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OPERATIONAL SUPPORT

Doxycycline prophylaxis for bacterial sexually transmitted infections: a guide for data collection in the EU/EEA

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This guide was produced by ECDC in response to a request from the Robert Koch Institute (RKI), and with its scientific input. The work was coordinated by Otilia Mårdh (ECDC) and Klaus Jansen (RKI), who also contributed to the conceptualisation of the guide and its writing.

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Abbreviations

AE	Adverse event
AMR	Antimicrobial resistance
AST	Antimicrobial susceptibility testing
CHIP	Centre of Excellence for Health, Immunity and Infections
CLSI	Clinical and Laboratory Standards Institute
CTCAE	Common Terminology Criteria for Adverse Events
Doxy-PEP	Doxycycline post-exposure prophylaxis
Doxy-PrEP	Doxycycline pre-exposure prophylaxis
EACS	European AIDS Clinical Society
ECDC	European Centre for Disease Prevention and Control
EMIS-2024	European Men-Who-Have-Sex-With-Men and Trans People Internet Survey
EU/EEA	European Union/European Economic Area
EUCAST	European Committee on Antimicrobial Susceptibility Testing
Euro-GASP	European Gonococcal Antimicrobial Surveillance Programme
GoE	Group of Experts
HAV	Hepatitis A Virus
HBV	Hepatitis B Virus
HIV	Human immunodeficiency virus
HIV-PrEP	HIV pre-exposure prophylaxis
HPV	Human papillomavirus
MIC	Minimum inhibitory concentration
MLST	Multilocus sequence typing
MRSA	Methicillin-resistant *Staphylococcus aureus*
NAAT	Nucleic acid amplification test
NG-MAST	*Neisseria gonorrhoeae* multi-antigen sequence typing
NG-STAR	*Neisseria gonorrhoeae* sequence typing for antimicrobial resistance
PCR	Polymerase chain reaction
RCT	Randomised clinical trial
RKI	Robert Koch Institute
RPR	Rapid plasma reagin
STI	Sexually transmitted infection
VDRL	Venereal Disease Research Laboratory
WGS	Whole-genome sequencing
WHO	World Health Organization

Executive summary

Purpose and scope

This guide provides a harmonised, non-prescriptive framework for data collection on doxycycline prophylaxis for the prevention of bacterial sexually transmitted infections (STIs) in the European Union/European Economic Area (EU/EEA). It is intended to support monitoring, surveillance, research and evaluation activities in settings where doxycycline prophylaxis (primarily doxycycline post-exposure prophylaxis, doxy-PEP) is used, whether by prescription or informally.

The guide does not promote or discourage the provision of doxycycline prophylaxis, nor does it replace national clinical guidelines, regulatory decisions or antimicrobial-stewardship policies. Instead, it aims to improve the comparability, interpretability and quality of data generated across countries and settings, thereby strengthening the evidence base available for public-health decision-making at the national and EU/EEA level. ECDC public health considerations (January 2026) recommend individual-level, shared decision-making for those at highest risk of contracting an STI, particularly for syphilis prevention among gay, bisexual and other men who have sex with men, and transgender women, and emphasise the need for ongoing monitoring of STI trends, antimicrobial resistance (AMR), antimicrobial consumption and behavioural indicators.

Why harmonised data collection is needed

Interest in doxycycline prophylaxis for STI prevention is increasing across the EU/EEA, alongside growing concerns about antimicrobial resistance (AMR), the potential impact on the human microbiome, longer-term safety, and equity of access. Available evidence to date is uneven across populations, outcomes and settings. Most efficacy data come from randomised trials conducted among gay, bisexual and other men who have sex with men and transgender women living with HIV or using HIV pre-exposure prophylaxis (HIV PrEP). Evidence on effectiveness in real life settings is emerging but is often derived from heterogenous observational or implementation contexts.

Fragmented or inconsistent data collection across settings limits the ability to:

- compare findings across countries or programmes;
- pool data to evaluate infrequent outcomes (e.g. specific adverse events, microbiological endpoints);
- distinguish programme-related effects from underlying epidemiological trends;
- assess population-level benefits, risks and unintended effects, including AMR.

This guide addresses these challenges by proposing standardised variables, operational definitions and minimum datasets that can be applied across diverse study designs and implementation contexts.

What the guide contains

The guide is organised into three modules:

- Module A: Epidemiological, microbiological and clinical variables

Covers uptake and use patterns, demographics and equity, prescribing practices, clinical effectiveness outcomes, safety and adverse events, AMR impacts and (optionally) microbiome outcomes.

