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Partner notification

(and the ‘arrested immunity’ hypothesis)

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Outline

- The ‚arrested immunity' hypothesis
- Partner notification definitions and history
- Partner notification aims and outcomes
- Effectiveness
- Discussion

The ‚arrested immunity' hypothesis

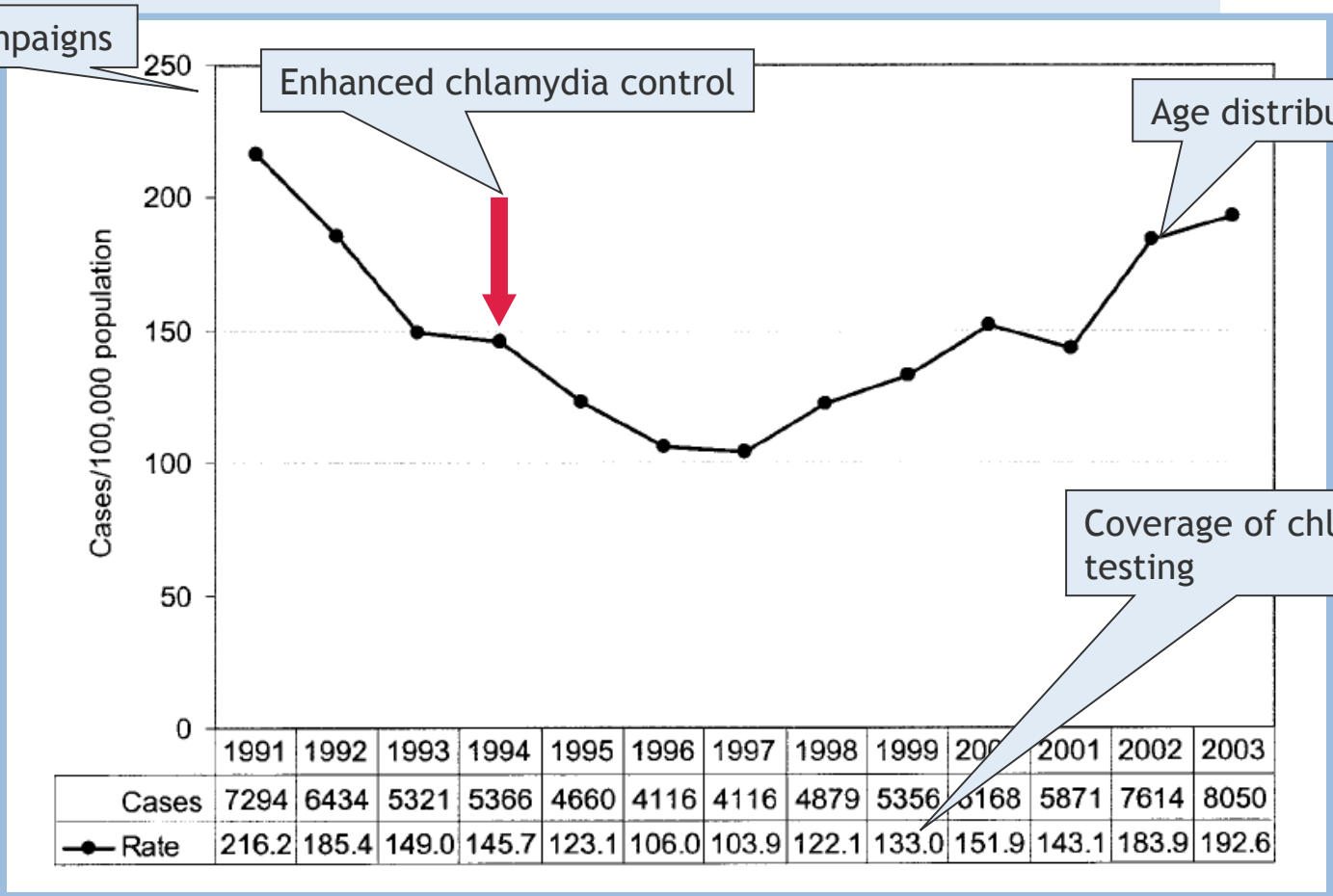
> "Early, expanded treatment interrupts the natural immune response enhancing population susceptibility to infection as susceptible patients re-enter the same sexual networks."[1]

In other words, when we treat Chlamydia early we reduce the body's ability to fully respond immunologically and this increases the likelihood of reinfection upon re-exposure. This is most important for patients who return to the same or similar sexual networks with the same or similar sexual risk patterns, as is often the case. There are five lines of evidence that support this intriguing proposition.[2]

- Assumes population level data exist to demonstrate that
  - —A programme of chlamydia screening and treatment reached enough of the population of British Columbia to reduce chlamydia prevalence over time
  - —Re-infection rates have increased in the population
  - —A mathematical model incorporating immunity is plausible

1. Brunham RC et al. *J Infect Dis* 2005; 2. Rekart ML & Brunham RC. *Sex Transm Infect* 2008

Chlamydia surveillance, British Columbia



	1991	1992	1993	1994	1995	1996	1997	1998	1999	200	2001	2002	2003
Cases	7294	6434	5321	5366	4660	4116	4116	4879	5356	5168	5871	7614	8050
Rate	216.2	185.4	149.0	145.7	123.1	106.0	103.9	122.1	133.0	151.9	143.1	183.9	192.6

