Why COVID-19 Will Not Mean the End of the STI Epidemic (and May Make It Worse)

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Learning Objectives

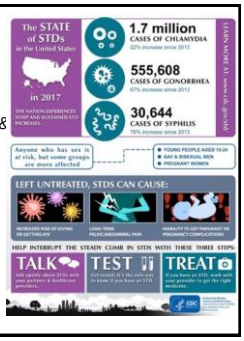
After attending this presentation, learners will be able to:

- Describe changes to the management of gonococcal infection
- State the appropriate method to monitor response to treatment of syphilis
- Screen people living with HIV for sexually transmitted infections (STIs)

Slide 3 of 33

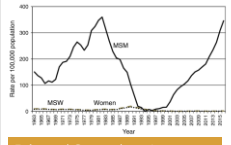
Discussion

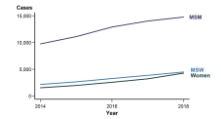
- Epidemiologic trends
  - Continued STI crisis
  - What will happen during the pandemic?
- Concerns specific to HIV management & prevention
  - Operational challenges
    - Asymptomatic nature of most STI; burden of extragenital infection
    - Cost of screening & treatment
    - Management in setting of a pandemic
  - High index of suspicion for antimicrobial resistance → treatment failure



The U.S. Syphilis Epidemic: 2018

Primary / Secondary Syphilis in Men

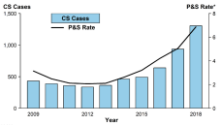




- 88% of cases
- 80% in MSM
- 46% in MSM HIV+

Primary/ Secondary & Congenital Syphilis in Women

- Primary / Secondary: 156% increase compared with 2013
- Congenital syphilis: 154% increase



- >1300 congenital cases
- >50% of cases without prenatal care
- Strong links to meth, heroin

CDC

Source: http://www.cdc.gov/std

Centers for Disease Control and Prevention
MMWR Morbidity and Mortality Weekly Report
Weekly / Vol. 69 / No. 22 June 5, 2020

TABLE 2. Missed congenital syphilis prevention opportunities among mothers of infants with congenital syphilis, by U.S. Census region* — United States, 2018

	Census region No. (%†)				
Missed prevention opportunity	**Total**	**South**	**West**	**Midwest**	**Northeast**
No timely prenatal care and no timely syphilis testing	**368 (28.2)**	136 (19.9)	**191 (41.1)**	25 (24.3)	16 (30.2)
No timely syphilis testing despite receipt of timely prenatal care	**116 (8.9)**	47 (6.9)	53 (11.4)	8 (7.8)	6 (11.3)
No adequate maternal treatment despite a timely syphilis diagnosis	**401 (30.7)**	235 (34.3)	133 (28.6)	26 (25.2)	7 (13.2)
Late identification of seroconversion during pregnancy§	**146 (11.2)**	73 (10.7)	30 (6.5)	22 (21.4)	21 (39.6)
Missed prevention opportunity not identified					
Clinical evidence of congenital syphilis despite maternal treatment completion¶	**46 (3.5)**	33 (4.8)	9 (1.9)	4 (3.9)	0 (0.0)
Insufficient information**	**229 (17.5)**	161 (23.5)	47 (10.1)	18 (17.5)	3 (5.7)
Total	**1,306**	**685**	**465**	**103**	**53**

