CORE
Community Response to End Inequalities

Updating & Simplifying Testing Algorithms: how to reach the first 95 and close the gaps in HIV diagnosis

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World Health Organization
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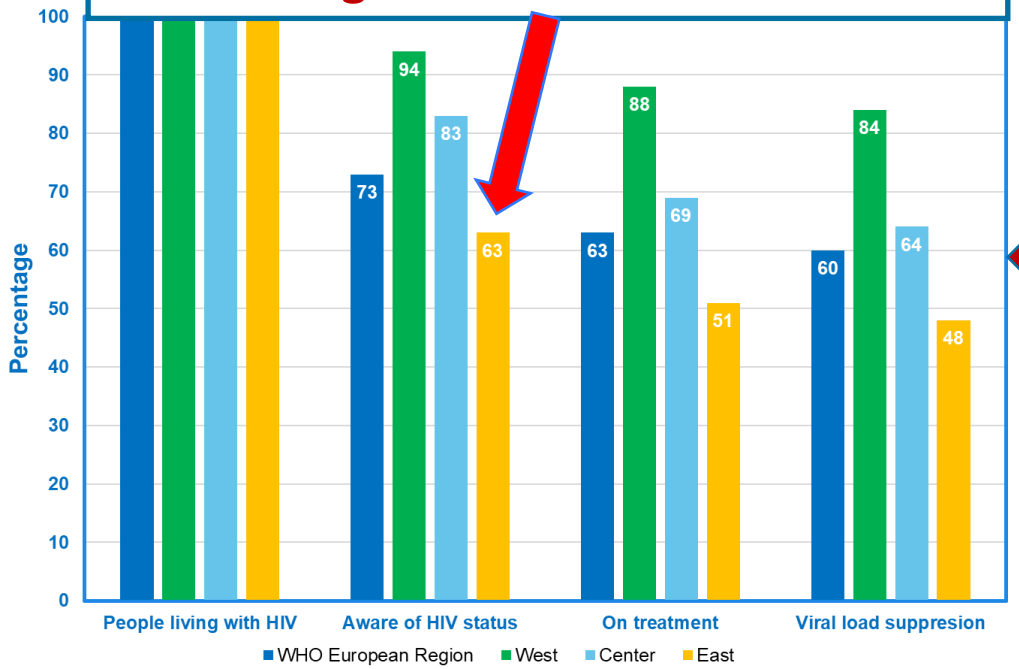
Testing and treatment cascade



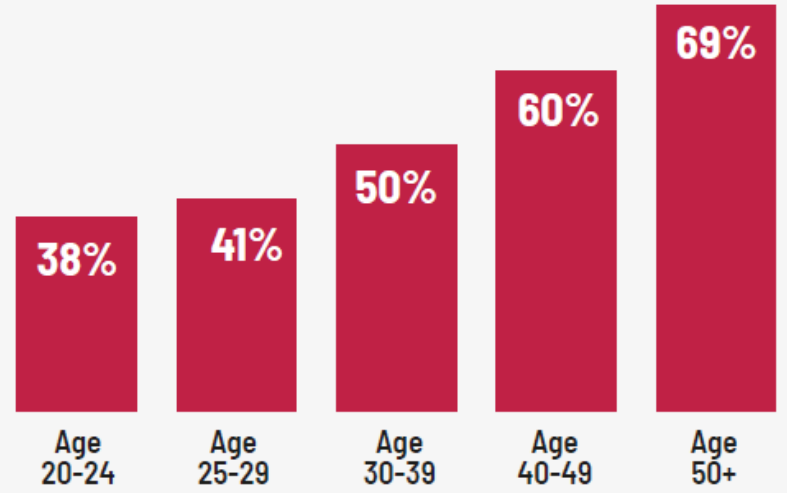
Context

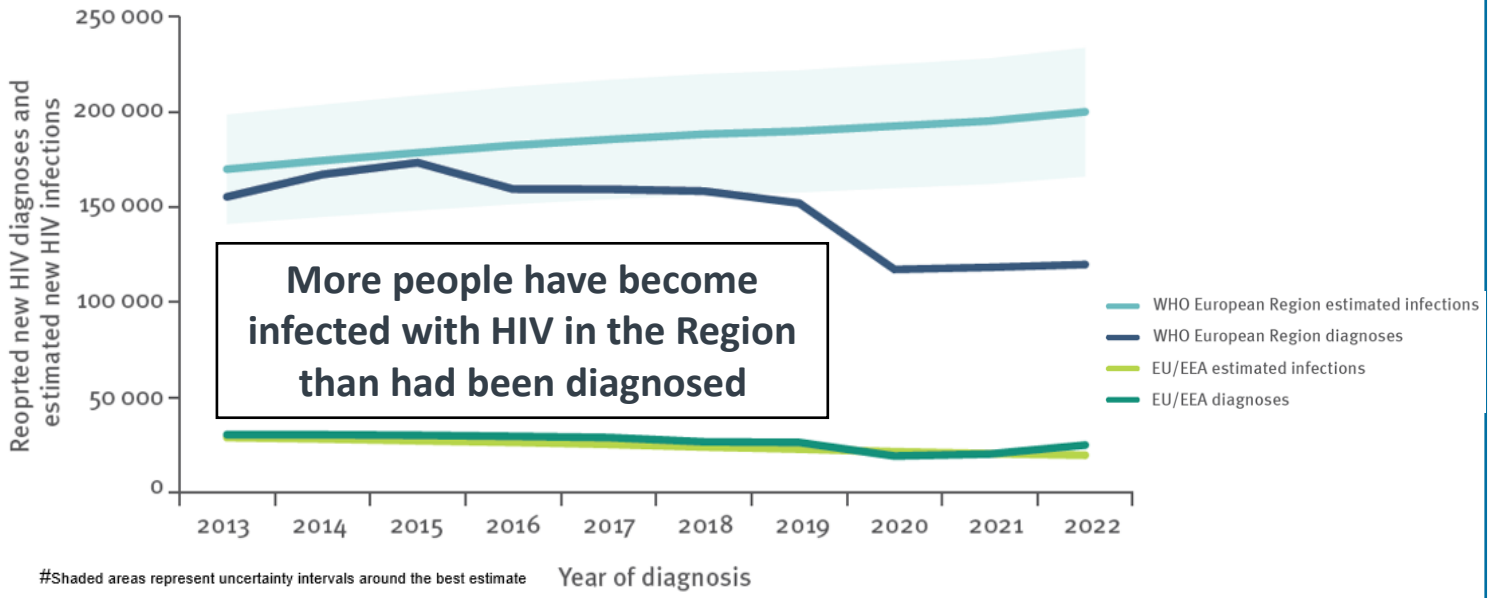
LATE DIAGNOSIS

delays treatment and increases the risk of AIDS and death

54%

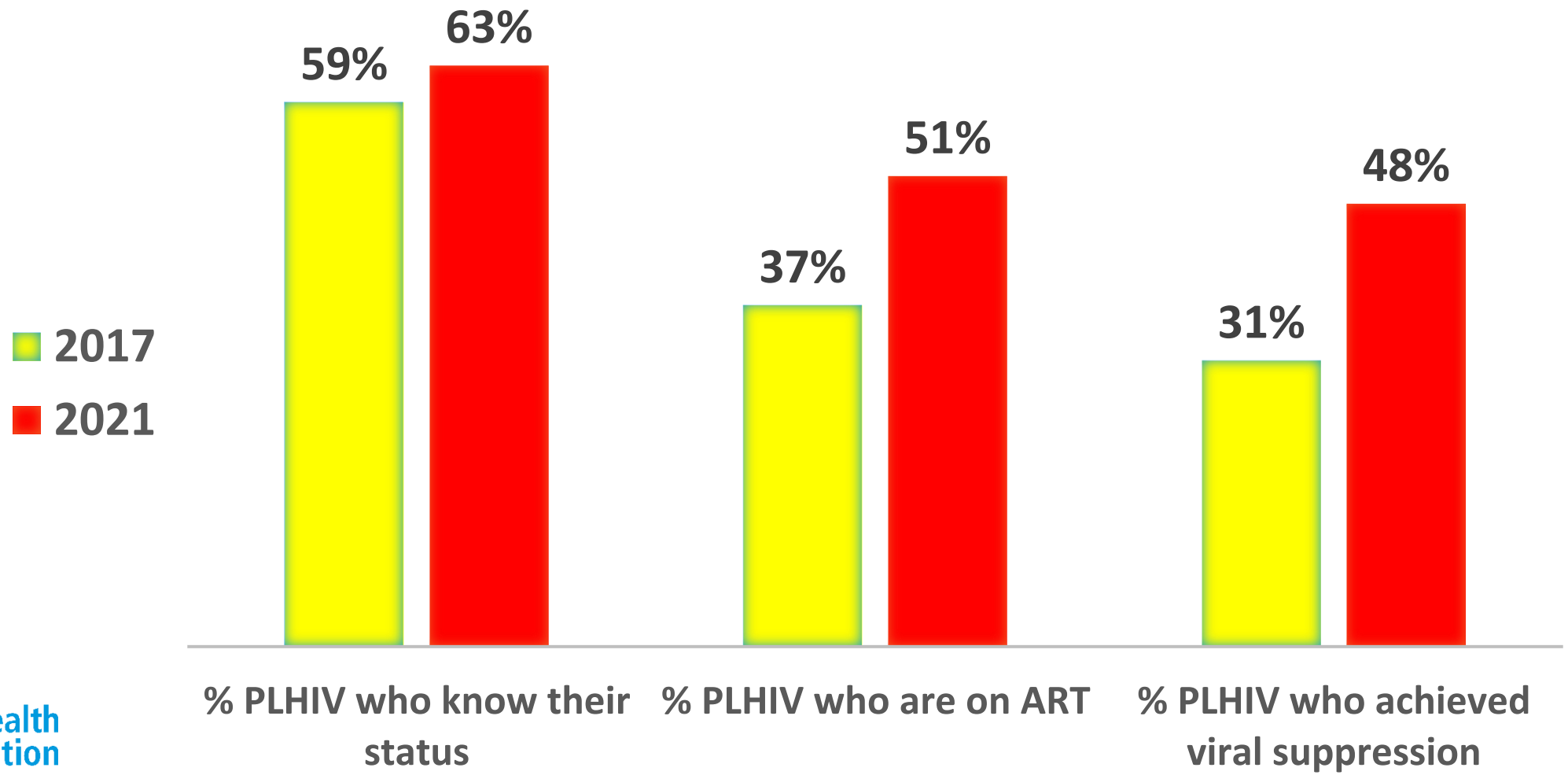
Percentage of people diagnosed late with HIV increases with age and is highest in people over age 50.





