



*Training course in sexually transmitted infections, HIV/AIDS 2018*

*Toward global prevention of  
sexually transmitted infections:  
the need for STI vaccines*

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# STIs and global public health

- ❑ STIs have profound impact on sexual, reproductive, and maternal-child health
- ❑ STI control is a core component of WHO's Global Strategy on Reproductive Health
- ❑ Essential to achieving MDGs 4 (child health), 5 (maternal health), 6 (HIV prevention)
- ❑ STI control remains challenging in most settings



# HPV and HBV vaccines: major advances

- ❑ Safe, highly efficacious vaccines against HPV and HBV have been major advances in STI prevention
- ❑ Limitations of other interventions provide important reasons for working toward new STI vaccines

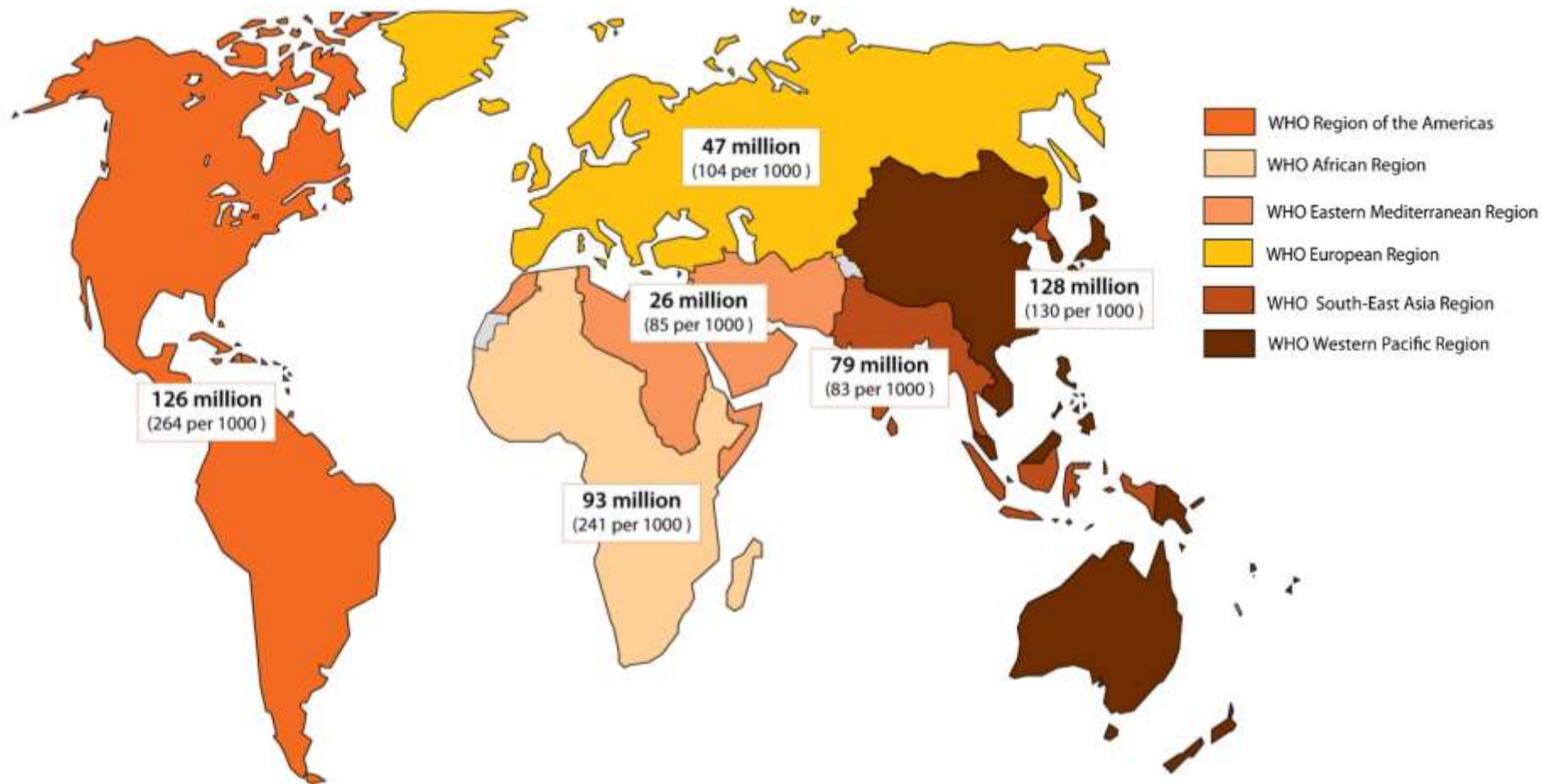


# Outline

- ❑ Global epidemiology of STIs and STI-associated complications
- ❑ Challenges to existing interventions for STI control
- ❑ The need for new STI vaccines for future prevention efforts

# Global epidemiology of STIs

# WHO estimates 499 million new cases of curable STIs in 2008



Curable STIs: chlamydia, gonorrhoea, syphilis, trichomoniasis

# Curable STIs: a global snapshot

- Individual curable STIs, 2008

106 million	Chlamydia
106 million	Gonorrhoea
11 million	Syphilis
276 million	Trichomoniasis

- Overall, numbers not decreasing compared with 2005 estimate of 448 million

Source: WHO. Global incidence and prevalence of selected curable sexually transmitted infections - 2008.

# Viral STIs: large proportion of prevalent STIs

- ❑ HSV-2 infection affects an estimated 536 million people globally
- ❑ An estimated 291 million women have HPV infection at any point in time
  - Numbers of men likely similar
- ❑ Approximately 360 million people suffer chronic HBV infections
  - Most acquired perinatally



# STI-associated complications

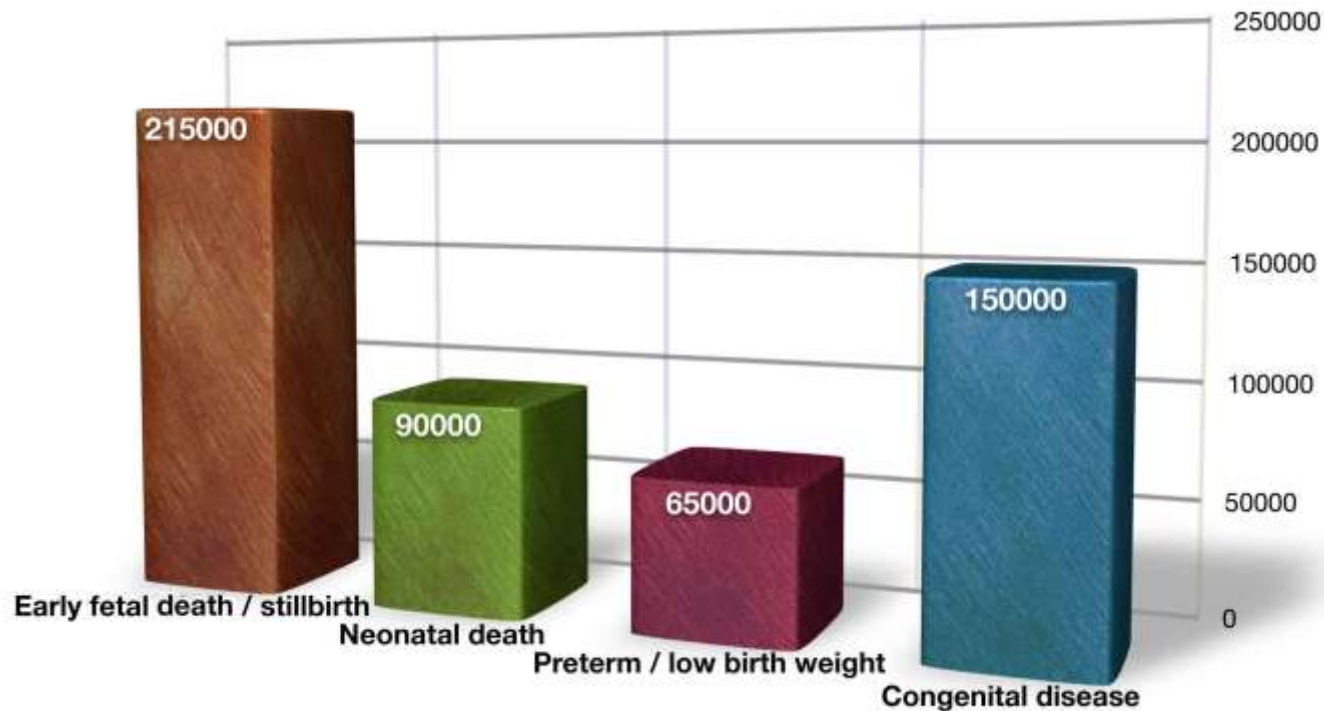
# Genital symptoms

- ❑ Most STIs asymptomatic or unrecognized
- ❑ When symptoms occur, can have important impact on quality of life

