

# Expedited Partner Therapy for Gonorrhea & Chlamydia



Matthew R. Golden MD, MPH  
Center for AIDS & STD, University of WA  
Public Health – Seattle & King County

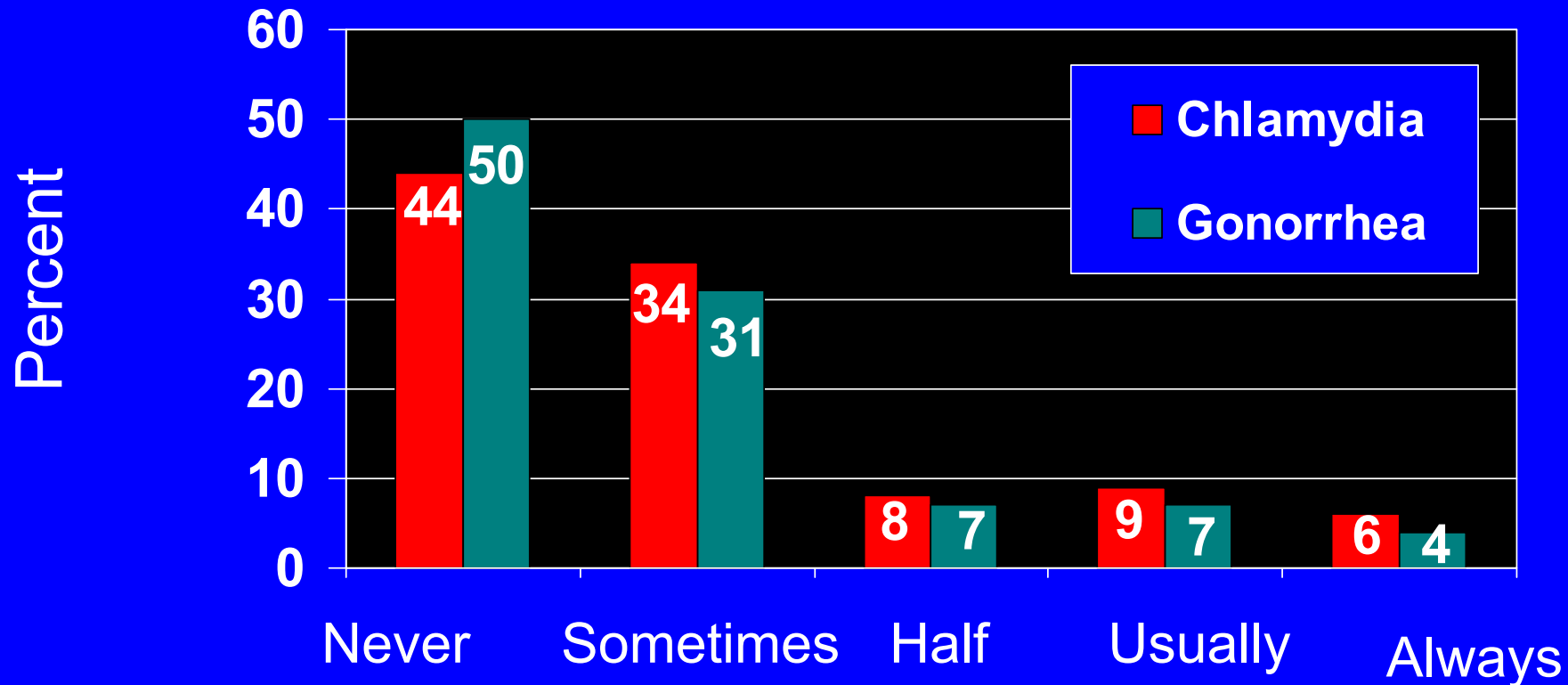
# Overview

- Background
- State of PN in the U.S.
- Expedited Partner Therapy Trials
- Scale-up
- Preliminary results WA State community-level trial

# Expedited Partner Therapy (EPT)

- Global term for process of treating partners without their mandatory prior examination
- Patient delivered partner therapy (PDPT) – index patient gives meds to partners
  - Most common form of EPT
- Accelerated partner therapy
  - Procedures designed to speed the treatment of partners while maintaining some contact between partners and health care professionals
  - Under study in UK

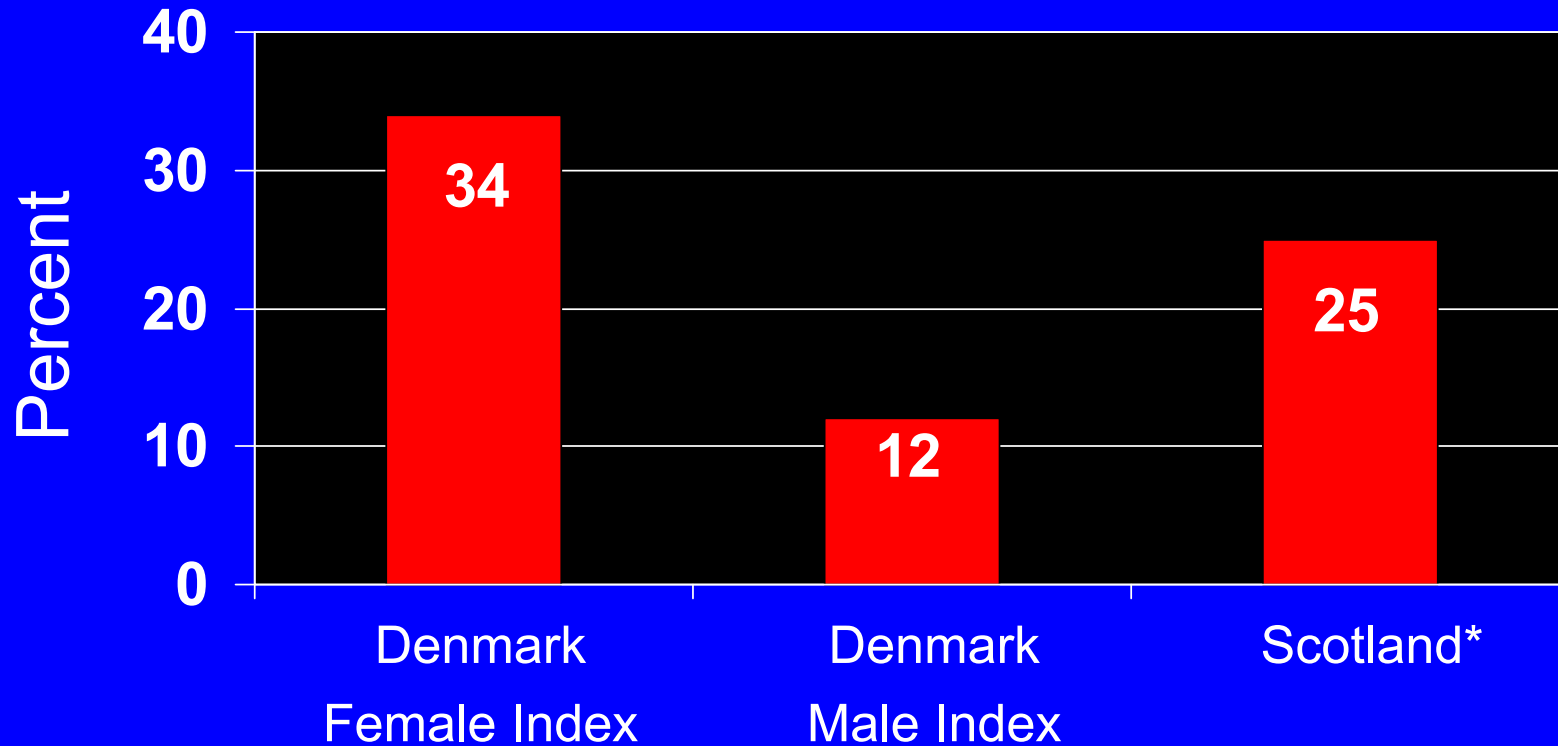
# Proportion of patients with chlamydial infection to whom physicians give medications for their sex partners



