



Training Course in Sexual and Reproductive Health Research 2014
**Module: Principles and Practice of Sexually Transmitted Infections
Prevention and Care**

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

Sami Gottlieb - WHO



SHR Department of Reproductive Health and Research



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

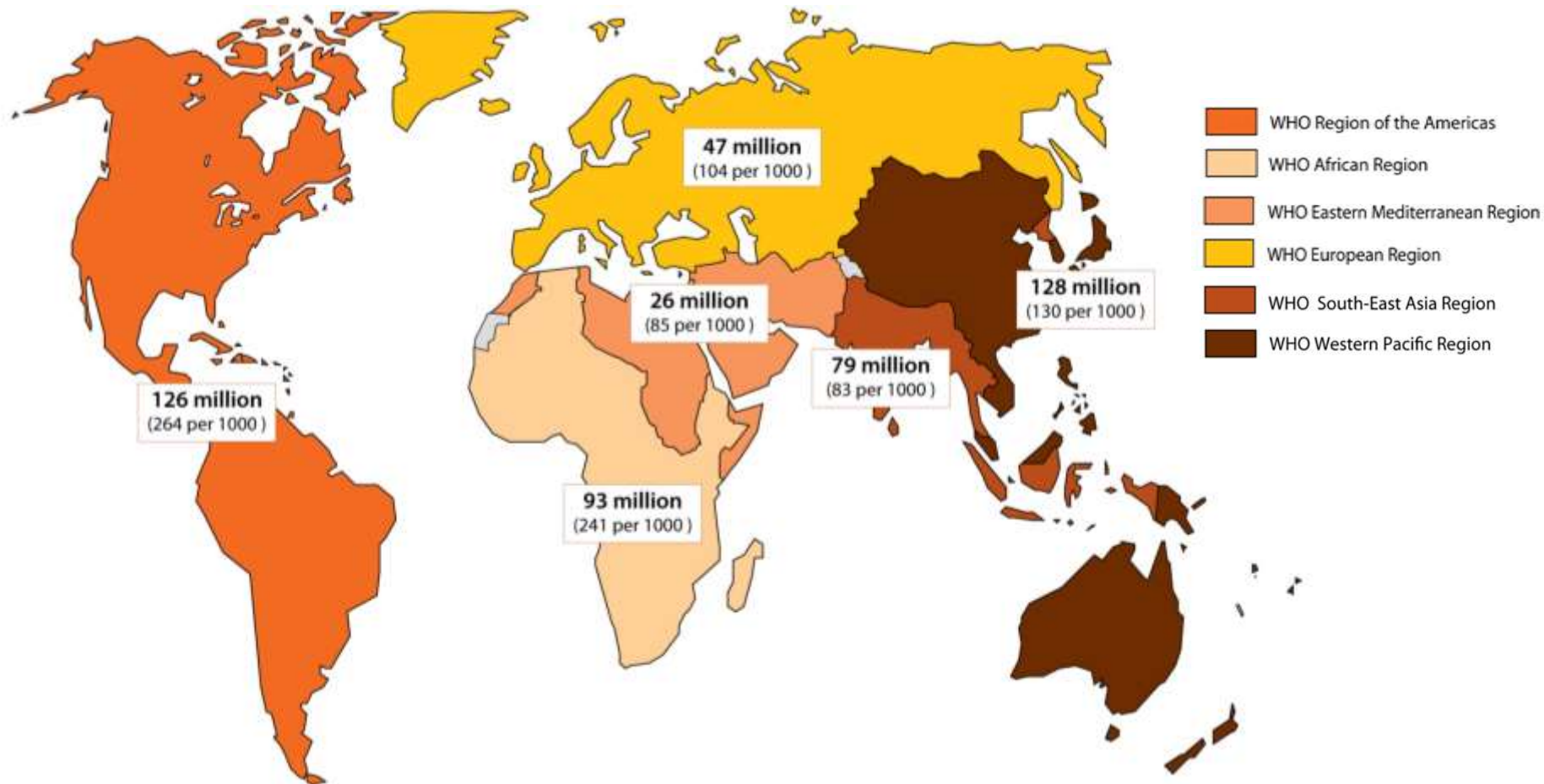


Outline