Chlamydia, gonorrhea, trichomoniasis	Vaginal discharge syndromes, urethritis
HSV, syphilis	Genital ulceration
HPV	Genital warts

# Pregnancy complications

- Untreated syphilis in pregnancy leads to more than half a million adverse outcomes each year



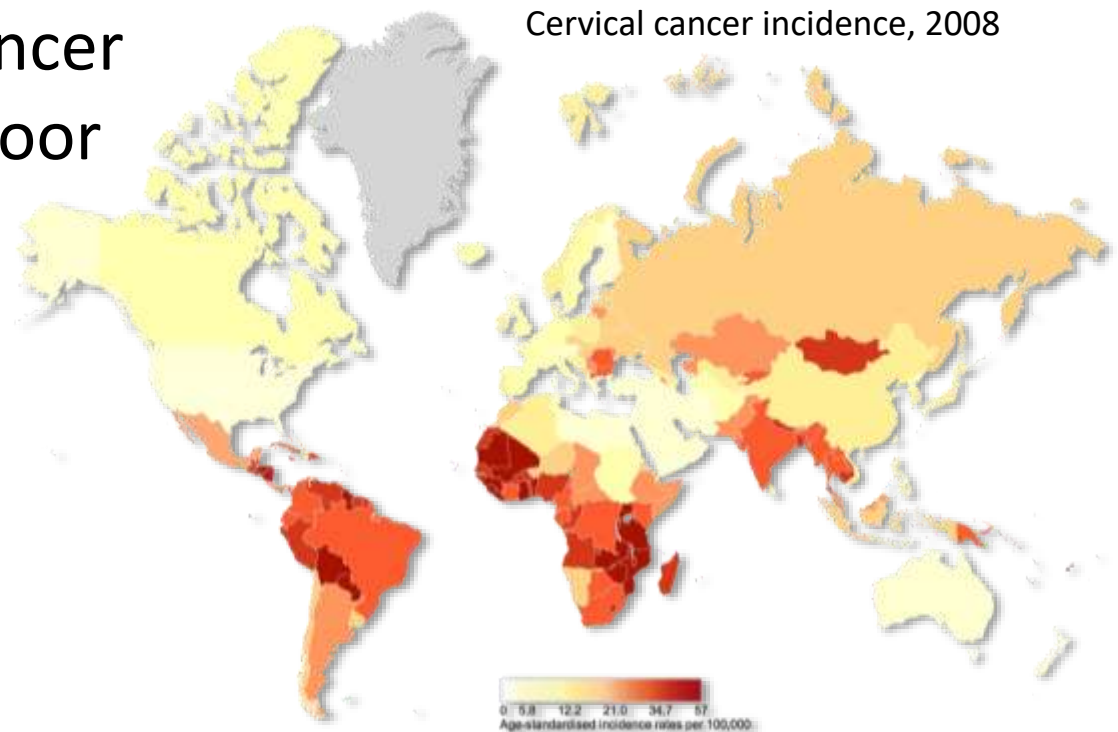
# Pregnancy complications

- Remaining STIs can lead to variety of adverse maternal-child outcomes

Curable STIs	Preterm labor
Chlamydia, gonorrhea	Ophthalmia neonatorum
Chlamydia	Neonatal pneumonia
HSV	Neonatal herpes

# Cancer

- ❑ HPV and HBV are oncogenic
- ❑ HPV infection: 530,000 cervical cancer cases and 275,000 cervical cancer deaths each year
- ❑ Highest cervical cancer rates in resource-poor settings

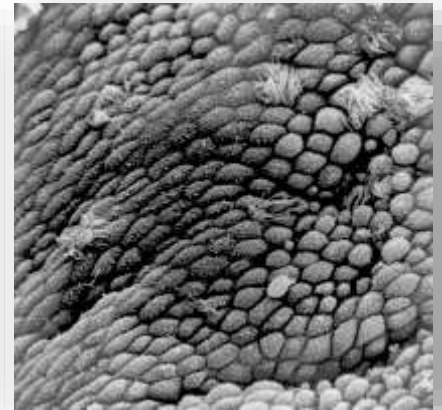


# Upper genital tract disease

- ❑ Chlamydia, gonorrhea can ascend to upper genital tract and cause pelvic inflammatory disease (PID)
- ❑ Long-term sequelae
  - Tubal factor infertility
  - Ectopic pregnancy
  - Chronic pelvic pain

