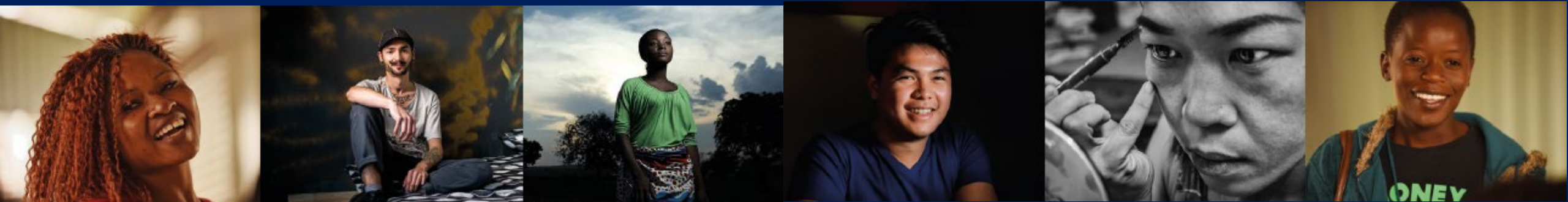


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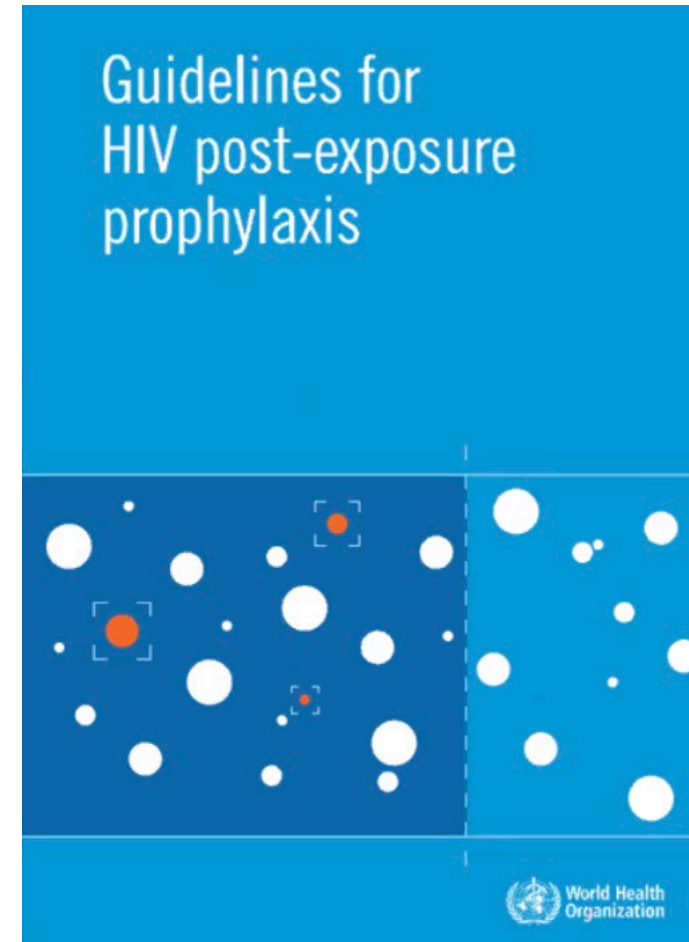
# Levels of evidence needed for guideline development: PEP



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# Guidelines and guidance for Post-exposure prophylaxis (PEP)

- **2014: Guidelines on HIV PEP** - TDF/XTC preferred as backbone regimen
- **2016: Consolidated HIV Guidelines – PEP** recommendation update to include DTG as 3rd drug
- **2024: Guidelines for implementation of PEP in community settings and task shifting**