- ❑ 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

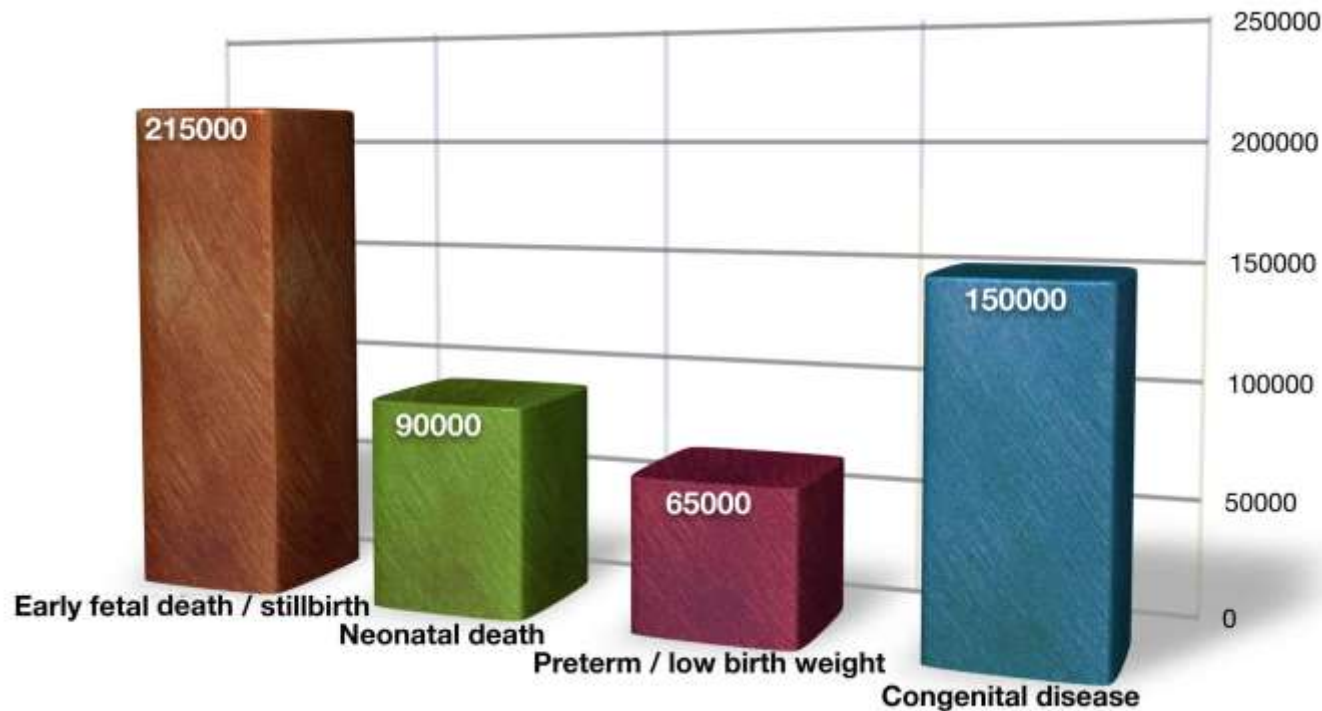
Genital symptoms

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

Chlamydia, gonorrhoea, 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



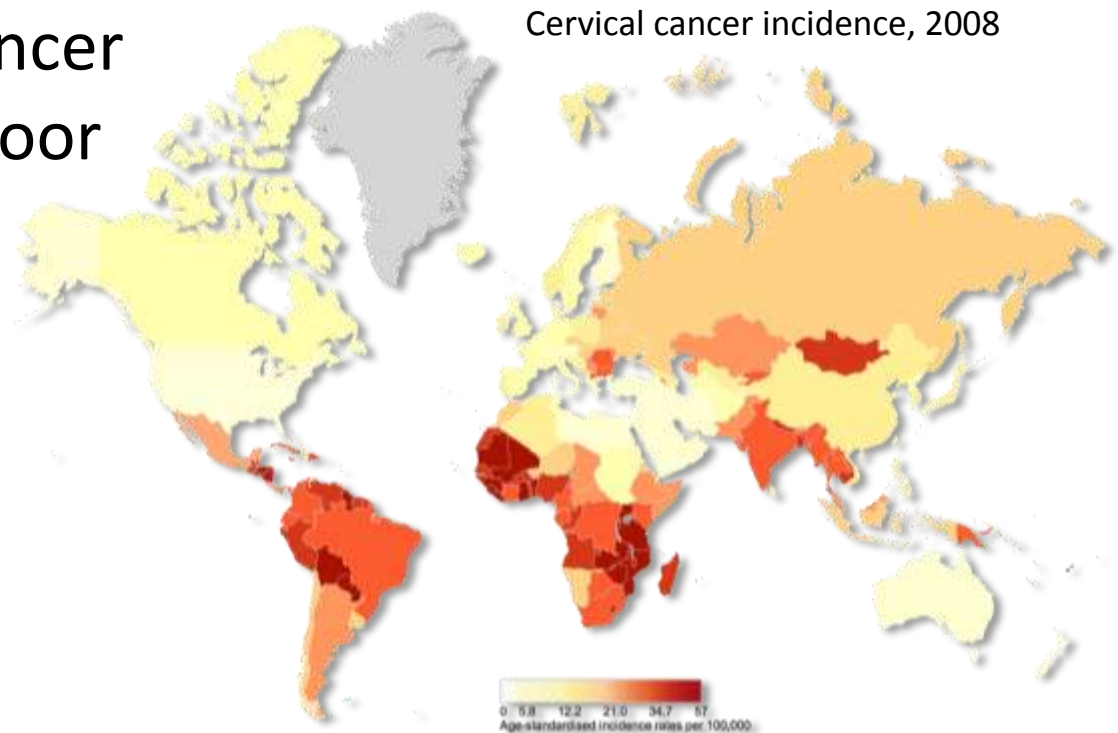
Pregnancy complications

- 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

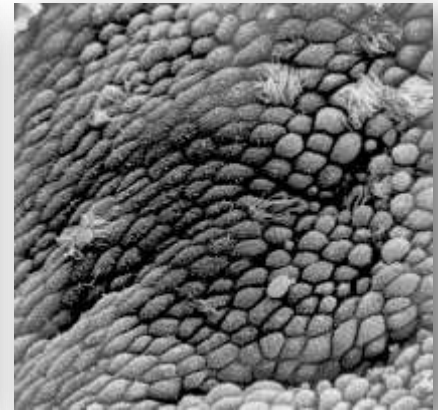