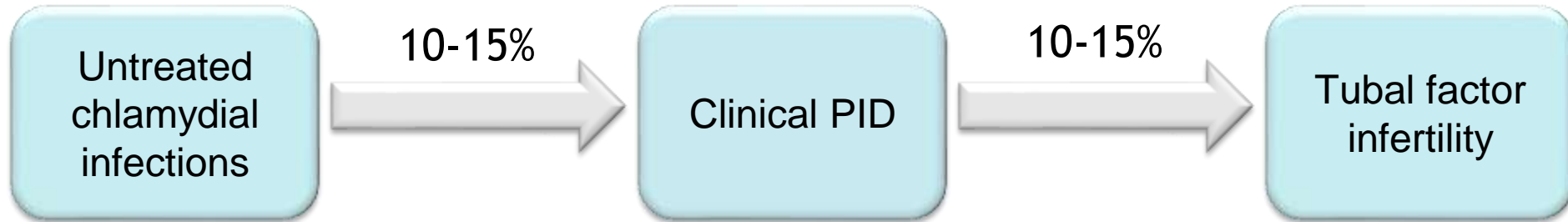


Normal tubal tissue, 1200x

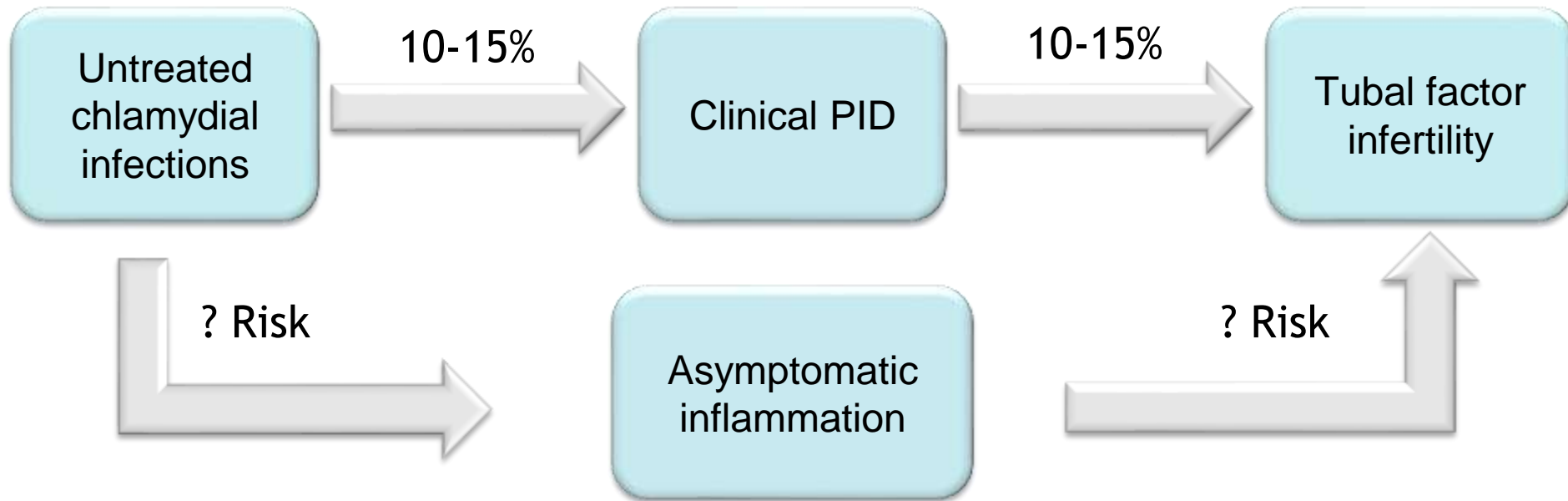


Post-PID, 1200x

# Upper genital tract disease

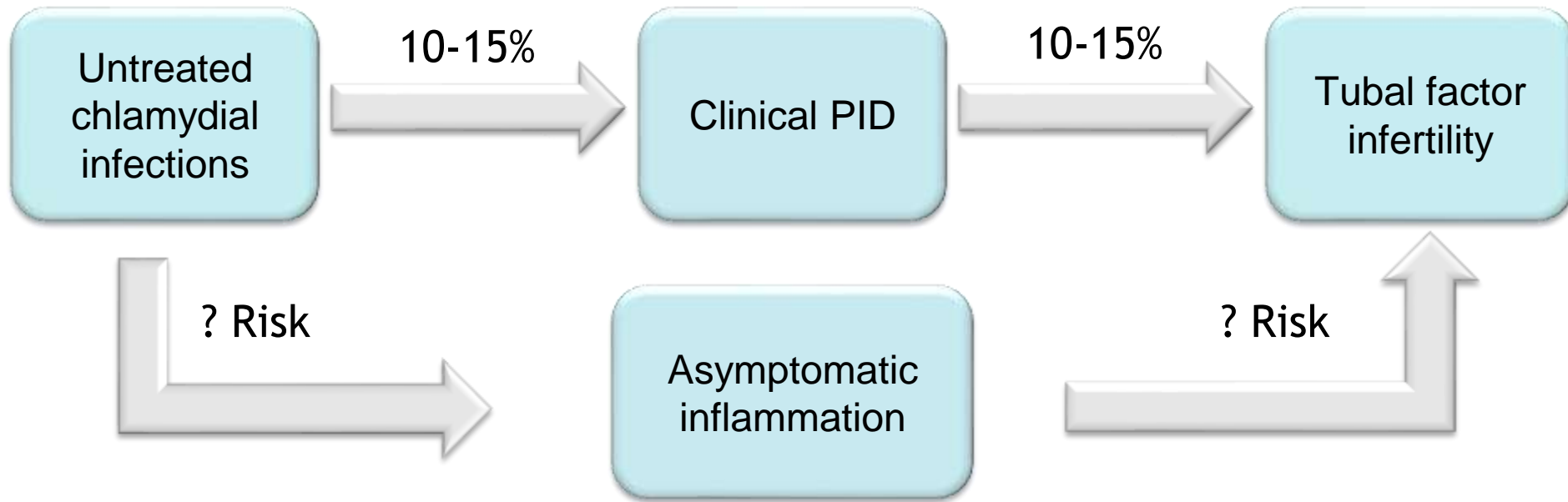


# Upper genital tract disease





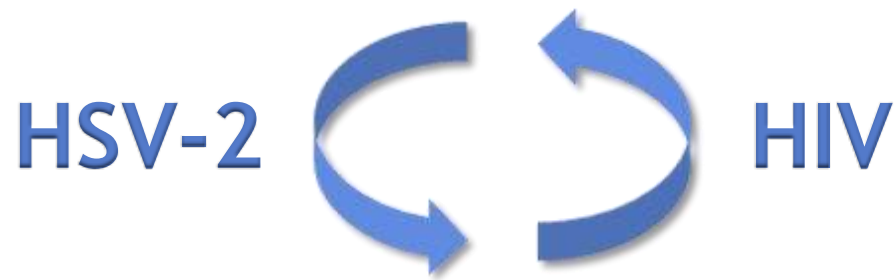
# Upper genital tract disease



- Almost 100 million chlamydia & gonorrhoea infections among women globally each year

# Increased HIV risk

- HSV-2 infection: 3-fold increased risk of acquiring HIV
  - Co-infection: more likely to transmit HIV



- Curable STIs may also be associated with increased HIV acquisition, by up to 2- to 3-fold
  - Urethritis and cervicitis increase HIV shedding

# Psychosocial consequences

- ❑ Difficult to quantify profound psychosocial impact
- ❑ STI diagnosis: stigma, shame, decreased self-worth
- ❑ Anxiety about sexual relationships, future reproductive health
- ❑ Disruption of partnerships, even intimate partner violence