## 2014 PEP recommendations

| Number of antiretroviral drugs   |             |                 |
|--|-------------|-----------------|
| An HIV post-exposure prophylaxis regimen with two antiretroviral drugs is effective, but three drugs are preferred.  | Conditional | Low             |
| Preferred antiretroviral regimen for adults and adolescents <sup>a</sup>   |             |                 |
| TDF + 3TC (or FTC) is recommended as the preferred backbone regimen for HIV post-exposure prophylaxis among adults and adolescents.  | Strong      | Low to moderate |
| LPV/r or ATV/r is recommended as the preferred third drug for HIV post-exposure prophylaxis among adults and adolescents.<br>Where available, RAL, DRV/r or EFV can be considered as alternative options.                | Conditional | Very low        |
| Preferred antiretroviral regimen for children $\leq 10$ years old <sup>b</sup>   |             |                 |
| AZT + 3TC is recommended as the preferred backbone regimen for HIV post-exposure prophylaxis among children 10 years and younger.<br>ABC + 3TC or TDF + 3TC (or FTC) can be considered as alternative regimens.          | Strong      | Low             |
| LPV/r is recommended as the preferred third drug for HIV post-exposure prophylaxis among children younger than 10 years.<br>An age-appropriate alternative regimen can be identified among ATV/r, RAL, DRV, EFV and NVP. | Conditional | Very low        |
| Prescribing frequency  |             |                 |
| A 28-day prescription of antiretroviral drugs should be provided for HIV post-exposure prophylaxis following initial risk assessment.  | Strong      | Very low        |
| Adherence support  |             |                 |
| Enhanced adherence counselling is suggested for all individuals initiating HIV post-exposure prophylaxis.  | Conditional | Moderate        |

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# Drug regimen: Number of drugs and which drugs

Start early:

PEP should be offered, and as early as possible, **ideally within 24 hours** but not later than 72 hours.

## 4.3 Number of ARV drugs prescribed for post-exposure prophylaxis

### Recommendations

A regimen for post-exposure prophylaxis for HIV with two ARV drugs is effective, but three drugs are preferred.

*(Conditional recommendation, very-low-quality evidence)*

## 4.4 Post-exposure prophylaxis ARV regimens – adults and adolescents

### Recommendations

TDF + 3TC (or FTC) is recommended as the preferred backbone regimen for HIV post-exposure prophylaxis for adults and adolescents.

*(Strong recommendation, low-quality evidence)*

LPV/r or ATV/r is recommended as the preferred third drug for HIV post-exposure prophylaxis for adults and adolescents.

*(Conditional recommendation, very-low-quality evidence)*

Where available RAL, DRV/r or EFV can be considered as alternative options.

## Recommendations (2016)

### Overall

**An HIV PEP regimen with two ARV drugs is effective, but three drugs are preferred** *(conditional recommendation, low-certainty evidence).*<sup>a</sup>

### Adults and adolescents

**TDF + 3TC (or FTC) is recommended as the preferred backbone regimen for HIV PEP** *(strong recommendation, low-certainty evidence).*<sup>a</sup>

**DTG is recommended as the preferred third drug for HIV PEP** *(strong recommendation, low-certainty evidence).*

**When available, ATV/r, DRV/r, LPV/r and RAL may be considered as alternative third drug options for PEP** *(conditional recommendation, low-certainty evidence).*

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## 4.6 Prescribing frequency

### Recommendations

A 28-day prescription of antiretroviral drugs should be provided for HIV post-exposure prophylaxis following initial risk assessment.

*(Strong recommendation, low-quality evidence)*

## 4.7 Adherence strategies

### Recommendations

Enhanced adherence counselling is suggested for individuals initiating HIV post-exposure prophylaxis.

*(Conditional recommendation, moderate-quality evidence)*

# 2024 guidelines : Re-thinking / Re-invigorating PEP

## Uptake challenges

- Low knowledge of PEP by health care workers
- Low knowledge about PEP among groups at risk of HIV
- Low access and uptake (esp outside HCW services)
- Limited PEP delivery points
- High cost in private sector
- Complexities for access (eligibility check lists etc)
- Late start
- Low completion

## Low completion of PEP course

- 56.6% [95% (CI 50.9-62.2%) people considered eligible for PEP completed 28-day course
- PEP completion rates highest for nonoccupational exposures (65.6%, 95% CI 55.6-75.6%)
- lowest for sexual assault (40.2%, 95% CI 31.2-49.2%)
- higher rates of PEP completion reported for MSM (67.2%, 95% CI 59.5-74.9%).

Ford N, Irvine C, Shubber Z, Baggaley R Adherence to HIV postexposure prophylaxis: a systematic review and meta-analysis. *AIDS*, 2014



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# WHO PEP guidance and recommendations (2024)

To increase access to HIV PEP

**HIV PEP should be delivered in community settings.** *(strong recommendation, very low certainty of evidence)*

- Community settings can include a **wide range of options**, including but not limited to pharmacies, community-based organizations, drop-in centres, mobile clinics, online delivery

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## WHO PEP guidance and recommendations (2024)

**Task sharing should be employed to dispense, distribute, provide and monitor PEP** (*strong recommendation, very low certainty of evidence*)

