AETC AIDS Education & Training Center Program Mountain West

Expedited Partner Therapy in 2022: Updated Guidance and Practical Realities

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Disclosures

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Advisory Committee: Nabriva

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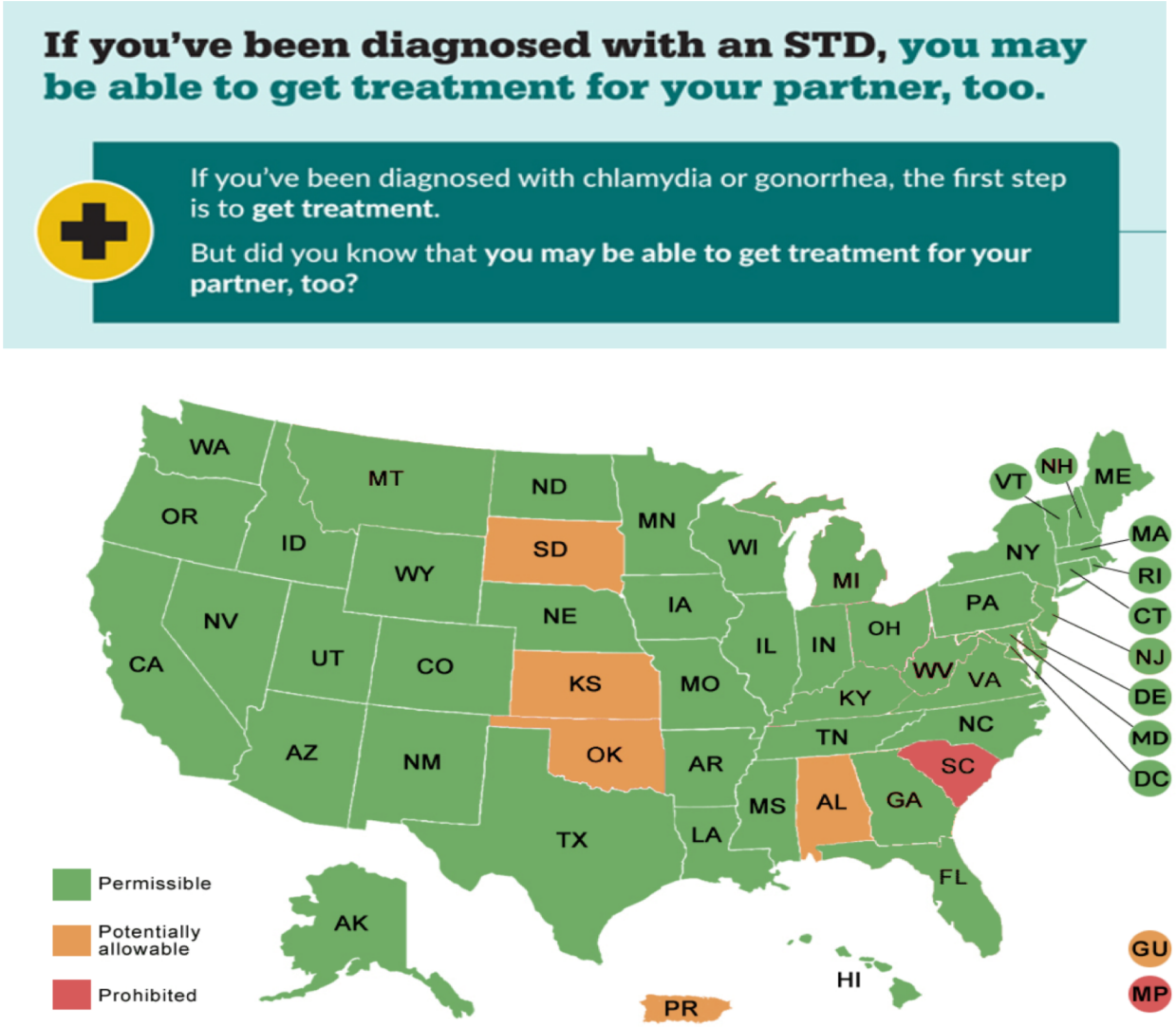
What is Expedited Partner Therapy (EPT)?

