 -0.32%

ABT
ABBOTT LABORATORIES
$61.57 USD -0.66 -1.07%

Company Lookup
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Testing: what do we need to know?

Many research questions

- Do gay men (and others at high risk) know about the benefits of early treatment, and is this related to frequency of testing?
- What are gay men's preferences for how testing should be offered?
- What is the doctor's role in testing?
- How can we reduce the time between risk events and testing?
- How can we reduce the time between infection and testing?
- What are the characteristics of men who are at risk of HIV infection but never tested or tested less frequently?

- **How do we measure the effectiveness of the new testing models being trialled?**
  - Shop front; venue-based; rapid v conventional; one-stop

Treatment revolution

United States guidelines on Initiating Antiretroviral Therapy in Treatment-Naive Patients: when to start (revised March 2012)

- Antiretroviral therapy (ART) is recommended for all HIV-infected individuals. The strength of this recommendation varies on the basis of pre-treatment CD4 cell count:
  - CD4 count <350 cells/mm^3 (AI; strong recommendation, based on RCT)
  - CD4 count 350 to 500 cells/mm^3 (AII; strong recommendation, based on observational evidence)
  - CD4 count >500 cells/mm^3 (BIII; moderate recommendation, based on expert opinion)

Treatment revolution

United States guidelines on Initiating Antiretroviral Therapy in Treatment-Naive Patients: treatment as prevention

- " Effective ART also has been shown to prevent transmission of HIV from an infected individual to a sexual partner; therefore, ART should be offered to patients who are at risk of transmitting HIV to sexual partners
  - AI [heterosexuals; strong recommendation, based on RCT]
  - AIII [other transmission risk groups; strong recommendation, based on expert opinion]; "

HIV treatment guidelines

CD4 count	US DHHS since March 2012	Australian commentary on US DHHS May 2012	EACS Oct 2011	BHIVA (April 2012)	WHO (since Nov 2009 and updated Apr 2012)
< 350	ART recommended at any CD4+, strength of recommendation varies by CD4 count	ART recommended	ART recommended	ART recommended	ART recommended
350-500		Defer unless certain conditions exist…..	use of ART should be considered…..	Defer unless certain conditions exist…..	Defer unless certain conditions exist…..
> 500		Defer unless certain conditions exist…..	Defer ART unless meets one of the criteria described…..		Defer unless certain conditions exist…..

Australian commentary on new US guidelines

- When to start
  - "The panel did not achieve consensus on this comment"
  - "The panel notes that the currently available data addressing the issue of when to commence therapy above this level are predominantly observational. Randomised controlled studies are underway but results are not yet available."
  - "There is accumulating observational data suggesting benefit in terms of mortality and AIDS free survival when antiretroviral therapy is commenced at a CD4 cell count between 350 and 500 cells /μL"

- Treatment as prevention
  - "The panel did not achieve consensus on this comment."
  - "Differences in the capacity of ART to reduce HIV transmission between the subjects studied in that trial and Australian MSM may exist and some clinicians reasonably take the view that initiation of ART in Australian MSM primarily to prevent HIV transmission is premature"

My 2 cents worth...

Should we be starting treatment earlier?

- Untreated, HIV is (virtually) uniformly fatal
- All people with HIV will require treatment sooner or later
- The difference between starting at 400 and starting and 600 is about 3 years (out of 35+ years of treatment for the average 30 old with new HIV infection)
- There is a transmission benefit, and we should be telling our patients about it
  - Many/some of our positive patients will want it
  - A fully informed decision on “when to start” should be informed by the transmission evidence

The new treatment as prevention landscape

(treatment as) prevention belongs in the clinic

- Increased treatment
  - Information giving about the likely reduction in transmissibility associated with treatment
  - PLWHIV given the option of starting treatment early
  - We need new and revamped
    - Individuals/couples prevention counselling
    - community education
- Doctors are the gatekeepers for these new techniques
  - will we/they recommend treatment as prevention?
- Will PLHIV want to take it?

PrEP

Two proposals currently under consideration for funding

- Trial with wait list controls

or

- Demonstration projects

- Measure
  - Adherence
  - Toxicity
  - Behaviour change
  - Real world efficacy
  - Who should/who wants to take it

Pre-exposure prophylaxis

Research questions

- Do gay men want it, and will they take it everyday?
- What happens in the real world (demonstration projects)?
  - Does risk behaviour increase?
  - Do transmissions happen?
  - Do men tend to take it intermittently rather than continuously?

Treatment as prevention

Research questions

- Does it work in gay men?
  - Opposites attract study recruiting now!
- What are doctors attitudes to early treatment, and how does this influence decisions to start.
- Attitudes of PLWHIV to early treatment.
- How will we monitor whether it is happening?
- How will we monitor whether it is effective?