- Module B: Psychosocial and behavioural variables

Covers sexual behaviours and exposure patterns, acceptability and adherence, provider attitudes and awareness, and the use of specific psychoactive substances to enhance sexual experiences ('chemsex').

- Module C: Cross-cutting considerations

Provides guidance on implementation contexts, study design, data quality, governance, ethics, interpretation and harmonisation, without introducing additional variables.

Across Modules A and B, each variable domain includes:

- the public health relevance and objectives;
- a summary of existing evidence at state of publication;
- proposed variables with definitions, timing, coding schemes and priority level;
- identification of a core minimum dataset to support harmonised implementation.

The annexes summarise the core dataset and provide an example illustrating how the variables can be applied in a clinical cohort setting, with extended variables available for implementation where capacity allows.

Intended users

The guide is intended for:

- national and subnational public-health authorities;
- academic and public health researchers;
- sexual health services and HIV-PrEP programmes conducting monitoring or evaluation;
- surveillance networks and laboratories contributing STI or AMR data;
- institutions coordinating multicounty or multisite studies.

It may also be informative for policymakers and guideline developers, while recognising that it is not a policy or clinical recommendation document.

Introduction

This guide provides a high-level framework to support harmonised data collection on doxycycline prophylaxis for the prevention of bacterial sexually transmitted infections (STIs) across clinical and community settings and within surveillance and research contexts in the EU/EEA. Its purpose is to define a standardised set of variables to enable the generation of comparable, high-quality evidence on use, effectiveness, safety, antimicrobial resistance (AMR), microbiological outcomes (including impacts on the human microbiome) and behavioural impacts (including the use of specific psychoactive substances to enhance sexual experiences). Harmonised datasets will facilitate pooled analyses across countries and programmes, increasing sample size and analytical power. This is essential for assessing infrequent clinical events, microbiological endpoints and AMR-related outcomes that are less likely to be robustly evaluated within single-site studies. The guide is intended to support evidence generation and enhance comparability across settings, and to inform future study design and public health evaluation of doxycycline prophylaxis for STI prevention at national and EU/EEA levels.

Doxycycline post-exposure prophylaxis (doxy-PEP) refers to the use of a single 200 mg dose of doxycycline taken as soon as possible after condomless sexual contact (preferably within 24 hours and no later than 72 hours, with a maximum dose of 200 mg in any 24-hour period) as a biomedical prevention strategy to reduce the risk of specific bacterial STIs [1,2]. The rationale is based on the antimicrobial activity of doxycycline against *Chlamydia trachomatis* and *Treponema pallidum*. Although doxy-PEP may also have some effect on *Neisseria gonorrhoeae*, its overall effectiveness against gonorrhoea is highly region-dependent and limited by widespread tetracycline resistance (for example, approximately 55% efficacy in United States trials, compared with limited or no significant reduction in French trials) [1,3]. Doxy-PEP is distinct from doxycycline pre-exposure prophylaxis (doxy-PrEP), which refers to continuous daily use of doxycycline (typically 100 mg taken once daily) before, during and after periods of potential exposure [1]. Evidence on the effectiveness, safety, AMR and other population-level impacts of doxy-PrEP remains limited and is still emerging [4].

Evidence from randomised clinical trials indicates that doxy-PEP can reduce incident syphilis and chlamydia among gay, bisexual and other men who have sex with men and transgender women living with HIV or using HIV pre-exposure prophylaxis (HIV-PrEP), and who are at increased risk of STIs (for example, those with a history of an STI) [5-7]. Conversely, a randomised clinical trial evaluating doxy-PEP among cisgender women in Kenya failed to show a significant reduction in bacterial STIs, a finding largely attributed to low medication adherence, though a recent observational study in Japan suggested effectiveness for cisgender female sex workers [8,9]. Early observational data from implementation settings similarly suggest reductions in syphilis and chlamydia incidence following wider community use but limited or no reduction in incident gonorrhoea cases [10-13]. However, these findings are based on relatively short observation periods, and evidence on longer-term effectiveness, sustainability of use and population-level impacts remains limited.