Upper genital tract disease

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

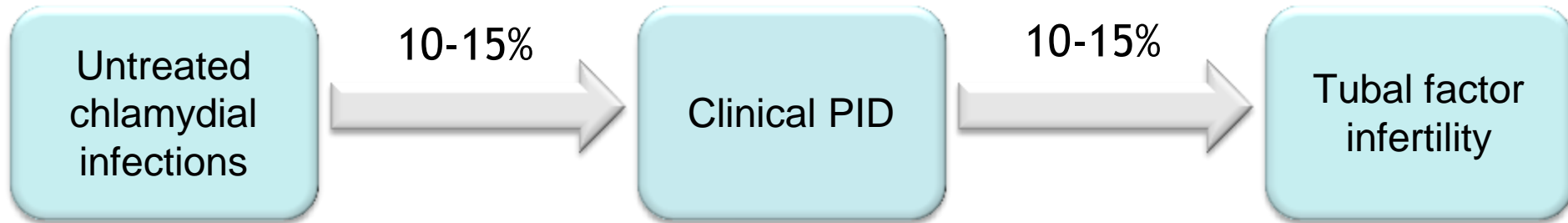


Normal tubal tissue, 1200x

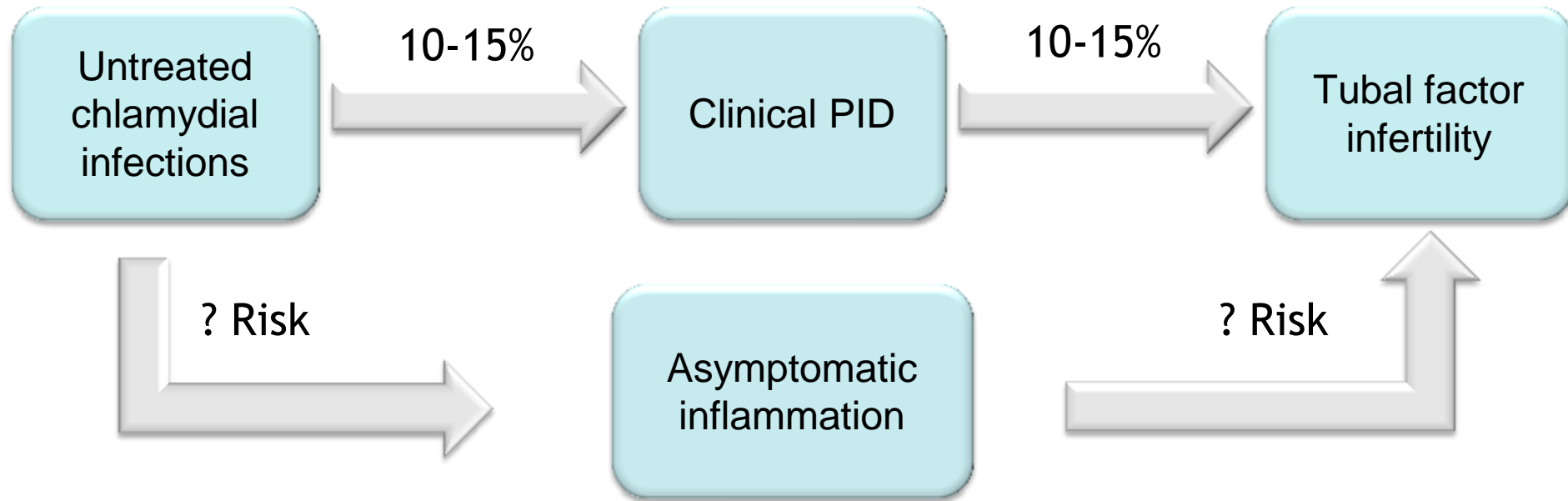


Post-PID, 1200x

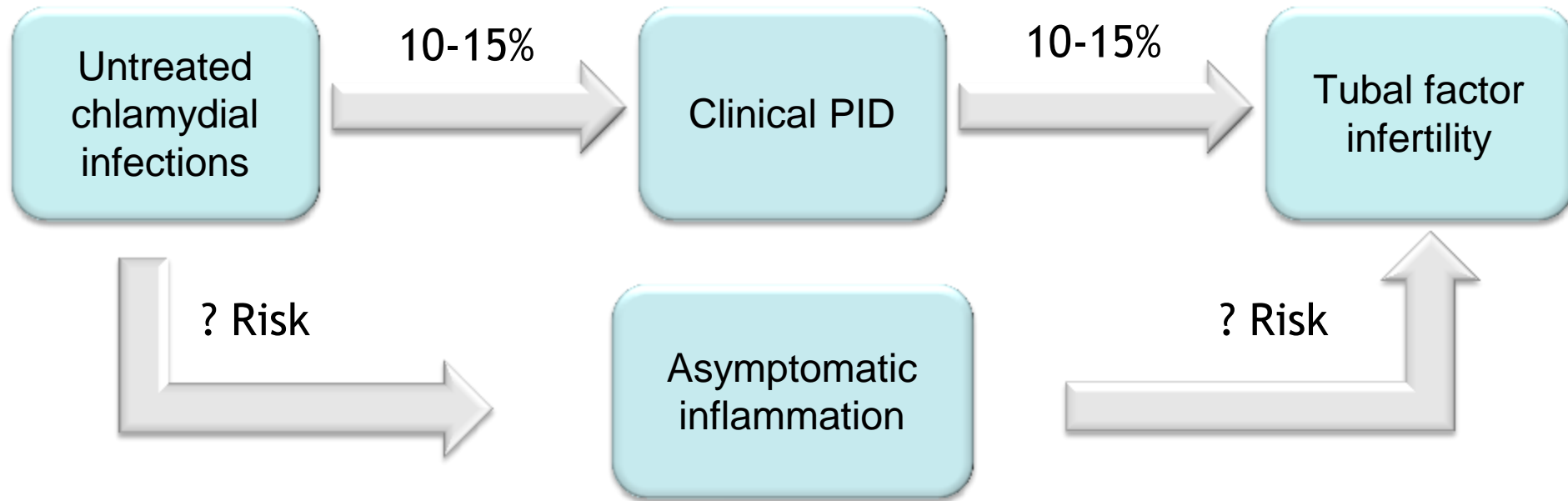
Upper genital tract disease



Upper genital tract disease



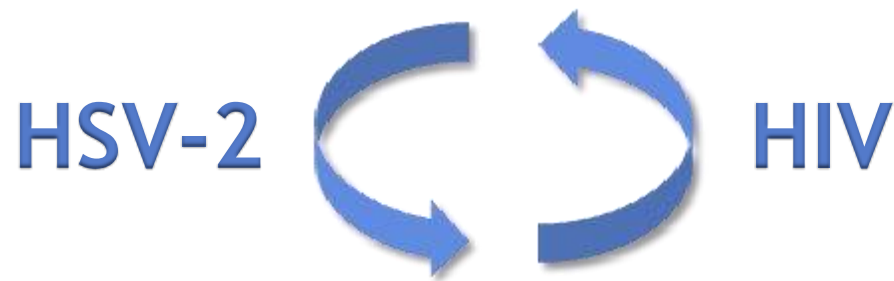
Upper genital tract disease