Prescription of STI treatment to partners of patient with STI.

Rx written WITHOUT examining sex partner.

Legality varies from state to state.

EPT for gonorrhea and chlamydia has been shown to reduce recurrent STI in patient.*



*Golden et al, NEJM, 2005; Golden et al. PLoS Med 2015, Schillinger et al 2003, Kissinger et al 2005

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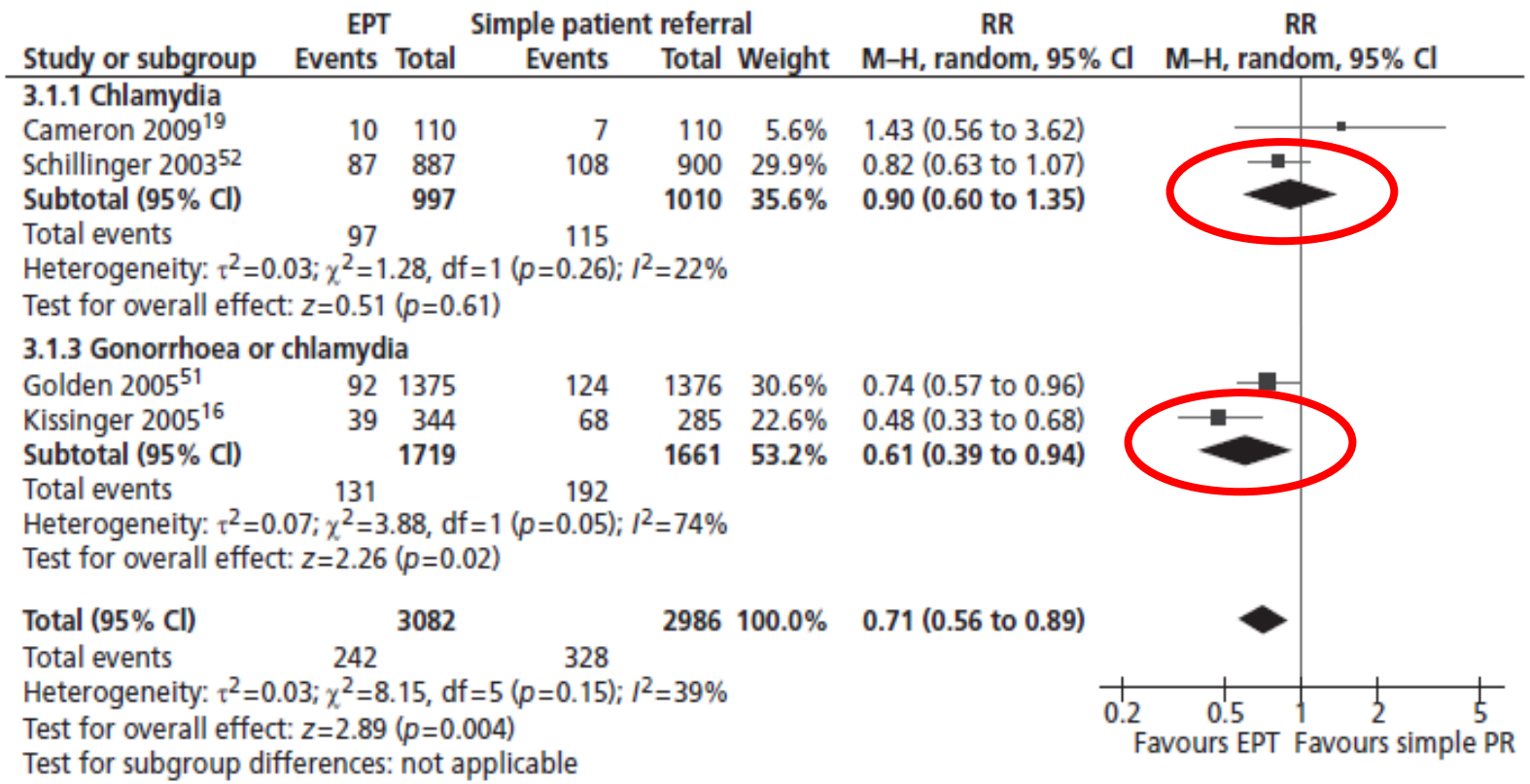
Evidence for EPT's effectiveness: a meta-analysis