Emerging evidence suggests that doxy-PEP use may contribute to changes in antimicrobial resistance [14-18]. Concerns relate not only to the development of resistance to doxycycline itself, but also to the potential for selection or co-selection of resistance to other antimicrobial classes, including third-generation cephalosporins (such as decreased susceptibility to cefixime and ceftriaxone in *N. gonorrhoeae*), through increases in minimum inhibitory concentrations (MICs) and the emergence or enrichment of shared resistance mutations or genes (for example, the co-selection of the tetM gene alongside mosaic penA alleles) [19-21]. Uncertainties remain regarding the extent and clinical relevance of these potential AMR impacts in *Neisseria gonorrhoeae*, *Mycoplasma genitalium* and other relevant pathogens, as well as effects on commensal bacteria and the human microbiome [15,16,22-26]. In addition, potential implications for longer-term behavioural patterns, health service utilisation and antimicrobial consumption at the population level remain insufficiently characterised.

Across EU/EEA countries, interest in doxycycline prophylaxis is increasing, with both prescribed use and informal use (i.e. use outside formal clinical programmes) already occurring in multiple countries and settings across the EU/EEA [1]. Several national and international bodies have issued provisional clinical guidance recommending shared decision-making and ongoing monitoring where doxycycline prophylaxis is provided[i] [1]. This highlights the need for coordinated, systematic and harmonised data collection (including variables such as user demographics, prescribing practices, adherence behaviours and impacts on the human microbiome) to ensure that evidence generated from research projects, pilot programmes, surveillance activities and clinical monitoring is comparable and suitable for pooled interpretation. Such harmonisation is particularly important to support assessment of population-level benefits and risks and outcomes that require larger sample sizes. These outcomes include potential reductions in bacterial STI incidence, AMR trends, changes in clinical presentation and equity of access.

[i] For a list of relevant guidelines, recommendations and statements published up to January 2026, see Annex 3 of ECDC (2026), *Public health considerations on the use of doxycycline for post-exposure prophylaxis for bacterial sexually transmitted infections in the EU/EEA*.

In January 2026,the European Centre for Disease Prevention and Control (ECDC) issued public health considerations on doxy-PEP that recommend individual-level decision-making guided by clinical judgement and national guidelines, and specifically advise that use should focus on syphilis prevention among gay, bisexual and other men who have sex with men and transgender women at the highest risk of infection; a population-level intervention is not recommended at this time [1]. National public health authorities are advised to maintain oversight of doxy-PEP use and its impact on STI incidence, antimicrobial resistance and antimicrobial consumption through robust surveillance. The same document also presents the broader evidence base and identifies a set of priority research questions to guide future evidence generation, including questions related to effectiveness, AMR, behavioural impacts and implementation models [1].

This guide focuses on harmonised data collection for monitoring and research and does not promote or discourage doxycycline prophylaxis. In line with ECDC's approach, it supports evidence generation by providing a standardised approach to variable definitions, measurement methods and operational procedures that can be applied across study designs and data collection contexts. The guide is explicitly intended to support monitoring and research rather than to recommend clinical implementation and is intended for use across EU/EEA settings to facilitate comparable data collection and alignment of future research efforts [27]. This guide was developed in response to a request from the Robert Koch Institute (RKI) through the ECDC country support mechanism, in collaboration with the European AIDS Clinical Society (EACS) and the Centre of Excellence for Health, Immunity and Infections (CHIP).

The three modules provide background information, core and extended datasets, variable specifications and methodological considerations to support implementation across diverse study designs and health system contexts. As evidence continues to evolve, regular review and adaptation of this guide will be necessary. Early priorities may include integrating the core minimum dataset into planned research, pilots or monitoring activities, and strengthening mechanisms for secure, General Data Protection Regulation (GDPR)-compliant data sharing and pooled analyses [28].

This guide is intended as a living resource. Users are encouraged to apply the core minimum dataset as the standard foundation, adapting extended elements according to feasibility, capacity and national context. Across modules, variables are aligned with priority research questions identified by ECDC and RKI to ensure that harmonised data collection supports both immediate monitoring needs and longer-term public health decision-making.

Methods

This document was produced by ECDC in response to a request from the Robert Koch Institute (RKI), under the coordination and scientific contributions from both ECDC and RKI experts. A draft version was developed by the European AIDS Clinical Society (EACS), with contributions from the Centre of Excellence for Health, Immunity and Infections (CHIP).

This guide was developed through a structured, multi-step process that combined evidence review, expert consultation and iterative drafting. The approach was to ensure that the content was based on the best available evidence, informed by relevant stakeholders and feasible for use across diverse EU/EEA settings. The guide does not promote the implementation of doxycycline prophylaxis but is intended to support informed decision-making in settings where its use is being considered or is already occurring.