# Challenges to existing interventions for STI control

# Public health approach to STI control

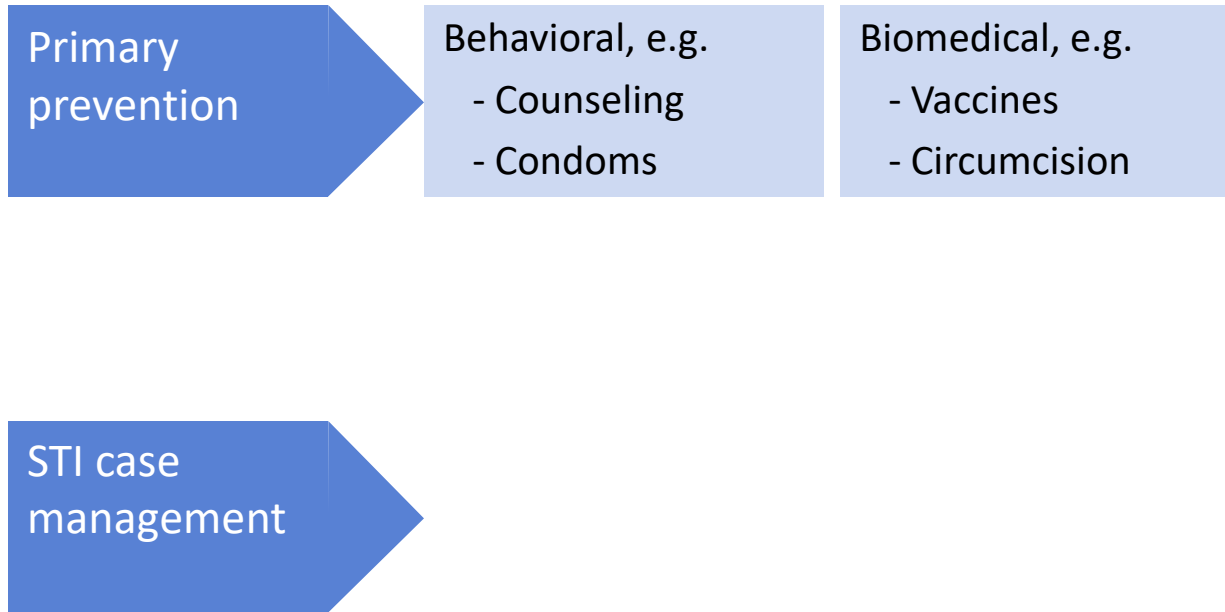


Primary  
prevention

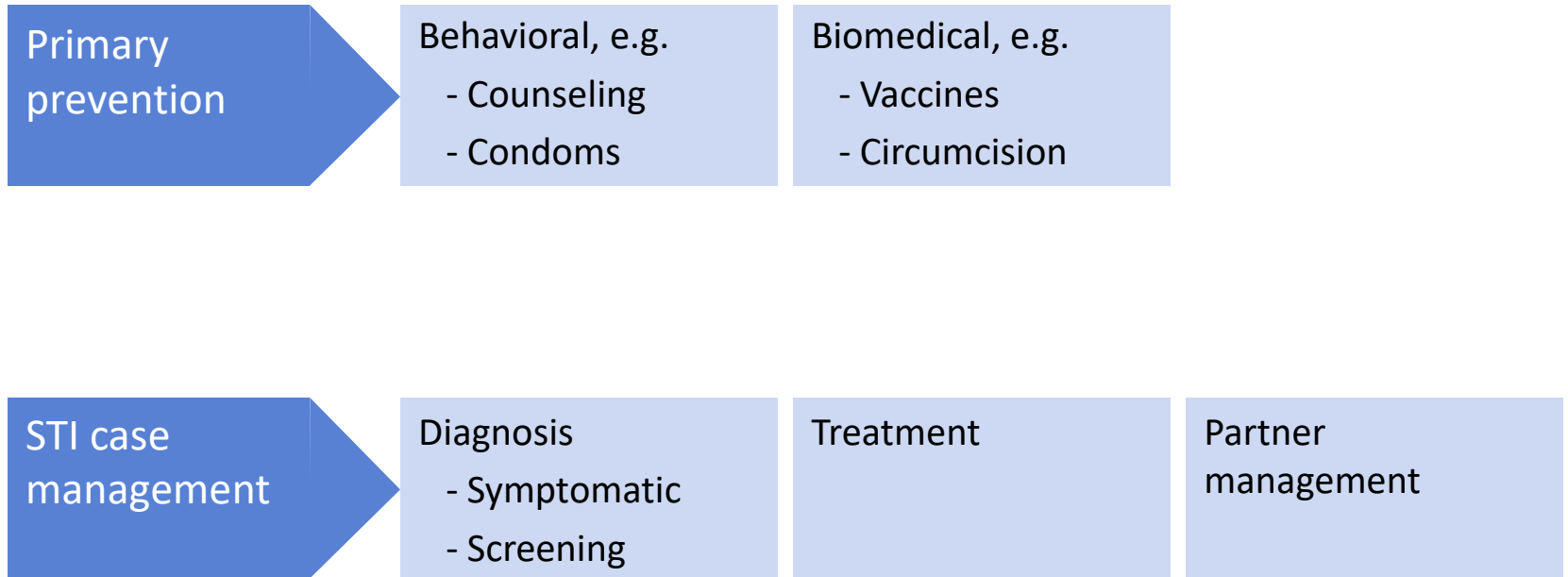


STI case  
management

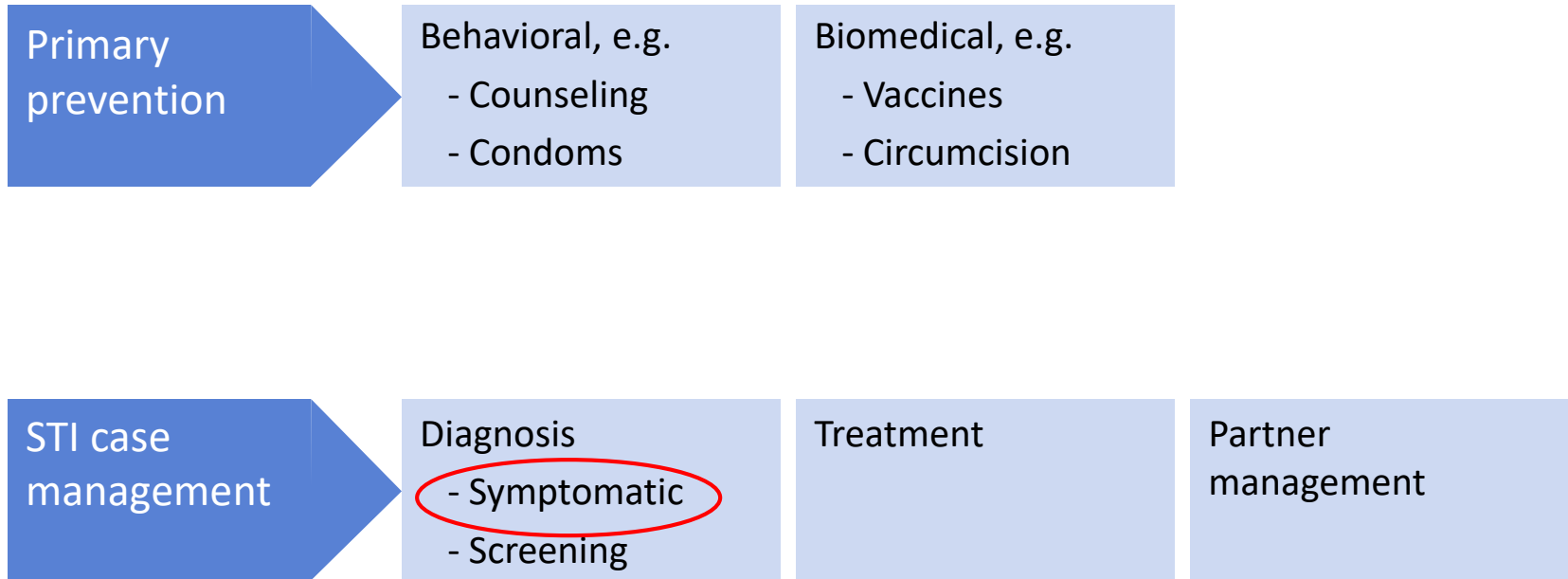
# Public health approach to STI control



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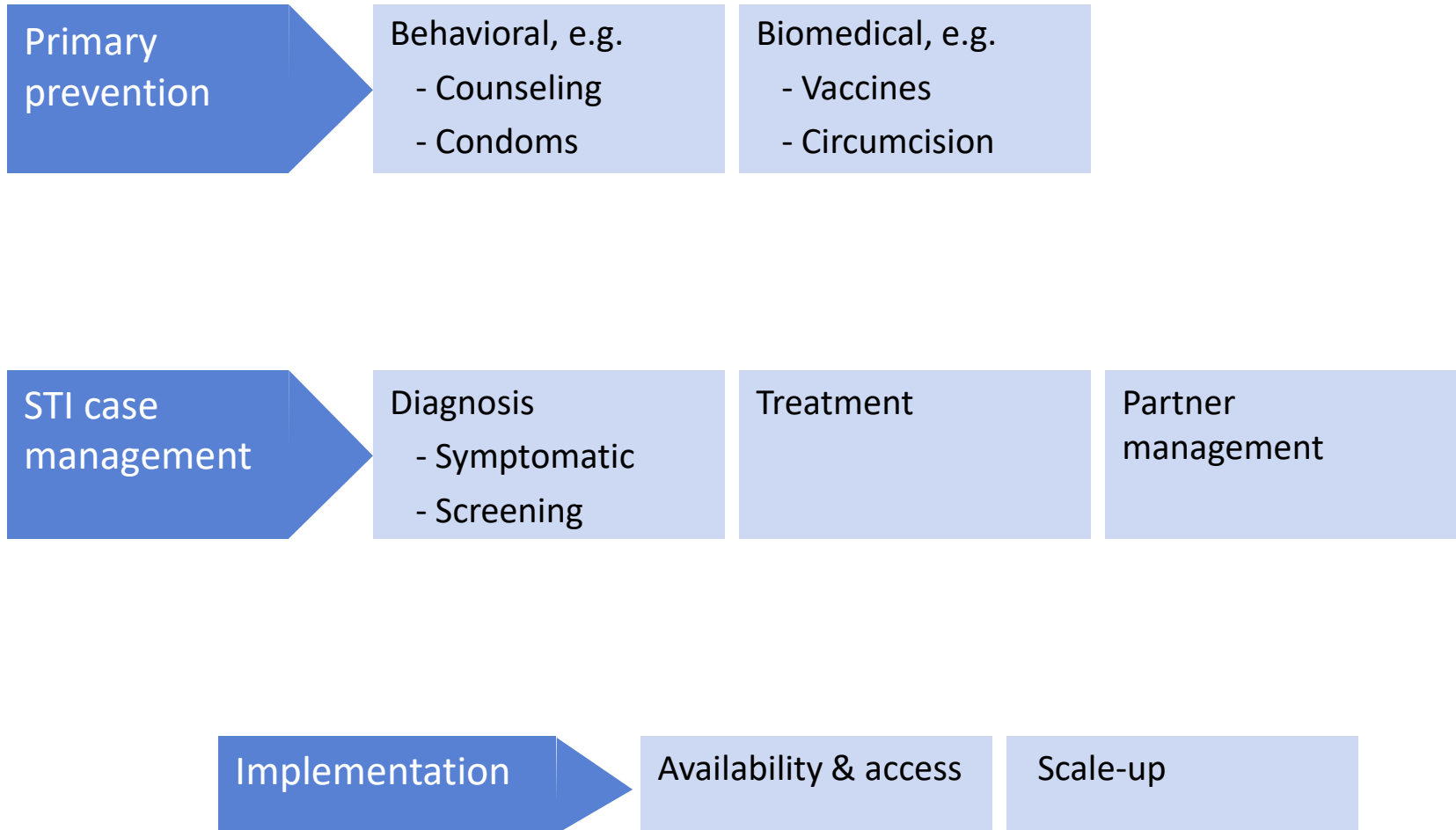