The most fundamental change in the HIV epidemic since 1996

A major challenge for the HIV partnership

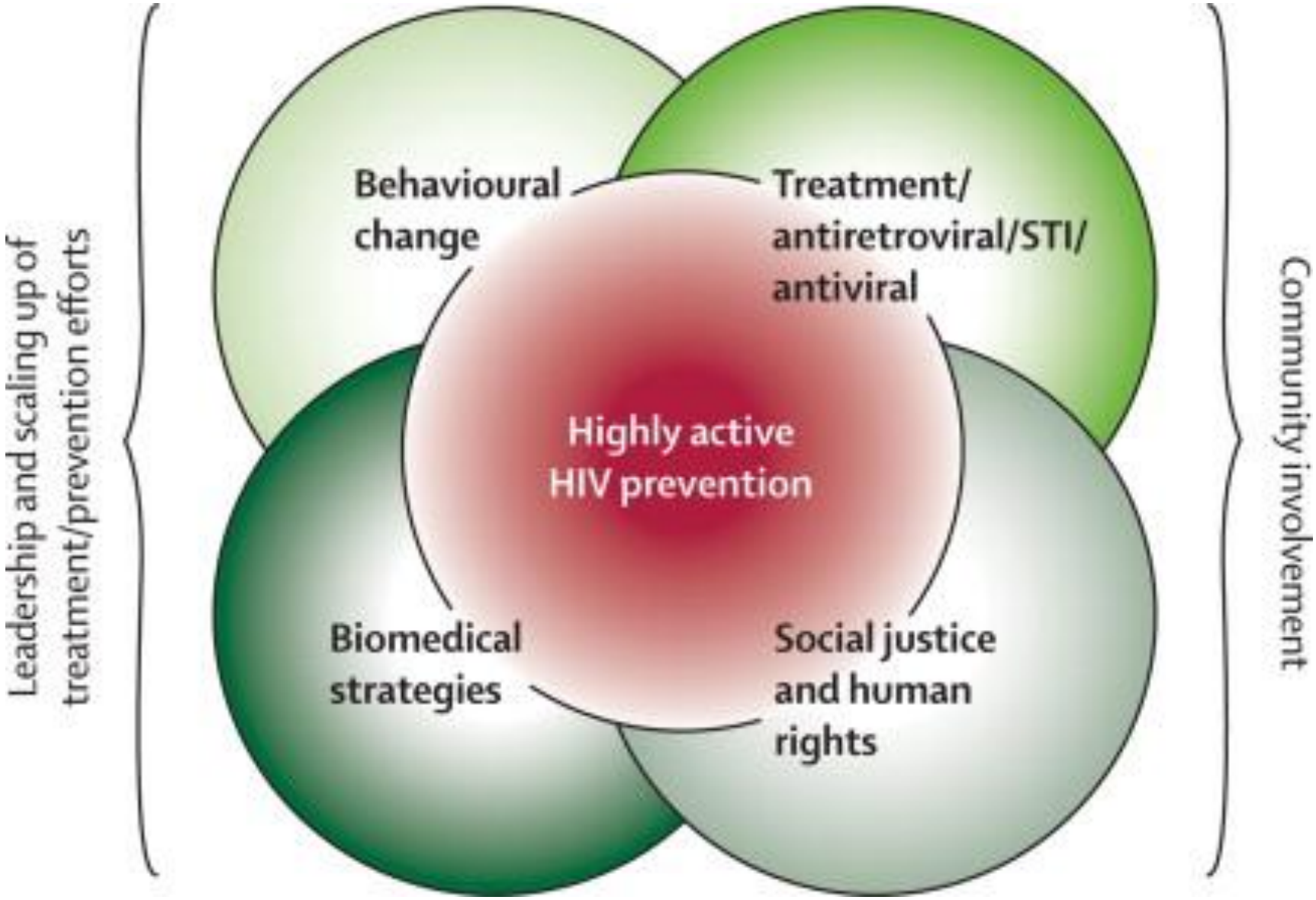
- Policy makers
  - What reduction in transmission should we be aiming for?
  - What will give the best bang for buck?
  - How can we do this without investing (much) more money?
  - Can we act with imperfect evidence?

- Clinical
  - A fundamental re-alignment is necessary to address HIV prevention issues in the clinic
  - Prevention and treatment are closely aligned.
  - What should I tell my patients?

The most fundamental change in the HIV epidemic since 1996

A major challenge for the partnership

- Research/science
  - What works?
  - What about behaviour and social factors?
  - How do monitoring and surveillance need to change?
- Community
  - How do we ensure community members will receive the benefits of this change?
  - How do we educate the community and couples and individuals?
  - What is the role of activism?
- Industry
  - How can we fund preventive therapies?


Leadership and scaling up of treatment/prevention efforts
Behavioural change
Treatment/ antiretroviral/STI/ antiviral
Highly active HIV prevention
Biomedical strategies
Social justice and human rights
Community involvement

Thanks to...

- Garrett Prestage, Ian Down, Kathy Triffit, Rebecca Guy, Mary Poynten, Iryna Zablotska, Jeff Jin, Ben Bavinton, Michelle McKechine, Lara Cassar, David Templeton

- David Wilson

- All those who have heard a version of this talk before today!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