N=2,538 CT N=1,873 GC

Source: Sex Trans Dis 2005;32:101

# Use of PDPT in Europe



Danish data on specific patients. Scottish data=ever used

# 4 RCTs of Expedited Partner Therapy (EPT)

<b>Study</b>	<b>Population</b>	<b>Intervention</b>	<b>Outcome</b>	<b>Follow-up</b>
<b>Multi-city CT in ♀<sup>1</sup></b>	♀ screened CT positive – FP clinics	Patient-delivered partner therapy (PDPT)	- Partner Rx* - Infection at 1 & 4 months	90% 1 month 55% 3-4 months
<b>Seattle CT/GC<sup>2</sup></b>	Population-based  Men & Women	Offered PN assistance 1) PDPT 2) Partners contacted by hlth. dept. offered direct Rx	- Partner Rx* - Infection at 3-4 months	68% at 10-18 weeks
<b>New Orleans urethritis<sup>3</sup></b>	STD clinic patients	2 Interventions 1) Informational booklet 2) PDPT	- Partner Rx* - Infection at 1-2 months	85% Interview 30% specimen
<b>Edinburgh CT Study<sup>4</sup></b>	Women in GUM and FP clinics	2 Interventions 1) Partner mailed testing 2) PDPT	-Partner Rx - infection 3-12 months	44% interview, 65% tested

# Impact of PDPT on Index Patient GC/CT Reinfection in 4 Randomized Controlled Trials

CT in women

0.62 **0.8** 1.05

GC or CT in men or women

0.59 **0.76** 0.98

Urethritis in men

0.19 **0.38** 0.74

CT in women

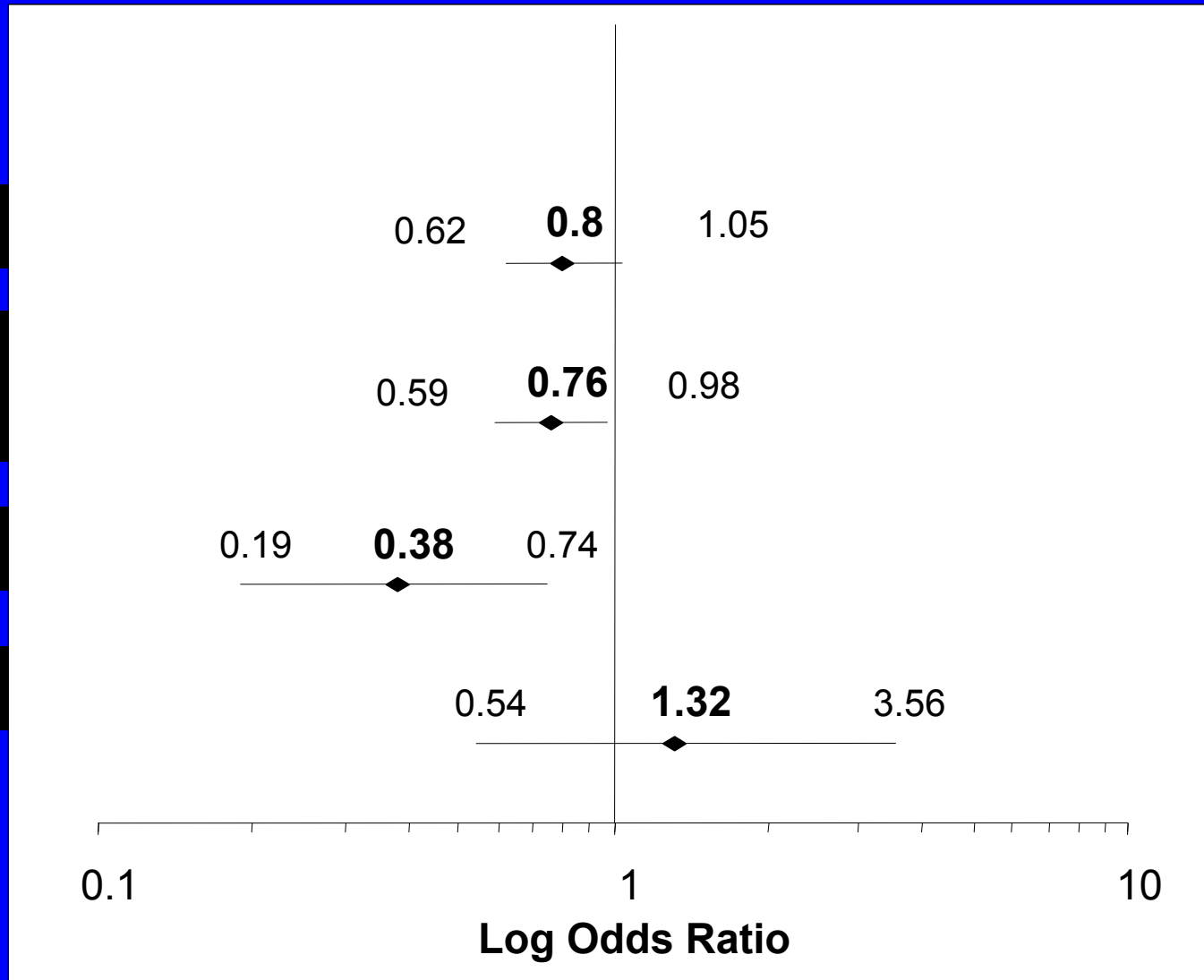
0.54 **1.32** 3.56

0.1

1

10

Log Odds Ratio



# Impact of PDPT on Index Patient Report that Partner was Treated in 4 Randomized Controlled Trials

<u>Study</u>	<u>PDPT</u>	<u>Control</u>	<u>P-value</u>
Multi-city CT in ♀	86%	57%	0.001
Seattle CT/GC	64%	52%	0.001
New Orleans urethritis	56%	34%	0.001
Scottish CT in ♀*	94%	78%	0.02

\* Outcome is all partners contacted, not treated



# Cost Effectiveness of EPT (Male Index Patients)

	Costs (per 100 index pts)*	QALYs Lost (per 100 index pts)	Cost-effectiveness Ratio (\$/QALY saved)*
<b>Payer perspective (includes costs borne by an individual payer)</b>			
Standard	\$24,392	3.08	
EPT	\$23,546	2.72	<b>-\$2351 (cost-saving)</b>
<b>Health care system (includes all direct medical costs, regardless of who pays)</b>			
Standard	\$45,317	3.08	
EPT	\$39,988	2.72	<b>-\$14,803 (cost-saving)</b>
<b>Societal perspective (includes all medical and lost productivity costs)</b>			
Standard	\$59,243	3.08	
EPT	\$48,834	2.72	<b>-\$28,914 (cost-saving)</b>