Brunham RC et al. *J Infect Dis* 2005

Chlamydia test coverage in British Columbia

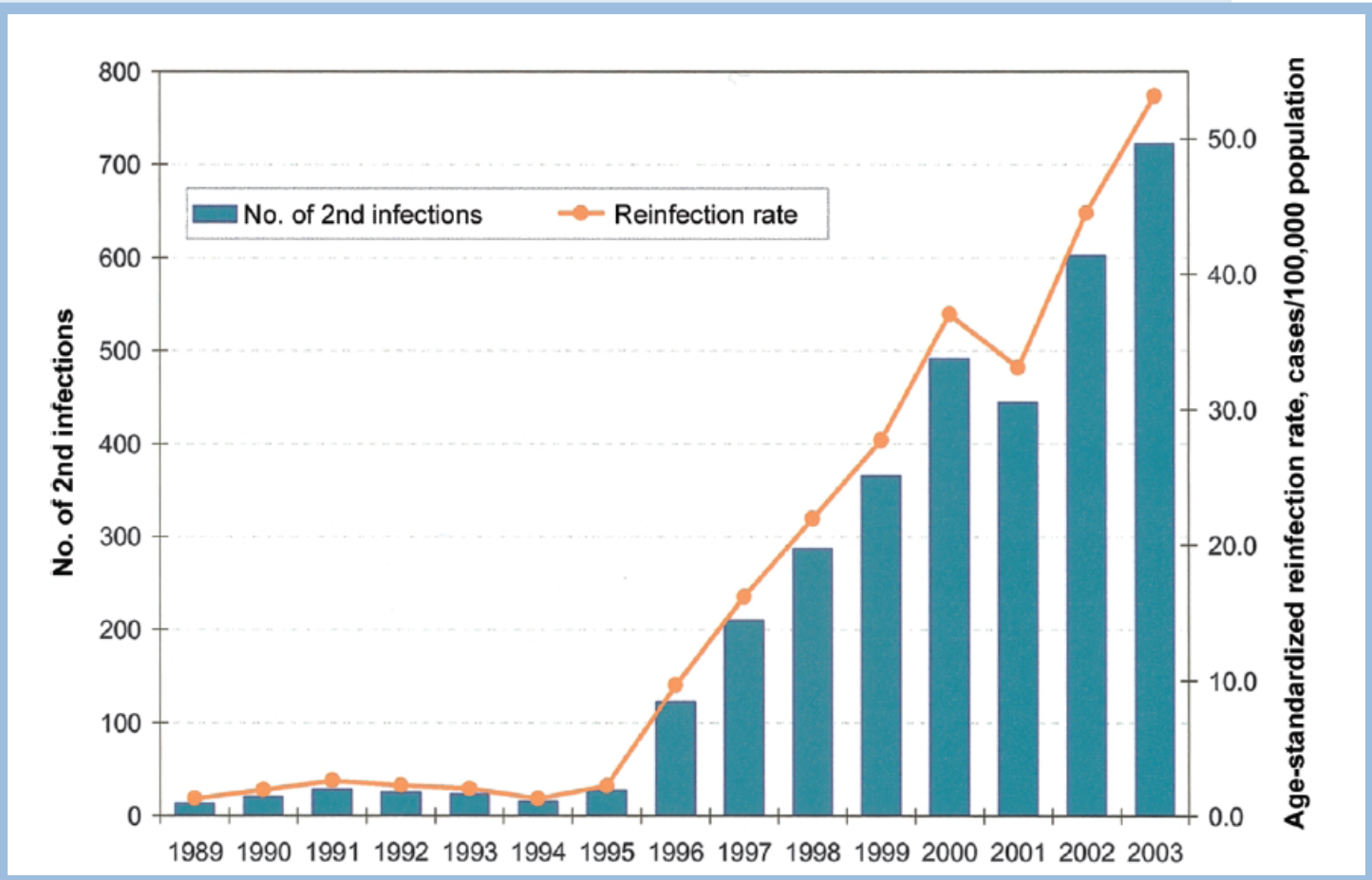
Year	Chlamydia	Total rate	Total pop	15-34 years*	Expected cases**	Expected % detected
1991	7294	216.2	3373500	1044000	52200	14
1992	6434	185.5	3468400	1059300	47669	13
1993	5321	149.2	3567400	1076900	43076	12

* Assume all chlamydia tests in 15-34 year olds; ** Assume prevalence 5%

- Coverage of population each year 10-20%
  - —i.e. Leaving 80-90% untested each year is sufficient to reduce prevalence
- Mathematical model reproduces surveillance trend at coverage of 80% per year