- 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

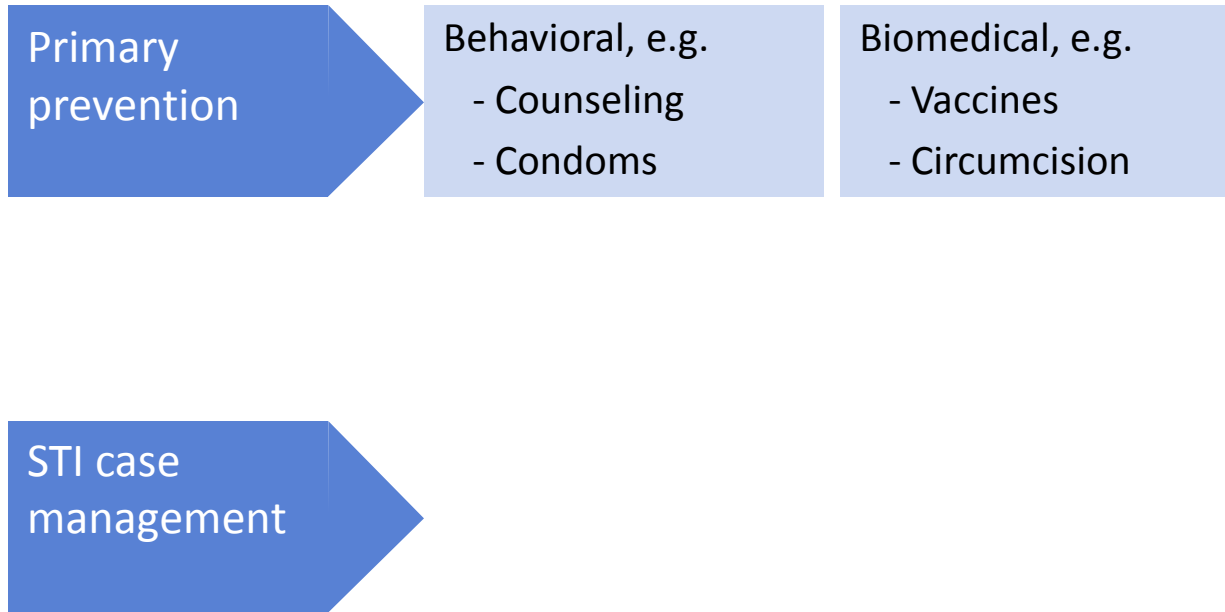


Primary
prevention

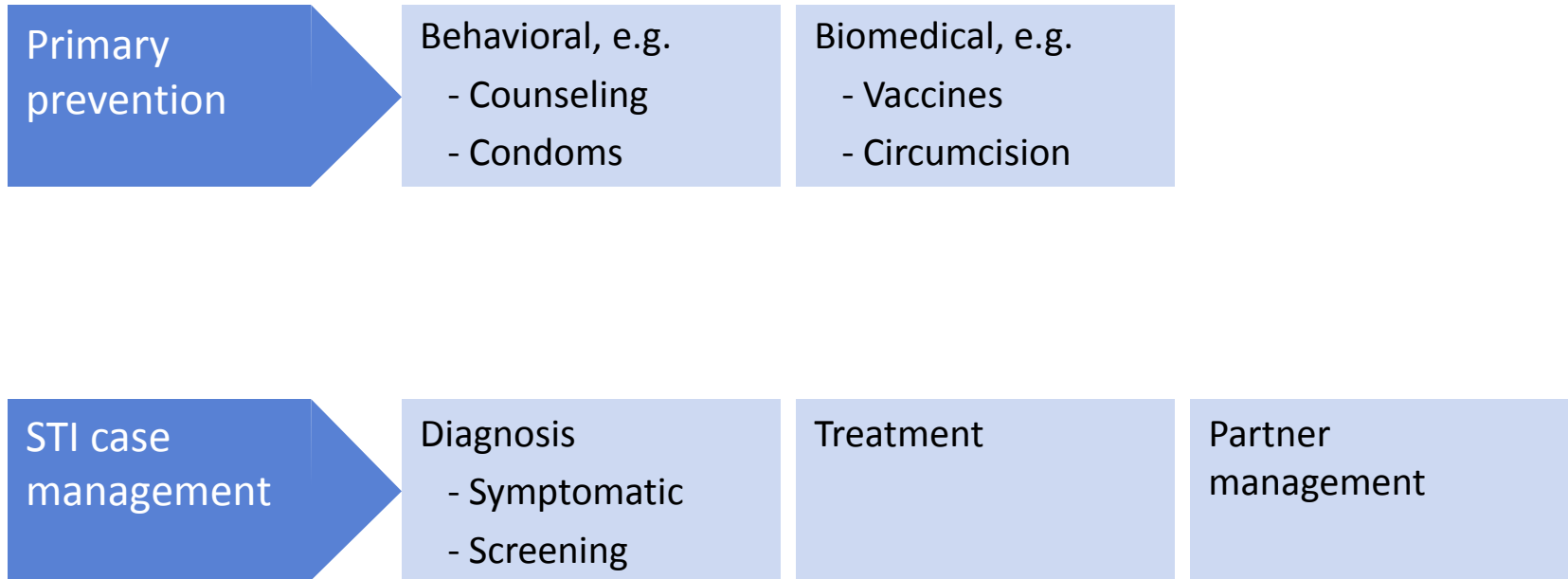


STI case
management

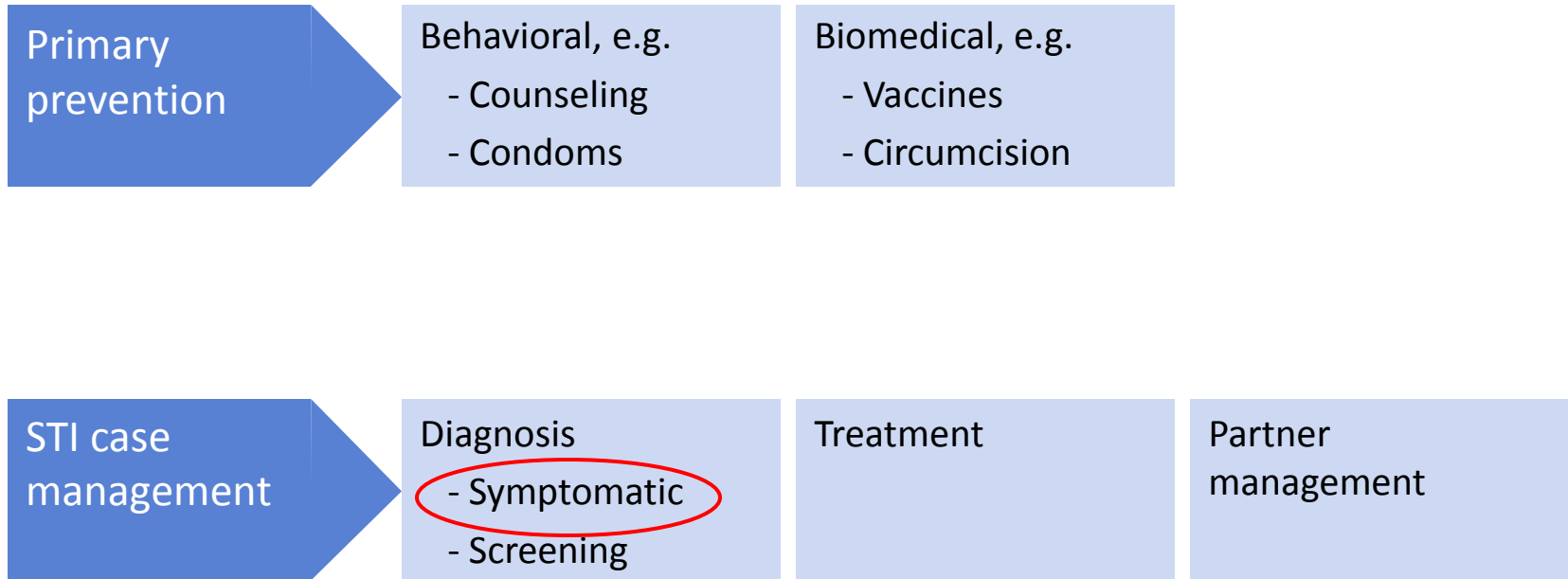
Public health approach to STI control



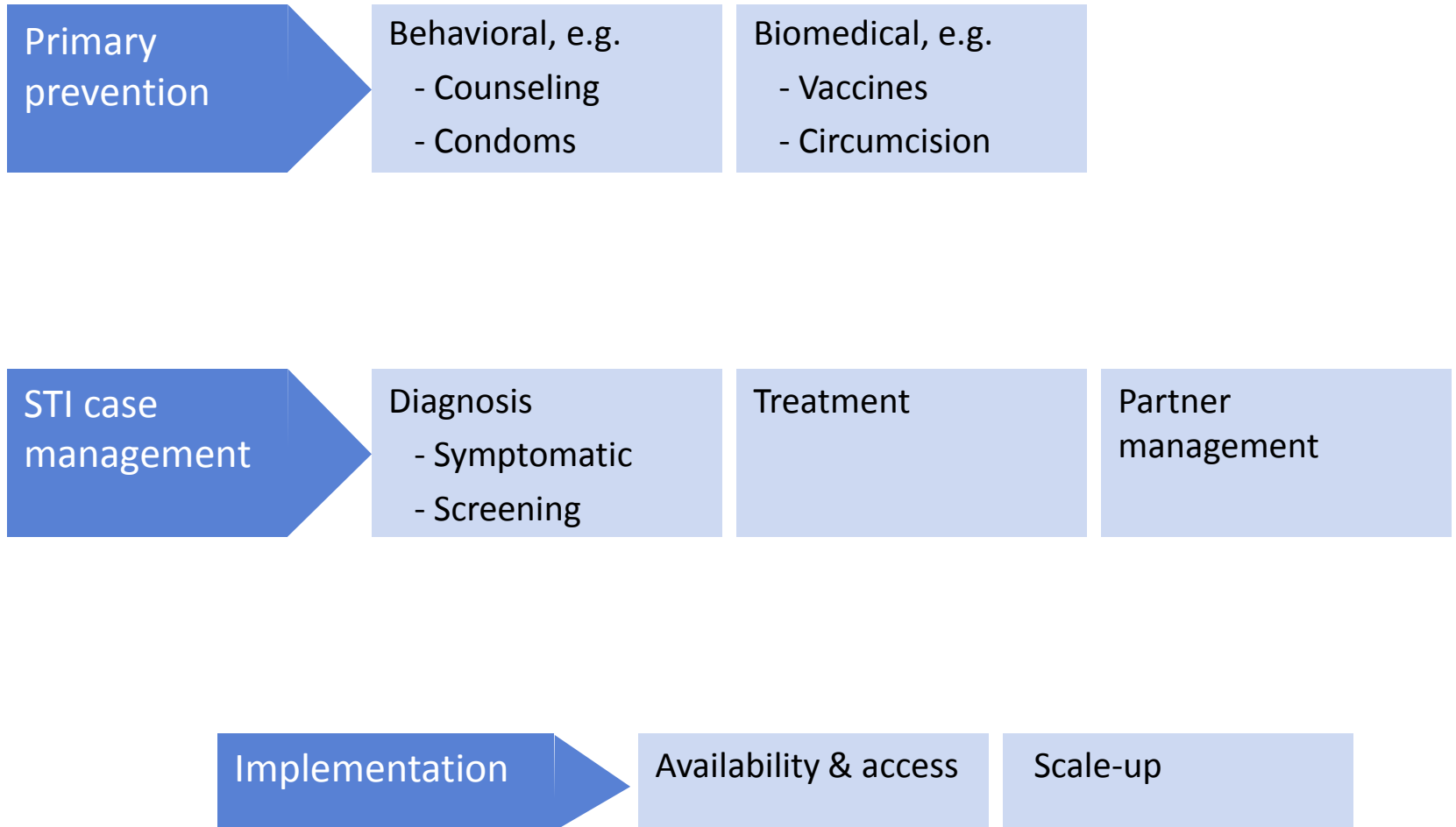
Public health approach to STI control



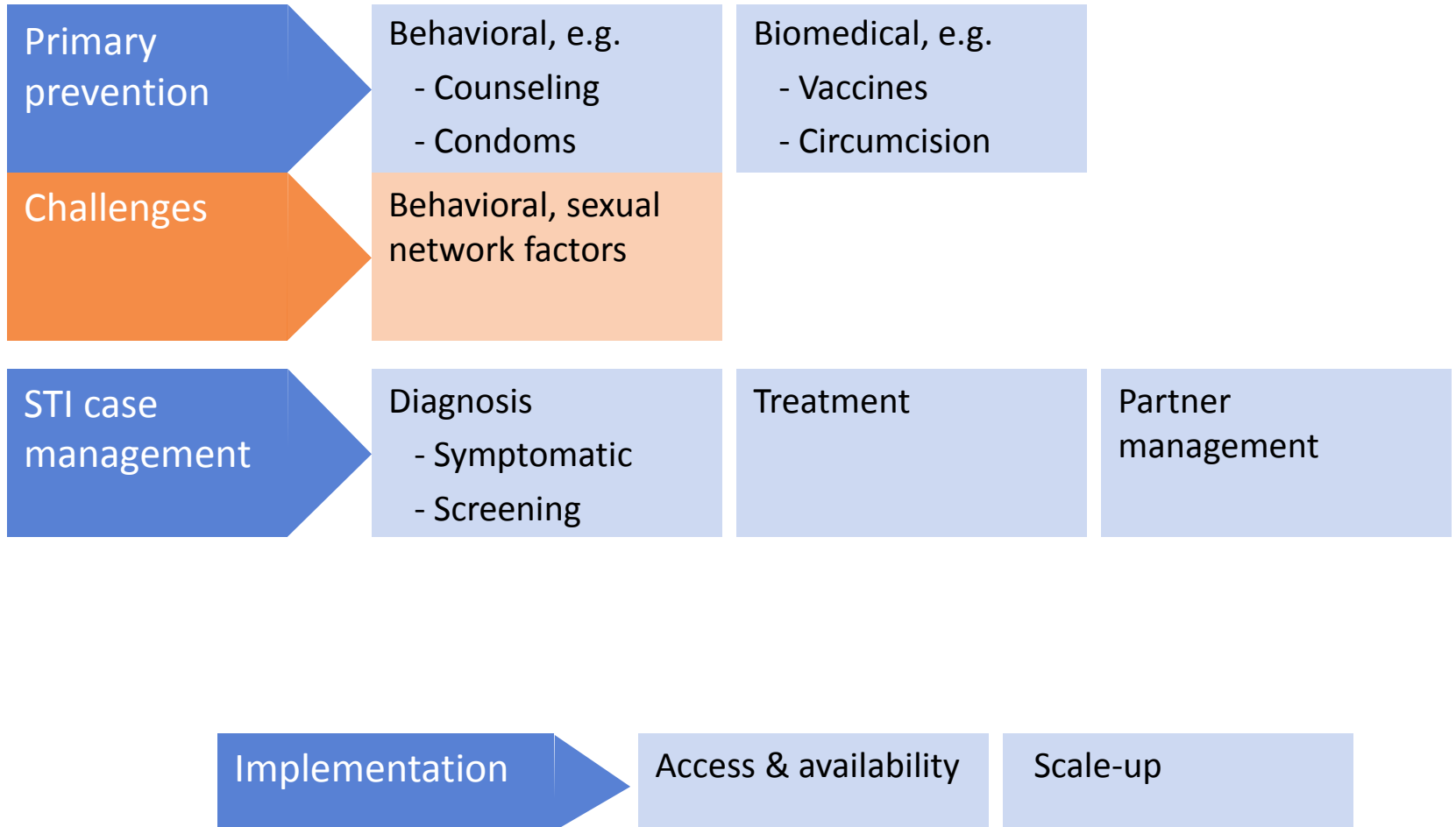
Public health approach to STI control