* South: Alabama, Arkansas, Delaware, District of Columbia, Florida, Georgia, Kentucky, Louisiana, Maryland, Mississippi, North Carolina, Oklahoma, South Carolina, Tennessee, Texas, Virginia, and West Virginia; West: Alaska, Arizona, California, Colorado, Hawaii, Idaho, Montana, Nevada, New Mexico, Oregon, Utah, Washington, and Wyoming; Midwest: Illinois, Indiana, Iowa, Kansas, Michigan, Minnesota, Missouri, Nebraska, North Dakota, Ohio, South Dakota, and Wisconsin; Northeast: Connecticut, Maine, Massachusetts, New Hampshire, New Jersey, New York, Pennsylvania, Rhode Island, and Vermont.
† Percentages might not sum to 100 because of rounding.
§ Must have had a negative syphilis test early in pregnancy and a positive syphilis test <30 days before delivery, at day of delivery, or ≤90 days after delivery to be classified as having a seroconversion during pregnancy.
¶ Infant indications of infection include direct detection of *Treponema pallidum* by dark field microscopy or special stains; a reactive nontreponemal test and any one of these signs or symptoms of congenital syphilis: condyloma lata, snuffles, syphilitic rash, hepatosplenomegaly, jaundice/hepatitis, pseudoparalysis, or edema on physical exam; long bone radiograph findings consistent with congenital syphilis; abnormal protein or white blood cell count in the cerebrospinal fluid; or reactive venereal disease research laboratory test in the cerebrospinal fluid.
** Insufficient information submitted to CDC related to maternal prenatal care, testing, or treatment to categorize.

TABLE 2. Missed congenital syphilis prevention opportunities among mothers of infants with congenital syphilis, by U.S. Census region* — United States, 2018

Summary

What is already known about this topic?

Timely identification and treatment of maternal syphilis can prevent congenital syphilis; however, the number of congenital syphilis cases in the United States increased 261% during 2013–2018.

What is added by this report?

Nationally, the most commonly missed opportunities for prevention of congenital syphilis are a lack of adequate maternal treatment despite timely diagnoses of syphilis (31%) and a lack of timely prenatal care (28%), followed by late identification of seroconversions (11%); prevalences of these missed opportunities differ regionally and by race/ethnicity.

What are the implications for public health practice?

Halting continued increases in congenital syphilis requires understanding the missed prevention opportunities and implementing tailored interventions based on local experience.

JAMA | Original Investigation

Association of HIV Preexposure Prophylaxis With Incidence of Sexually Transmitted Infectio Among Individuals at High Risk of HIV Infection

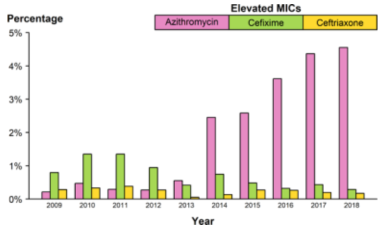
JAMA April 9, 2019:321(14)

Table 2. Incidence of Sexually Transmitted Infections During Follow-up Among Included Participants (N = 2981)

	No. of Infections	Person-Years of Follow-up (n = 3185.0)[a]	Incidence Rate per 100 Person-Years (95% CI)
All STIs	2928		91.9 (88.7-95.3)
Chlamydia	1434		45.0 (42.7-47.4)
Rectal[b]	1091		34.3 (32.3-36.3)
Urethral[b]	381		12.0 (10.8-13.2)
Pharyngeal[b]	127		4.0 (3.3-4.7)
Gonorrhea	1242		39.0 (36.9-41.2)
Rectal[b]	719		22.6 (21.0-24.3)
Urethral[b]	233		7.3 (6.4-8.3)
Pharyngeal[b]	629		19.7 (18.3-21.3)
Syphilis	252	3140.8	8.0 (7.1-9.0)
Site[b]			
Rectal infections	1810		56.8 (53.4-60.4)
Urethral infections	614		19.3 (17.4-21.3)
Pharyngeal infections	756		23.7 (22.0-25.6)
Age group, y[c]			
18-24 (n = 307)	161	186.1	86.5 (74.6-101.5)
25-29 (n = 634)	554	536.3	103.3 (94.9-112.1)
30-34 (n = 620)	733	684.4	107.1 (99.8-115.3)
35-39 (n = 482)	495	593.2	83.4 (76.4-91.2)
40-44 (n = 356)	354	432.2	81.9 (73.8-90.9)
45-49 (n = 437)	486	548.0	88.7 (81.2-97.1)
≥50 (n = 145)	145	204.7	70.8 (60.2-83.4)