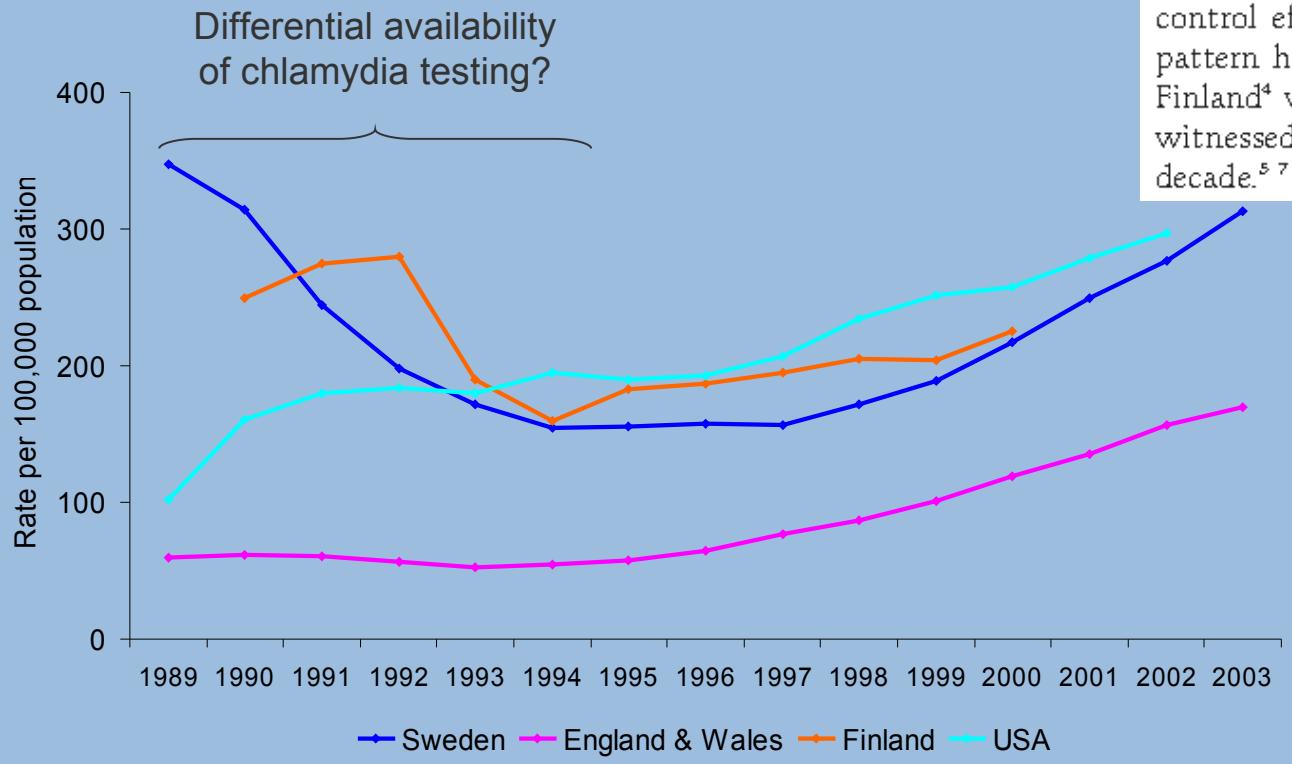
Low N. *Sex Transm Infect* 2008

Re-infection and testing rates



Brunham RC et al. *J Infect Dis* 2005

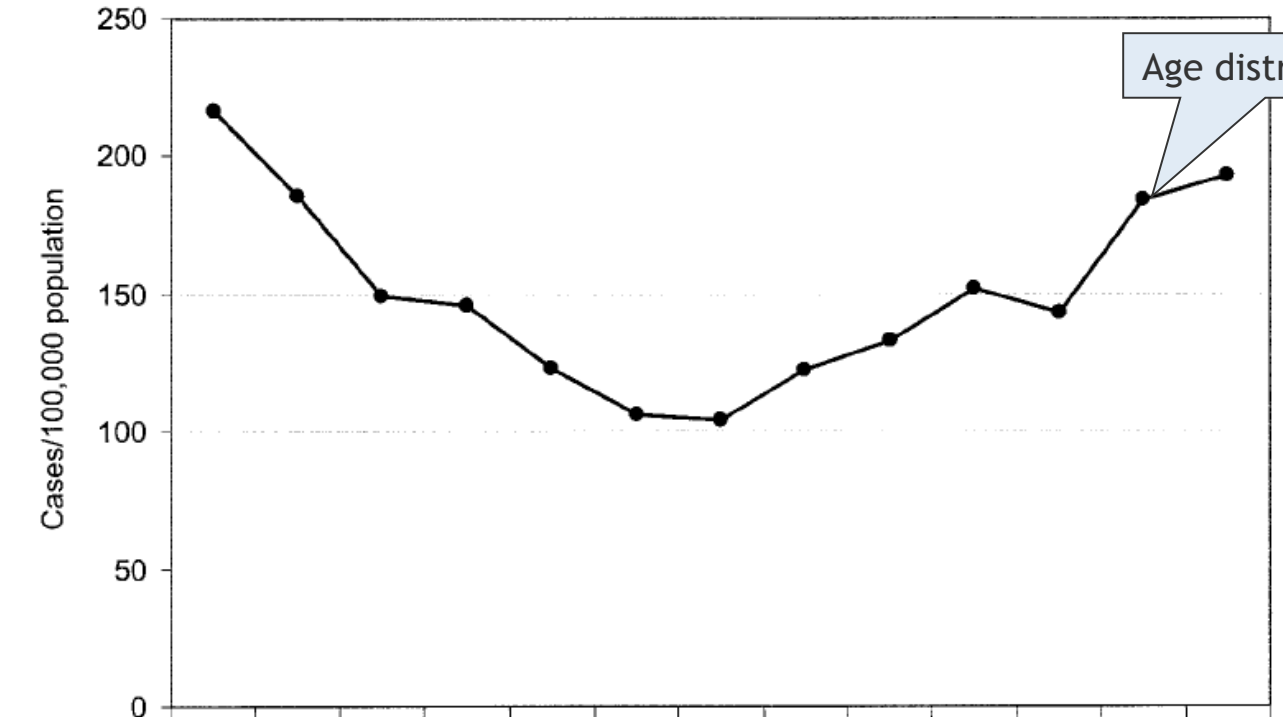
Chlamydia reports, 1989 to 2003



From 1985 2005, Sweden witnessed a very similar trend of decreasing cases followed by increasing cases in the face of enhanced awareness and control efforts (fig 1).[2 3] This downward-upward pattern has also been reported from Norway and Finland[4] whereas the USA, the UK and Australia witnessed steady increases throughout the last decade.[5 7] For developing countries, the World

Adapted from Low N. Eurosurveillance http://www.eurosurveillance.org/ew/2004/041007.asp#5

Age at infection



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Brunham RC et al. *J Infect Dis* 2005

Chlamydia rates decrease with age

condom usage. The evidence for immunity is strengthened by the finding that increasing years of sex work is protective against Chlamydia infection.[21] If natural immunity plays an

- Additional contributing factors
  - —? Lower rates of partner change at older ages
  - —? Increased condom use at older ages?
  - —? Lower risk of STI in male partners in older women

Rekart ML and Brunham RC. *Sex Transm Infect* 2008; 21. Brunham RC et al. *J Infect Dis* 1996

Interest in vaccine development

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1. authors also assert that the long term goal of prevention of Chlamydia will require the development of a vaccine and that *C trachomatis* immuno-epidemiology has emerged as an urgent research priority.[35]

2. population level. Nevertheless, we conclude that, with the data in hand, research and development of a vaccine remains an important and perhaps the necessary solution to halt the spread of *C. trachomatis* infection at the population level.