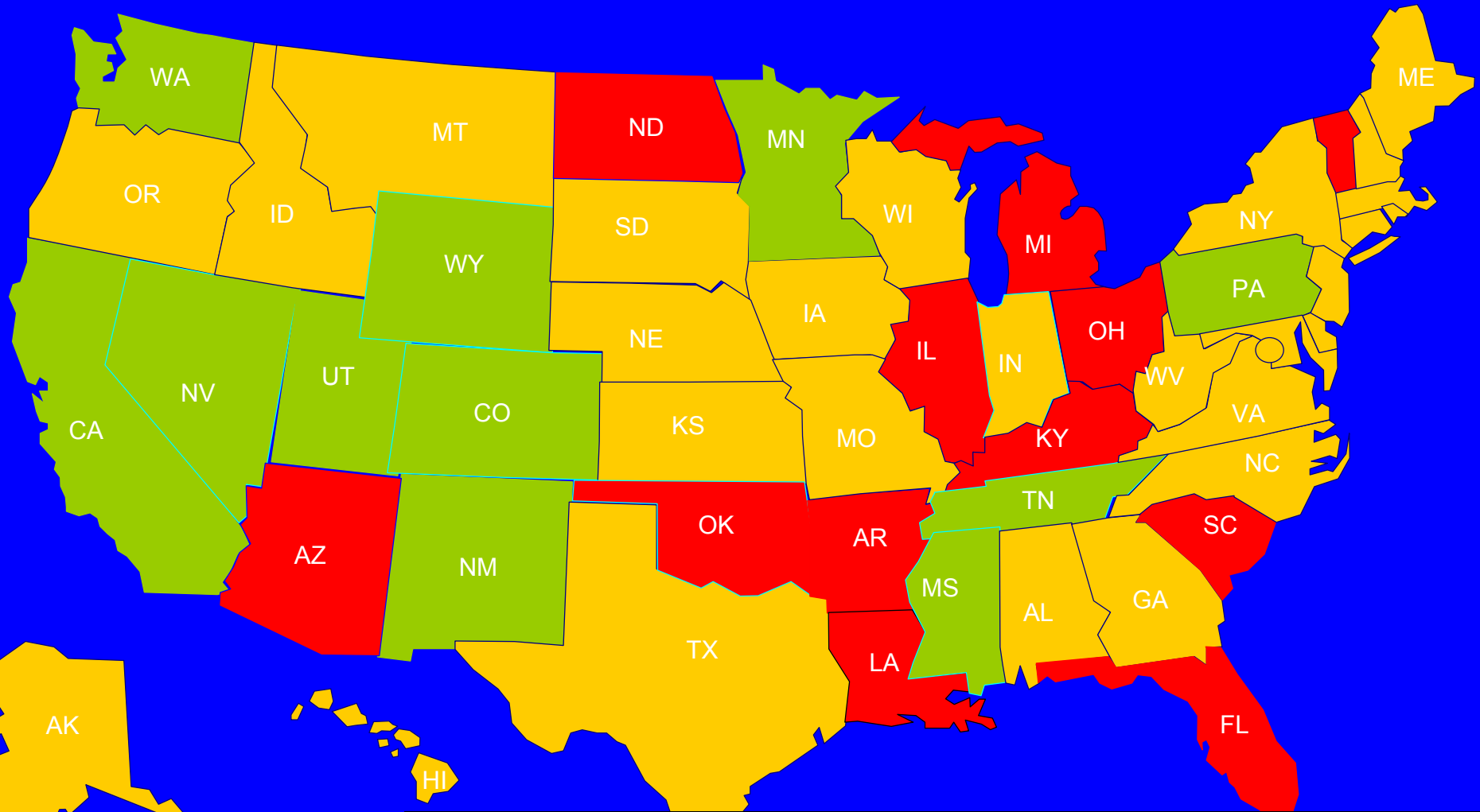
\*All costs in 2008 dollars

Source: Gift T. 02-S4.04

# Barriers

- Is this legal, and are providers liable?
- Is this an acceptable standard of medical care?
- Will EPT promote antimicrobial resistance?
- Is this ethical?

# Legal Status of EPT in the United States



EPT Permissible

EPT Prohibited

EPT legal status uncertain

EPT newly legal

EPT under consideration

# Is EPT a Good Standard of Care?

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- A complete evaluation of all partners would be best
- Are we missing concurrent diagnoses?
- Are we placing partners at significant risk of adverse drug reactions?

# STD Diagnoses in Persons Presenting as Contacts to Bacterial STD\* in Two Studies

	Women		Hetero Men		MSM	
	US	Australia	US	Australia	US	Australia
	N=2507	N=195	N=3511	N=243	N=460	N=188
Gonorrhea	3.9%	1%	3.1%	0	6.1%	8%
PID	3.7%	3.1%	NA	NA	NA	NA
HIV	0	0	0.2%	0	5.5%	5.1%
Syphilis	<0.1%	0	0	0	0.4%	0.5%

\* U.S. Study include contacts to CT, GC and NGU.  
 Australian study includes only contacts to CT

Sources: Stekler J. CID 2005;40:787.  
 McNulty A. STD 2008;35:834

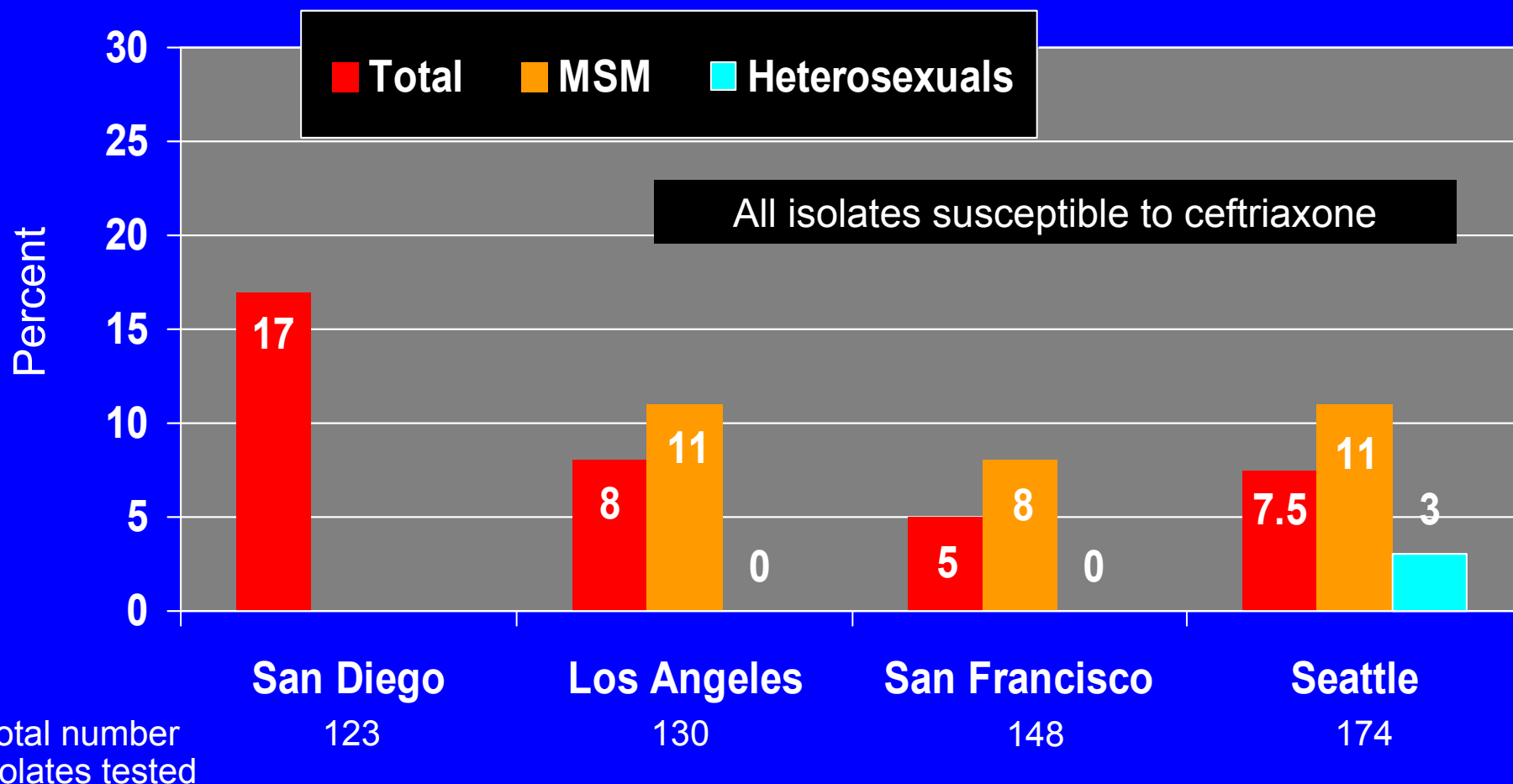
# Adverse Drug Reactions

- Anaphylaxis to macrolides is very rare
- PCN
  - Anaphylaxis with cephalosporins is rare (0.1-0.0001%)
  - ~10% of people report having a PCN allergy
  - Cross reactivity to 3<sup>rd</sup> gen cephalosporins 1-3%
  - Only avertable reactions are those occurring in persons with a known allergy who take meds despite written warnings
- No cases anaphylaxis to date in CA and WA