- Similar increases in incidence
- Antimicrobial resistance
- Challenge of extragenital infections
- Low efficacy of all but CTX at pharynx
- Limited options for alternative antibiotic regimens

***Neisseria gonorrhoeae* — Percentage of Isolates with Elevated MICs to Azithromycin, Cefixime, and Ceftriaxone, Gonococcal Isolate Surveillance Project (GISP), 2009–2018**



NOTE: Elevated MIC = Azithromycin: ≥2.0 μg/mL; Cefixime: ≥0.25 μg/mL; Ceftriaxone: ≥0.125 μg/mL.

CDC

CDC STD Treatment Guidelines, 2015
Gonorrhea Dual Therapy
Uncomplicated Genital, Rectal, or Pharyngeal Infections

Ceftriaxone 250 mg IM in a single dose **PLUS*** Azithromycin 1 g orally (preferred) or ~~Doxycycline 100 mg BID x 7 days~~

- Regardless of chlamydia test result

CDC 2015 STD Treatment Guidelines
www.cdc.gov/std/treatment

CDC STD Treatment Guidelines, 2020
Gonorrhea Therapy
Uncomplicated Genital, Rectal, or Pharyngeal Infections

500
Ceftriaxone ~~250~~ mg IM in a single dose **PL**

Azith omycin ally rred) or ne 100 x 7 ays

Addresses concerns of:
- Increasing azithromycin resistance
- Potential for increasing MICs to CTX
- Better pharyngeal coverage (?)
- Antimicrobial stewardship

Gonorrhea: When Cephalosporins Are Contraindicated

PO Gentamicin 240 IM/ Azithromycin 2.0g

(IM Administration/Toxicity)

PO Gemifloxacin 340 mg/Azithromycin 2.0g

(GI Toxicity; unavailable)

Novel Antimicrobials Under Study for Gonorrhea

- **Zoliflodacin** (AZ D0914)
  - Spiropyrimidinetrione (topoisomerase inhibitor)
  - Activity at rectum; limited at pharynx
  - Activity vs. *C. trachomatis*, *M. genitalium*
  - Phase II trial completed (Taylor SA NEJM 2018); III underway
- **Gepotidacin** (BTZ116576)
  - Triazaacenaphthylone (topoisomerase inhibitor)
  - High efficacy potential – 3 separate ribosomal targets
  - Phase II trial completed (Taylor SA CID 2018)
- **Solithromycin**
  - Fluoroketolide; inhibits protein synthesis
  - Initial Ph 3 trial did not show non-inferiority to standard-of-care; no resistance but given structural similarity to telithromycin, strains with high-level azithromycin resistance are concern (Hook EW CID 2015)
- **Delafloxacin**
  - Ineffective as single-dose therapy (Hook Sex Transm Dis 2019)

Single-Dose Zoliflodacin (ETX0914) for Treatment of Urogenital Gonorrhea

Stephanie N. Taylor, M.D., Jeanne Marrazzo, M.D., M.P.H., Byron E. Batteiger, M.D., Edward W. Hook, III, M.D., Arlene C. Seña, M.D., M.P.H., Jill Long, M.D., M.P.H., Michael R. Wierzbicki, Ph.D., Hannah Kwak, M.H.S., Shacondra M. Johnson, B.S.P.H., Kenneth Lawrence, Pharm.D., and John Mueller, Ph.D.