Public health approach to STI control



Public health approach to STI control

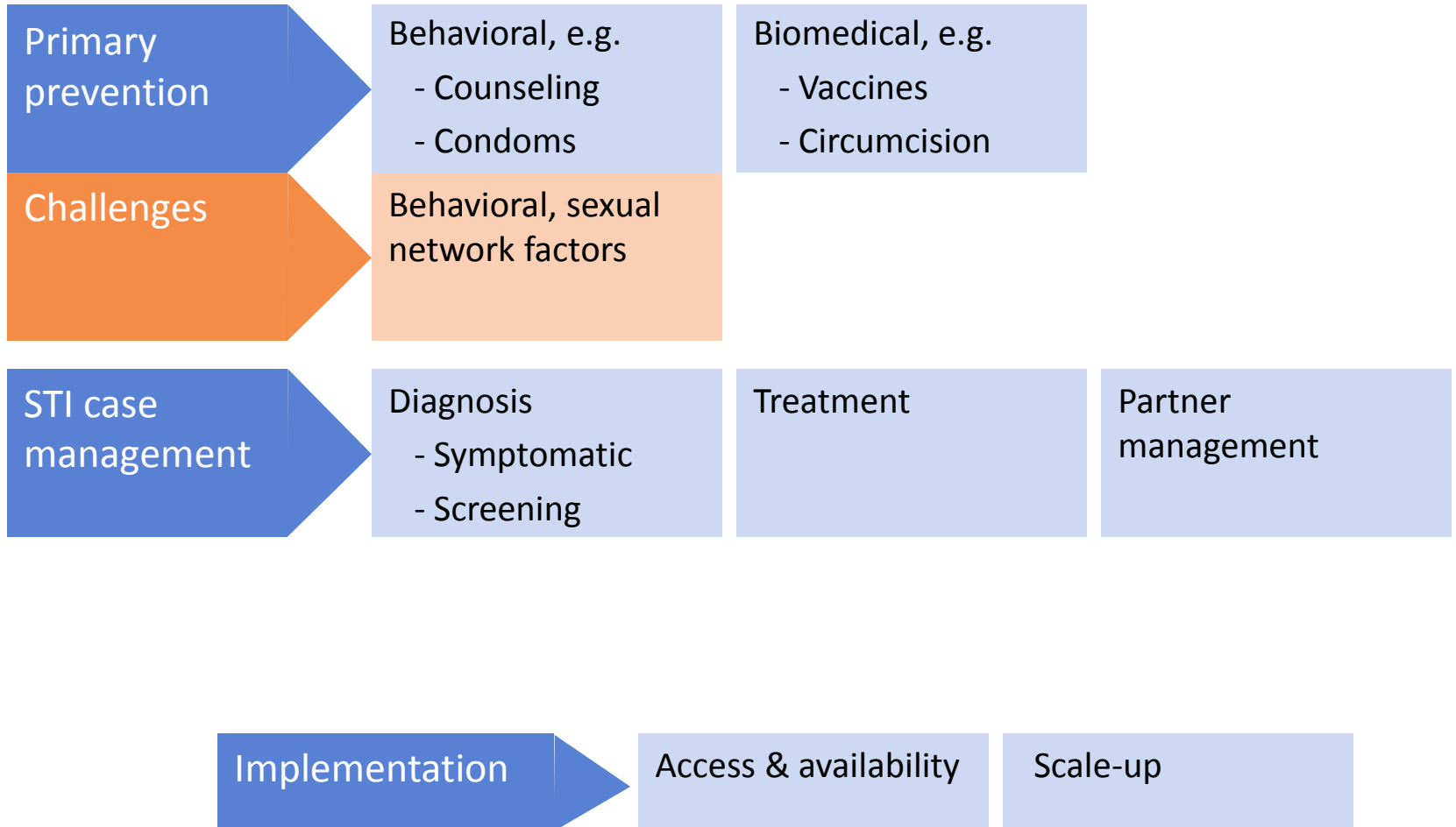


Challenges: behavioral and network factors

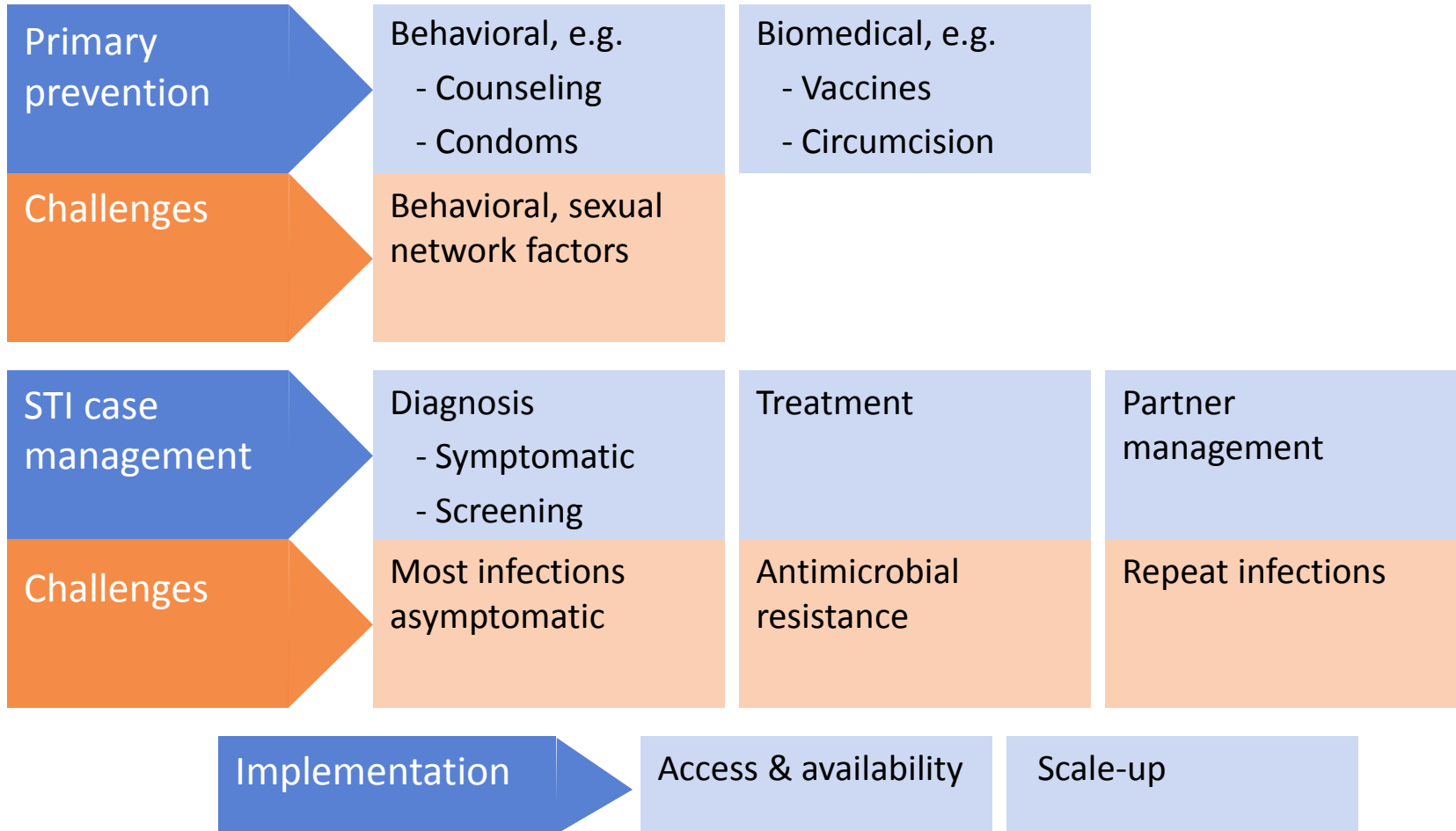
- ❑ Limits to progress made with condom promotion as main primary prevention measure
- ❑ Cultural factors affect acceptability of condoms, comfort level with discussing sex
- ❑ Sustainability of behavior change