Evidence review and scoping

An initial desk review was conducted to identify existing evidence relevant to doxycycline prophylaxis, including randomised clinical trials, observational studies, AMR surveillance reports, implementation studies and behavioural research. Relevant EU/EEA surveillance frameworks, including those for STIs, AMR and behavioural indicators, were reviewed to explore opportunities for alignment with existing data structures and reporting systems. This review informed the definition of key content domains and identified areas requiring further expert input. Where applicable, variables were adapted from existing instruments or indicators, including ECDC monitoring indicators and measures from the 'European Men-Who-Have-Sex-With-Men and Trans People Internet Survey (EMIS-2024)'. All other variables were developed specifically for this guidance by the project team.

Establishment of the Group of Experts

An international, multidisciplinary Group of Experts was convened by the Robert Kock Institute (RKI), with support from EACS, CHIP and ECDC to contribute to the development of this guide. Members included specialists in clinical STI care, infectious disease epidemiology, microbiology and AMR surveillance, behavioural and psychosocial research, clinical trial methodology, public health surveillance and community organisations. Selection aimed to ensure geographical and disciplinary diversity and to reflect settings with differing levels of experience in research and/or implementation of doxycycline prophylaxis. A full list of members is provided in Annex 1.

Stakeholder engagement

To complement the desk review, a series of online group interviews was conducted in October–November 2025 with five thematic stakeholder groups: civil society representatives and psychosocial researchers; microbiology, AMR and microbiome specialists; clinical care providers; clinical trial researchers; and public health policy and surveillance specialists.

The interviews explored current practice, feasibility considerations, priority data needs and anticipated challenges in collecting harmonised data. Outputs were synthesised across groups to identify areas of agreement, divergence, and emerging issues, informing both variable selection and operationalisation.

Drafting and review process

A zero draft of the guidance structure and proposed variables was developed based on the desk review and stakeholder interview findings. This draft was reviewed by representatives from ECDC and RKI, followed by written input from the Group of Experts. Feedback addressed clarity, feasibility, operational definitions and alignment with existing EU/EEA surveillance and research systems.

A subsequent in-person meeting with RKI and other experts from Germany, held on 20 January 2026, refined variable specifications, methodological options and the distinction between core and extended datasets. Following further revisions, an updated draft was reviewed and discussed during a dedicated online Group of Experts meeting, with an opportunity for participants to provide additional input following the meeting. The document was then updated before finalisation.

Adaptation and applicability

This guide is intended for use across a range of clinical, surveillance, research and other data collection settings in the EU/EEA with the capacity and regulatory approval to contribute data. The core minimum dataset is designed to support comparability across sites and countries. Extended dataset elements and methodological options may be used in studies according to local priorities, infrastructure and regulatory requirements.

The overarching objective of harmonised data collection is to generate comparable, high-quality evidence on doxy-PEP use, effectiveness, safety, AMR impacts and behavioural outcomes. Standardisation enables pooled analyses across countries and programmes, strengthens the assessment of rare or microbiological outcomes and supports evidence-based public health and policy decision-making at national and EU/EEA levels.

Limitations

The development of this guide was shaped by the current and evolving evidence base on doxycycline prophylaxis. Substantial uncertainties persist regarding AMR, long-term behavioural impacts and potential population-level effects. Most available data come from studies among gay, bisexual and other men who have sex with men and transgender women, with limited data available for other populations or exposure groups. The harmonised data collection proposed in this guide is intended to support efforts to address several of these gaps by enabling consistent monitoring of effectiveness, safety, AMR dynamics, behavioural outcomes and patterns of use across EU/EEA settings.

Limitations inherent to prospective real-world data collection may include variability in data completeness, representativeness, feasibility and resource availability. Differences in national regulatory frameworks, clinical pathways and laboratory infrastructure may also influence implementation. Given these considerations, the guide should be updated as new evidence and operational experience become available.

Overview of the modules

The following modules present harmonised variables and operational definitions to support consistent data collection on doxycycline prophylaxis across EU/EEA settings. The priority domains were identified through an initial request from RKI and align with priority research questions identified by ECDC [1]. The proposed variables were refined through consultation with the multidisciplinary Group of Experts to ensure that harmonised data collection supports both immediate monitoring needs and longer-term public health evidence generation.