CLINICAL EFFECTIVENESS OF PARTNER NOTIFICATION



Study or subgroup	EPT Events	EPT Total	Simple patient referral Events	Simple patient referral Total	Weight	RR M–H, random, 95% CI
3.1.1 Chlamydia						
Cameron 2009[19]	10	110	7	110	5.6%	1.43 (0.56 to 3.62)
Schillinger 2003[52]	87	887	108	900	29.9%	0.82 (0.63 to 1.07)
Subtotal (95% CI)		**997**		**1010**	**35.6%**	**0.90 (0.60 to 1.35)**
Total events	97		115			
Heterogeneity: τ^2=0.03; χ^2=1.28, df=1 (p=0.26); I^2=22%						
Test for overall effect: z=0.51 (p=0.61)						
3.1.3 Gonorrhoea or chlamydia						
Golden 2005[51]	92	1375	124	1376	30.6%	0.74 (0.57 to 0.96)
Kissinger 2005[16]	39	344	68	285	22.6%	0.48 (0.33 to 0.68)
Subtotal (95% CI)		**1719**		**1661**	**53.2%**	**0.61 (0.39 to 0.94)**
Total events	131		192			
Heterogeneity: τ^2=0.07; χ^2=3.88, df=1 (p=0.05); I^2=74%						
Test for overall effect: z=2.26 (p=0.02)						
Total (95% CI)		**3082**		**2986**	**100.0%**	**0.71 (0.56 to 0.89)**
Total events	242		328			
Heterogeneity: τ^2=0.03; χ^2=8.15, df=5 (p=0.15); I^2=39%						
Test for overall effect: z=2.89 (p=0.004)						
Test for subgroup differences: not applicable						

FIGURE 3 Forest plot of randomised controlled trials of EPT vs. simple patient referral, by infection and overall. PR, patient referral. Source: Reproduced from Ferreira A, Young T, Mathews C, Zunza M, Low N. Strategies for partner notification for sexually transmitted infections, including HIV. *Cochrane Database Syst Rev* 2013; 10: CD002843 http://dx.doi.org/10.1002/14651858/CD002843.pub2 with permission from John Wiley and Sons.[44]

HEALTH TECHNOLOGY ASSESSMENT

VOLUME 18 ISSUE 2 JANUARY 2014
ISSN 1366-5278

Effectiveness and cost-effectiveness of traditional and new partner notification technologies for curable sexually transmitted infections: observational study, systematic reviews and mathematical modelling

Christian L Althaus, Katherine ME Turner, Catherine H Mercer, Peter Auguste, Tracy E Roberts, Gill Bell, Sereina A Herzog, Jackie A Cassell, W John Edmunds, Peter J White, Helen Ward and Nicola Low

EPT decreases reinfection with gonorrhea or chlamydia in the index patient by ~40%

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CAVEATS

- Data is from trials from early 2000s. Therefore, before…
  - Azithromycin and cephalosporin reduced susceptibility GC
  - Our understanding about doxy v azithro for rectal CT and rectal CT in cis-women
- Only studied in cisgender heterosexuals
- Treatment regimens were
  - Chlamydia: Azithromycin 1g
  - Gonorrhea: Cefixime 400mg plus 1g Azithromycin
- When chlamydia was examined individually, not statistically significant

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2021 STI Treatment Guidelines: What's new for EPT?