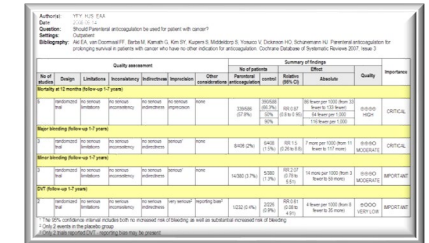
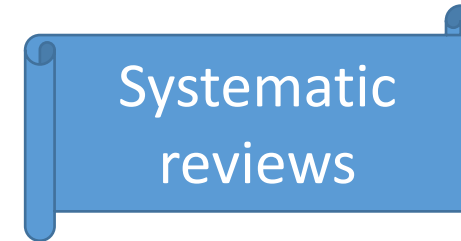
- Tasks can be shared with a range of health workforce teams, including **pharmacists, nurses, doctors and trained lay and peer health workers**

# Decision-making in WHO Guidelines

**GRADE**

# GRADE Evidence to Decision-making

- ❖ Balance of benefits versus harms
- ❖ Certainty of evidence
- ❖ Values & Preferences (cultural, social, special populations)
- ❖ Resource use
- ❖ Feasibility
- ❖ Equity & Human Rights
- ❖ Acceptability



| Study ID                              | Stage | Limitations | Quality assessment |              |             |                      |        | No. of patients |          | Summary estimates |  | Reference |
|---------------------------------------|-------|-------------|--------------------|--------------|-------------|----------------------|--------|-----------------|----------|-------------------|--|-----------|
|                                       |       |             | Inconsistency      | Indirectness | Imprecision | Other considerations | Number | Relative risk   | Absolute | Quality           |  |           |
| <b>Summary of results: 17 studies</b> |       |             |                    |              |             |                      |        |                 |          |                   |  |           |
| No. of patients: 10000                |       |             |                    |              |             |                      |        |                 |          |                   |  |           |
| Relative risk: 0.10                   |       |             |                    |              |             |                      |        |                 |          |                   |  |           |
| Absolute: 1000                        |       |             |                    |              |             |                      |        |                 |          |                   |  |           |
| Quality: High                         |       |             |                    |              |             |                      |        |                 |          |                   |  |           |
| Reference: [1-17]                     |       |             |                    |              |             |                      |        |                 |          |                   |  |           |
| <b>Summary of results: 17 studies</b> |       |             |                    |              |             |                      |        |                 |          |                   |  |           |
| No. of patients: 10000                |       |             |                    |              |             |                      |        |                 |          |                   |  |           |
| Relative risk: 0.10                   |       |             |                    |              |             |                      |        |                 |          |                   |  |           |
| Absolute: 1000                        |       |             |                    |              |             |                      |        |                 |          |                   |  |           |
| Quality: High                         |       |             |                    |              |             |                      |        |                 |          |                   |  |           |
| Reference: [1-17]                     |       |             |                    |              |             |                      |        |                 |          |                   |  |           |

# Evidence to Decision-making Table

| Domain  | Judgement  |
|---|--|
| Benefits vs Harms                             | Benefits > Harms; Benefits = Harms; Harms > Benefits   |
| Certainty of Evidence                         | High, Moderate, Low, Very Low                          |
| Values & Preferences                          | No Major Variability OR Major Variability OR Uncertain |
| Resource use                                  | More or Less resources required                        |
| Feasibility                                   | Yes OR No OR Uncertain                                 |
| Equity & Human Rights                         | More OR less equitable OR Uncertain                    |
| Acceptability                                 | No Major Variability OR Major Variability OR Uncertain |
| RECOMMENDATION                                | <b>In favour OR Against OR No Recommendation</b>       |
| Strength                                      | <b>STRONG OR CONDITIONAL</b>                           |
| Research Gaps / Implementation considerations |  |

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# Considerations for WHO guidelines on a new PEP product

- Current WHO recommendations are based on the drug (TDF/FTC as the backbone)
- For future products, considerations include
  - Which drug – One drug only, or need to paired with other drugs ?
  - Time after exposure?
  - Duration - 1 month? More than 1 month?
  - Drug resistance ?
  - HIV testing - Timeline for confirmation for a negative test ?
- Biological plausibility
  - We will not have RCTs
  - Possibility for PK/PD, animal models ?
- How to do a systematic review without data?
- Ethical issues
- Need for regulatory? Off label?
- 2024 recommendations will still apply for delivery and access

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# Thank you for your attention

## Acknowledgements

**WHO:** Heather-Marie Schmidt, Rachel Baggaley, Virginia MacDonald, Nathan Ford

**2014** and **2024** Guideline Development Groups