Source: ECDC/WHO (2022). HIV/AIDS Surveillance in Europe 2022 (2021 data)

EECA HIV cascade of care in 2017 and 2021



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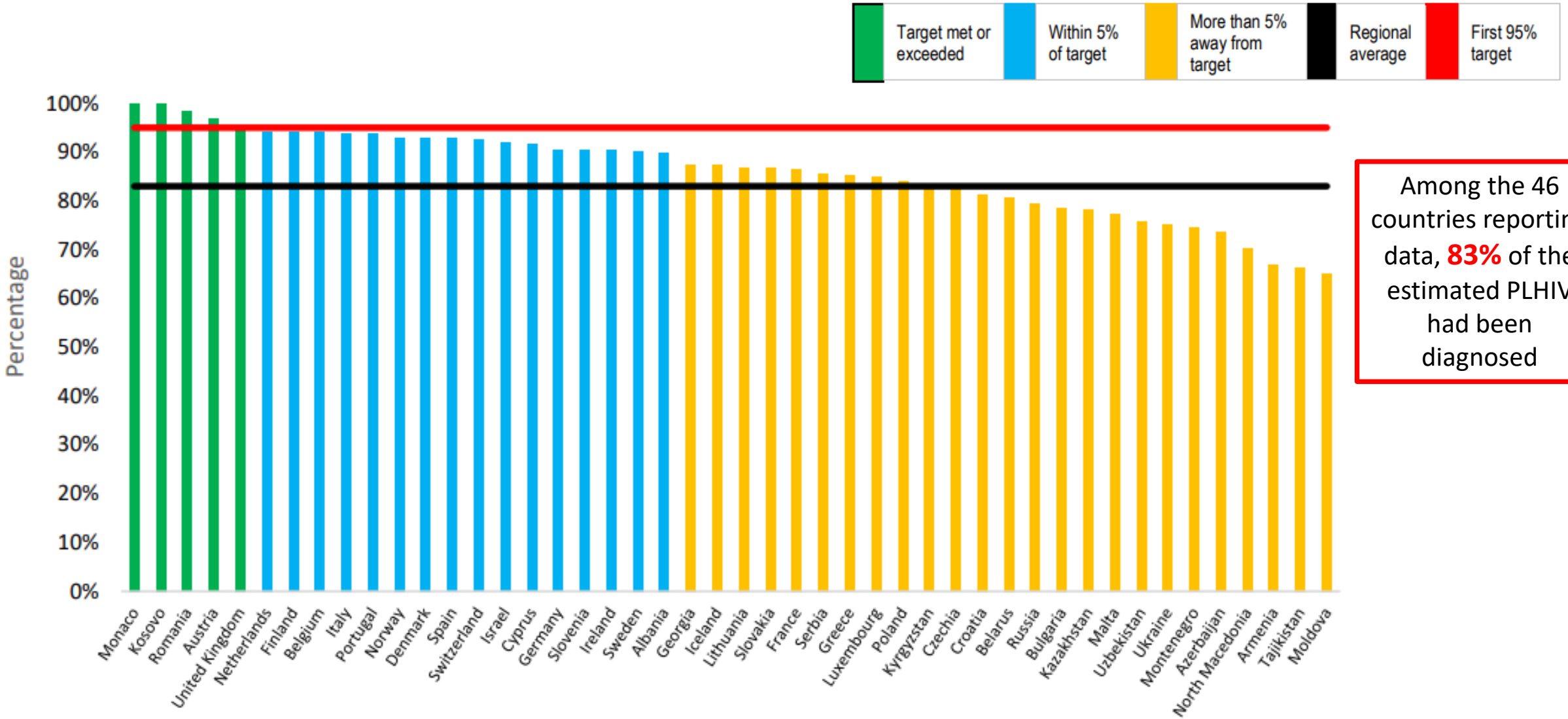
Data Source: UNAIDS 2022 GAM available on https://aidsinfo.unaids.org/

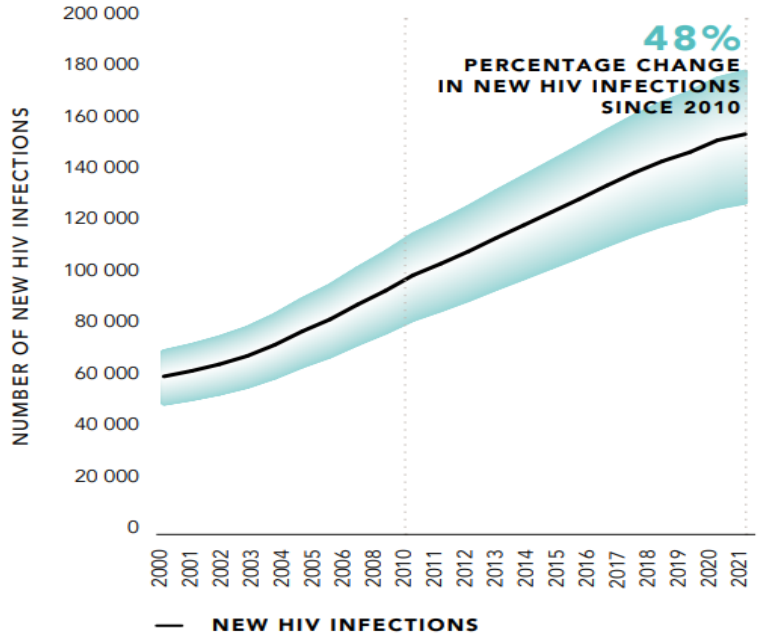
Proportion of PLHIV who had ever been diagnosed in 46 countries of Europe and Central Asia, based on data as of 2023



Among the 46 countries reporting data, **83%** of the estimated PLHIV had been diagnosed

Source: European Centre for Disease Prevention and Control. Continuum of HIV care. Monitoring implementation of the Dublin Declaration on partnership to fight HIV/AIDS in Europe and Central Asia: 2023 progress report. Stockholm: ECDC; 2024.

Countries of EECA have had the **fastest growing HIV epidemic in the world** over the last decade and contributed to 78% of new HIV diagnoses reported in WHO European region in 2021



Source: UNAIDS epidemiological estimates, 2022 (https://aidsinfo.unaids.org/)

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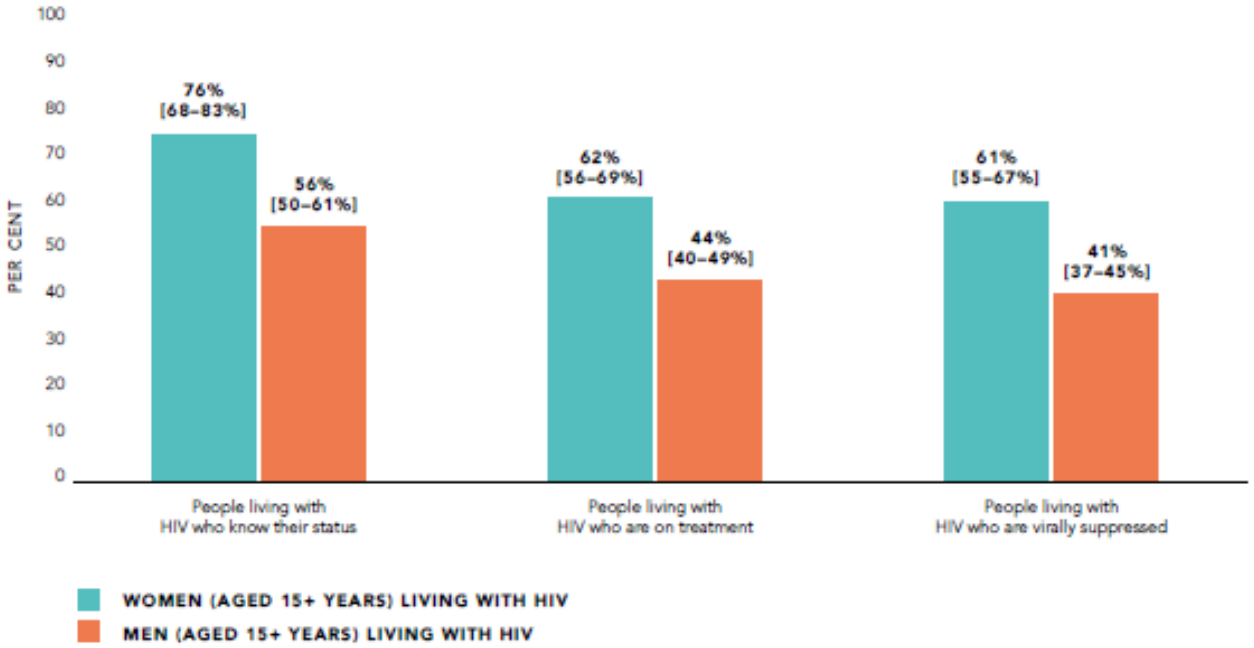
Source: ECDC/WHO (2022). HIV/AIDS Surveillance in Europe 2022 (2021 data)

What populations tend to be missed in HIV diagnosis?