Gepotidacin for the Treatment of Uncomplicated Urogenital Gonorrhea: A Phase 2, Randomized, Dose-Ranging, Single-Oral Dose Evaluation

Stephanie N Taylor, David H Morris, Ann K Avery, Kimberly A Workowski, Byron E Batteiger, Courtney A Tiffany, Caroline R Perry, Aparna Raychaudhuri, Nicole E Scangarella-Oman, Mohammad Hossain, ... Show more

Clinical Infectious Diseases, Volume 67, Issue 4, 1 August 2018, Pages 504–512, https://doi.org/10.1093/cid/ciy545

A Phase 2 Trial of Oral Solithromycin 1200 mg or 1000 mg as Single-Dose Oral Therapy for Uncomplicated Gonorrhea

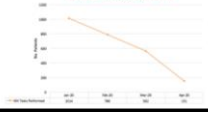
Sexual health during the pandemic

- Major disruption of clinical services
- Diversion of resources (especially public health) to COVID19 efforts
- Access to prevention (including PrEP, contraception) compromised

https://www.cdc.gov/std/prevention/disruptionGuidance.htm

Impact of COVID-19 on HIV PrEP Care at a Boston Community Health Center

Krakower DS, Solleveld P, Mayer KH IAC 2020



- Fenway CHC EMR Jan 1-Apr 30; 3,520 people
- Mostly cis men, White, priv insurance
- PrEP refill lapses associated with younger age, multi- or NR race, Hispanic ethnicity, public insurance

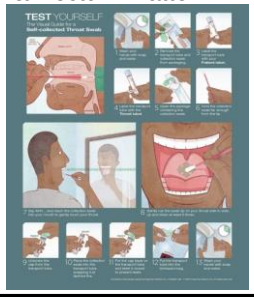
Syndrome	Preferred Treatment In clinic, or other location where injections can be given*	Alternative Treatment When only oral medications are available&
Male urethritis syndrome	Ceftriaxone 250mg intramuscular (IM) in a single dose **PLUS** Azithromycin 1g orally in a single dose (If azithromycin is not available and patient is not pregnant, then doxycycline 100 mg orally twice a day for 7 days is recommended). If cephalosporin allergy is reported, gentamicin 240 mg IM in a single dose **PLUS** azithromycin 2 g orally in single dose is recommended. *When possible, clinics should make arrangements with local pharmacies or other clinics that are still open and can give injections.	Cefixime 800 mg orally in a single dose PLUS Azithromycin 1g orally in a single dose (If azithromycin is not available and the patient is not pregnant, doxycycline 100 mg orally twice a day for 7 days is recommended). **OR** Cefpodoxime 400 mg orally q 12 hours x 2 doses **PLUS** Azithromycin 1g orally in a single dose (If azithromycin is not available and the patient is not pregnant, doxycycline 100 mg orally twice a day for 7 days is recommended). If oral cephalosporin is not available or cephalosporin allergy is reported, azithromycin 2g orally in a single dose. &Alternative regimens should be considered when recommendations treatments from CDC 2015 Treatment Guidelines are not available

Syndrome	Preferred Treatment In clinic, or other location where injections can be given*	Alternative Treatment When only oral medications are available &
Genital ulcer disease (GUD) Suspected primary or secondary syphilis ++^ ++ All pregnant women with syphilis must receive Benzathine penicillin G. ^ If clinical signs of neurosyphilis present (e.g. cranial nerve dysfunction, auditory or ophthalmic abnormalities, meningitis, stroke, acute or chronic altered mental status, loss of vibration sense), further evaluation is warranted	Benzathine penicillin G, 2.4 million units IM in a single dose. *When possible, clinics should make arrangements with local pharmacies or other clinics that are still open and can give injections	Males and non-pregnant females: Doxycycline 100 mg orally twice a day for 14 days. Pregnant: Benzathine penicillin G, 2.4 million units IM in a single dose. &Alternative regimens should be considered when recommendations treatments from CDC 2015 Treatment Guidelines are not available