# Public health approach to STI control

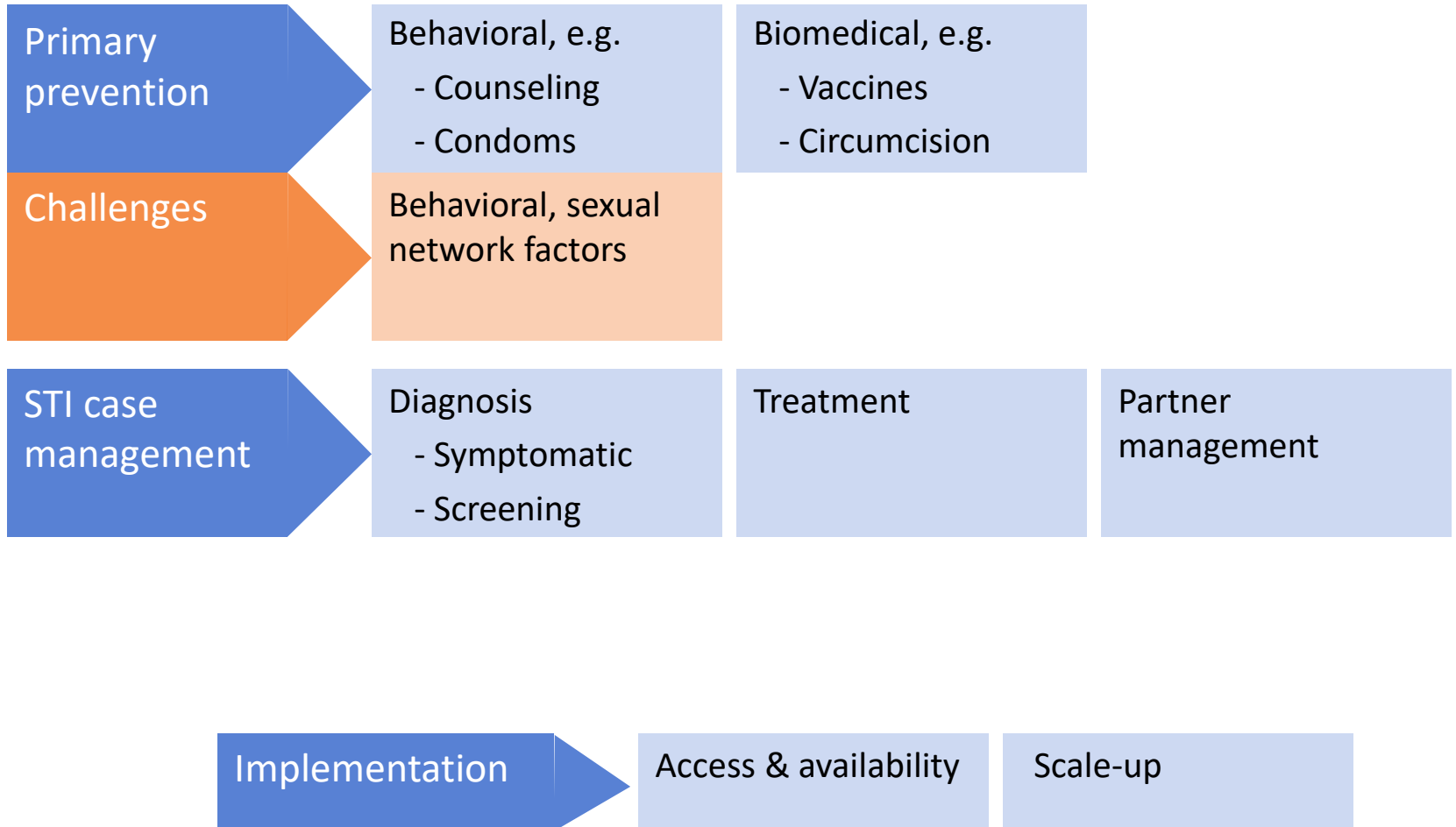




# Public health approach to STI control



# Public health approach to STI control

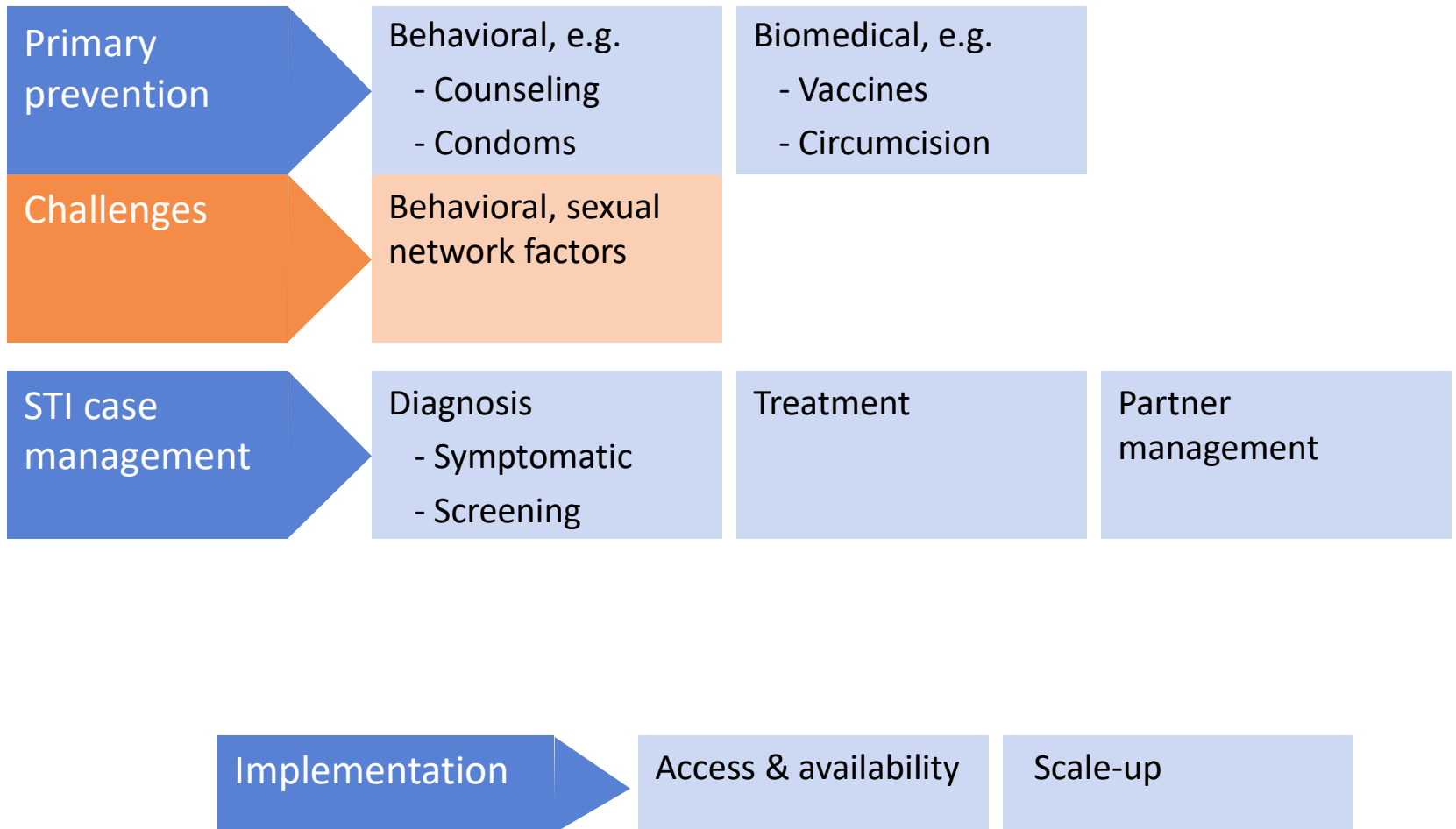


# Challenges: behavioral and network factors

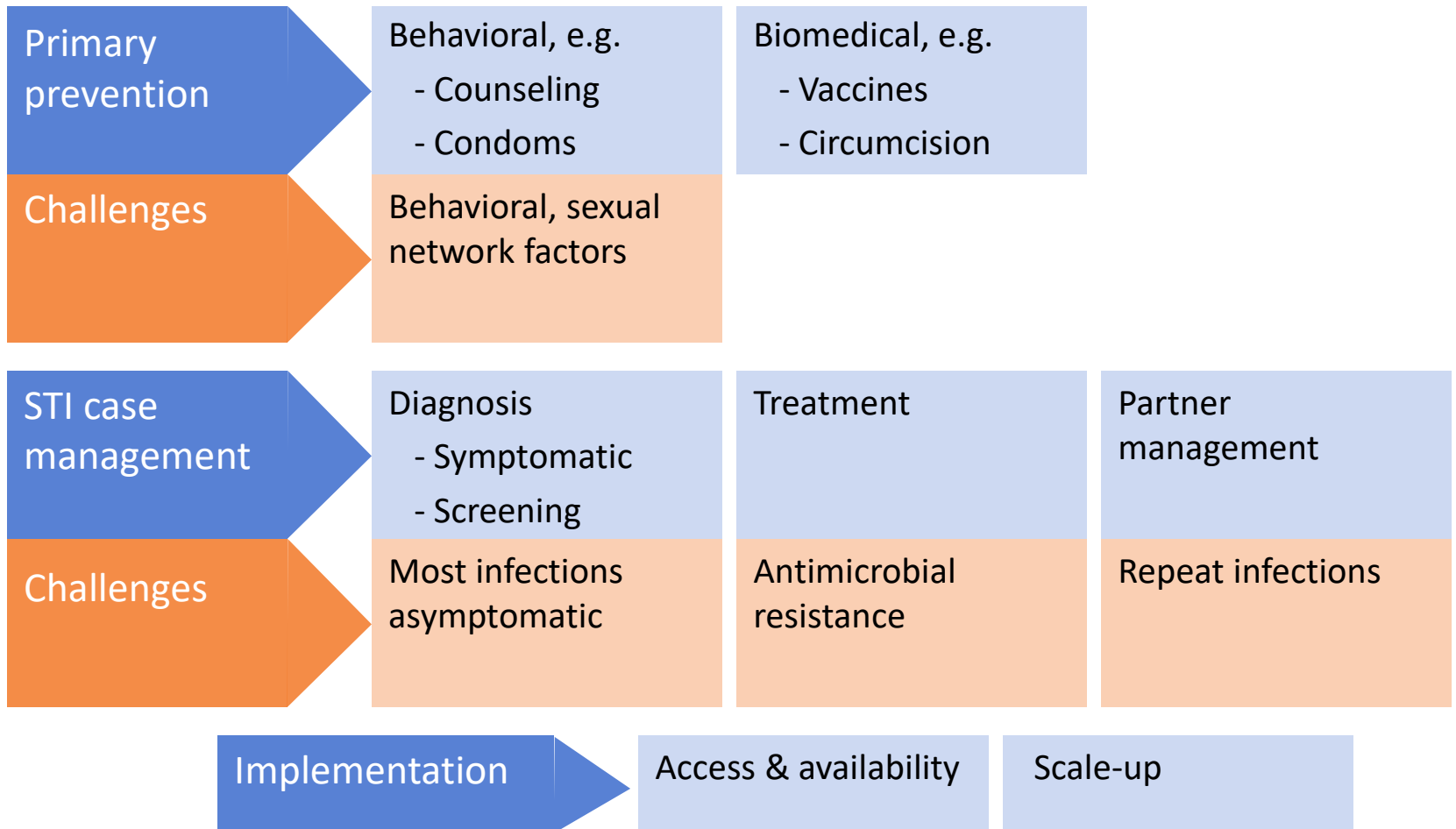
- ❑ Limits to progress made with condom promotion as main primary prevention measure
- ❑ Cultural factors affect acceptability of condoms, comfort level with discussing sex
- ❑ Sustainability of behavior change
- ❑ Individual behavior may be less important than network risk