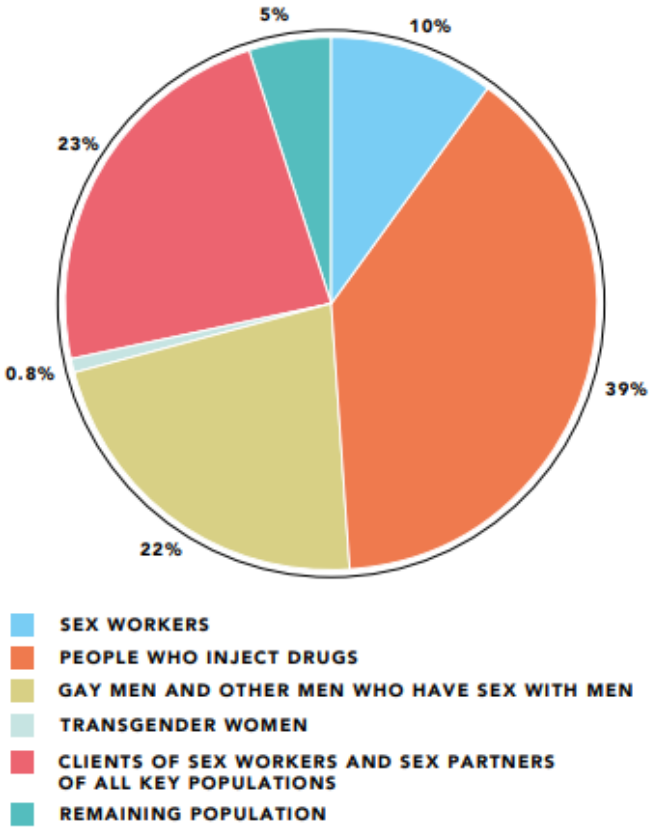
FIGURE 12.5 HIV testing and treatment cascade, women (aged 15+ years) compared to men (aged 15+ years), eastern Europe and central Asia, 2021



Knowledge of HIV status in men < women

95%

Proportion of new infections among key populations and their partners in EECA



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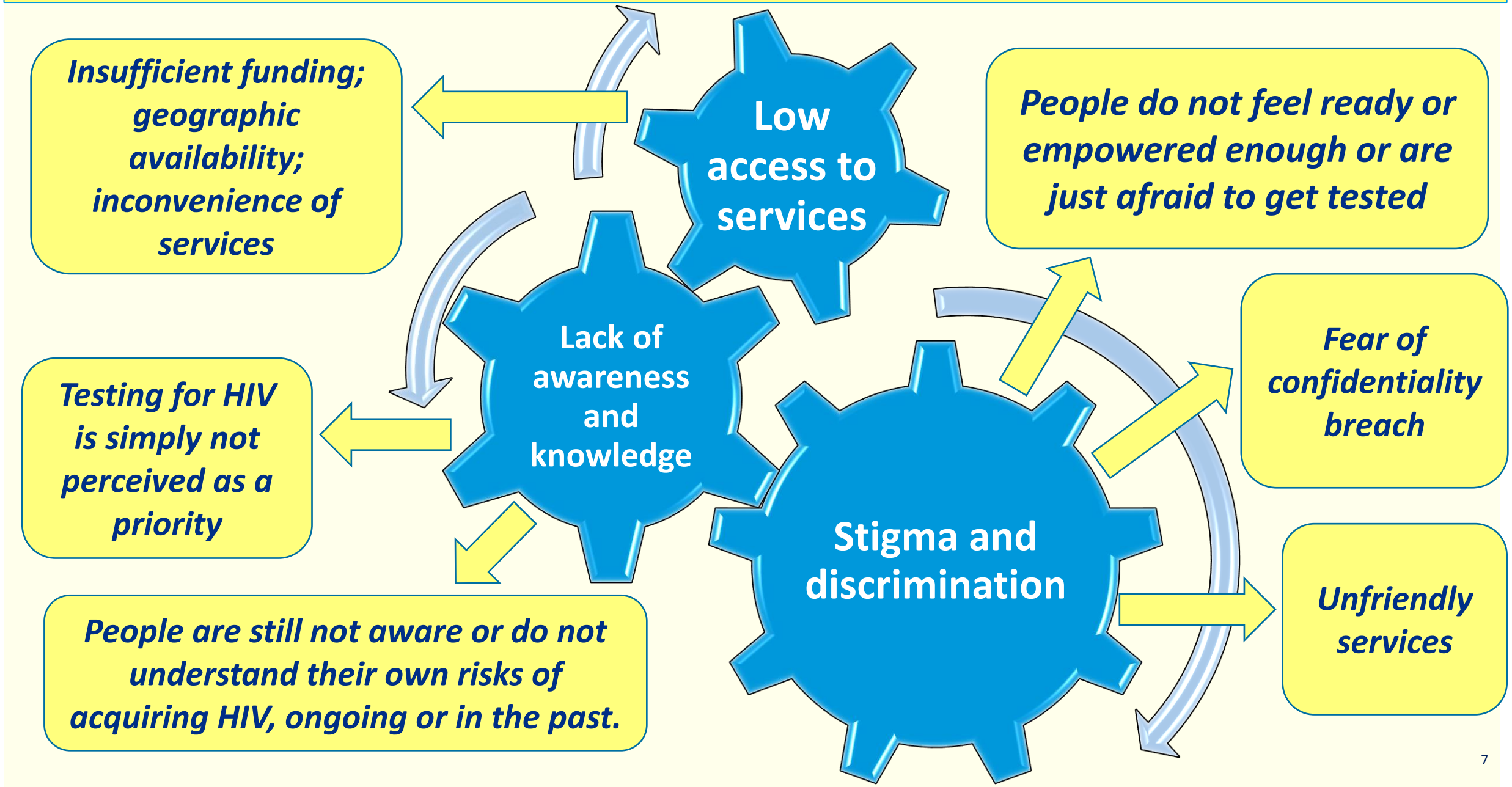
Men and Key population are the most affected in EECA

UNAIDS Global update 2022; https://www.unaids.org/sites/default/files/media_asset/2022-global-aids-update_en.pdf

Main reasons behind the remaining gaps in HIV case detection



Solutions

Increasing funding; geographic availability; decentralization of services

Low access to services

"Normalization of HIV". But: changing societal attitudes, norms and stereotypes in order to tackle stigma takes time. Starting from healthcare settings

Lack of awareness and knowledge

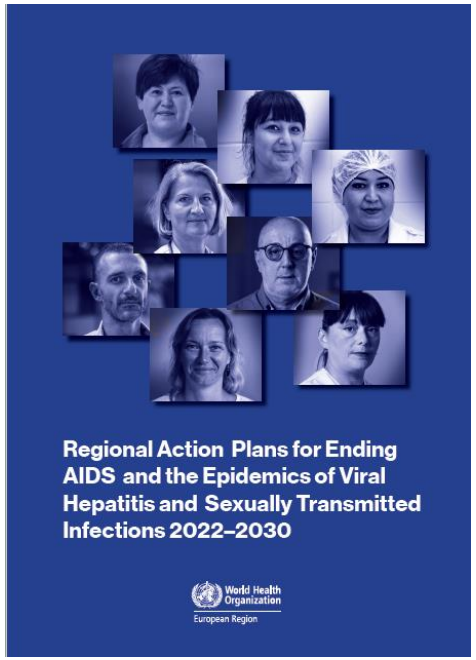
Activities to reach 10-10-10 targets

Stigma and discrimination

Demand generation: information campaigns, wide use of digital solutions and social applications, sexuality education programmes

Expansion of friendly, safe, confidential services

Priority actions for countries for Strategic Direction 1 (a shared response to HIV, VH and STIs)



1.5. Ensure accessible, decentralized diagnostic and laboratory services

- Develop strategic laboratory plans across disease programmes to clarify the role of reference laboratories, while decentralizing and integrating testing and optimizing the use of the available molecular diagnostic platforms including point-of-care testing (POCT) and rapid testing for HIV, TB, VH, STIs and other communicable diseases.
- Ensure quality standards for decentralized testing strategies and appropriate professional competencies.
- Implement laboratory information management systems that are linked to patient data systems to deliver timely results.

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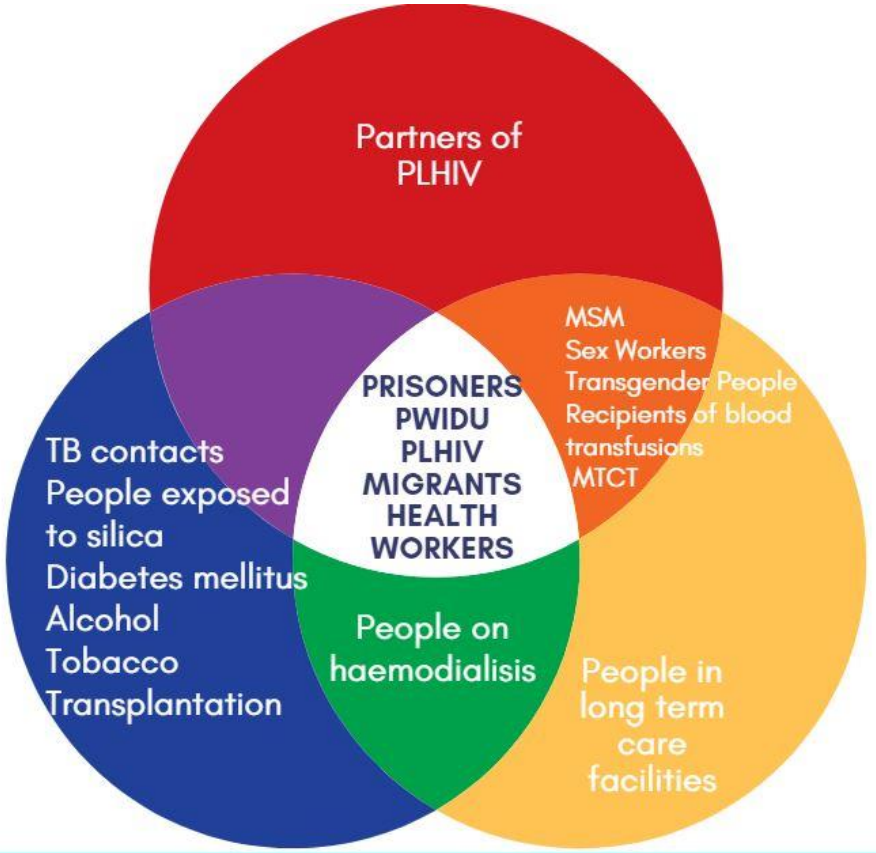
Why integrated testing for HIV, viral hepatitis and STIs?

- HIV, VH and STIs share **common modes of transmission** and determinants, and many of the populations affected by these diseases overlap.
- Integrated HIV, VH and STIs testing allows synergies to be created in times of **constrained resources**.