>Vaccine development desirable but difficult

>In a mouse model, antibiotic treatment of chlamydial infection impairs development of protective immune response

1. Brunham RC and Rekart ML. *Sex Transm Infect* 2008; 35. Brunham RC and Rekart ML. *Sex Transm Dis* 2008
2. Brunham RC et al. *J Infect Dis* 2005

Summary

- No empirical evidence for a population level effect of early treatment
  - Surveillance data inappropriate for validation
  - Insufficient coverage of chlamydia control
- Reducing rates of PID are inconsistent with increased susceptibility to re-infection and immunologically mediated tubal damage
  - But are consistent with changing treatment patterns
- Treatment of infected individuals still needed
- Another way of reducing re-infection rates...

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Partner notification

Partner notification – contact tracing

- The process of
  - identifying sex partners of people with sexually transmitted infections;
  - informing them of their potential exposure;
  - ensuring evaluation and/or treatment;
  - providing advice about preventing future infections.

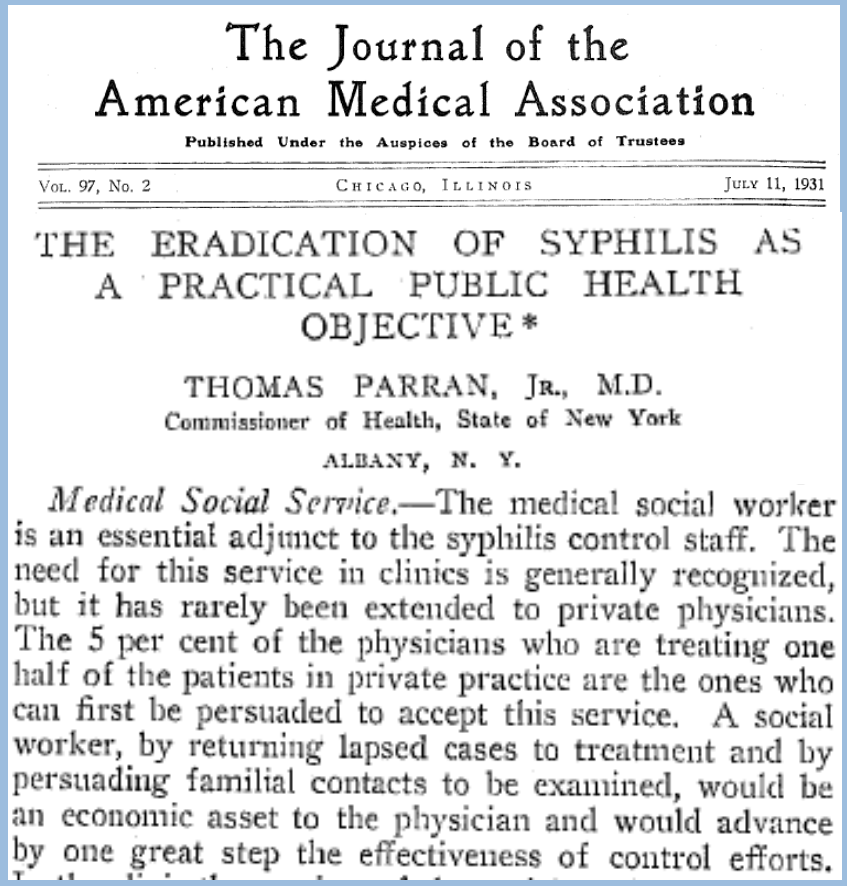
WHO/UNAIDS. Best Practice Collection, 1999

Partner notification origins

- 18th century
  - Danish priests worked with local governmental authorities to "notify persons known or suspected of being infected" with syphilis
- 19th century
  - Sweden, linked to compulsory treatment and free medical care
- 1930s
  - USA, included in "Platform for action" for syphilis control
  - UK, World War II – following efforts to control venereal disease in American troops
- 1960s onwards
  - Subsequently extended to include gonorrhoea
- now… chlamydia, trichomonas, HIV

Parran T. *JAMA* 1931; Shadow on the Land 1937; Wigfall AS. *Br J Ven Dis* 1972

Model for modern contact tracing



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THE ERADICATION OF SYPHILIS AS A PRACTICAL PUBLIC HEALTH OBJECTIVE *