The modules address three complementary areas:

- **Module A:** Epidemiological, microbiological and clinical variables
  - **A1.** Uptake and use patterns
  - **A2.** User demographics and equity
  - **A3.** Provider prescribing practices
  - **A4.** Clinical effectiveness outcomes
  - **A5.** Safety and adverse events
  - **A6.** Antimicrobial resistance (AMR) impacts
  - **A7.** Microbiome impacts
- **Module B:** Psychosocial and behavioural variables
  - **B1.** Sexual behaviours and exposure patterns
  - **B2.** Acceptance, adherence and perceptions
  - **B3.** Provider attitudes and awareness
  - **B4.** Use of specific psychoactive substances to enhance sexual experiences (chemsex)
- **Module C:** Cross-cutting considerations
  - **C1.** Implementation contexts and use cases
  - **C2.** Study design and analytical considerations
  - **C3.** Data quality, governance and ethical considerations
  - **C4.** Interpretation and unintended effects
  - **C5.** Harmonisation and data comparability

Several variables across Modules A and B are interdependent. For example, sexual behaviour indicators inform the interpretation of clinical effectiveness outcomes, and provider attitudes and access pathways influence uptake, continuation and patterns of use. These interdependencies should be considered when selecting variables for implementation and when designing analyses or combining datasets, particularly where data are intended to address cross-cutting research questions related to effectiveness, equity, safety, behavioural dynamics and AMR.

To support harmonised implementation, each module outlines the purpose and relevance of the variable domain, key objectives, existing evidence or data sources and proposed variables with operational definitions and suggested coding schemes. A core minimum dataset is identified for consistent use across settings to enable comparability and pooling of data. Extended variables may be selected according to feasibility, capacity, infrastructure and specific research, surveillance or monitoring objectives.

Module A. Epidemiological, microbiological and clinical variables

This module presents variables for epidemiological, microbiological and clinical data collection related to doxycycline prophylaxis. For each domain, the module outlines: (i) relevance for monitoring and evaluation; (ii) key objectives; (iii) existing evidence or available data sources; and (iv) proposed variables, including operational definitions, coding schemes, data sources and priority classification (core or extended).

The objective of this module is to support a harmonised core minimum dataset that enables comparability across studies, clinical programmes and EU/EEA settings. Sites with additional capacity may implement extended variables to support more detailed analyses, methodological triangulation, sentinel surveillance or exploratory research questions, according to local priorities and feasibility.

A1. Uptake and use patterns

Overview

Monitoring uptake and patterns of doxycycline prophylaxis use is essential for assessing feasibility, user engagement and potential population-level impact. Key indicators include the proportion of individuals who initiate doxycycline prophylaxis, frequency and recency of use, and patterns of dosing, including event-driven use. Where feasible, information on dosing behaviour and adherence can support interpretation of clinical outcomes, antibiotic stewardship considerations and programme performance.

Understanding discontinuation or periods of non-use, including reasons for stopping or pausing, may inform clinical guidance, identify barriers to appropriate use (such as gastrointestinal side effects, user concerns regarding AMR, or perceived stigma), and support the design of user support strategies. Documentation of eligibility criteria, screening processes and access pathways (e.g. provider-initiated offer, user request, or use outside formal clinical programmes) can contribute to assessments of equitable access and responsible use in line with national guidance.

Doxycycline prophylaxis may also be used outside study cohorts or formal healthcare pathways, including among individuals who are not enrolled in studies, do not receive prescriptions, or do not undergo baseline STI testing. Although such use is methodologically challenging to capture, indirect indicators of non-prescribed or informal use are relevant, as intermittent single-dose antibiotic use in individuals with undiagnosed infections may have implications for AMR development.

Objectives

The objectives of this sub-module are to:

- Measure uptake among individuals who receive or use doxycycline prophylaxis in participating settings.
- Estimate or contextualise the size of populations eligible for use, using available clinical, surveillance or programme-level indicators where feasible.
- Characterise patterns of use, including timing relative to sexual exposure, dosing behaviour and adherence where feasible.
- Identify reasons for discontinuation or periods of non-use, including tolerability, perceived need, access barriers or provider recommendation.
- Document eligibility criteria and pathways to access, including prescription-based provision, user-requested provision and use outside formal clinical programmes.
- Capture contextual information on the use of other antimicrobials for STI prevention or self-treatment where feasible.

Note: Estimation of the population eligible for doxycycline prophylaxis may not be feasible in all settings (eligibility criteria may differ between countries and over time). Any such estimates should be interpreted in light of national clinical recommendations, service models and data availability.

Existing data

While published evidence on uptake and continuation of doxycycline prophylaxis remains limited, recent observational data from large-scale implementation programmes suggest broader adoption in practice [10,29]. Randomised clinical trials for doxy-PEP have typically followed participants for approximately 9–14 months [5-7]; however, patterns of use, persistence and discontinuation outside trial settings and within routine care remain uncertain. Early observational reports from implementation contexts outside the EU/EEA describe high initial uptake among eligible or targeted individuals, with continuation varying according to service model, user experience and programme support [10,12,13,29].