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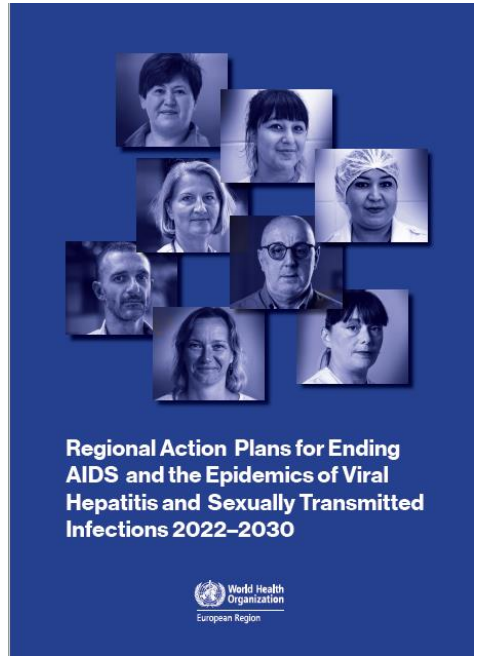
RAP: Priority populations for HIV, VH and STIs

- people exposed through **sexual transmission**, including
  - **young people** and adolescents;
  - men who have sex with men **(MSM)**;
  - **sex workers** and their clients; **transgender** people;
  - people in **prisons** and other closed settings;
  - and people whose sexual behaviour is mediated by drug or alcohol use;
- people exposed through **unsafe blood** supplies and/or **unsafe medical** injections and procedures;
- people who inject and use **drugs**;
- children exposed through **vertical (mother-to-child) transmission** or early childhood infection;
- **pregnant and breastfeeding** women;
- women and girls, including adolescent girls and young women, who face risks associated with gender inequalities and exposure to **violence**, in conjunction with increased biological risks on the basis of sex;
- people of all ages, including men, who are less likely to use health services; **migrants**, mobile populations, and people **affected by conflict** and civil unrest; indigenous peoples;
- people with **disabilities.**



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Essential health and enabling recommendations for key populations,

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Essential for impact: enabling interventions

Removing punitive laws, policies and practices

Reducing stigma and discrimination

Community empowerment

Addressing violence

Essential for impact: health interventions

Prevention of HIV, viral hepatitis and STIs

Harm reduction (needle and syringe programmes (NSPs), opioid agonist maintenance therapy (OAMT) and naloxone for overdose management)

Condoms and lubricant

Pre-exposure prophylaxis (PrEP) for HIV

Post-exposure prophylaxis (PEP) for HIV and STIs

Prevention of vertical transmission of HIV, syphilis and HBV

Hepatitis B vaccination

Addressing chemsex

Diagnosis

HIV testing services

STI testing

Hepatitis B and C testing

Recommended packages of interventions for each key population

	MSM	PWID	TGD	SW	PRIS
Diagnosis					
HIV testing services	x	x	x	x	x
STI testing	x	x	x	x	x
Hepatitis B and C testing	x	x	x	x	x
Screening, diagnosis, treatment and prevention of HIV associated tuberculosis (TB)	x	x	x	x	x

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Consolidated guidelines on HIV, viral hepatitis and STI prevention, diagnosis, treatment and care for key populations: policy brief. Geneva: World Health Organization; 2022. Licence: CC BY-NC-SA 3.0 IGO.

In each context, we need to decide which testing approaches can be attractive and perceived as safe by potential clients, even in settings with current high levels of HIV-related stigma and discrimination.

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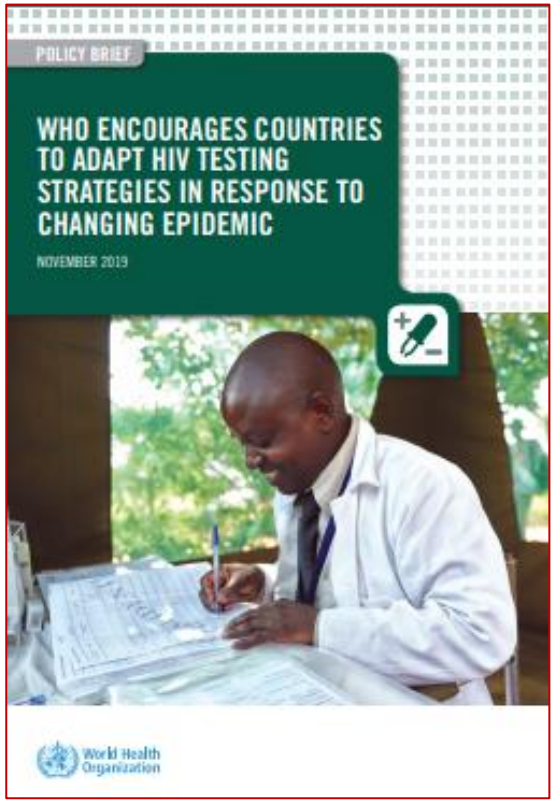
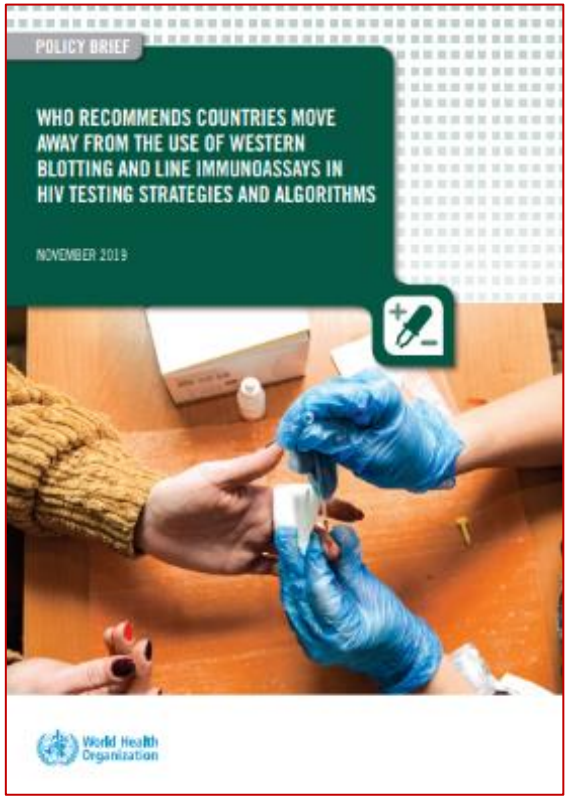
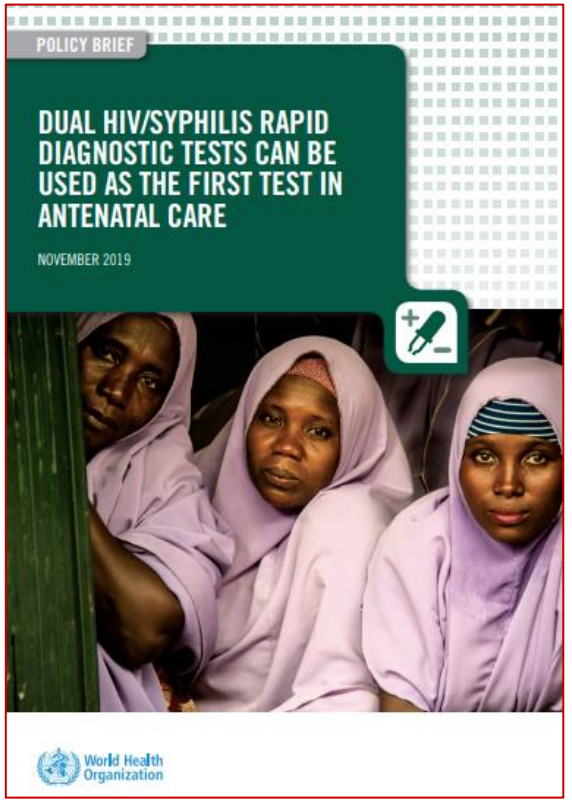
Consolidated guidelines on HIV testing services



Universal 3 tests strategy



Moving away from WB/IB



Dual HIV RDT in ANC (and now KP) settings

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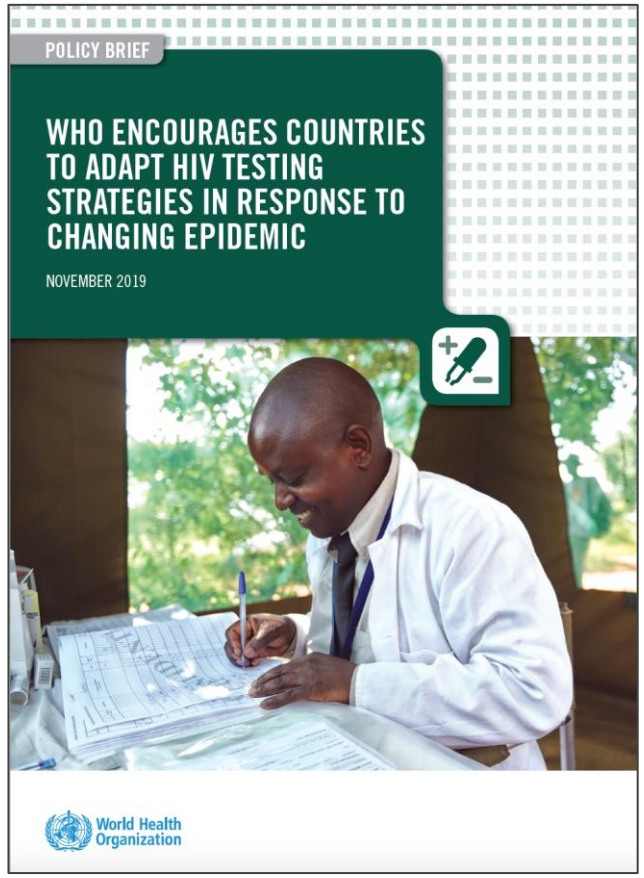
Adapting national HIV testing strategies



Confirmation of HIV infection = **combination** of **3** **"reactive"** IA/RDT results
(not an individual confirmatory test)