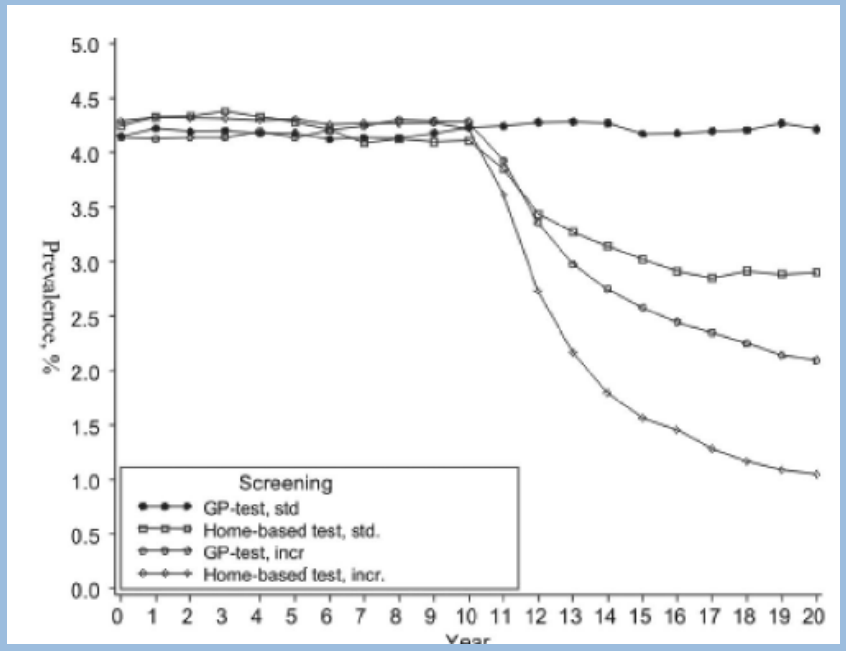
THOMAS PARRAN, JR., M.D.
Commissioner of Health, State of New York
ALBANY, N. Y.

Medical Social Service.—The medical social worker is an essential adjunct to the syphilis control staff. The need for this service in clinics is generally recognized, but it has rarely been extended to private physicians. The 5 per cent of the physicians who are treating one half of the patients in private practice are the ones who can first be persuaded to accept this service. A social worker, by returning lapsed cases to treatment and by persuading familial contacts to be examined, would be an economic asset to the physician and would advance by one great step the effectiveness of control efforts.

- "Shoe leather epidemiology"
- Medical social workers, health visitors, public health nurses
  - —Disease intervention specialists (USA), health advisers (UK)
- Visits to homes of sexual contacts of people with syphilis
- Treatment of incubating (90 days) syphilis

Parran T. *JAMA* 1931, Shadow on the Land 1937

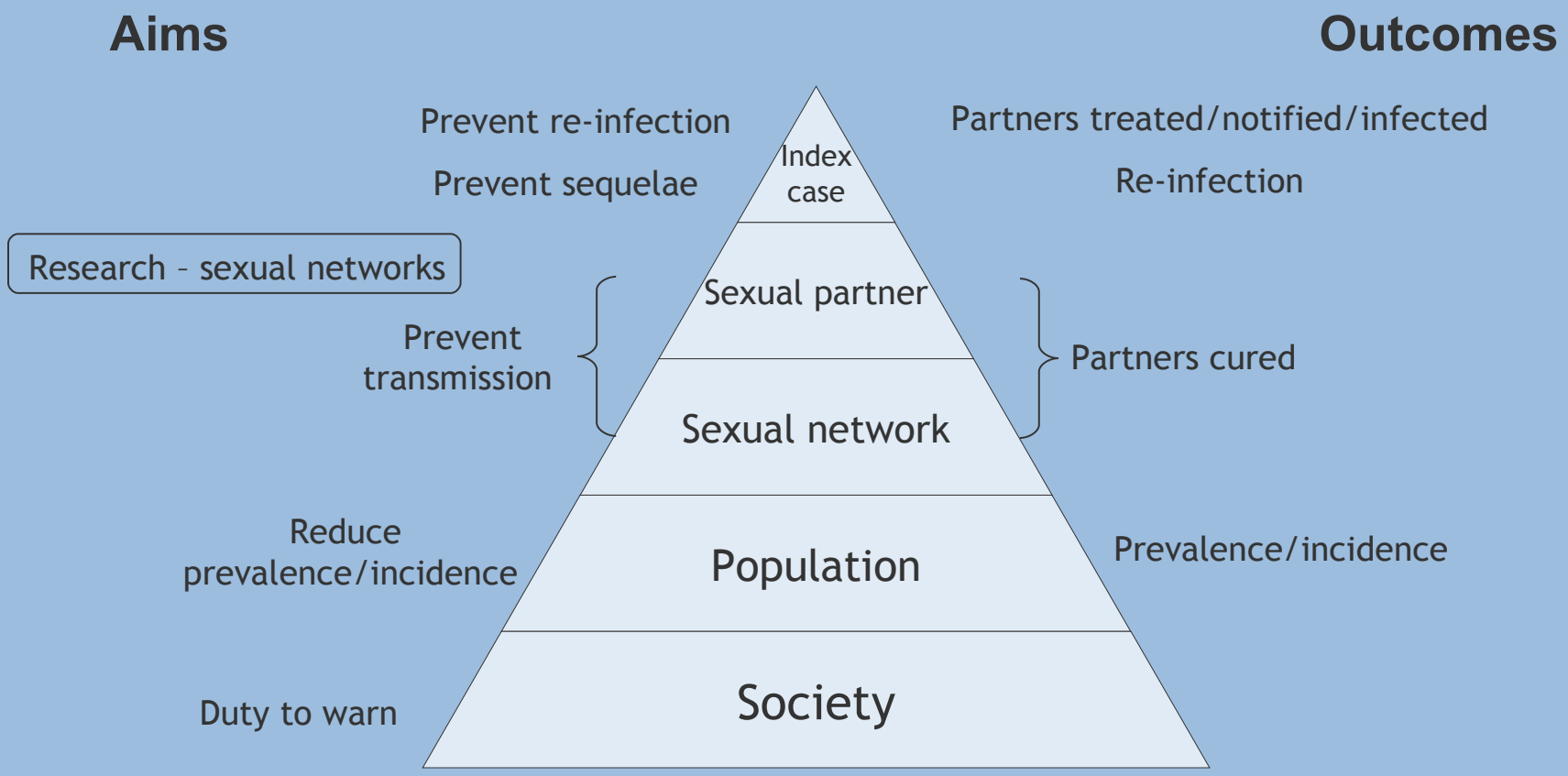
Rationale for contact tracing



- Integral part of STI control
- $R_0 = \beta * c * D$
- Reduce duration of infection
- Interrupt transmission through sexual networks
- Partner notification should have independent benefit in controlling transmission of infection
- No empirical data yet

Andersen B et al. *Sex Transm Dis* 2006;33:407-15.