# Public health approach to STI control



# Public health approach to STI control



# Challenges: asymptomatic infection

- ❑ Vast majority of STIs cause few or no symptoms
  - But can still lead to harmful sequelae
- ❑ Symptomatic case management just “tip of the iceberg”
- ❑ Syndromic management inaccurate for syndromes like vaginal discharge



# Challenges: antimicrobial resistance

- ❑ Drug-resistant gonorrhoea is major threat to STI control globally
  - Resistance to cephalosporins, only first-line drugs, increasingly reported
- ❑ Nitroimidazoles only class active against trichomoniasis
  - Low-level resistance being reported

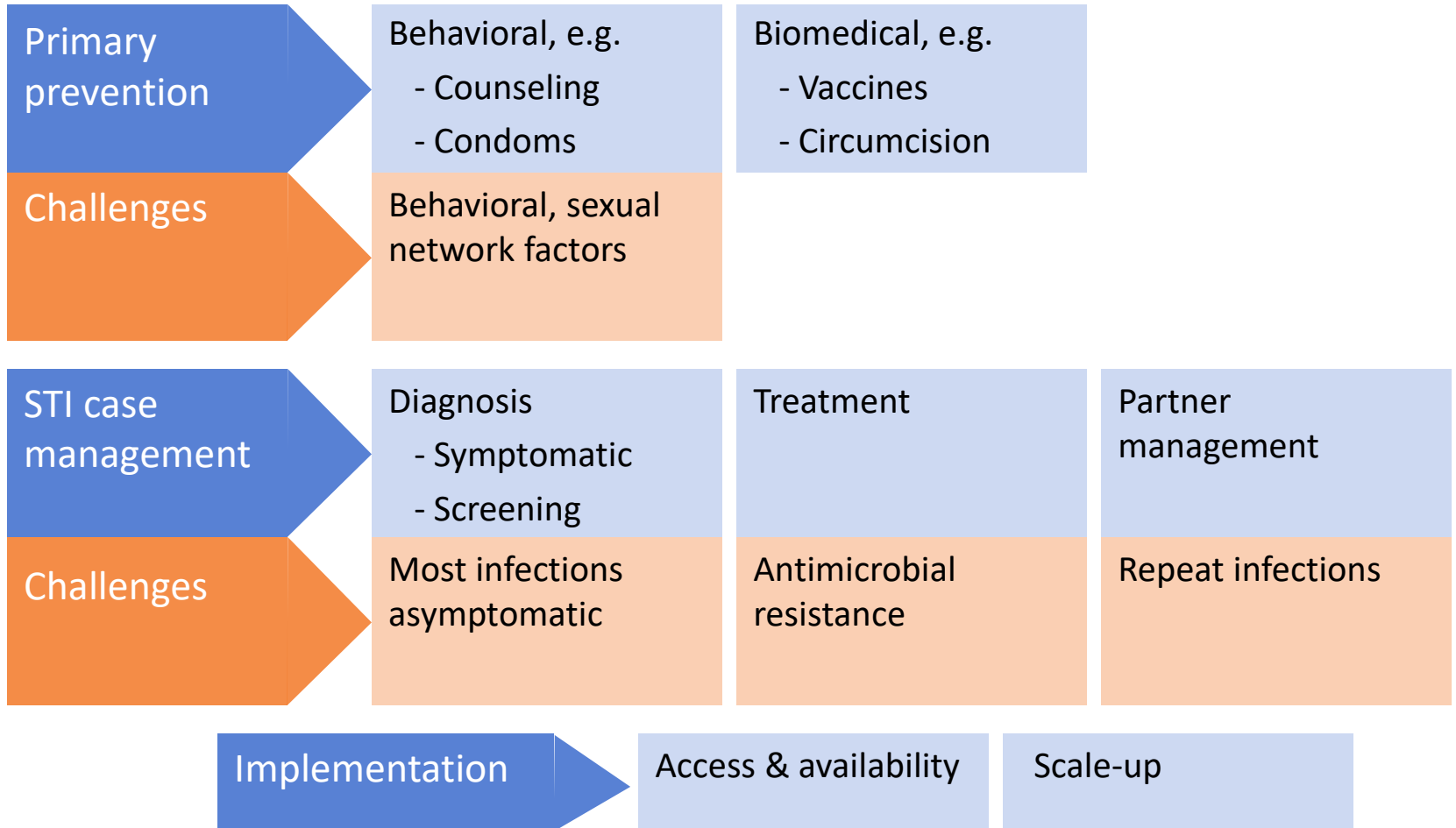


# Challenges: repeat infections

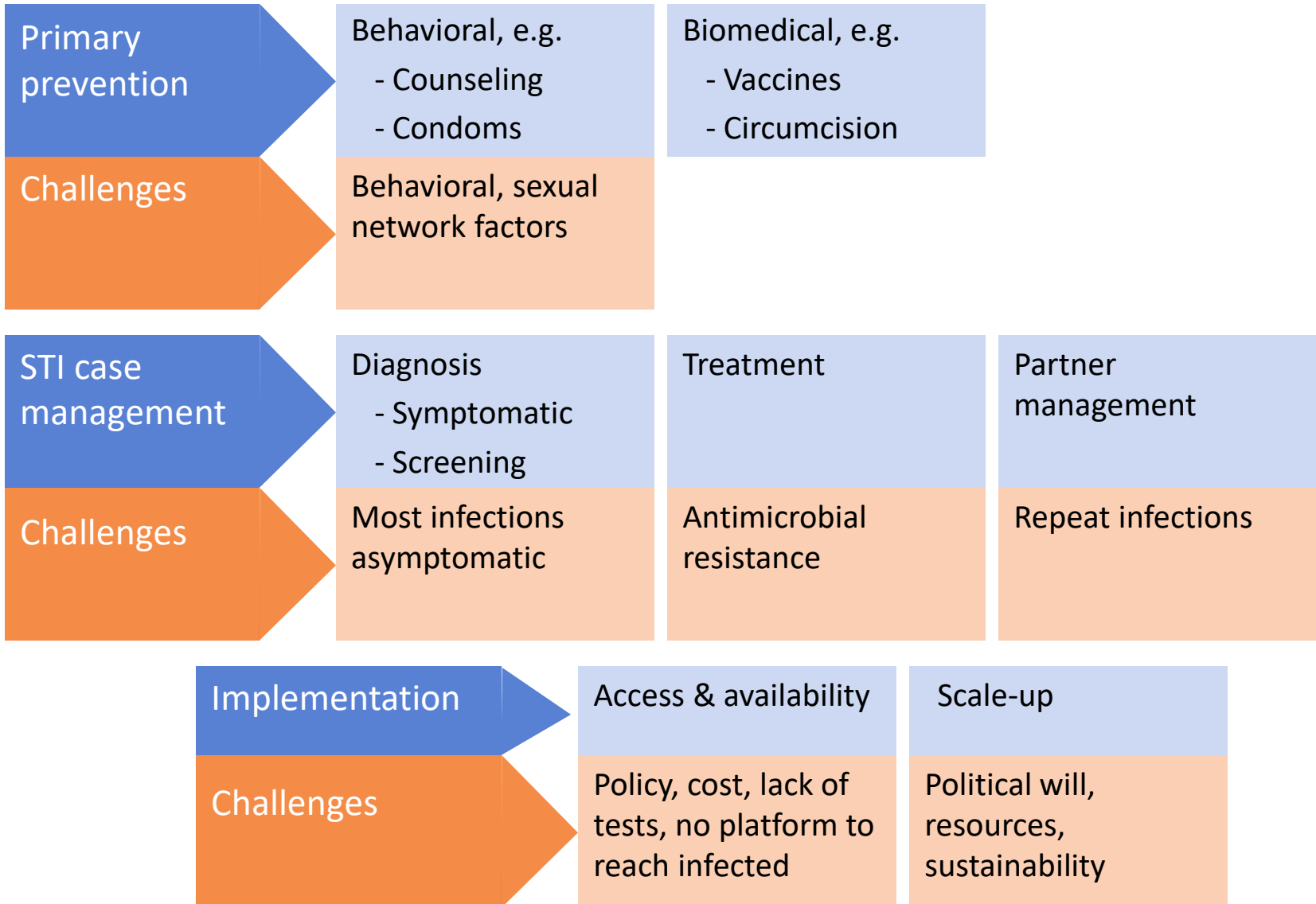
- ❑ Curable STIs do not result in strong, lasting protective immunity
- ❑ Repeat infection rates for chlamydia, gonorrhoea, trichomoniasis: 10-20% after treatment
- ❑ Repeat infection more common when little attention to partner management
  - Challenging in most settings