- **Ensure that the testing strategy has a positive predictive value ≥99% (PPV)**
  - Meaning of the persons classified as HIV+, ≥99% will truly be living with HIV
  - PPV depends on positivity rate among testing population

- **Quality assured assays, such as WHO prequalified, should be used:**
  - **≥99% sensitivity:** fewer than 1 *'false negative'* for 100 truly positive
  - **≥98% specificity:** fewer than 2 *'false positive'* for 100 truly negative
  - Either rapid diagnostic tests (RDTs) or immunoassay (EIA, CLIA, ECL)

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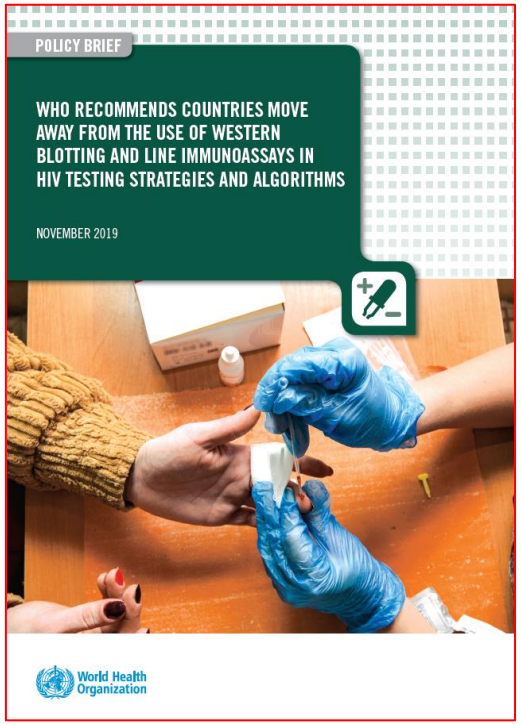
Moving away from WB: Systematic review of published data



Pooled estimates from bivariate mixed-effects meta-analysis

	Comparator (with WB/LIA)				Index (without WB/LIA)			
	Estimate	Std error	95% CI		Estimate	Std error	95% CI	
Sensitivity (%)	98.6	0.8	95.9	99.6	99.2	0.5	97.6	99.7
Specificity (%)	99.9	0.1	99.7	100.0	100.0	<0.01	99.7	100.0
Indeterminate	81				0			

- **Comparator (with WB/LIA) produced 81 indeterminate diagnosis**
- *37 of 81 INDs (46%) were from specimens that were Positive*
- *44 of 81 (54%) were from specimens that were Negative.*

Performance:

- **Sensitivity and specificity is comparable**
- **But high-rate indeterminate results with an algorithm containing WB**

Western blot limitations

- Higher frequency of **indeterminate** results
- Lower sensitivity in the early stages of infection
- **Longer testing procedure than RDT/ELISA**
- More time-consuming, the need for specially trained staff
- Cost per test is higher than RDT/ELISA
- **Higher loss to follow-up, and lower linkage to care** with WB algorithms

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Estimated mean window period (time from HIV infection to immunological reactivity, in days)

Test generation	Median
4 generation	17,8
3 generation	23,1
2 generation	31,1
2 generation additional essays	33,4
Western blot	36,5

Delaney K, Время от заражения ВИЧ-1 до появления реактивных тестов на ВИЧ: практические следствия для интерпретации результатов и повторного тестирования после контакта, 2017.

Verification studies – good examples

- WHO is currently supporting HIV testing verification studies in **Armenia, Kazakhstan, Georgia**

It is suggested to conduct a **verification study of the new testing algorithms** in order to:

1. Identify the **combination of products which have minimum possible common cross-reactivity** to reduce the risk of false HIV-positive diagnosis. (Note: *Products from the same manufacturer should not be used as part of the testing algorithm to minimize common cross-reactivity*)
2. Identify **flexible algorithms**: replacement tests in case of a "problem" with one of the selected tests, e.g. stock out, lot recall, etc. One for A1 and one for A2/A3
3. **Not intended to reevaluate sensitivity and specificity of individual products**!

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Why lay provider testing and rapid testing?

- **Better uptake & prefered by clients (especially KP) = more people know their status**
  - In all studies individuals preferred RDTs over lab-based methods (EIA & WB)
- **Low cost & affordablity**
- **Accurate diagnosis**
  - equivalent accuracy to laboratory methods (EIA/WB)
- **Same day start**
  - RDTs have much faster turnaround time than lab-based testing
  - RDTs enable decentralization of confirmation testing which is key
  - People get to start PrEP & ART same day

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Using rapid diagnostic tests, the diagnosis can be confirmed within one day

WHO recommends:

Treatment should be prescribed on the day of confirmation of the diagnosis of HIV infection (and no later than 7 days from the confirmation of the diagnosis – if additional examinations are necessary).*

* Differences in tuberculosis and cryptococcal meningitis

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WHO recommendation:

HIV self-testing should be offered <u>as an approach</u> to HIV testing services

(strong recommendation, moderate quality evidence)

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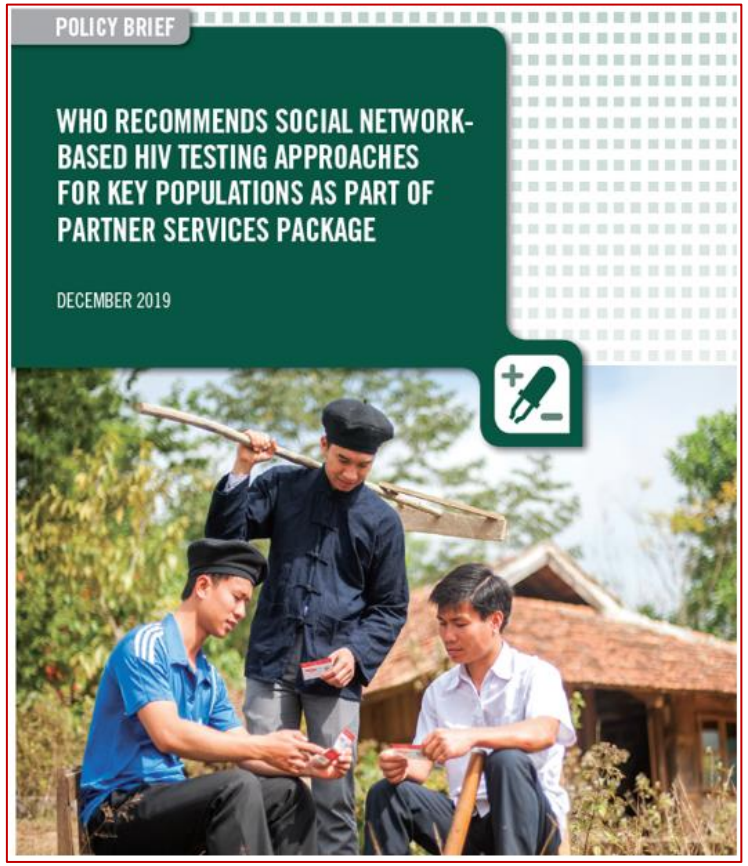
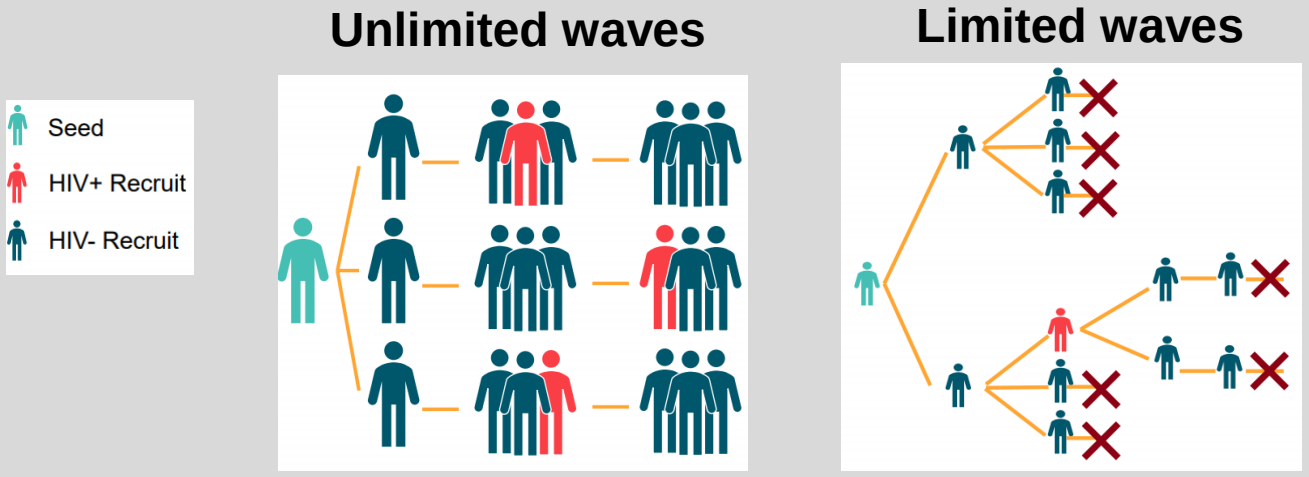
Self-testing is now the new normal!