Behavioural survey data from European settings indicate increasing awareness of and interest in doxycycline prophylaxis, although non-prescribed, intermittent and informal use remains difficult to quantify [30-33]. Existing datasets, including large behavioural surveys (e.g. EMIS-2024), may provide baseline indicators of awareness, willingness to use and past self-reported use of antibiotics for STI prevention [34]. However, systematic programme- and study-level data collection will be required to adequately characterise uptake, patterns of use and determinants of continuation across EU/EEA settings.

In this context, systematic monitoring of uptake, continuation and patterns of doxycycline prophylaxis use directly addresses priority research questions related to the population-level impact of doxy-PEP and to methods for assessing benefits and risks over time. Harmonised data on initiation, persistence, discontinuation and informal use are essential for interpreting observed clinical and AMR outcomes, for distinguishing programme-related effects from background trends, and for supporting evidence-informed decision-making regarding future public health guidance.

Proposed variables

Table 1. Variables for uptake and patterns of use

Variable description	Values and coding	Priority
Doxy_Offered • Definition: Whether doxycycline prophylaxis was offered to or discussed as an option with the individual. • Timing: Baseline. • Possible source: Clinical record or provider report.	No/Yes	Core
Doxy_Received • Definition: Whether the individual received doxycycline intended for prophylaxis (e.g. prescription issued, medication dispensed or documented non-prescribed acquisition). • Timing: Baseline or follow-up. • Possible source: Prescription record, dispensing data or participant report.	No/Yes	Core
Doxy_Regimen_Type • Definition: Type of doxycycline prophylaxis regimen used for STI prevention. • Timing: Baseline and updated during follow-up if the regimen changes. • Possible source: Participant self-report, prescribing clinic records, pharmacy/administrative data. Possible categories: none; event-driven doxy-PEP; daily doxy-PrEP; both event-driven and daily use; unknown / not reported	Categories	Core
Doxy_Initiation_Reason • Definition: Primary reason for initiating or obtaining doxy-PEP. • Timing: Baseline. • Possible source: Participant interview or survey. Possible categories: recent STI history; partner STI risk; multiple partners; user request; provider recommendation; peer use; harm reduction use; sex work; other	Categories	Extended
Doxy_Use_Recency • Definition: Recency of self-reported doxycycline prophylaxis use. • Timing: Each follow-up. • Possible source: Participant self-report. Possible categories: within the last 24 hours; within the last seven days; within the last four weeks; within the last three months; within the last six months; within the last 12 months; within the last five years; longer ago; never *Note:This variable is also included in B1. In A1, it is used to monitor recency of prophylaxis use within programme or clinical follow-up.*	Categories	Core

Variable description	Values and coding	Priority
Doxy_Use_Frequency • Definition: Number of times doxycycline prophylaxis was used within the defined recall period (e.g. past three months). • Timing: Each follow-up. • Possible source: Participant self-report.	Numerical	Core
Doxy_Current_Use • Definition: Derived indicator of any current doxycycline prophylaxis use within the pre-defined recall period. • Timing: Each follow-up. • Possible source: Derived from Doxy_Use_Recency or Doxy_Use_Frequency.	No/Yes	Extended (derived)
Doxy_Exposure_Coverage • Definition: Self-reported extent to which doxycycline prophylaxis was used as intended in relation to relevant sexual exposures during the recall period. • Timing: Each follow-up. • Possible source: Participant self-report. Possible categories: all relevant exposures; most exposures; some exposures; no use despite exposures; no sexual exposures	Categories	Core
Doxy_Doses_Distributed • Definition: Quantity of doxycycline doses provided for prophylactic use. • Timing: Baseline and follow-up or refill visits. • Possible source: Dispensing data, prescription record or participant report. *Note: Treatment-related doxycycline prescriptions (e.g. for diagnosed STIs) should be recorded separately where feasible.*	Numerical (number of doses given)	Core
Other_Antimicrobial_Prophylaxis • Definition: Use of other antimicrobials for STI prevention or prophylaxis. • Timing: Baseline and follow-up. • Possible source: Participant self-report.	No/Yes/Unknown (if yes, specify)	Extended
Doxy_SelfTreatment_STI • Definition: Self-initiated use of doxycycline for STI symptoms without testing or clinical assessment. • Timing: Baseline and follow-up. • Possible source: Participant self-report.	No/Yes/Unknown	Extended
Doxy_Cost_Coverage • Definition: Primary mode of payment for doxycycline used for prophylaxis. • Timing: Baseline. • Possible source: Participant report or administrative data. Possible categories: public insurance; private insurance; out-of-pocket; mixed; unknown	Categories	Extended