# Public health approach to STI control



# Public health approach to STI control



# Challenges: policy and political will

- ❑ STIs are stigmatizing; lack of champions
- ❑ Many STI interventions either not fully effective or difficult to quantify impact
  - Harder to garner support

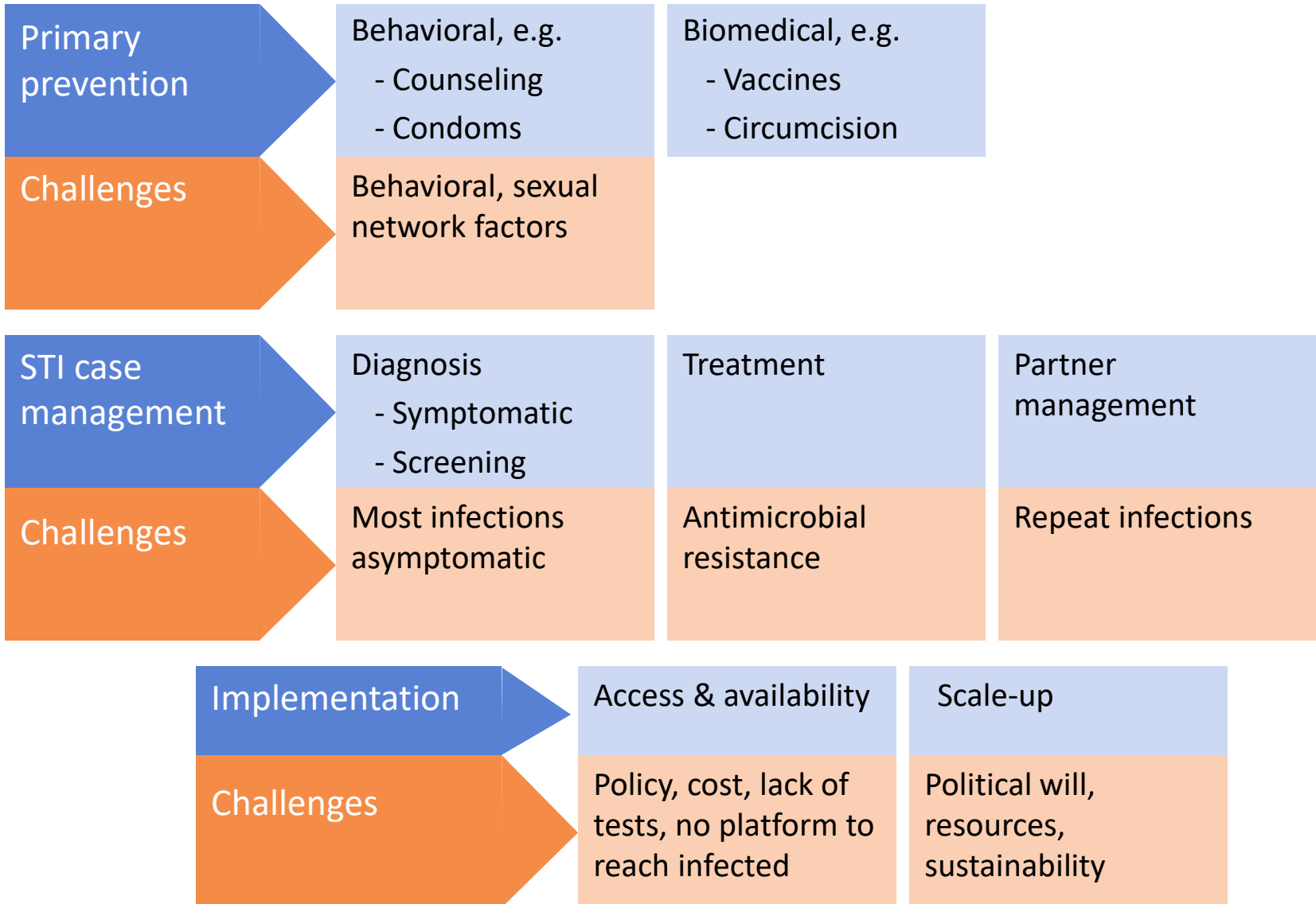


# Challenges: implementation factors

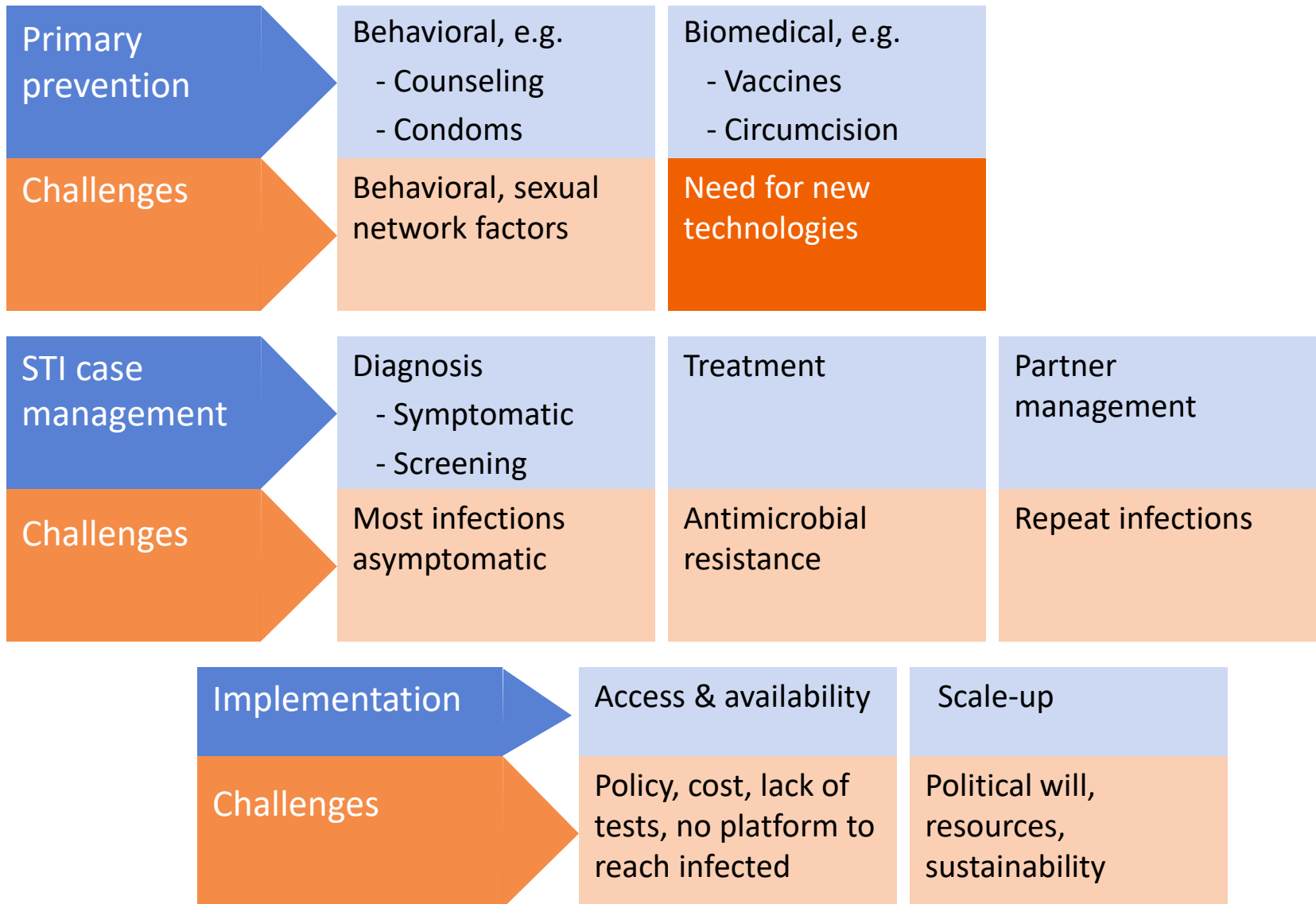
- ❑ Lack of availability and access to affordable, easy-to-use diagnostic tests in much of world
  - New rapid tests for syphilis
  - Rapid tests for others may be on horizon
- ❑ Availability does not ensure effective implementation
  - Platform to access target population
  - Commitment, resources for scale-up
  - Sustainability