WHO RECOMMENDATION:
Social network-based approaches can be offered as an approach to HIV testing for key populations as part of a comprehensive package of care and prevention

Social network approach (**SNA**): process where individuals (including those newly with diagnosed, with established infection or HIV negative) at high ongoing risk of HIV (such as key populations) are enlisted to encourage and offer HIV testing to social, sexual, drug injecting contacts in their network who may be at risk for HIV

SNA Types



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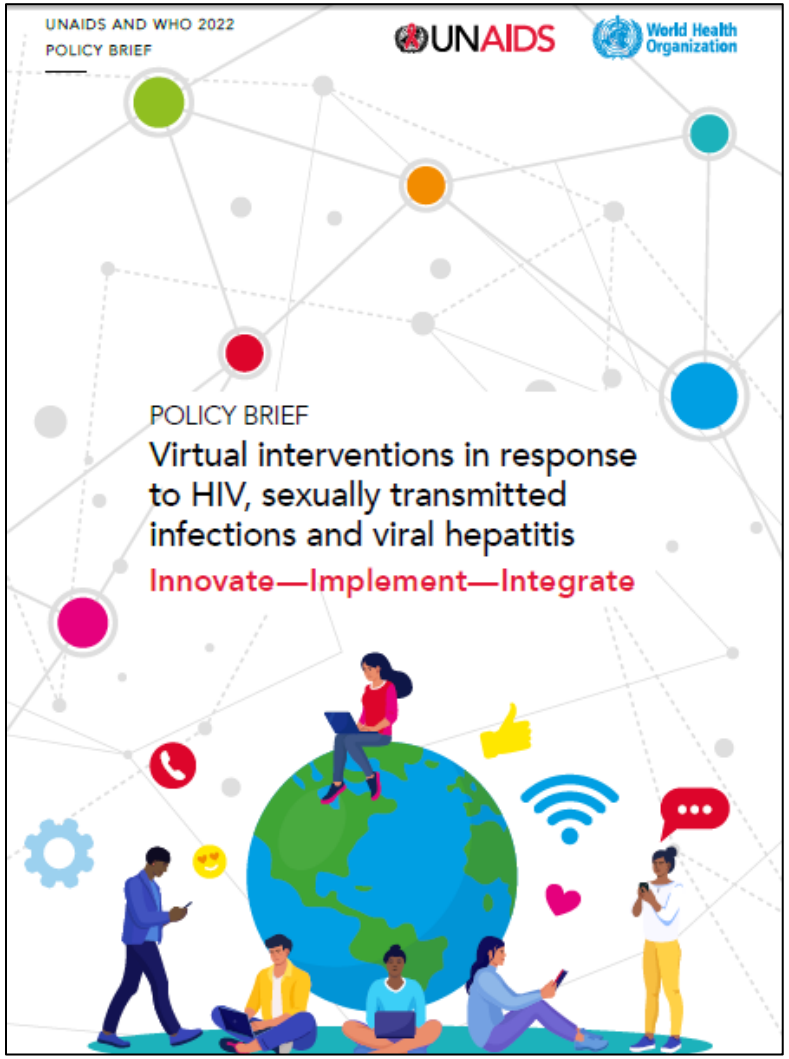

What are virtual interventions?

Internet and phone-based ways of communicating

Why should we go virtual?

- **4.80 billion internet users** (61% of total population)
- 4.48 active social media users (99% mobile users)
- **2.5 hours on social media**
- Reach broader audience
- Targeted reach
- **Offers choices**
- Improved efficiency
- Less opportunity costs for clients
- Less time consuming

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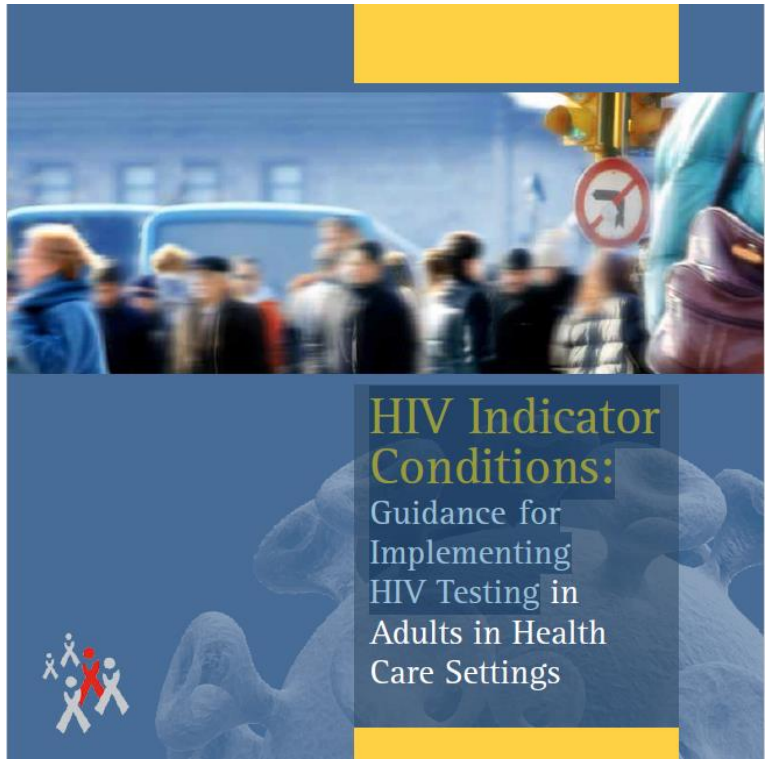

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1. Conditions which are AIDS defining among PLHIV*

Strongly recommend testing:

Neoplasms:
- Cervical cancer
- Non-Hodgkin lymphoma
- Kaposi's sarcoma

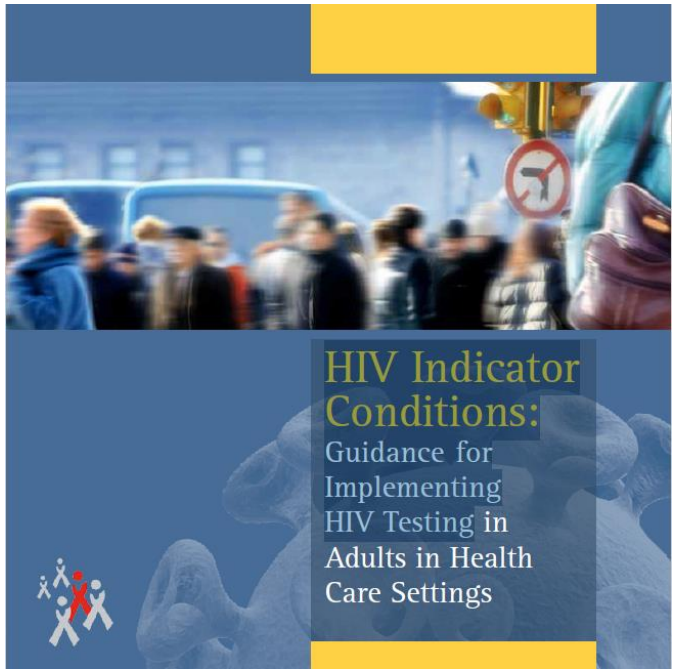
Bacterial infections
- Mycobacterium Tuberculosis, pulmonary or extrapulmunary
- Mycobacterium avium complex (MAC) or Mycobacterium kansasii, disseminated or extrapulmonary
- Mycobacterium, other species or unidentified species, disseminated or extrapulmunary
- Pneumonia, recurrent (2 or more episodes in 12 months)
- Salmonella septicaemia, recurrent

Viral infections
- Cytomegalovirus retinitis
- Cytomegalovirus, other (except liver, spleen, glands)
- Herpes simplex, ulcer(s) >I month/bronchitis/pneumonitis
- Progressive multifocal leucoencephalopathy

Parasitic infections
- Cerebral toxoplasmosis
- Cryptosporidiosis diarrhoea, >1 month
- Isosporiasis, >1 month
- Atypical disseminated leismaniasis
- Reactivation of American trypanosomiasis (meningoencephalitis or myocarditis)

Fungal infections
- Pneumocystis carinii pneumonia
- Candidiasis, oesophageal
- Candidiasis, bronchial/ tracheal/ lungs
- Cryptococcosis, extra-pulmonary
- Histoplasmosis, disseminated/ extra pulmonary
- Coccidiodomycosis, disseminated/ extra pulmonary
- Penicilliosis, disseminated

HIV in Europe. *HIV Indicator Conditions: Guidance for Implementing HIV Testing in Adults in Health Care Settings.* Copenhagen: HIV in Europe; 2012.



2a. Conditions associated with an undiagnosed HIV prevalence of >0.1 %**

Strongly recommend testing:

- Sexually transmitted infections
- Malignant lymphoma
- Anal cancer/dysplasia
- Cervical dysplasia
- Herpes zoster
- Hepatitis B or C (acute or chronic)
- Mononucleosis-like illness
- Unexplained leukocytopenia/ thrombocytopenia lasting >4 weeks
- Seborrheic dermatitis/exanthema
- Invasive pneumococcal disease
- Unexplained fever
- Candidaemia
- Visceral leishmaniasis
- Pregnancy (implications for the unborn child)

2b. Other conditions considered likely to have an undiagnosed HIV prevalence of >0.1%

Offer testing:

- Primary lung cancer
- Lymphocytic meningitis
- Oral hairy leukoplakia
- Severe or atypical psoriasis
- Guillain–Barré syndrome
- Mononeuritis
- Subcortical dementia
- Multiplesclerosis-like disease
- Peripheral neuropathy
- Unexplained weightloss
- Unexplained lymphadenopathy
- Unexplained oral candidiasis
- Unexplained chronic diarrhoea
- Unexplained chronic renal impairment
- Hepatitis A
- Community-acquired pneumonia
- Candidiasis

3. Conditions where not identifying the presence of HIV infection may have significant adverse implications for the individual's clinical management despite that the estimated prevalence of HIV is most likely lower than 0.1%

Offer testing:

- Conditions requiring aggressive immuno-suppressive therapy:
  - Cancer
  - Transplantation
  - Auto-immune disease treated with immunosuppressive therapy
- Primary space occupying lesion of the brain.
- Idiopatic/Thrombotic thrombocytopenic purpura

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Missed opportunities for diagnosis at different levels

Health Contact and Missing opportunities according to HIV Rapid Test Result in DRIVE 01 study					
Health Contact (N 5329)		Overall	Negative	Positive	P
Any Health Care Contact in last two years	Yes (%)	94.4	94.4	90,9	0.478
In Hospital Emergency Room	Yes (%)	46.5	46,4	55	0.443
Primary Care Center	Yes (%)	91	91	70	0.001
Specialist Physician	Yes (%)	39.9	40	35	0.648
Occupational Health Physician	Yes (%)	11.3	11.4	0	0.109
Number of Health care Contacts	Mean ±SD	8.9±0,15	8.9±0,15	8.1± 1,9	0.71
Prior HIV testing	Yes (%)	29.9	29.7	59.1	0.003
			(OR: 3.4, 95% CI: 1.5-8,02)		

- 18 - 60 years old who received services at a PHC Center or in a Hospital Emergency room in **Madrid**.
- Almost **91%** of patients with new HIV diagnosis had had **at least one health care contact** in the last two years before their HIV diagnosis.
- During this period, the same patients reported that **59%** of them had been **tested for HIV before**.
- At least **32%** of HIV infected patients had **missed opportunities** to be HIV diagnosed

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Missed Opportunities: 90.9% - 59.1% = **31.8%**

Source: Pérez Elías MJ, et all, Prevalence of Hidden HIV Infection and Prior Sanitary Contact in DRIVE Study of Voluntary Routine HIV Diagnosis 14th European AIDS Conference. Brussels 15-19 October. 2013. PS8/3

Brighton Study 2000-2005: Missed opportunities for diagnosis

62% accessed **secondary care** in the preceding year:

- 26% with an HIV-related problem;

80% had been seen in **primary care**

- 60% with an HIV-related problem

Ottewil, BHIVA 2006l

BMJ Open

Missed opportunities for earlier diagnosis of HIV in patients who presented with advanced HIV disease: a retrospective cohort study

Itzchak Levy,[1,2] Yasmin Maor,[3,2] Naim Mahroum,[1,2] Liraz Olmer,[4] Anat Wieder,[1] Vladislav Litchevski,[1] Orna Mor,[5,2] Galia Rahav[1,2]

- Old age and being heterosexual were significant risk factors for being diagnosed late.
- **All patients with advanced disease** had at least one clinical indicator disease (CID) that did not lead to an HIV test in the 5 years prior to AIDS diagnosis.
- The median time between CID and AIDS diagnosis was **24 months** (IQR 10–30).
- **60%** of CIDs were missed by a general practitioner and **40%** by a specialist.