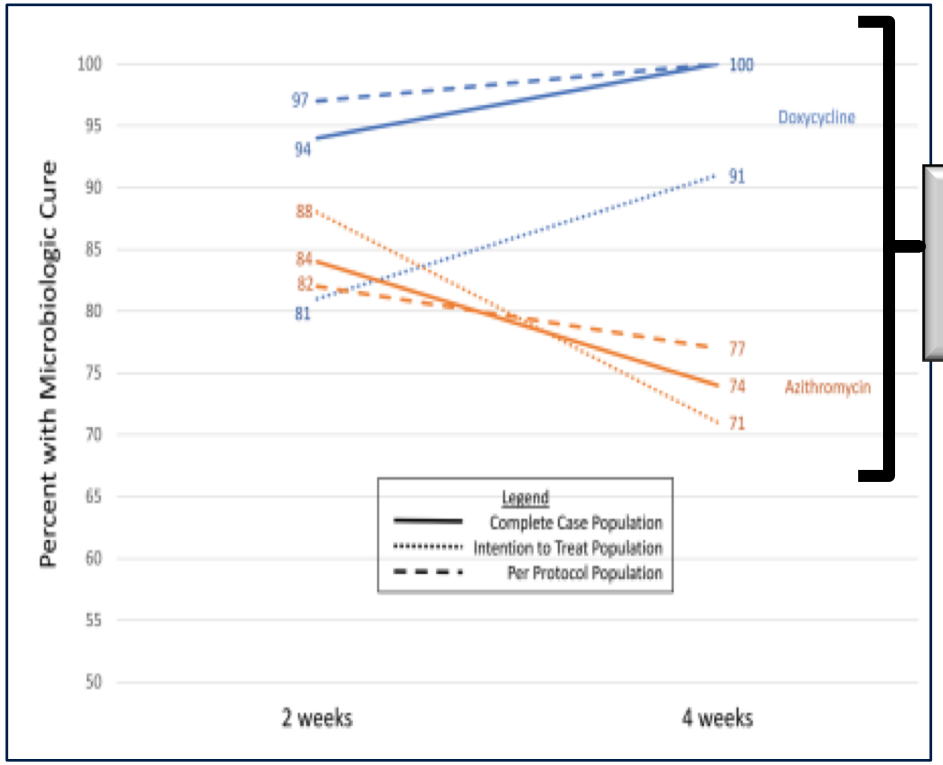
- Chlamydia:
  - Use doxycycline 100mg PO BID x 7 days
- Gonorrhea:
  - Use cefixime 800mg PO x 1
  - Add doxy if chlamydia cannot be excluded
- MSM :
  - Use shared decision-making

Why change Chlamydia treatment regimen?

Clinical Infectious Diseases
MAJOR ARTICLE

Doxycycline Versus Azithromycin for the Treatment of Rectal Chlamydia in Men Who Have Sex With Men: A Randomized Controlled Trial

Julia C. Dombrowski,[1,2] Michael R. Wierzbicki,[3] Lori M. Newman,[4] Jonathan A. Powell,[3] Ashley Miller,[5] Dwyn Dithmer,[2] Olusegun O. Soge,[6] and Kenneth H. Mayer[7,8]



Risk Difference 26%
(95% CI:16-36%)
p<0.001

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Azithromycin versus Doxycycline for Urogenital *Chlamydia trachomatis* Infection

William M. Geisler, M.D., M.P.H., Apurva Uniyal, M.A., Jeannette Y. Lee, Ph.D., Shelly Y. Lensing, M.S., Shacondra Johnson, B.S.P.H., Raymond C.W. Perry, M.D., M.S.H.S., Carmel M. Kadrnka, D.O., and Peter R. Kerndt, M.D., M.P.H.