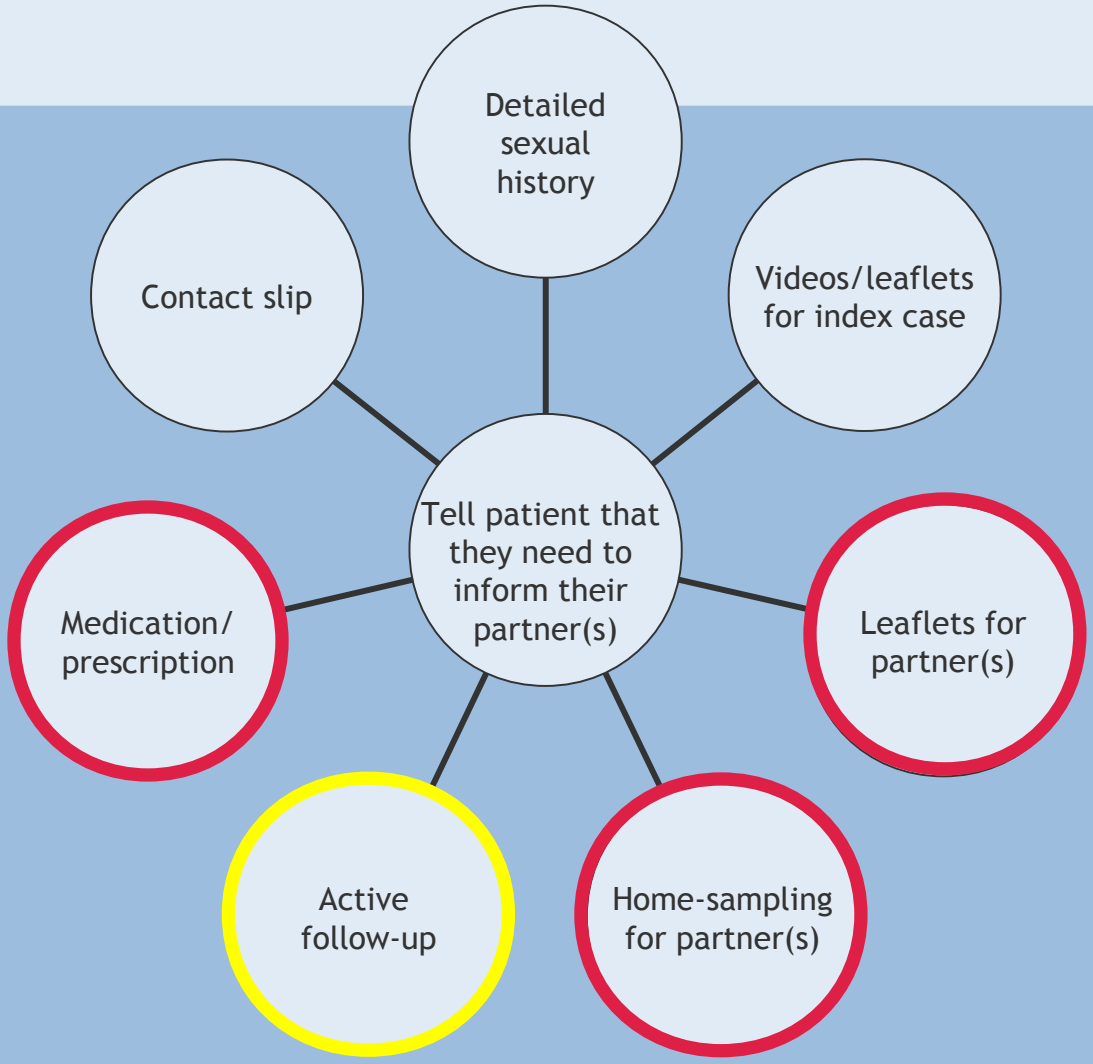
Partner notification aims and outcomes



Partner notification methods

- Provider referral
  - Health professional notifies sexual contacts of index case
  - Originally developed for syphilis control
  - Still done for syphilis and HIV
- Patient referral
  - Index case informs sexual contacts
  - Most commonly used method for bacterial STI
- Conditional/contract referral
  - Index case informs sexual contacts, but if not done within an agreed time period, health professional will do so
  - Pragmatic alternative to provider referral

What is patient referral?



Expedited partner therapy

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- Patient-delivered partner therapy
  - Medication
  - Prescription
  - Legal status uncertain in many settings
- Belgium, Denmark, Finland, Netherlands, Ireland, Norway, Portugal, Scotland, Spain, USA at least sometimes, mainly for chlamydia
- In UK, 'accelerated partner therapy' legal if partner assessed before receiving medication
  - By phone
  - By a pharmacist

Golden M et al. Chapter 54, Sexually Transmitted Diseases (4th Ed.); Arthur G et al. *Sex Transm Dis* 2005; Estcourt C, personal communication.

Who does partner notification and how often?