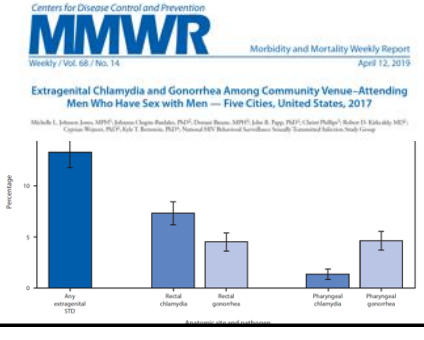
Syndrome	Preferred Treatment In clinic, or other location where injections can be given*	Alternative Treatment When only oral medications are available&
Vaginal discharge syndrome in women without lower abdominal pain, dyspareunia or other signs concerning for pelvic inflammatory disease (PID)	Treatment guided by examination and lab results. *When possible, clinics should make arrangements with local pharmacies or other clinics that are still open and can give injections.	Discharge suggestive of bacterial vaginosis or trichomoniasis (frothy, odor): Metronidazole 500 mg orally twice a day for 7 days. Discharge cottage cheese-like with genital itching: Therapy directed at candida. &Alternative regimens should be considered when recommendations treatments from CDC 2015 Treatment Guidelines are not available.

Syndrome	Preferred Treatment In clinic, or other location where injections can be given*	Alternative Treatment When only oral medications are available[&]
Proctitis syndrome [#]	Ceftriaxone 250mg IM in a single dose **PLUS** doxycycline 100 mg orally twice a day for 7 days. If doxycycline not available or the patient is pregnant, azithromycin 1g orally in single dose recommended.	Cefixime 800 mg orally in a single dose **PLUS** doxycycline 100 mg orally bid for 7 days (if doxycycline not available or the patient is pregnant, azithromycin 1g orally in single dose recommended). **OR** Cefpodoxime 400 mg orally q 12 hours x 2 doses **PLUS** doxycycline 100 mg orally bid for 7 days (if doxycycline not available or the patient is pregnant, azithromycin 1g orally in single dose recommended).
[#]Consider adding therapy for herpes simplex virus if pain present	*When possible, clinics should make arrangements with local pharmacies or other clinics that are still open and can give injections	[&]Alternative regimens should be considered when recommendations treatments from CDC 2015 Treatment Guidelines are not available

Do STIs at the Pharynx & Rectum Matter?



- Recommend screening at all sites relevant to sexual activity on annual basis at minimum
- Oropharyngeal screening for chlamydia not recommended (but treat if + reported)


Centers for Disease Control and Prevention

MMWR

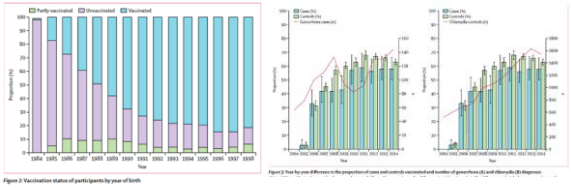
Morbidity and Mortality Weekly Report

Weekly / Vol. 68 / No. 14 April 12, 2019

Extragenital Chlamydia and Gonorrhea Among Community Venue–Attending Men Who Have Sex with Men — Five Cities, United States, 2017

Does the Group B Meningococcal Vaccine Protect Against Gonorrhea?

Retrospective case-control study of subjects immunized with NZ MenB OMV vaccine (2004-2014)



- 877 diagnoses of gonorrhea, 772 diagnoses of gonorrhea/chlamydia co-infection in participants
- Effectiveness of MenB vaccine against gonorrhea estimated to be 33%
- No reduced risk in individuals with gonorrhea/chlamydia coinfection

Petousis-Harris, *Lancet* July 2017

Will an "Optimized" Group B Meningococcal Vaccine Protect Against Gonorrhea?