# Antimicrobial Resistance

- Standard of care is to treat contacts to GC & chlamydia without awaiting test results
  - EPT increases antimicrobial use by increasing appropriate treatment of partners
  - Rising MICs to oral cephalosporins in US and Europe and increasing emphasis on ceftriaxone for GC treatment
- No known chlamydial resistance to azithro
  - In 2005, 55 million prescriptions for Azithro; 3 million cases of chlamydia in U.S.
  - Recent trial showing doxy superior to azithro (Schwebke CID 2011;52:163)

# Proportion of *N. gonorrhoeae* Isolates with Elevated MICs to Oral Cephalosporins, 2010



Elevated MIC = cefixime or cefpodoxime MIC  $\geq 0.25 \mu\text{g/ml}$

Alert values based on cefpodoxime alone in ~50% isolates

Source: GISP Collaborators



# Ethics

Respect for Patient Autonomy

Beneficence

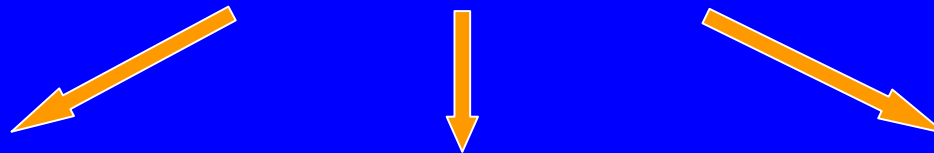
Nonmaleficence

Justice

- Insofar as RCTs show decreased reinfection in index cases given EPT, EPT is a superior standard of care
- Is EPT better for the partner? Can partners make an informed decision?

# Accelerated Partner Therapy

226 Index Cases with  
296 partners



**46% Hotline**

Partner talks to nurse +/-  
prescribing doc



**59% Partners  
Treated**

**15% Pharmacy**

Partner goes to pharmacy,  
counseled and treated



**66% Partners  
Treated**

**39% Routine**

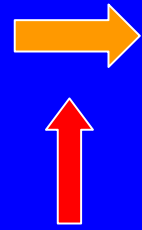
Index patient talks to health  
advisor and partner goes to  
clinic



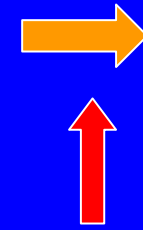
**36% Partners  
Treated**

# Scheme of PN Barriers & Interventions

Index patient  
diagnosed &  
treated



Partner Notified



Partner Treated

*BARRIERS* Doesn't know partner(s)  
Doesn't like partner(s)  
Can't reach partner(s)  
Afraid of partner(s)

Access to care  
(clinic hrs, transportation)  
Partner asx - not concerned

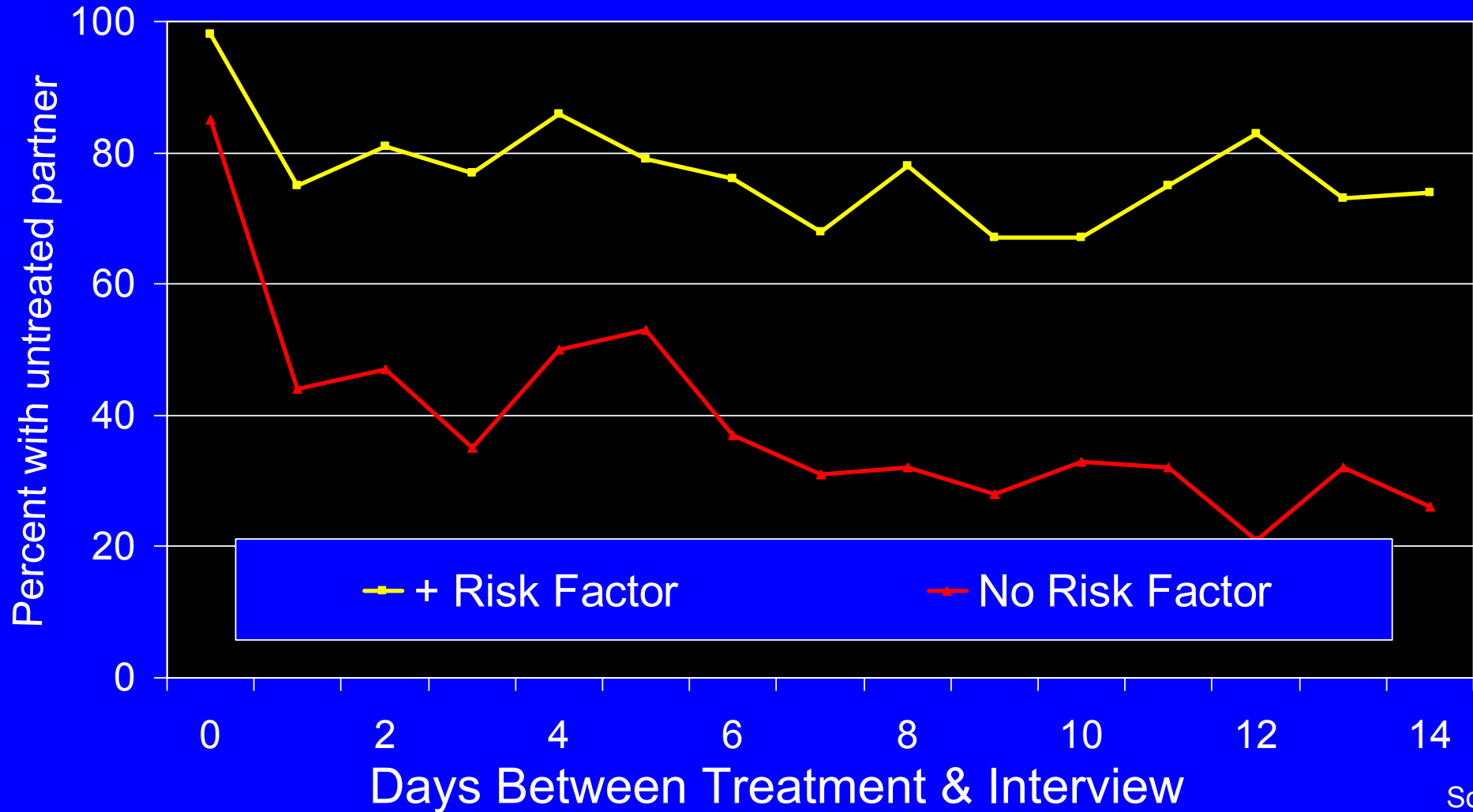


*INTERVENTION*

DIS

Pt Delivered Rx

# Proportion of Patients with Untreated Partners at Time of Study Interview




Source: STD  
2001;28:658

Risk factors: > 1 sex partner 60 days or pt does not anticipate sex with partner in future