A2. User demographics and equity

Overview

Collecting of demographic and equity-related variables is important for understanding who is accessing doxycycline prophylaxis and whether uptake, continuation and outcomes differ across population groups. These data support monitoring of equity in access and help identify whether populations with elevated STI risk are proportionately represented or potentially underserved. Demographic information also supports interpretation of use patterns, adherence behaviours and clinical outcomes, and enables appropriate adjustment for confounding in epidemiological and implementation analyses.

Relevant domains may include age, gender identity, sex assigned at birth, sexual orientation or partner choice, HIV status and use of HIV pre-exposure prophylaxis (HIV-PrEP), as well as selected indicators of social position or socioeconomic circumstances, such as ethnicity, migration background, education, insurance coverage or employment. These characteristics should be collected using self-reporting wherever possible and framed in a way that respects diversity, privacy and national legal constraints. Capturing these specific indicators can help identify structural barriers to access, which can contribute to disparities in implementation. Monitoring demographic and equity indicators over time can help assess the inclusiveness of implementation and inform service adaptation, targeted communication and outreach where inequities are identified.

Objectives

The objectives of this sub-module are to:

- Describe the demographic characteristics of individuals accessing doxycycline prophylaxis, including age, gender identity, sexual orientation or partner choice.
- Assess whether uptake, continuation and patterns of use vary across demographic and social groups.
- Identify whether populations with elevated STI risk are proportionately represented or remain underserved in implementation.
- Support equity monitoring and inform programme adaptation, targeted communication strategies and outreach activities.
- Enable adjustment for key demographic and social variables in epidemiological, clinical and implementation analyses.

Existing data

Available research and early implementation reports indicate that most doxy-PEP users to date are cisgender men who have sex with men, typically aged 25-49 years [5-7,10,12,13,29-33]. Data for transgender women remain limited, as they represented only a small proportion of participants in clinical trials, and evidence for cisgender women is mixed [6,8,9]. There is currently very little published information on transgender men, and data for other populations remain limited. This distribution reflects both the populations included in clinical trials to date and patterns of service access observed in early implementation studies.

Some international studies have reported differences in uptake associated with social and structural factors, including migration background or socioeconomic position [30,35-37]. Interpretation of such findings require caution, as these associations are unlikely to reflect biological differences and are more plausibly explained by intersecting determinants such as access to health services, education, stigma, legal and policy context and familiarity with biomedical prevention options. Recent implementation data note these equity concerns, highlighting the risk that doxy-PEP rollout could mirror existing disparities seen in HIV-PrEP access [11,38]. Routine collection of variables such as race or ethnicity varies across EU/EEA countries and may not be feasible or appropriate in all settings. Where direct measures are unavailable, alternative indicators, such as country of birth, years living in the reporting country or selected socioeconomic variables, may provide partial insight into equity-related patterns of access.

Socioeconomic factors, including education and employment, have rarely been included in doxy-PEP studies to date but may be relevant for interpreting adherence, access pathways and potential inequities. Existing European behavioural and cohort datasets, such as large online surveys and HIV-PrEP implementation programmes, may provide useful reference points for comparison. For example, preliminary findings from recent behavioural surveys suggest that current doxy-PEP users may represent a subgroup with higher levels of sexual activity, higher engagement in chemsex (i.e. use of specific psychoactive substances to enhance sexual experiences and greater familiarity with biomedical prevention options [30,31,39]. Systematic and harmonised data collection across EU/EEA settings will therefore be essential to better characterise demographic profiles, equity dimensions and determinants of access over time.

In this context, demographic and equity-related data collection directly supports priority research questions on willingness to use doxy-PEP across key populations, barriers and facilitators to initiation and continuation, and the inclusiveness and generalisability of the evidence base beyond populations currently overrepresented in clinical trials. Harmonised monitoring of demographic and social characteristics across EU/EEA settings is therefore essential for interpreting uptake patterns, for assessing equity in access, and for informing future public health decision-making.