N=567

0/283
Doxy TF

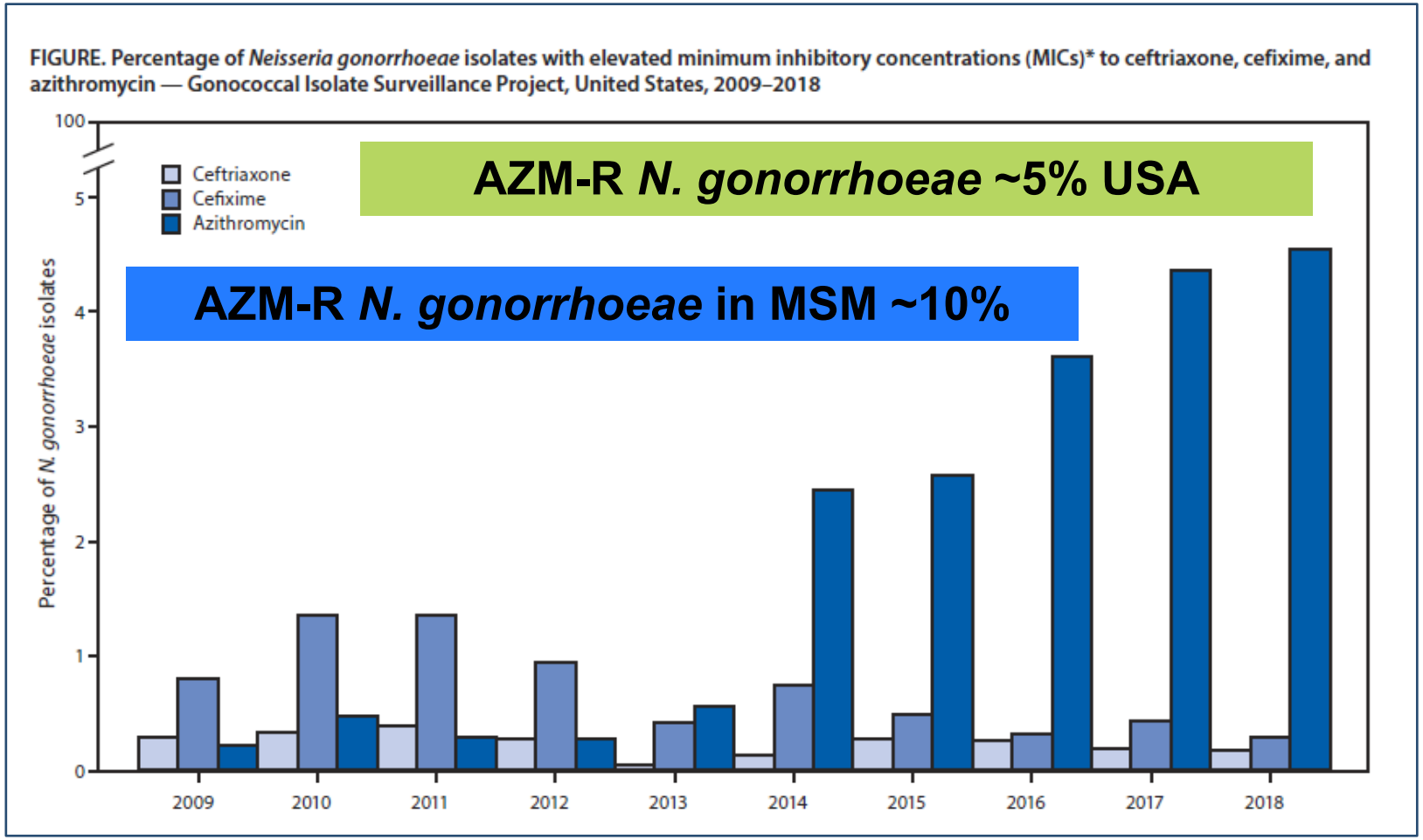
5/284
AZM TF

Doxy 100% effective vs. Azithromycin 97%

Azithromycin NOT non-inferior (difference 3.2%)

Why change Chlamydia treatment regimen?

- WHO and CDC guidance suggests removing drug when >5% resistance
- Antimicrobial Stewardship
  - AZM half-life ~68 hours
  - Resistance in many bacterial species
    Streptococci
    M. genitalium
    Shigella
    Campylobacter



Why change the Gonorrhea treatment regimen?

- Changes to first-line recommended GC treatment – Ceftriaxone Dose
  - Azithromycin resistance
  - New understanding in PK/PD
  - Mutant prevention concentration

PK/PD: fT>MIC

CHISHOLM (math model):
~20 hours

CONNOLLY (mouse model):
~24 hours

	Ceftriaxone 250 mg im		
MIC (mg/L)	median[a]	lower 95% CI	upper 95% CI
0.015	49.9	23.8	>90
0.03	41.4	19.7	86.5
0.06	32.8	15.1	68.8
0.125	24.1	10.5	52.2
0.25	15.4	5.3	34.3
0.5	6.0	0.0	19.8
1	0.0	0.0	6.5
2			
4			

Wide 95% CI Corresponds to Wide Inter-individual Pharmacokinetics

	Ceftriaxone im	
MIC mg/L	g	500 mg
0.008		67.2
0.015		58.7
0.03		49.9
0.06		41.3
0.125		32.8
0.25		24.3
0.5		15.6
1		6.6
2		0.0
4		0.0

Dark shading <10 h above MIC, light shading 10–20 h above MIC, no shading >20 h above MIC.