# PN CT & GC: where do we go from here?

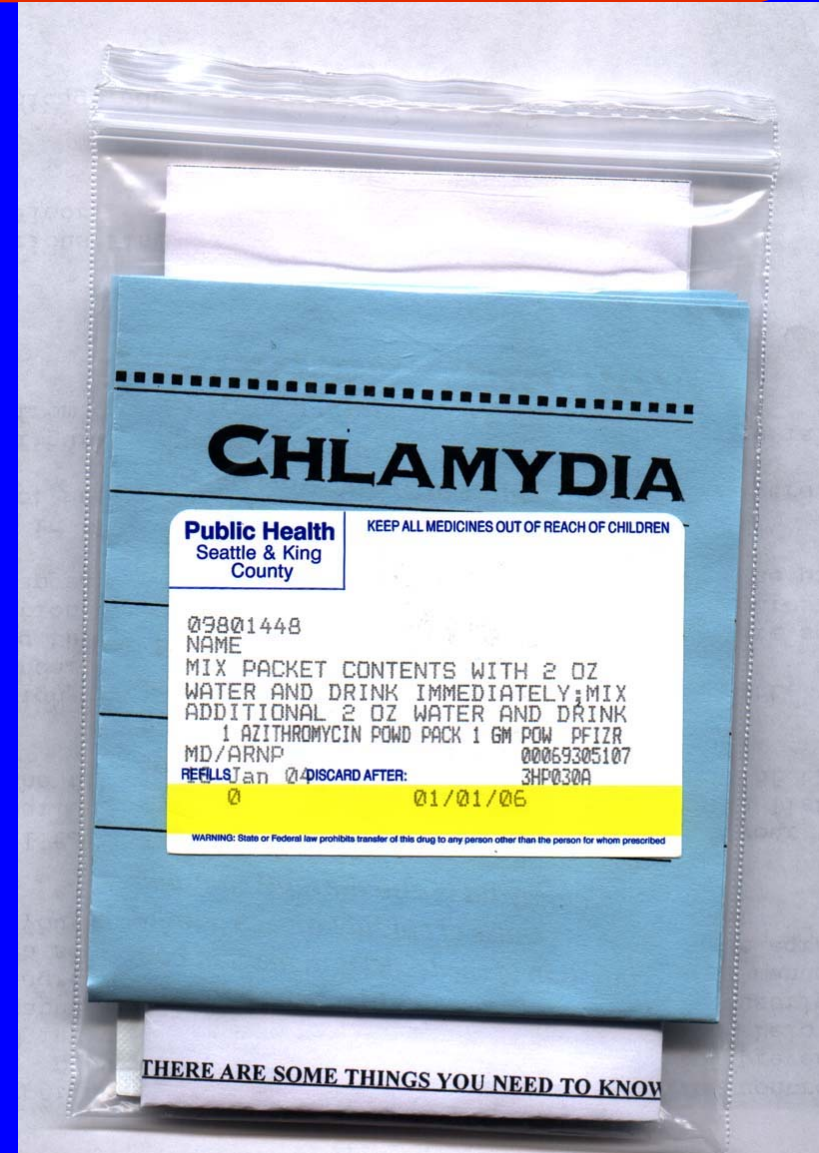
## CONFIDENTIAL SEXUALLY TRANSMITTED DISEASE CASE REPORT

<b>PATIENT DATA</b>	LASTNAME		FIRST NAME		INIT	C						
	ADDRESS			TELEPHONE ( )		REASON FOR EXAM: (CHECK ONE)						
	CITY/TOWN			STATE		<input type="checkbox"/> Symptomatic <input type="checkbox"/> Routine Exam—No Symptoms <input type="checkbox"/> Exposed to Infection						
DATE OF DIAGNOSIS MO   DAY   YR		ETHNICITY H   Non-His.   U		RACE - Check all that apply W   B   AI   AN   A   NHOPI   O   U		PATIENT HAS SEX WITH: M   W   B   UN						
						SEX M   F						
RACE: W—White; B—Black; AI—American Indian / AN—Alaskan Native; A—Asian; NHOPI—Native Hawaiian/Other Pacific Islander; O—Other; U—Unknown												
<b>DIAGNOSIS-DISEASE</b>	 <h3>Instructions</h3> <p><b><u>PARTNER MANAGEMENT PLAN</u></b>                      ✓ Select method of ensuring partner treatment</p> <p>1. <input type="checkbox"/> Health Department to assume responsibility for partner treatment.</p> <p>HEALTH DEPARTMENT ASSISTANCE <u>ONLY</u> RECOMMENDED IF:</p> <ul style="list-style-type: none"> <li>- Patient has had 2 or more sex partners in the last 60 days, or</li> <li>- Patient does not think he/she will have sex again with sex partners from the last 60 days, or</li> <li>- Patient is unable or unwilling to contact one or more partner, or</li> <li>- Patient is a man who has sex with other men.</li> </ul> <p>2. <input type="checkbox"/> Physician will ensure all partners treated (FREE medications available, see instructions).</p> <p>3. <input type="checkbox"/> All partners have already been treated.</p>		<b>GONORRHEA (lab confirmed)</b>				TREATMENT - ✓ all given/presc.		<b>SYPHILIS</b>			
			DIAGNOSIS - ✓ only one <input type="checkbox"/> Asymptomatic <input type="checkbox"/> Symptomatic - Uncomplicated <input type="checkbox"/> Pelvic Inflammatory Disease <input type="checkbox"/> Ophthalmia <input type="checkbox"/> Disseminated <input type="checkbox"/> Other Complications: DATE TESTED _____				SITE(S) - ✓ all that apply <input type="checkbox"/> Cervix <input type="checkbox"/> Urethra <input type="checkbox"/> Urine <input type="checkbox"/> Rectum <input type="checkbox"/> Pharynx <input type="checkbox"/> Ocular <input type="checkbox"/> Other		<input type="checkbox"/> Cefixime <input type="checkbox"/> Ceftriaxone <input type="checkbox"/> Ciprofloxacin <input type="checkbox"/> Ofloxacin <input type="checkbox"/> Azithromycin <input type="checkbox"/> Doxycycline <input type="checkbox"/> Other DATE RX _____		<input type="checkbox"/> Primary (Chancere, etc) <input type="checkbox"/> Secondary (Rash, etc) <input type="checkbox"/> Early Latent (<1 yr) <input type="checkbox"/> Late Latent (>1 yr) <input type="checkbox"/> Congenital <input type="checkbox"/> Neurosyphilis <input type="checkbox"/> Late DATE RX _____	
			<b>CHLAMYDIA TRACHOMATIS (lab confirmed)</b>				TREATMENT - ✓ all given/presc.		<b>HERPES SIMPLEX</b>			
			DIAGNOSIS - ✓ only one <input type="checkbox"/> Asymptomatic <input type="checkbox"/> Symptomatic - Uncomplicated <input type="checkbox"/> Pelvic Inflammatory Disease <input type="checkbox"/> Ophthalmia <input type="checkbox"/> Other Complications: DATE TESTED _____				SITE(S) - ✓ all that apply <input type="checkbox"/> Cervix <input type="checkbox"/> Urethra <input type="checkbox"/> Urine <input type="checkbox"/> Rectum <input type="checkbox"/> Pharynx <input type="checkbox"/> Ocular <input type="checkbox"/> Other		<input type="checkbox"/> Azithromycin <input type="checkbox"/> Doxycycline <input type="checkbox"/> Erythromycin <input type="checkbox"/> Ofloxacin <input type="checkbox"/> Other DATE RX _____		<input type="checkbox"/> Genital (Initial infection only) <input type="checkbox"/> Neonatal Laboratory Confirmation <input type="checkbox"/> Yes <input type="checkbox"/> No <b>OTHER</b> <input type="checkbox"/> Chancroid <input type="checkbox"/> Granuloma Inguinale <input type="checkbox"/> Lymphogranuloma Venereum	
			SUBMITTED BY (PROVIDER)				PERSON COMPLETING REPORT					
ADDRESS												
CITY		STATE		TELEPHONE ( )		<input type="checkbox"/> Need Additional Case Report Forms						

STATE OF WASHINGTON SEXUALLY TRANSMITTED DISEASE SERVICES

# PDPT Distribution

- Medication prepackaged to meet requirements of state pharmacy board
  - Allergy warning, info on STDs, complications & where to seek care, condoms
- Stocked in high-volume clinics and in 157 pharmacies, statewide
  - Pharmacies paid \$2-5 dispensing fee
- Preprinted prescriptions on case-report form and on faxable forms