- ❑ Individual behavior may be less important than network risk



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

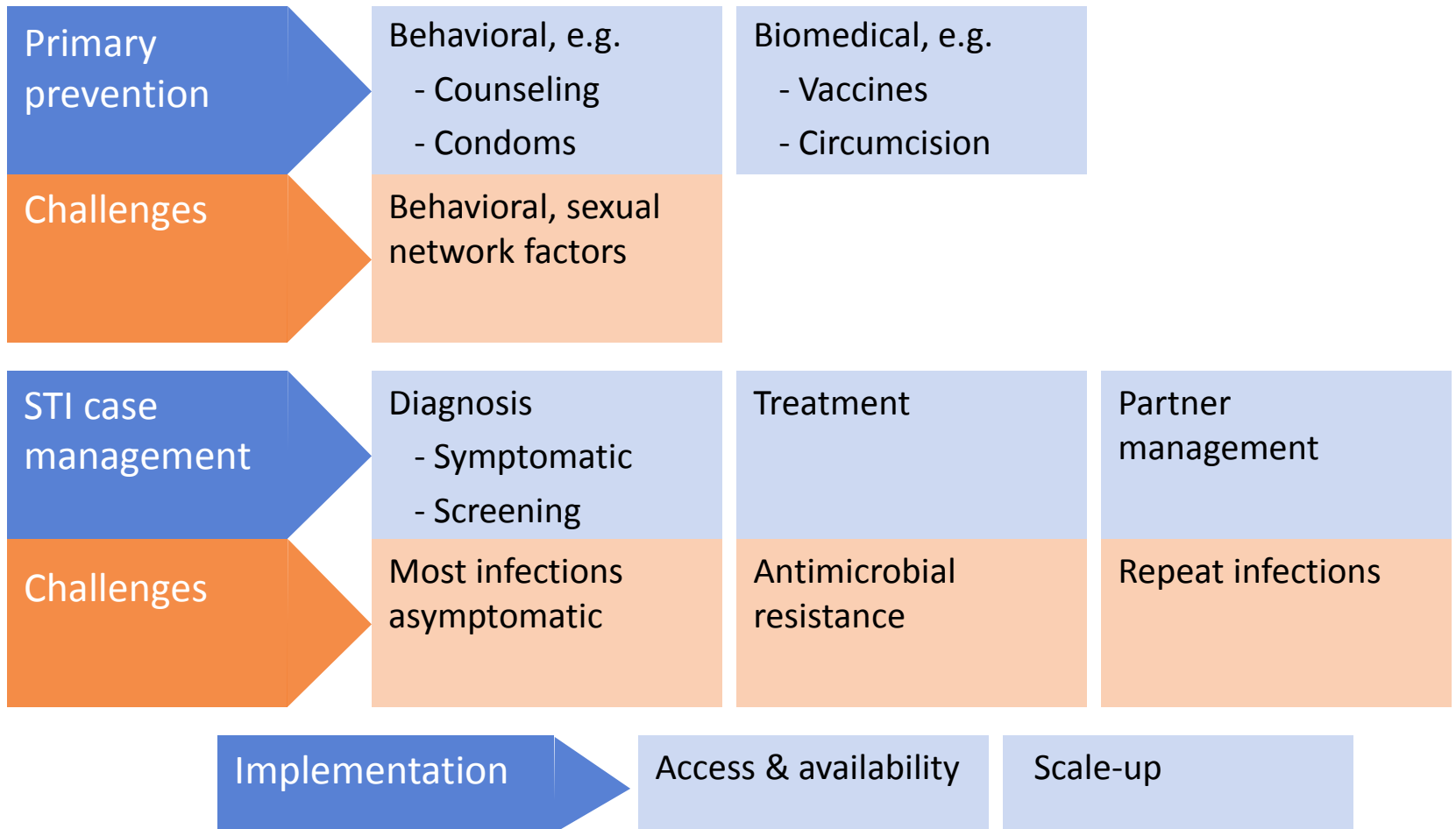
- ❑ Drug-resistant gonorrhoea is major threat to STI control globally
 - Resistance to cephalosporins, only first-line drugs, increasingly reported
- ❑ Nitroimidazoles only class active against trichomoniasis
 - Low-level resistance being reported