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Missed opportunities for HIV testing in people diagnosed with HIV in Estonia, 2014-2015

- Of 538 newly diagnosed HIV cases, **82%** had visited healthcare services at least once during the 2 years before HIV diagnosis; the mean number of visits was **9.1**.
- Of these, **31%** had at least **HIV indicator condition** on at least one of their treatment invoices.
- In 390 cases of HIV indicator conditions, **only 5% were tested for HIV**.

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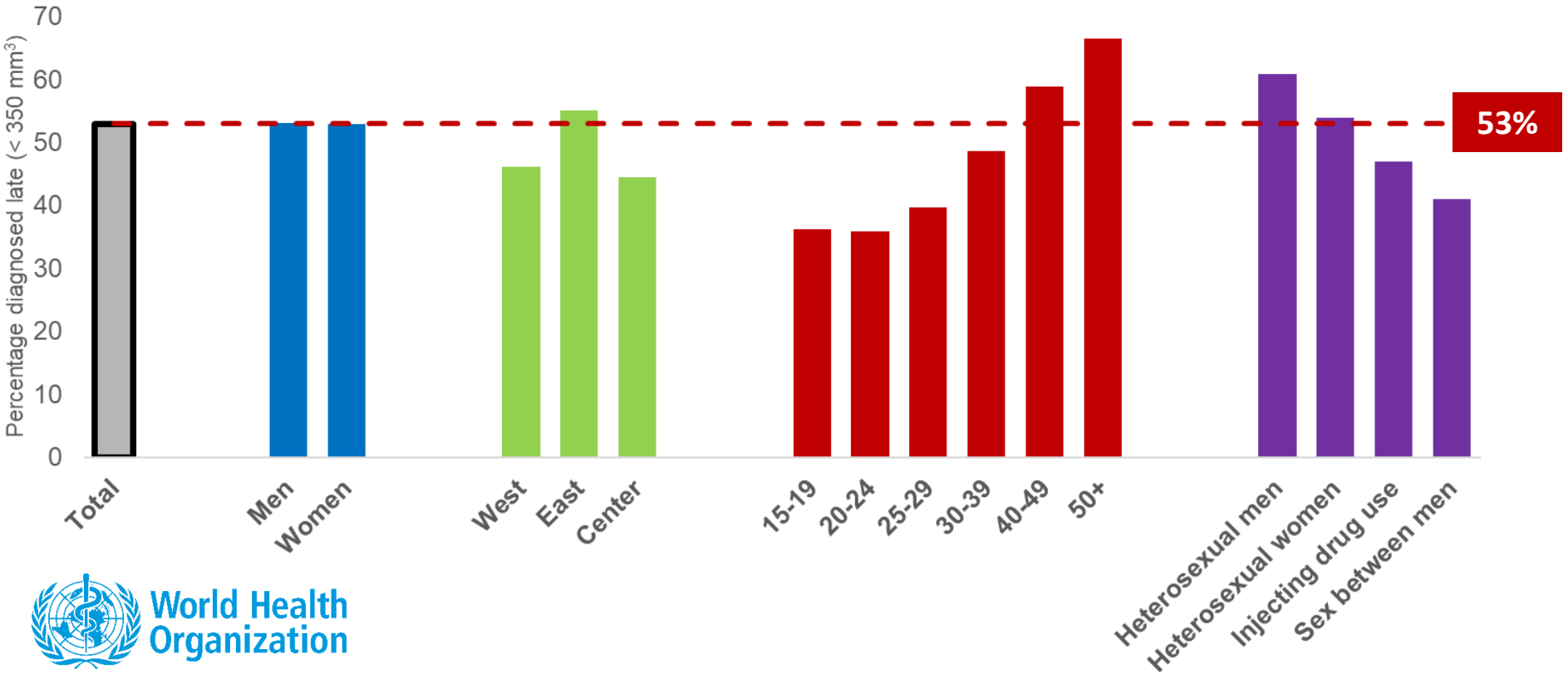
Missed opportunities for HIV testing in people diagnosed with HIV, Estonia, 2014 to 2015

Kristi Rüütel[1], Liis Lemsalu[1], Sirly Lätt[2], Jevgenia Epštein[3], on behalf of OptTEST by HiE[4]

https://www.eurosurveillance.org/content/10.2807/1560-7917.ES.2019.24.15.1800382

Late HIV diagnosis remains a challenge with variation across transmission mode & age

In 2022, 53% of reported diagnoses were diagnosed late, with CD4 < 350 cells/mm3 at diagnosis*



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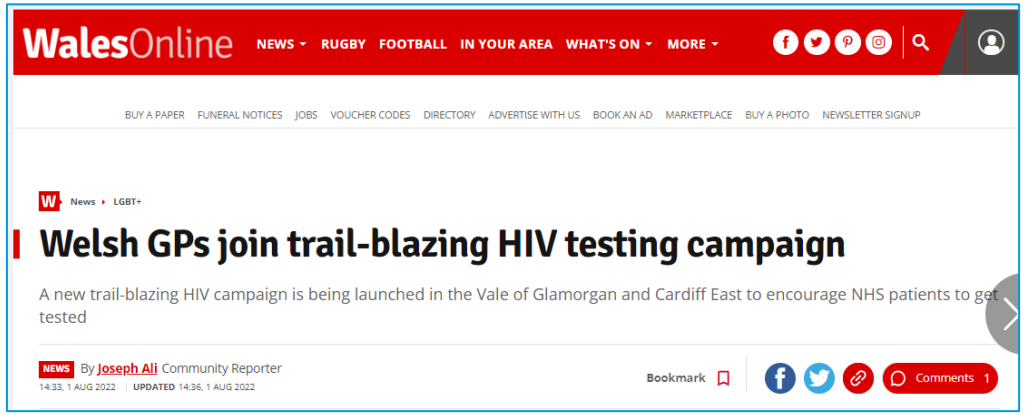
The percentage of people with HIV diagnosed late increases with age and is highest in people over the age 50

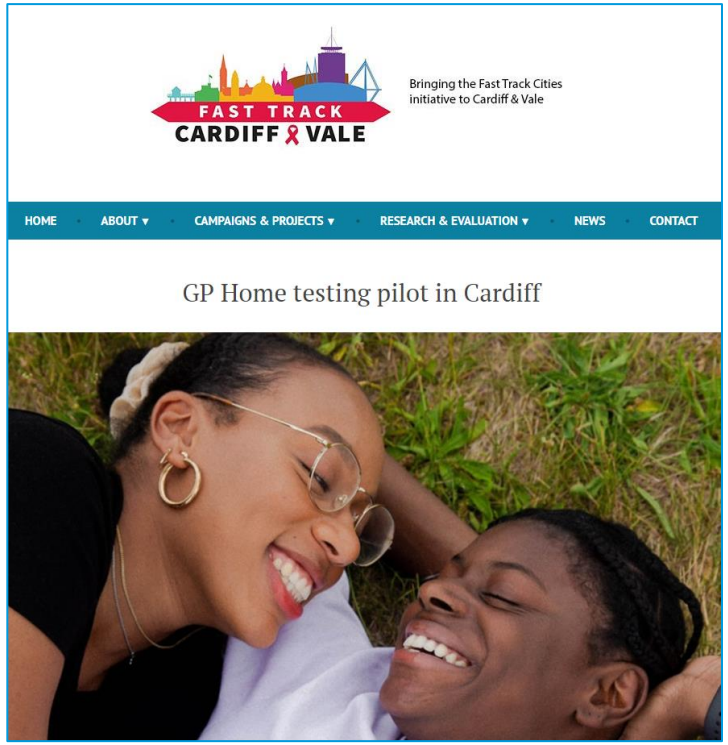
The percentage of people with HIV diagnosed late is highest among those infected heterosexually (for both men and women)

Source: ECDC/WHO (2023). HIV/AIDS Surveillance in Europe 2023 (2022 data)

Involving PHC in HIV testing in Wales
‘Texting 4 Testing’ project

- People aged 16+ years, served by GP practices in Cardiff & Vale, receive a text message offering a free HIV postal test kit.
- Those who receive a text message from their GP will be able to order a postal test kit from “Sexual Health Wales” online, through a link to their website.
- The kit will arrive in a discreet box which fits through a letterbox.
- Anyone who does not get a text can also order a free, confidential HIV test through “Sexual Health Wales”.





https://fasttrackcardiff.wales/campaigns-communities/21st-century-hiv/home-testing-in-cardiff/
https://www.walesonline.co.uk/news/welsh-gps-join-trail-blazing-24613803

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Testing as the Gateway to Prevention and Treatment

HIV TESTING

HIV testing determines the next steps and whether treatment or prevention is needed (including PrEP)