- USA
  - Public health clinics – Disease intervention specialist
  - Provider referral
  - 12% chlamydia, 17% gonorrhoea, 33% HIV, higher for syphilis
- UK
  - Genitourinary Medicine clinics – health advisers
  - Patient referral first choice for all infections
  - Most gonorrhoea, chlamydia, syphilis
  - 1997 – 15-20% HIV
  - Primary care – 1/3 refer, 1/3 treat
- Sweden
  - Partner notification legally required
  - Public health nurses
  - Not done in about 1/3 chlamydia cases
  - Conditional referral

Golden M et al. Chapter 54, Sexually Transmitted Diseases (4th Ed.); Arthur G et al. *Sex Transm Dis* 2005;32:734-41.

Partner notification yields

	United States	UK
	Infected partners/case treated mean (range)	Partners/case seen mean (95% CI)
Gonorrhoea	0.25 (0.09-0.58)	0.58 (0.47-0.71)
Chlamydia	0.22 (0.05-0.53)	0.61 (0.55-0.66)
Syphilis	0.22 (0.05-0.53)	NA
HIV	0.13 (0.03-0.75)	NA

Brewer DD. *Sex Transm Dis* 2005; Low N et al. *Sex Transm Infect* 2004

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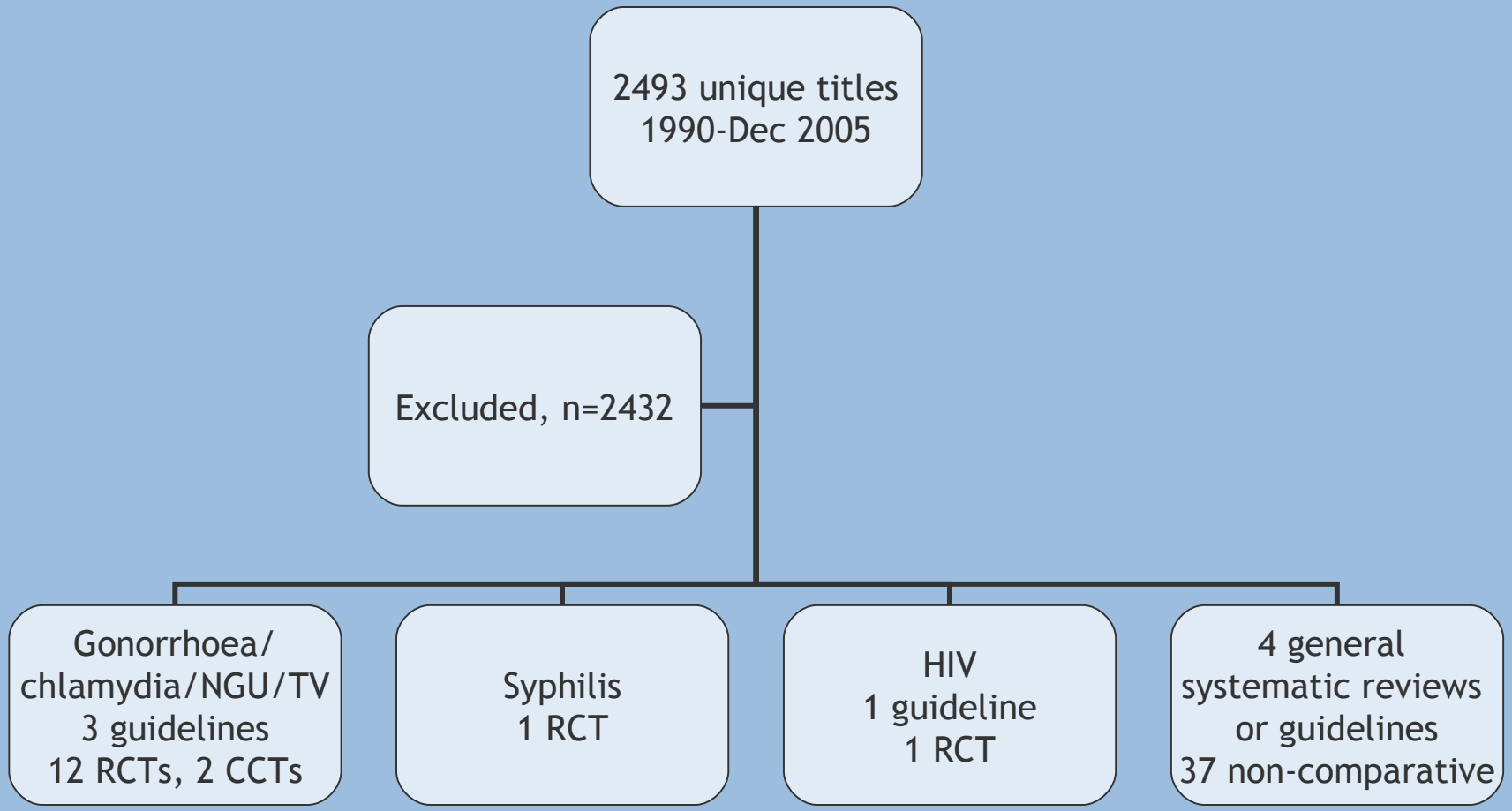
Improved effectiveness of partner notification for patients with sexually transmitted infections: systematic review

Sven Trelle,[1] Aijing Shang,[1] Linda Nartey,[1] Jackie A Cassell,[2] Nicola Low[1]

Trelle S et al. *BMJ 2007;* Trelle S et al. http://www.nice.org.uk, 2006

Search results



Which method of patient referral?