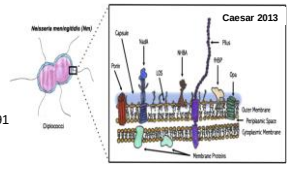
Composition of 4CMenB (Bexsero-GSK)

Outer membrane vesicles (OMV) from non-encapsulated strain MC58
(Group B, New Zealand epidemic strain)

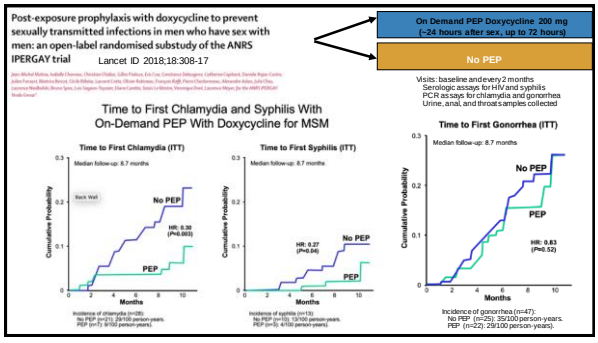
Three purified proteins

- rNadA
  Autotransporter, adhesion
- NHBA
  Neisserial heparin-binding protein; fused to GNA10030
- FHBP
  Factor H-binding protein; fused to GNA2091

Sexually Transmitted Infections (STI) Cooperative Research Centers (CRC): Vaccine Development MAGI Study: to start summer 2020



So what do we do while we wait for a vaccine?



Current Issues

Doxycycline Prophylaxis for Bacterial Sexually Transmitted Infections

Juliana S. Grant,[1] Chrysoulaoula Stafylis,[1] Connie Celum,[1,2,3] Troy Grennan,[4] Bridget Haire,[5] John Kaldor,[5] Anne F. Luetkemeyer,[6] John M. Saunders,[7] Jean-Michel Molina,[8,9] and Jeffrey D. Klausner[1,2,3]

2020;70(8):1247–53
Clinical Infectious Diseases
REVIEW ARTICLE

- Doxy-PEP reduced overall incidence of bacterial STI by 47% in MSM on PrEP (8.7 months of follow-up)
- No effect on gonorrhea, but strong reduction in chlamydia and syphilis
- Analysis of antibiotic resistance still pending
- Long-term benefit & harms not yet known
- No data in reproductive age women
- Several clinical trials planned or underway (www.clinicaltrials.gov); some health departments & providers already using it

Early diagnosis and risk factors of acute hepatitis C in high-risk MSM on preexposure prophylaxis

Julien Gras[a], Nadia Mahjoub[b], Isabelle Charreau[c], Laurent Cotte[d], Cécile Tremblay[e], Julie Chas[f], François Raffi[g], Eric Cua[h], Brigitte Guillon[i], Nicolas Guigue[b], Marie L. Chaix[b,j], Laurence Meyer[e], Jean M. Molina[a,j], Constance Delaugerre[b,j], the IPERGAY Study Group

AIDS January 2020

- High incidence 1.4 cases / 100 PYFU (429 men followed for median of 2.1 y)
- Associated with riskier sex, higher no of partners, chemsex*
- HCV Ag immunoassay & plasma HCV RNA were positive ~2 months before Ab detection, when men were asymptomatic and only 25% had increased ALT
- Direct tests might improve early diagnosis & facilitate therapy

* use of ecstasy/ cocaine/ GHB or GBL /ketamine /crack/ heroin/ speed/ LSD/ mephedrone or slam

Why Discuss STIs in the Era of PrEP and U=U?

JIAS

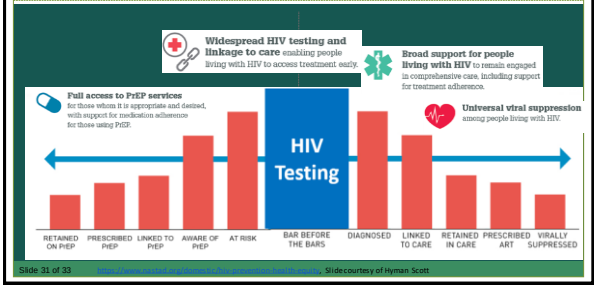
"…mantras like "Getting to Zero"…will never be achieved without addressing the potentiating role of STI in the global HIV pandemic, in addition to responding to other drivers of HIV spread, including economic and gender inequality, and other human rights challenges."