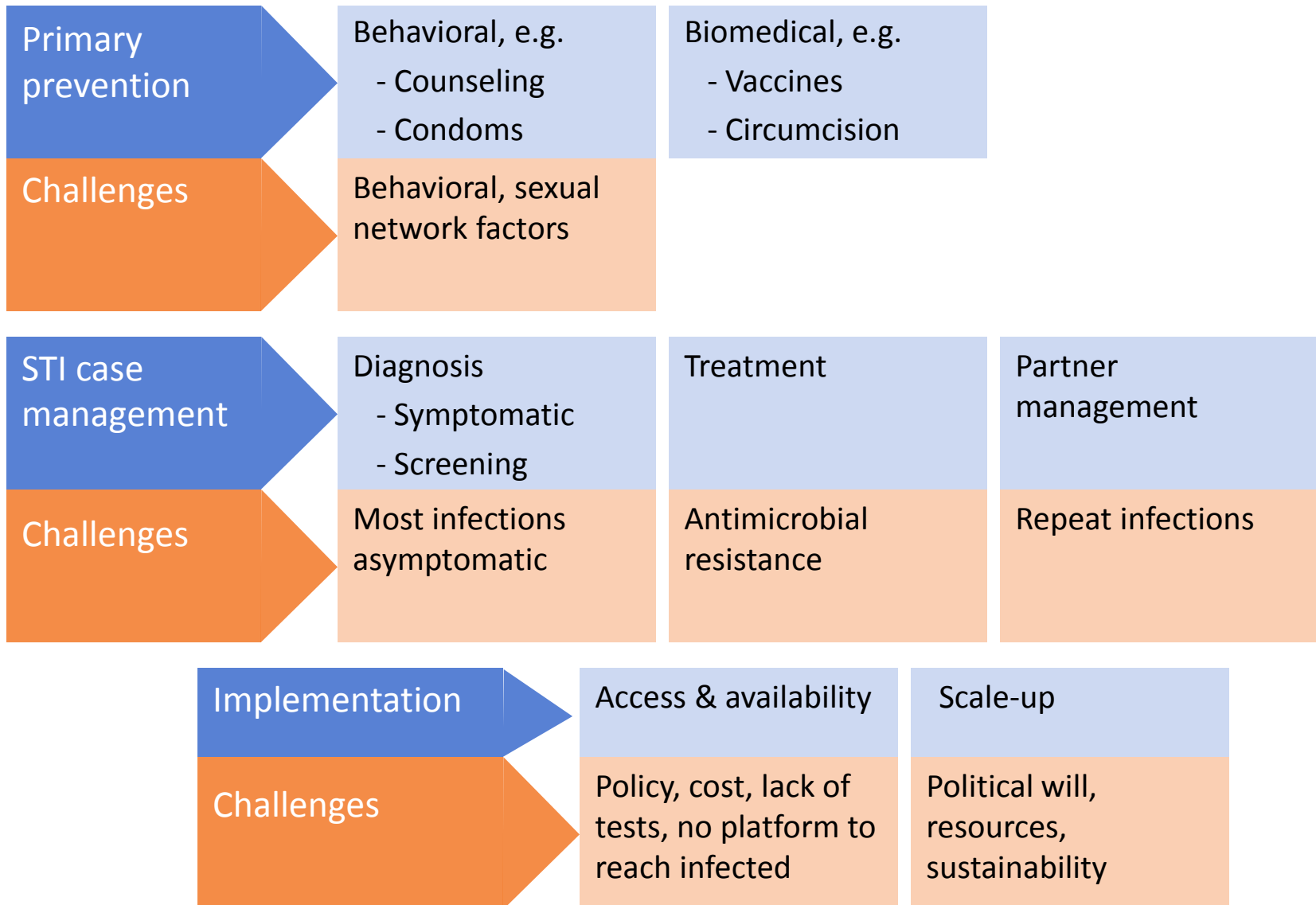
Challenges: repeat infections

- ❑ 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

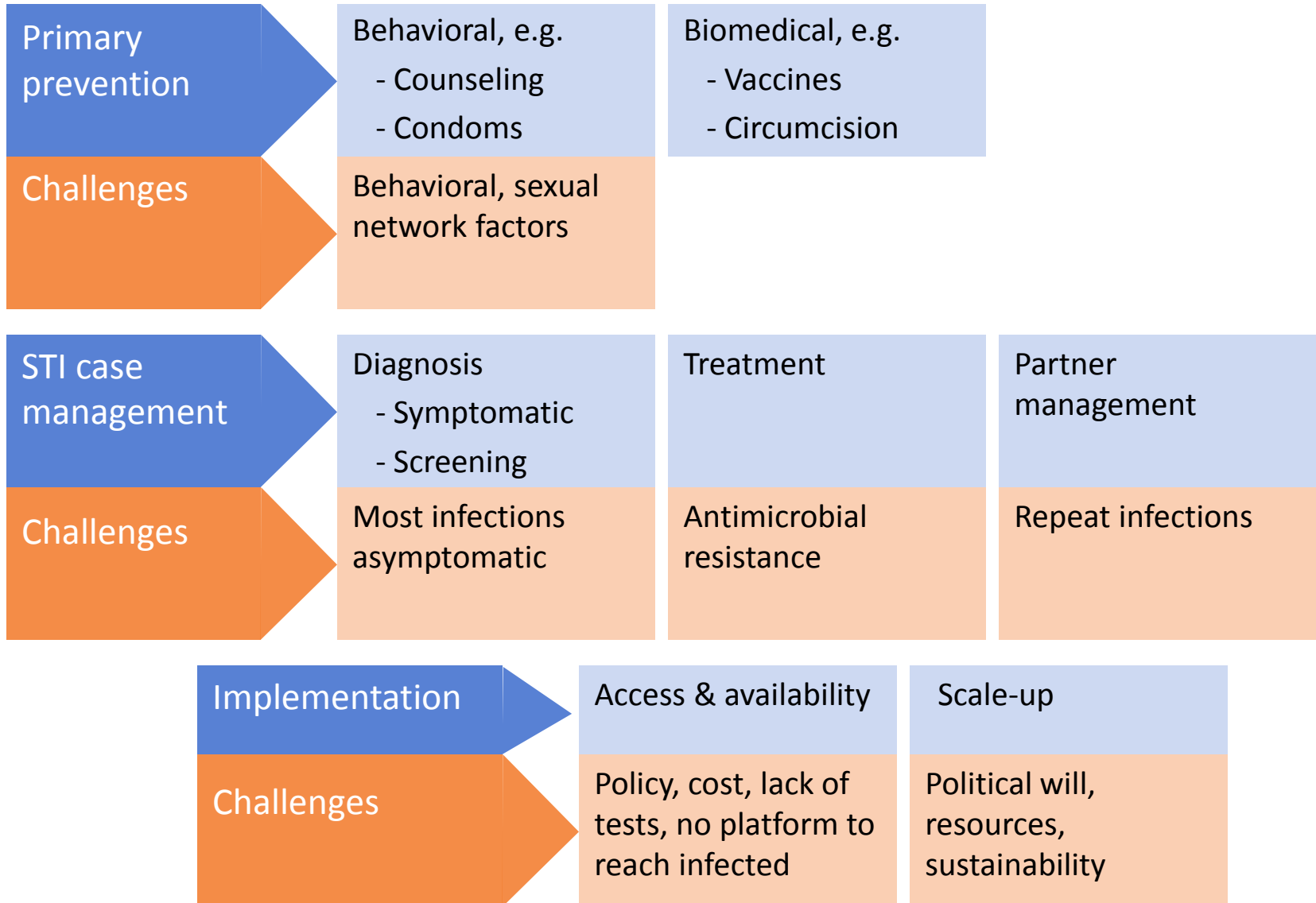


Challenges: implementation factors

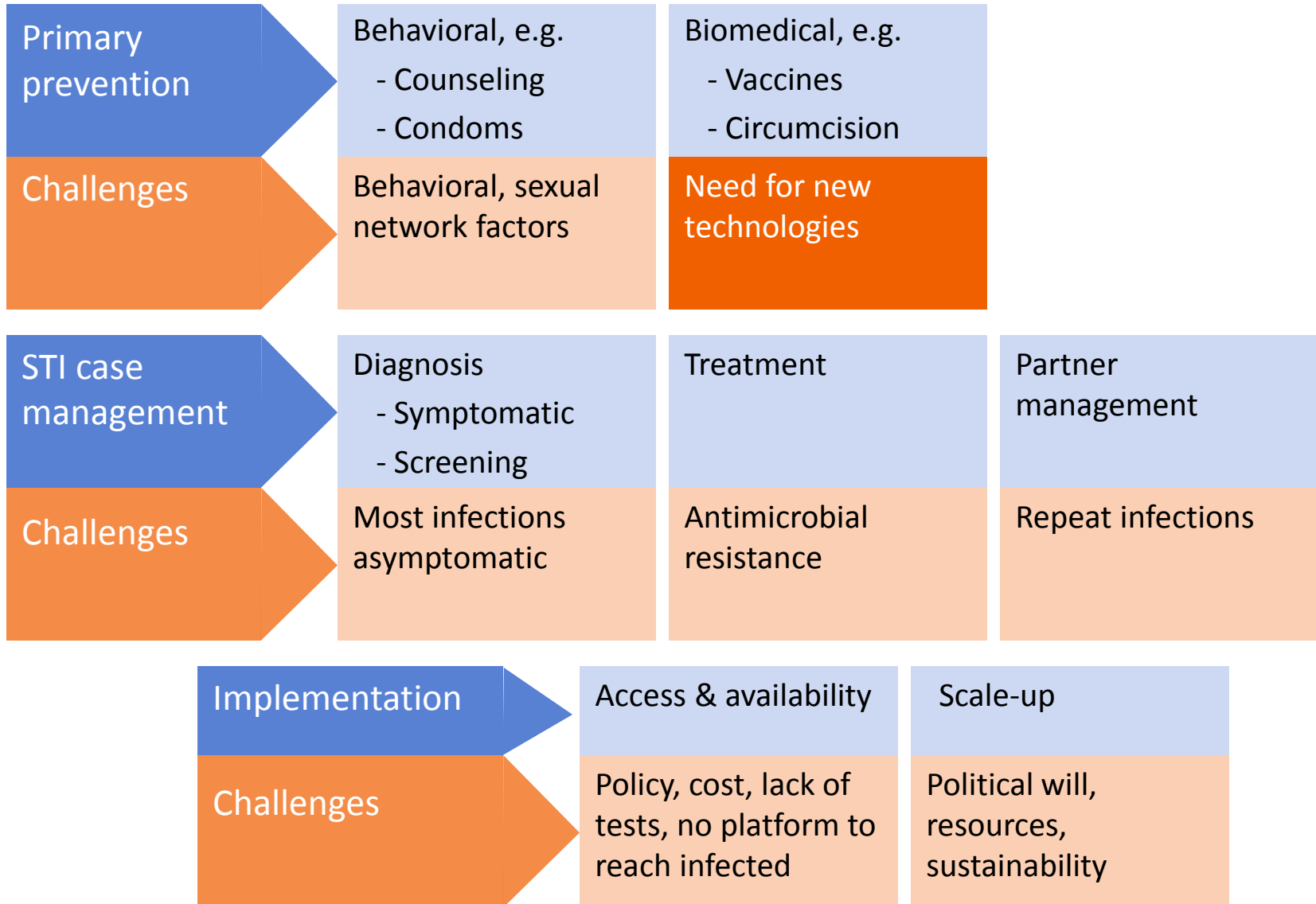
- ❑ Lack of availability and access to affordable, easy-to-use diagnostic tests in much of world
 - New rapid tests for syphilis
 - Rapid tests for others may be on horizon
- ❑ Availability does not ensure effective implementation
 - Platform to access target population
 - Commitment, resources for scale-up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



Public health approach to STI control



Public health approach to STI control



The need for new STI vaccines for future prevention efforts

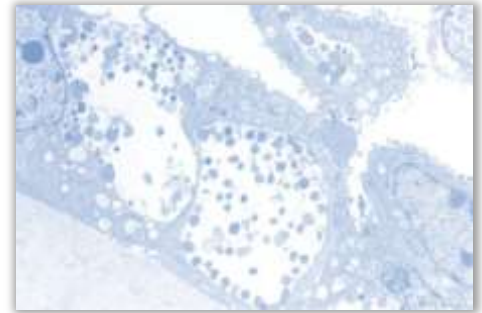
HSV-2 infection



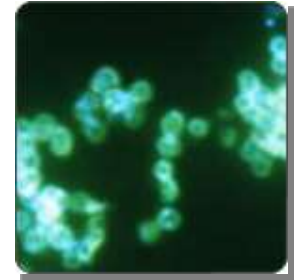
- ❑ >500 million HSV-2 infections globally
 - Incurable, lifelong
 - Marked synergy with HIV