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- 16 interventions in 14 trials
  - 8 trials comparing different forms of additional information
  - 2 trials comparing home-sampling for partners
  - 6 trials examining patient-delivered partner therapy
- 4 trials in Africa using syndromically diagnosed infections
  - 3 additional information
  - 1 patient-delivered partner therapy
- 4 trials reporting primary outcomes – re-infection
  - All patient-delivered partner therapy
- Differences in control interventions

Information to supplement patient referral

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- 6452 patients
- Additional written information for index patients to give to partners – 2 trials in USA
  - Gonorrhoea/chlamydia and trichomonas
  - Compared with minimal patient referral, no contact slips
- Counselling/interactive discussions for index cases – 2 trials in Africa
  - Syndromes
  - Compared with patient referral including contact slips
  - One included health care voucher for partner in intervention arm
- Structured verbal information – script or video
  - Compared with minimal patient referral with contact slips
- Combined methods of providing additional information

Home-sampling

- 658 participants in 2 trials in Denmark
- Index cases notified by post from microbiology lab
- Received home sampling kits to give to partners
  - Partner self-collects specimen and mails to lab
  - Partner takes kit to GP

Patient-delivered partner therapy

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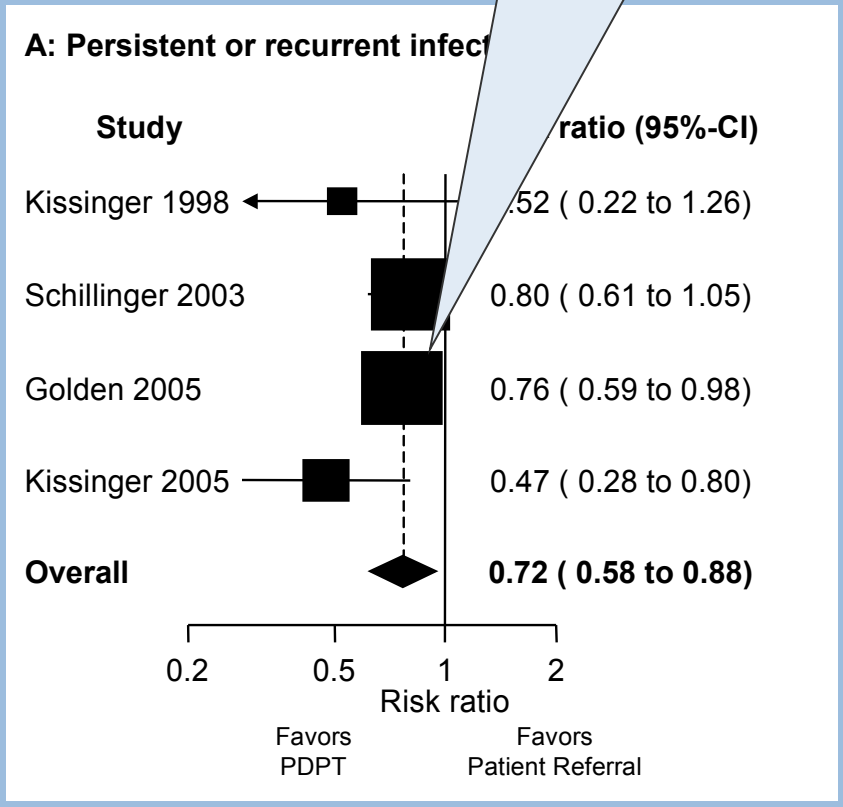
- >6000 patients in 6 trials
- Gonorrhoea/chlamydia; trichomonas; syndromic diagnosis
- Compared with minimal patient referral without contact slips
  - 2 trials also included comparison between patient-delivered partner therapy and patient referral supplemented by additional information that index cases gave to partner(s)
- 4 trials gave participants in experimental group additional information and/or condoms

Patient-delivered partner therapy – combined outcome

Effective for gonorrhoea but not chlamydia (p=0.04 for interaction)



Patient-delivered therapy was not more effective in reducing re-infection compared with providing additional information for index cases to give to partners (2 trials)

Adverse effects

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- 2 randomised trials – Uganda and Zimbabwe
  - Syndromically diagnosed infections
  - No differences according to method of partner notification
  - Quarrelling, fighting
  - No physical violence reported
- Non-randomised studies
  - Relationship breakdown
- Qualitative studies
  - Barriers - Stigma, fear
  - Patients in primary care prefer to have partner notification done there

Subgroups

- No consistent evidence of differences in outcomes between
  - African American and white
  - Men who have sex with men and heterosexual, but only for identified contacts
  - Younger and older adults
- Setting
  - 1 trial reporting similar/better outcomes in patients receiving patient referral from practice nurse than those referred to specialist sexual health advisers at genitourinary medicine clinic
  - 30% of patients referred to clinic defaulted

Discussion

- Partner notification is a difficult intervention
- Essential part of STI management
  - No evidence of reduction in transmission of infection at population level attributed to partner notification alone
  - Evidence that re-infection rates in index case can be reduced
- Methods of patient-referral that involve index case in informing partner show benefit over basic patient-referral
  - Patient-delivered therapy superior to minimal patient referral
  - Patient-delivered therapy not superior to patient-referral supplemented by additional information for partner(s)
  - Home sampling might be useful but comparison against standard patient-referral required

Discussion

- Potential new methods
  - Internet sites
  - Social networks
  - Home-sampling
- Resource poor settings
  - Better diagnostics
- Evaluations
  - Biological endpoints
  - Population effects

Thanks to…

- **The ClaSS project team, Universities of Bristol and Birmingham, UK –** especially Anne McCarthy, John Macleod, Paddy Horner, Karl Pye, Chris Salisbury, Anna Graham, Rona Campbell, Tracy Roberts, Pelham Barton, Matthias Egger
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