VIEWPOINT

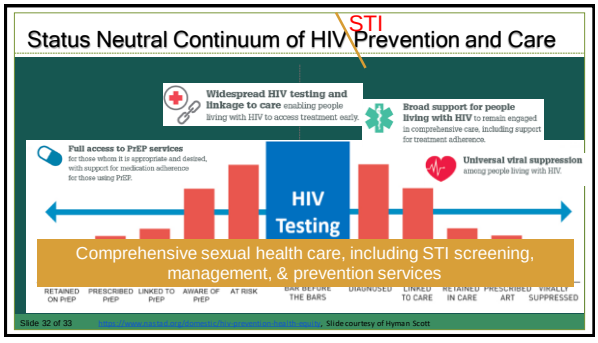
HIV and sexually transmitted infections: responding to the "newest normal"

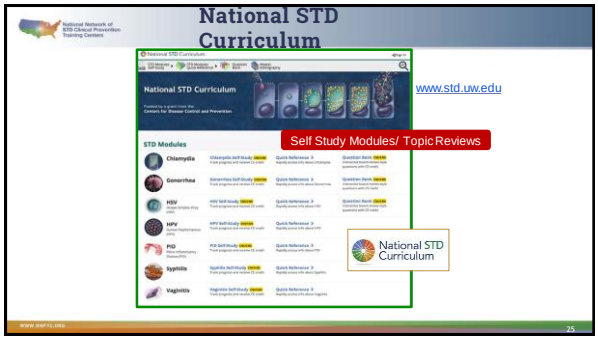
Kenneth H Mayer[1,2,3] and Henry de Vries[4,5,6]

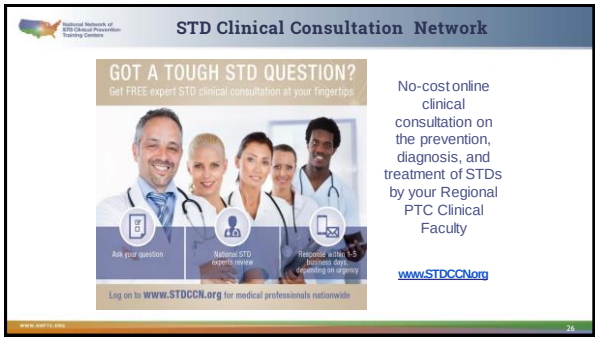
Status Neutral Continuum of HIV Prevention and Care



Slide 31 of 33 Slide courtesy of Hyman Scott


Status Neutral Continuum of HIV Prevention and Care
STI
Widespread HIV testing and linkage to care enabling people living with HIV to access treatment early.
Broad support for people living with HIV to remain engaged in comprehensive care, including support for treatment adherence.
Full access to PrEP services for those whom it is appropriate and desired, with support for medication adherence for those using PrEP.
Universal viral suppression among people living with HIV.
HIV Testing
Comprehensive sexual health care, including STI screening, management, & prevention services
RETAINED ON PrEP
PRESCRIBED PrEP
LINKED TO PrEP
AWARE OF PrEP
AT RISK
DIAGNOSED
LINKED TO CARE
RETAINED IN CARE
PRESCRIBED ART
VIRALLY SUPPRESSED
Slide 32 of 33
Slide courtesy of Hyman Scott


National STD Curriculum
www.std.uw.edu
Self Study Modules/ Topic Reviews
National STD Curriculum
STD Modules
Chlamydia
Gonorrhea
HSV
HPV
PID
Syphilis
Vaginitis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Ask your question
National STD experts review
Response within 1-5 business days depending on urgency
Log on to www.STDCCN.org for medical professionals nationwide
No-cost online clinical consultation on the prevention, diagnosis, and treatment of STDs by your Regional PTC Clinical Faculty
www.STDCCN.org

Question-and-Answer Session