# Public health approach to STI control

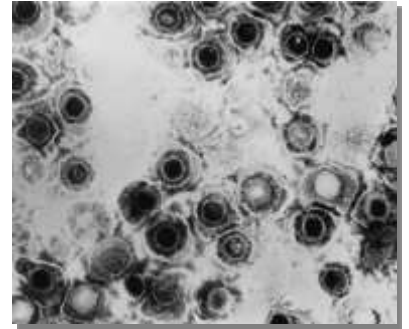


# Public health approach to STI control



# The need for new STI vaccines for future prevention efforts

# HSV-2 infection

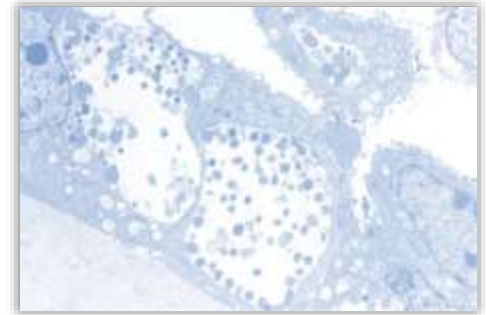


- ❑ >500 million HSV-2 infections globally
  - Incurable, lifelong
  - Marked synergy with HIV
- ❑ Current HSV-2 prevention strategies may not have feasible, sustainable population impact
- ❑ HSV vaccine could have impact on HIV spread, neonatal herpes, genital symptoms

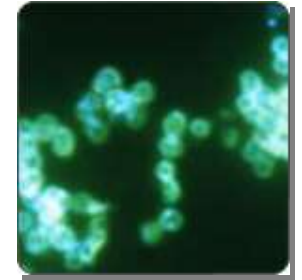


# Chlamydia

- ❑ Global burden of chlamydia-related PID, infertility likely very high
  - Lower-income countries: most chlamydia missed
- ❑ Screening programs difficult to bring to scale
  - Do not appear to have reduced chlamydia prevalence
- ❑ Repeat infections: arrested immunity?
- ❑ Complexities of current chlamydia control efforts highlight need for work toward chlamydia vaccine



# Gonorrhea

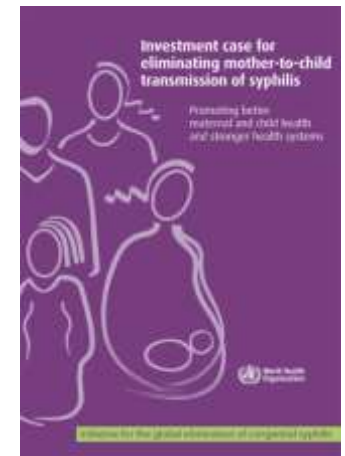


- ❑ Prevention threatened by antimicrobial resistance to only first-line drugs for 106 million cases/year
- ❑ Trials of new treatment regimens ongoing
  - *N. gonorrhoeae* has developed resistance to 4 different classes of antibiotics since first treatable
- ❑ Progress toward gonorrhea vaccine also needed

# Syphilis



- ❑ Over half a million adverse pregnancy outcomes/year
- ❑ New point-of-care diagnostic tests, cheap on-site treatment, antenatal care access
  - WHO: global strategy for elimination of mother-to-child transmission of syphilis
- ❑ If implementation remains challenging, no decrease in community transmission
  - Syphilis vaccine will be an important pursuit



# Trichomoniasis



- ❑ More cases of trichomoniasis than other curable STIs combined
  - Vaginal symptoms, preterm delivery, HIV enhancement
- ❑ Lack of diagnostic tests hampers control globally
- ❑ Reports of low-level nitroimidazole resistance worrisome; only one drug class
- ❑ New diagnostic tests and drug regimens needed, with continued work toward developing vaccine

# Summary

- ❑ More than half a billion STIs occur annually
- ❑ Large burden of sexual, reproductive, maternal-child health consequences
- ❑ Current STI control challenged by several behavioral, biological, and implementation factors
- ❑ Coordination and advancement of STI vaccines is a major priority for sustainable global STI control

# Acknowledgments

**Nicola Low**

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# 2010 Global Burden of Disease study

- Curable STIs accounted for 11 million DALYs lost

STI	DALYs in 1000s
Chlamydia	714
Gonorrhoea	282
Syphilis	9,600
Trichomoniasis	167

- Cervical cancer: another 6.4 million DALYs
- Did not calculate DALY estimates for HSV-2

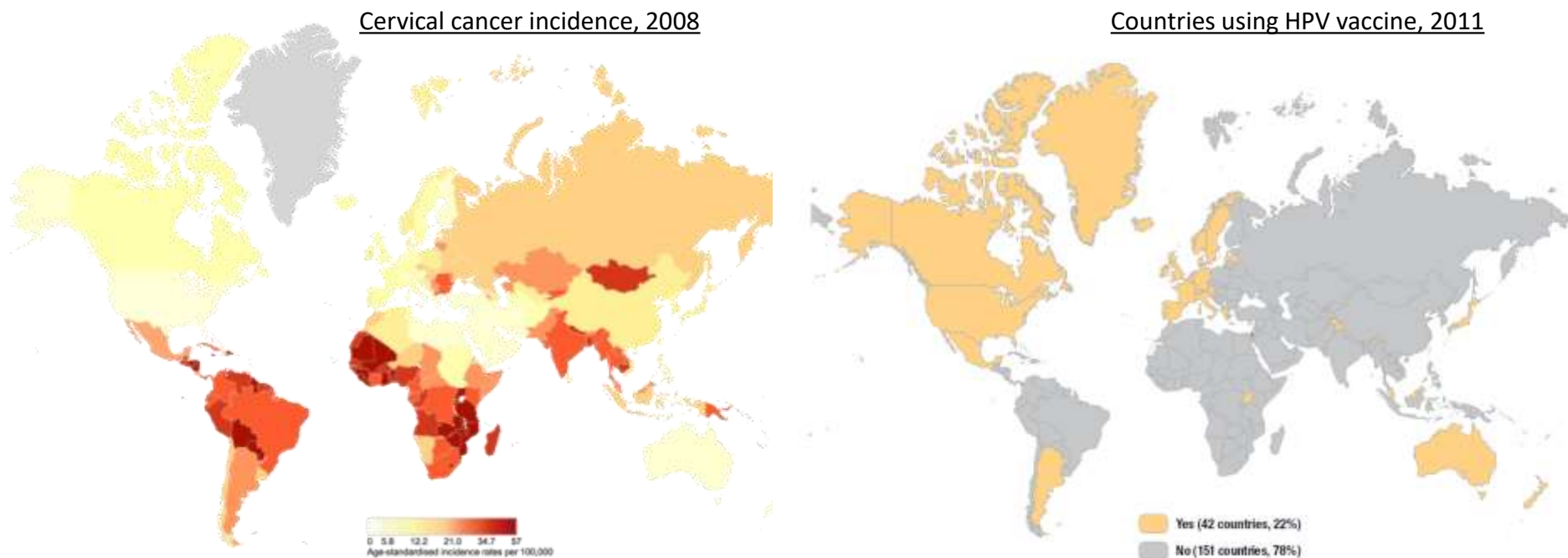
# Financial costs

- ❑ In US, \$3 billion in direct costs to diagnose and treat 19.7 million cases of STIs and complications
  - Excluding HIV and pregnancy-related outcomes
- ❑ Costs associated with adverse STI outcomes less well documented in resource-poor settings



# Implementation of STI vaccines

- ❑ HPV vaccine not yet implemented in countries with highest cervical cancer rates



- ❑ Lessons learned will inform future STI vaccine delivery