- ❑ Current HSV-2 prevention strategies may not have feasible, sustainable population impact
- ❑ HSV vaccine could have impact on HIV spread, neonatal herpes, genital symptoms

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

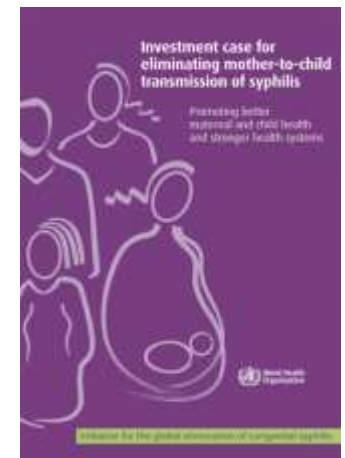


- ❑ Prevention threatened by antimicrobial resistance to only first-line drugs for 106 million cases/year
- ❑ Trials of new treatment regimens ongoing
 - *N. gonorrhoeae* has developed resistance to 4 different classes of antibiotics since first treatable
- ❑ Progress toward gonorrhea vaccine also needed

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

Lori Newman

Gail Bolan

Mary Kamb

Nathalie Broutet



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

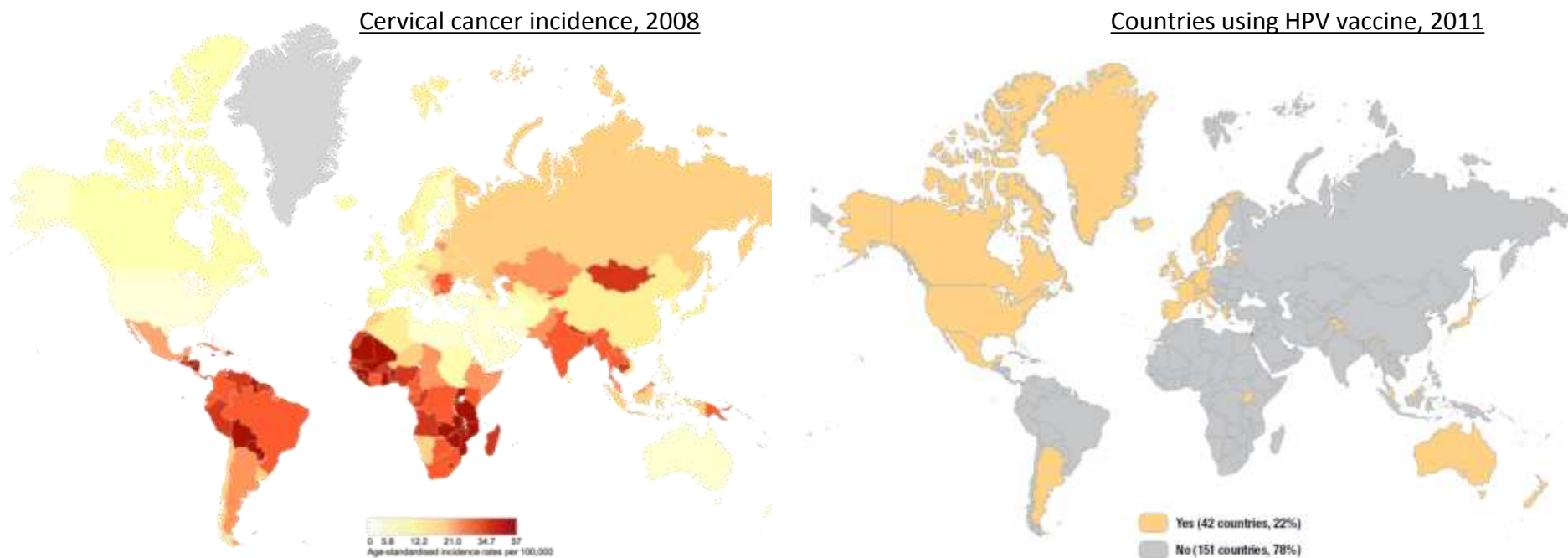
- Cervical cancer: another 6.4 million DALYs
- Did not calculate DALY estimates for HSV-2

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