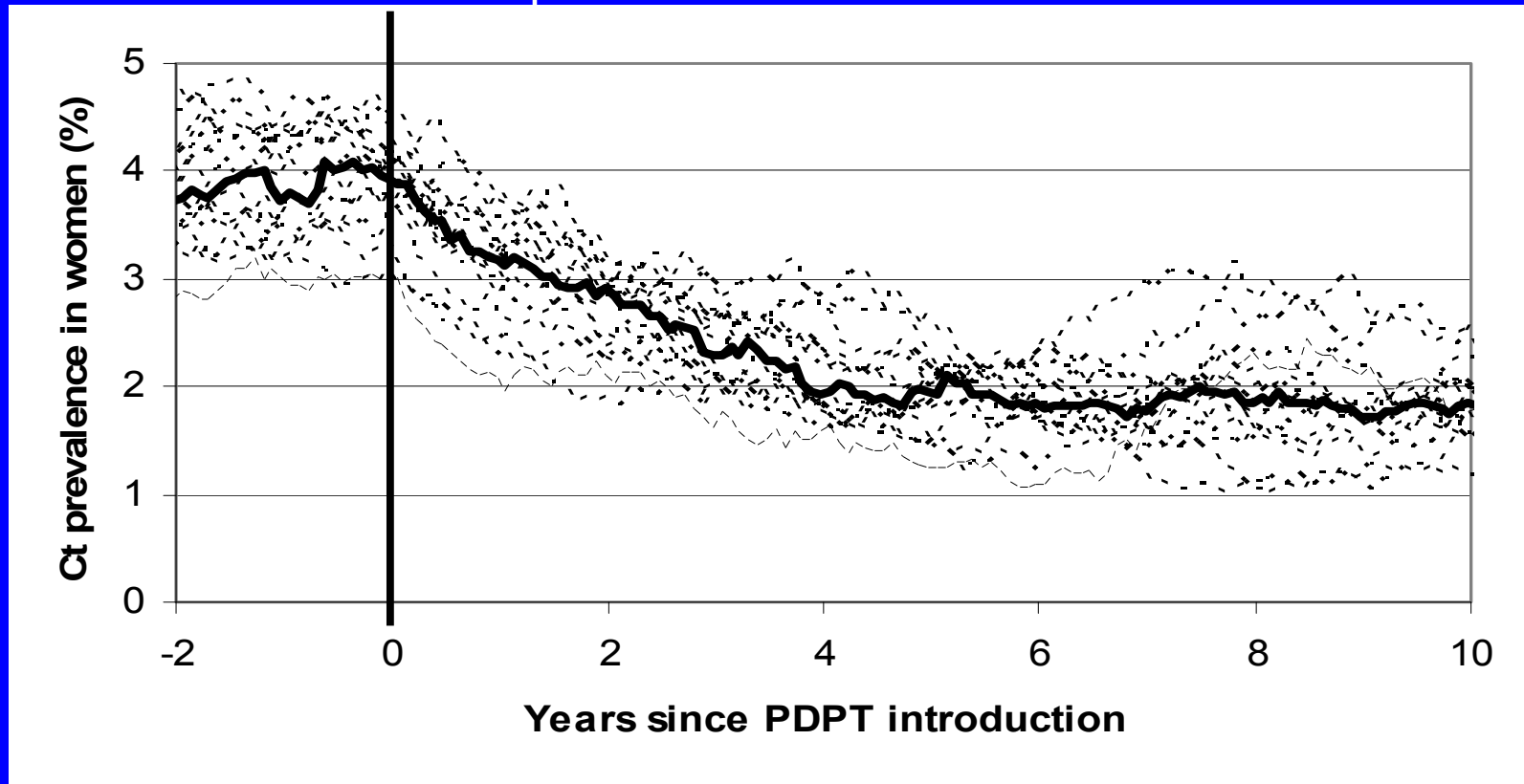


# EPT Scale-up in King County, WA

- Case report based triage
  - Providers completed case reports
  - Triage identified persons at high risk for having untreated partners and
- Estimated percentage of partners treated increased from 39% ->64%

# Assessment of Community-Wide EPT: Simulation Model

50% → 60% partners treated



15 realisations, thick line is median.

Includes annual Ct screening of 25% of women aged <26.

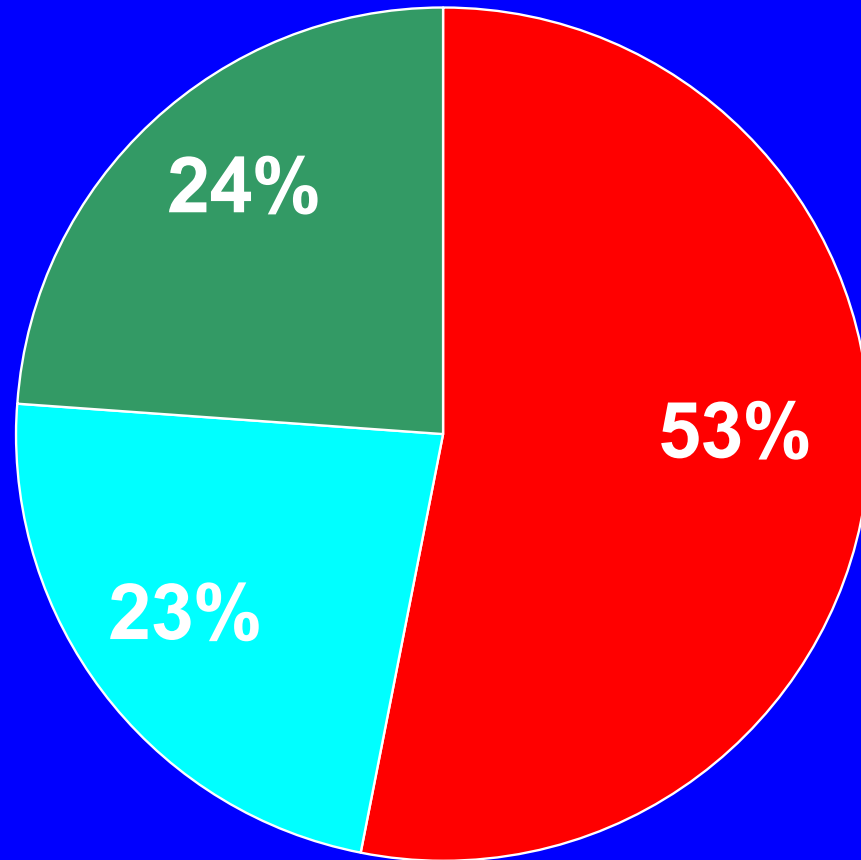
10% increase in partner treatment results in a ~25% reduction in CT prevalence at 2 years, and a ~50% reduction in 4 years



# Washington State Community-level Randomized Trial of EPT

- Goal - to determine if an EPT program can decrease the prevalence of chlamydia and/or the incidence of gonorrhea in the state's women
- Design – stepped-wedge community-level randomized trial
  - Order in which local health jurisdictions start intervention randomly assigned
  - Comparison of trends in places with and without the intervention
- Outcome
  - CT prevalence in sentinel clinics (IPP)
  - Reported incidence of gonorrhea