Key components of HIV control programs

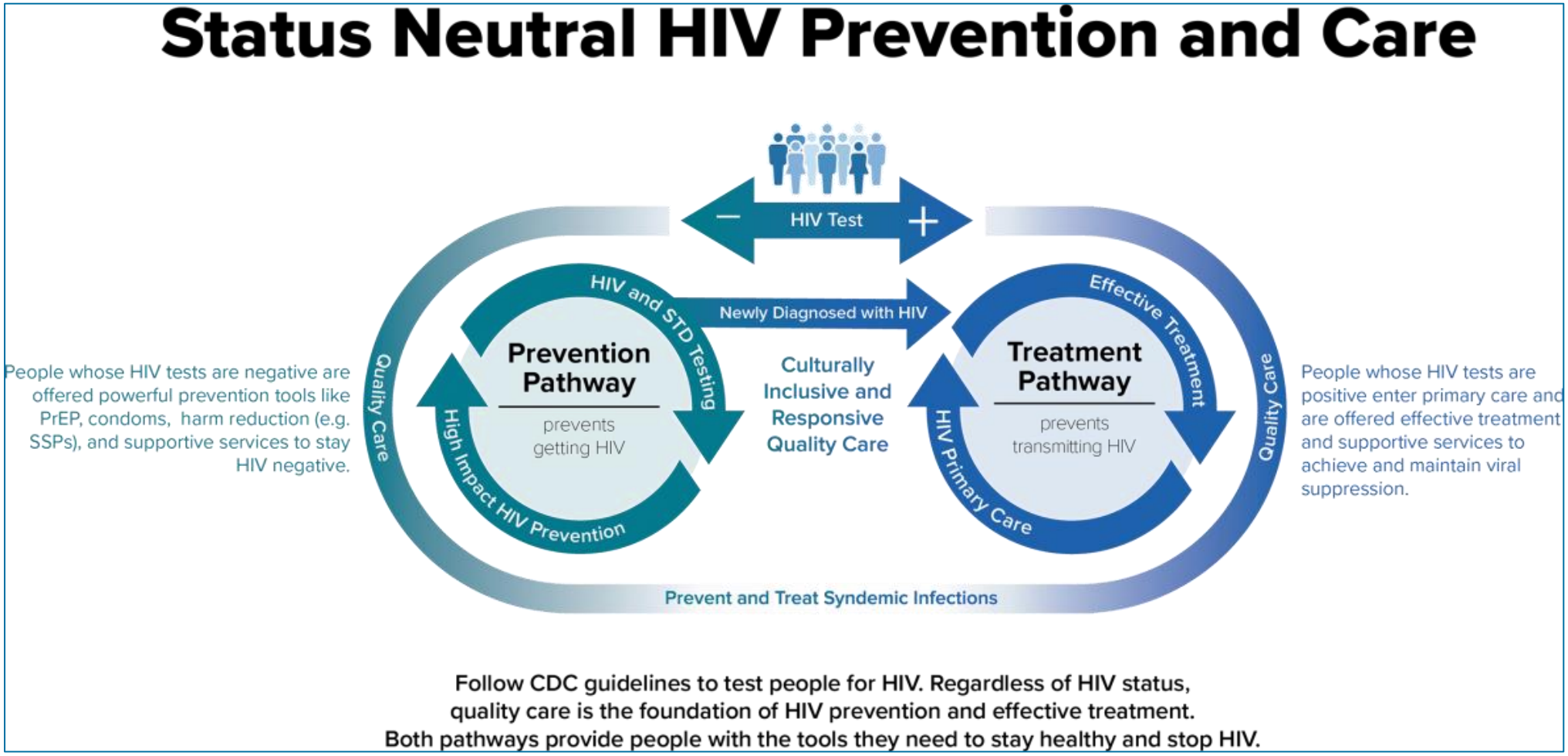
HIV TREATMENT

People diagnosed with HIV should receive daily ART to suppress viral load and prevent HIV transmission

PREVENTION

People without HIV, but at risk of becoming infected, can take PrEP for prevention. Basic combination prevention measures should be provided by the national HIV prevention program

- The status neutral approach to HIV prevention and care defines the entry point to care as the time of an HIV test.
- At this entry point, clients' needs are assessed, and they are engaged and linked to appropriate services based on these needs, regardless of whether their HIV test is positive or negative.



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Source: https://www.cdc.gov/hiv/effective-interventions/prevent/status-neutral-hiv-prevention-and-care/index.html

- **Decentralize** and **simplify** HIV testing to reach as earlier as possible those who are undiagnosed; introduce and expand **peer-led partner/contact tracing**
- Reduce delays in **diagnosis confirmation** (RDT, POCT, discontinuation of WB) and ensure rapid and effective **linkage to ART and care** (minimize losses to follow-up)
- Add and expand evidence-based approaches to **self-testing/self-sampling**
- Expand **indicator testing for HIV** in emergency care and other settings
- Ensure optimal **accuracy** of test results (WHO pre-qualification, verification studies)
- Use HIV testing as the pathway to both **prevention** and treatment **(status neutral** approach)

We shouldn't be afraid to switch from instrumental laboratory-based testing methods to a decentralized system using rapid tests!

New methods are replacing old ones - this is a natural process!

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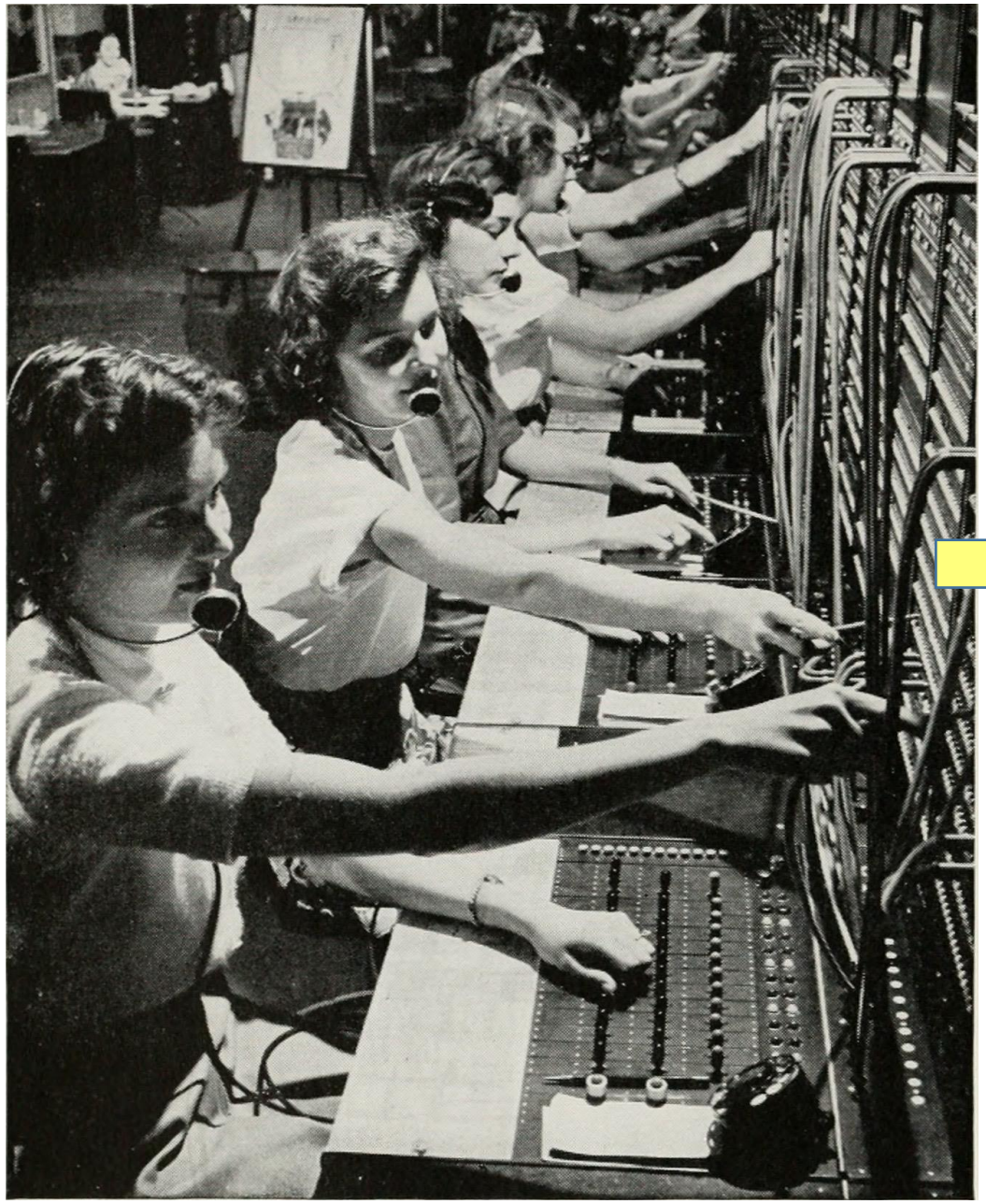
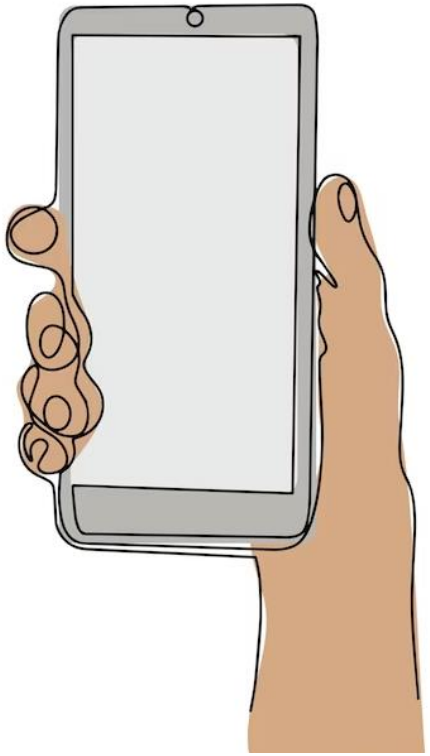
Progress cannot be stopped!





- https://rue.wikipedia.org/wiki/Телефонный коммутатор

Thank you for your attention!

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