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Why change the Gonorrhea EPT treatment regimen?

PK/PD Criterion: fT>MIC

Chisholm (math model): ~20 hours vs Connolly (mouse model): 38.6 hours

Known fT>MIC

400mg once dose:

MIC 0.008: 32.6 hours
MIC 0.03: 25.7 hours
MIC 0.25: 15.3 hours

800mg once dose:

MIC 0.008: unknown
MIC 0.03: unknown
MIC 0.25: unknown

		400mg	800mg
Cefixime Clinical Efficacy	Urogenital	96.2% (92.3% - 98.4%) (n=183, MIC ≤0.03)	97.9% (93.9% - 99.6%) (n=141, MIC ≤0.03)
	Rectal	90.1% (82.2% - 96.3%) (n=77, MIC ≤0.25)	Not enough data
	Pharyngeal	63.8% (53.3% - 73.5%) (n=94, MIC ≤0.25)	75% (42.8% - 94.5%) (n=12, MIC≤0.25)

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What is the evidence for EPT in MSM?

- Evidence remains limited
- One RCT compared EPT to passive partner notification in Peru
  - Not about efficacy based on reinfection

Clark *et al. BMC Medicine* (2017) 15:94
DOI 10.1186/s12916-017-0858-9

BMC Medicine

RESEARCH ARTICLE Open Access

CrossMark

Expedited Partner Therapy (EPT) increases the frequency of partner notification among MSM in Lima, Peru: a pilot randomized controlled trial

Jesse L. Clark[1,8*], Eddy R. Segura[1,2], Catherine E. Oldenburg[3], Jessica Rios[4], Silvia M. Montano[5], Amaya Perez-Brumer[6], Manuel Villaran[4], Jorge Sanchez[7], Thomas J. Coates[1] and Javier R. Lama[4]

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Considerations for 2021 EPT Recommendations

- Chlamydia regimen
  - Doxy has more potential side effects compared to Azithro
    - Photosensitivity
    - Pill esophagitis
    - Teratogenic in pregnancy
  - Doxy not studied for EPT
    - Concerns about adherence, inability to assess for pregnancy or counsel etc.

- Gonorrhea regimen
  - Limited efficacy at the pharynx
  - New data: Pharyngeal gonorrhea + 20-40%* of heterosexual contacts to GC
- EPT in MSM
  - Limited data
  - Pharyngeal GC common
  - Elevated antimicrobial resistance
  - High prevalence of co-infection with syphilis and HIV

*Chow et al STD 2019; McLaughlin et al CDC STD Prevention Conference 2020

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PHSKC's EPT Recommendations

- Chlamydia:
  - For cisgender female partners of cis-men: Use Azithromycin 1g
  - Doxy or azithromycin for male partners
- Gonorrhea:
  - Cefixime 800mg PO PLUS 2g Azithromycin
- MSM:
  - Ideally: Patients notify partners to seek testing (GC/CT/Syph and HIV) & treatment
  - Risk reduction: used shared decision-making

Barriers to EPT Use

Original Research ajog.org

GYNECOLOGY

Breakdown in the expedited partner therapy treatment cascade: from reproductive healthcare provider to the pharmacist

Okeoma O. Mmeje, MD; Jennifer Z. Qin, BA; Marisa K. Wetmore, MPP; Giselle E. Kolenic, MA; Clarissa P. Diniz, BS; Jenell S. Coleman, MD, MPH

- Interviewed pharmacists about EPT knowledge.
- About 23% knew what EPT was.
- About 14% had received a prescription for EPT.
- 85% would fill an EPT prescription for someone < 18 years old.
- After the call, 97% would fill a prescription for EPT.

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Time for Q&A

Acknowledgment

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