# Provider's Partner Management Plan as Indicated on the Case Report Form (n=40,718)

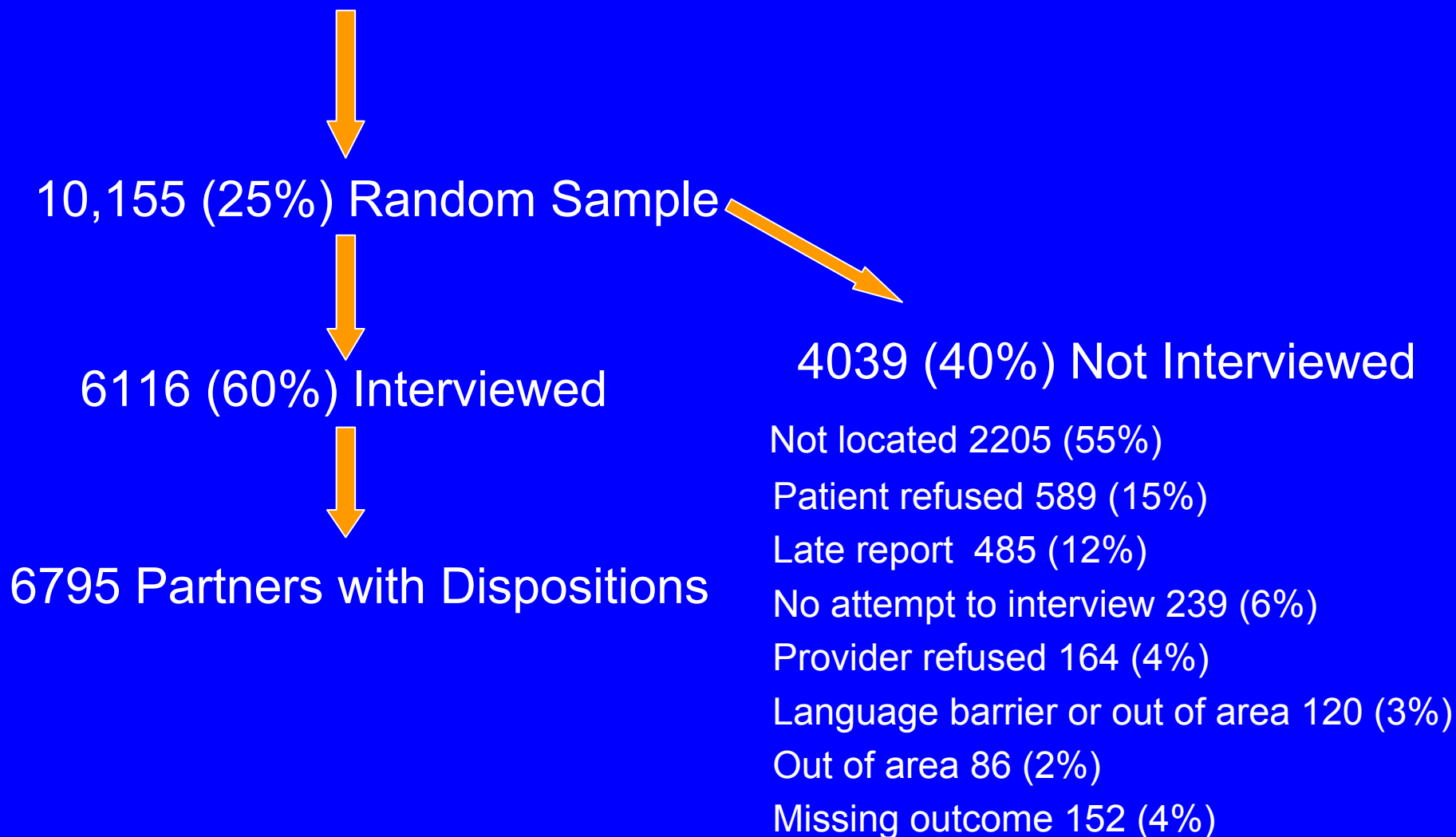


**90% of Forms Completed with a Partner Management Plan**

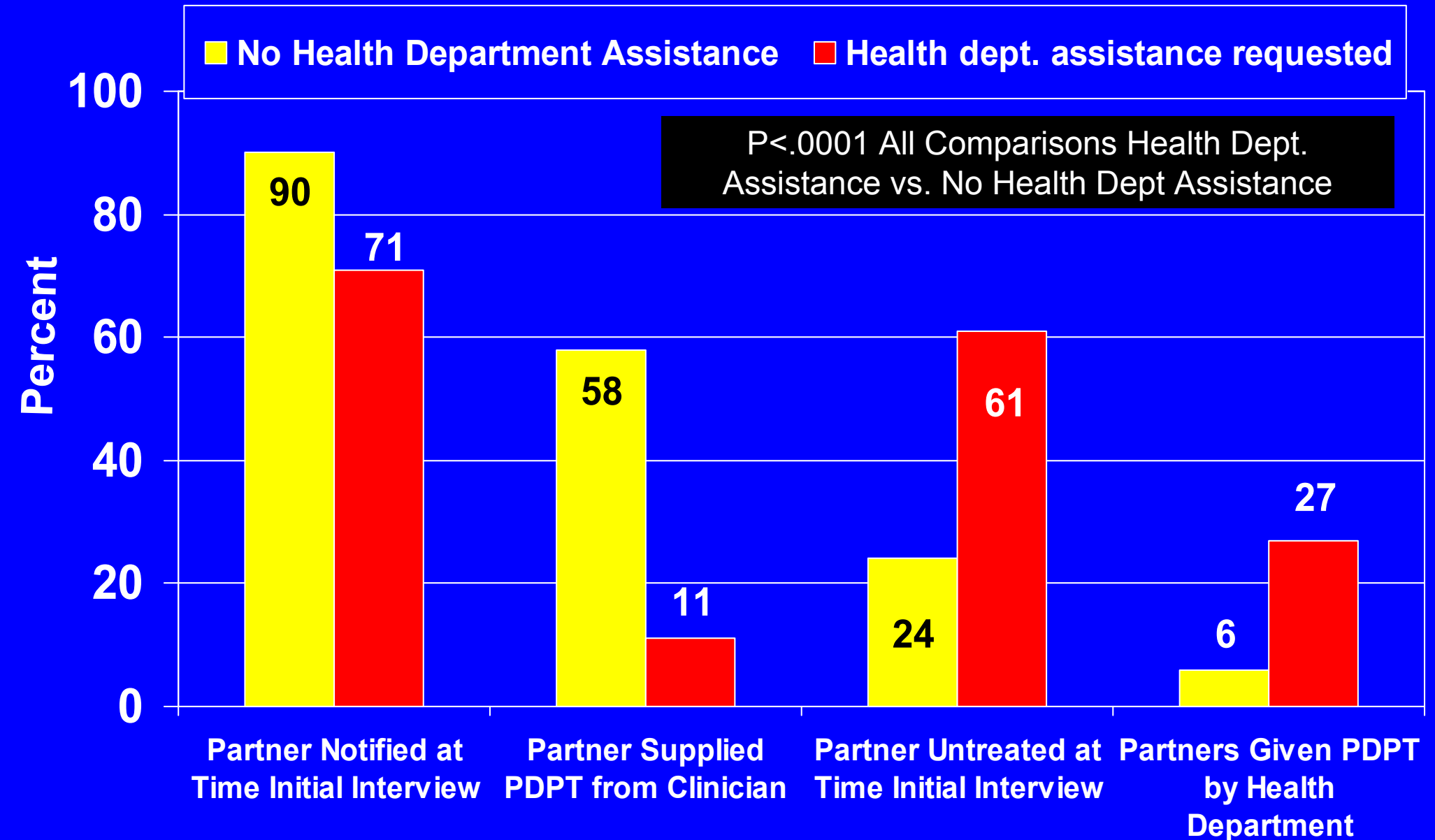
**Health Department    Provider    All Partners Treated**

# Process Outcome Evaluation: WA State EPT Trial

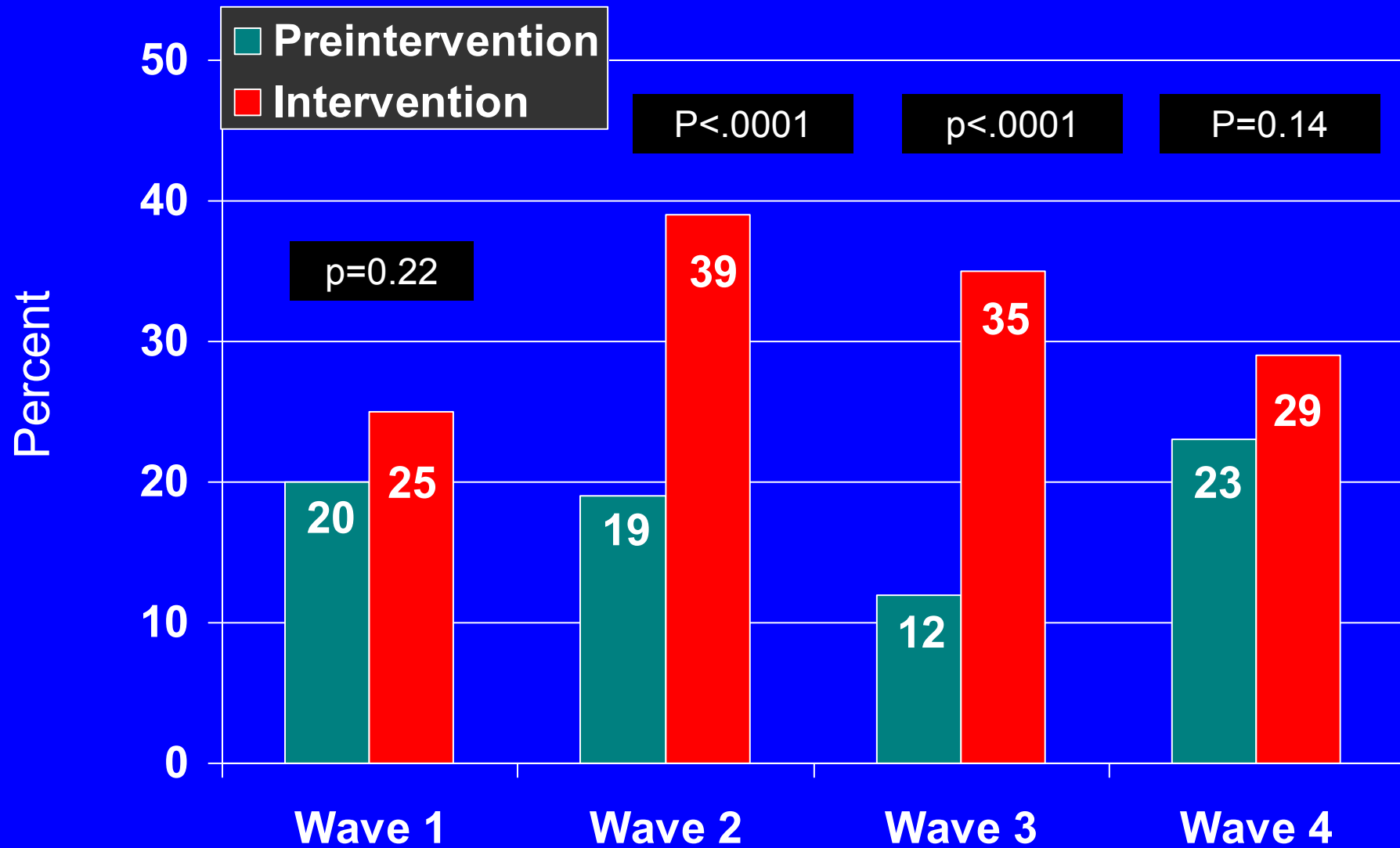
40,718 Cases GC/CT in Heterosexuals 1/1/07-12/31/09



# Association of PN Plan on Case Report Form with PN Outcomes

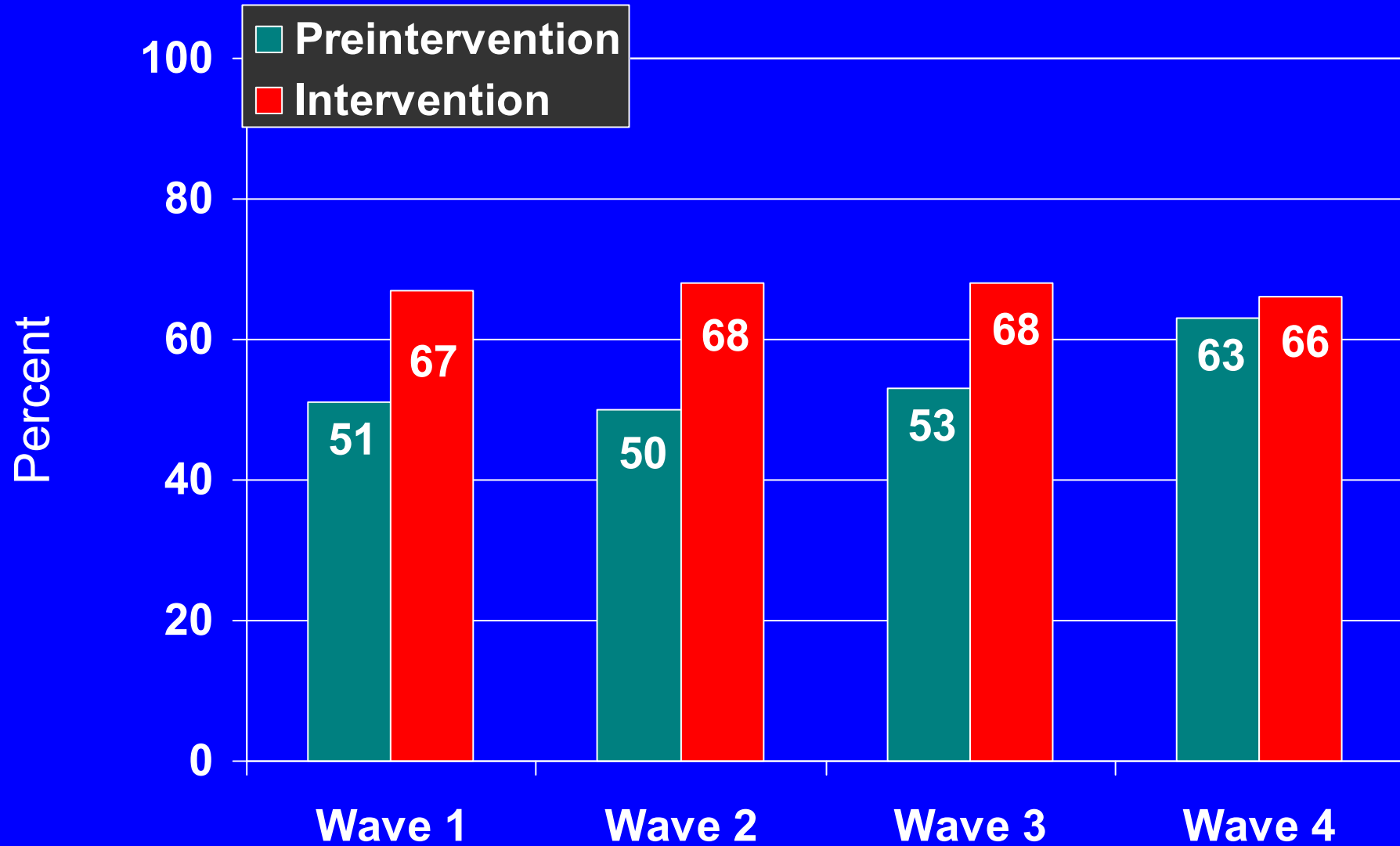


# Percentage of Index Cases Receiving PDPT From Medical Providers, Before and After an Intervention to Increase PDPT Use



GEE controlling for STD diagnosis

# Estimated Percentage of Sex Partners Treated, Before and After Intervention Initiation, by Wave



# Summary Community-level EPT Trial

- Final trial outcome in analysis
- Case report based triage appears to be working – confirms experience in King County
- Program increased PDPT use by providers and partner treatment, though not in all areas
- Effect on prevalence of infection yet to be defined

# Conclusions

- The development and roll out of EPT in the U.S. is an example of a relatively well organized, evidence-based change in public health practice
- Change remains very incomplete
  - Uncertain WA State program can be sustained
  - Uncertain whether changes in guidelines and laws in other states will result in a change in practice
- Substantial uncertainty persists on the effect of EPT on STD morbidity
  - Community-level trial may resolve this
- Rising antimicrobial resistance, particularly in GC, may limit the use of PDPT



# Contributors & Support

## Center for AIDS & STD, UW

King K. Holmes

James Hughes

Roxanne Kerani

H. Hunter Handsfield

William Whittington

Katherine Thomas

## CDC

Thomas Gift

Matthew Hogben

## Pharmacies

Rite-Aid Pharmacy

Bartell Drug

Fred Meyer

Safeway

## PHSKC STD Program

Cheryl Malinski

Angela Nunez

Allison Moore

Fred Koch

Barbara Krekeler

DIS staff

## WA State DOH

Mark Stenger

Mark Aubin

Katherine Gudgel

## Support

CDC, Division of STD Prevention

NIAID

# Is the Intervention Sustainable?

<b>Medications*</b>		<b>Cost</b>
Azithromycin (\$1.50 per 1000mg)	10,000	\$15,000
Cefixime (\$10 per 500mg)	3000	\$30,000
Pharmacy packing fees		\$49,000
Pharmacy distribution fees	3000	\$15,000
<b>Medication Subtotal</b>		<b>\$109,000</b>
<b>DIS working 50% cases in WA (n=~12,000)</b>	<b>10</b>	<b>\$607,500</b>
<b>Oversight and epi</b>	<b>1.25 FTE</b>	<b>\$107,200</b>
<b>Personnel subtotal</b>		<b>\$714,700</b>
<b>Total</b>		<b>\$823,700</b>

\*340B pricing AZM 500mg \$0.76, cefixime 500mg \$10. \$5 dispensing fee

DIS – Assumes DIS work 1200 cases/year – Salary \$45K + 35%