Proposed variables

Table 2. Demographic and equity variables

Variable description	Values and coding	Priority
Age • Definition: Age of the individual at enrolment. • Timing: Baseline. • Possible source: Participant self-report or clinical record. Possible categories: <20; 20–24; …; ≥65	Numerical (years) or categorised	Core
Gender_Identity • Definition: Self-identified current gender identity. • Timing: Baseline. • Possible source: Participant self-report or clinical record. Possible categories: man; woman; transgender man; transgender woman; non-binary; another identity; prefer not to say	Categories	Core
Sex_Assigned_Birth • Definition: Sex assigned at birth. • Timing: Baseline. • Possible source: Participant self-report or clinical record. Possible categories: male; female; intersex; unknown/prefer not to say *Note:* Together with Gender_Identity, this variable may support interpretation of gender categories for analytical purposes.	Categories	Extended
Gender_Partners • Definition: Gender identity or identities of sexual partners in the past 12 months. • Timing: Baseline. • Possible source: Participant self-report. Possible categories: cisgender men; cisgender women; transgender men; transgender women; non-binary people; no sexual partners	Categories	Core
Key_Population • Definition: Behaviourally defined key population, derived from reported sexual behaviour and context. • Timing: Baseline. • Possible source: Derived variable. Possible categories: gay, bisexual and other men who have sex with men; women who have sex with women; heterosexual men; heterosexual women; transgender women; transgender men; sex workers; other	Categories	Core
Migrant_Status • Definition: Whether the participant was born outside the reporting country. • Timing: Baseline. • Possible source: Participant self-report. *Note: Additional variables may be included to capture migration history, as relevant to the context (e.g. language spoken at home).*	No/Yes/Prefer not to say	Extended
Country_of_Birth • Definition: Country of birth of the participant. • Timing: Baseline. • Possible source: Participant self-report.	ISO country codes	Extended
Years_in_Country • Definition: Number of years living in the reporting country (if born outside the reporting country). • Timing: Baseline. • Possible source: Participant self-report.	Numerical (years)	Extended
Education_Level • Definition: Highest completed level of education. • Timing: Baseline. • Possible source: Participant self-report. Possible categories: low; medium; high (or ISCED-based categories)	Categories	Extended

Variable description	Values and coding	Priority
Employment_Status • Definition: Current employment situation. • Timing: Baseline. • Possible source: Participant self-report. Possible categories: employed full-time; employed part-time; self-employed; unemployed; student; retired; long-term sick leave; other	Categories	Extended
Sex_Work_Offered • Definition: Offering sex in exchange for money, goods or services within the specified recall period. • Timing: Baseline and follow-up. • Possible source: Participant self-report. Possible categories: never; past (not current); current	Categories	Extended
Sex_Work_Used • Definition: Paying for sex with money, goods or services within the specified recall period. • Timing: Baseline and follow-up. • Possible source: Participant self-report. Possible categories: never; past (not current); current	Categories	Extended
HIV_Diagnosis_Status • Definition: Ever diagnosed with HIV. • Timing: Baseline and updated if newly diagnosed. • Possible source: Participant self-report or clinical record.	No/Yes	Core
HIV_Diagnosis_Year • Definition: Year of initial HIV diagnosis (if applicable). • Timing: Baseline. • Possible source: Participant self-report or clinical record.	Year (yyyy)	Extended
HIV_PrEP_Status • Definition: Use of HIV pre-exposure prophylaxis (HIV-PrEP) among individuals not living with HIV. • Timing: Baseline and follow-up. • Possible source: Participant self-report or clinical record. Possible categories: never used; currently using daily PrEP; currently using event-based PrEP; previously used; long-acting injectable PrEP	Categories	Core
Prior_STI_History • Definition: History of diagnosed bacterial STIs in the 12 months prior to enrolment. • Timing: Baseline. • Possible source: Participant self-report or clinical record. Possible selections: syphilis; gonorrhoea; chlamydia; LGV; *Mycoplasma genitalium*; none; unknown	Multi-select	Core
Prior_STI_Symptom • Definition: Symptom status at the time of the most recent STI diagnosis. • Timing: Baseline. • Possible source: Participant self-report or clinical record. Possible categories: symptomatic; asymptomatic; unknown	Categories	Extended
Baseline_STI_Status • Definition: Laboratory-confirmed STI at baseline screening (if applicable). • Timing: Baseline. • Possible source: Laboratory testing.	Negative/Positive (by pathogen)	Core *(clinical cohorts only)*
Baseline_STI_Symptom • Definition: Presence of symptoms at time of baseline STI diagnosis. • Timing: Baseline. • Possible source: Clinical assessment or participant report. Possible categories: symptomatic; asymptomatic; unknown	Categories	Extended *(clinical cohorts only)*
STI_Complications_History • Definition: History of documented complications related to bacterial STIs. • Timing: Baseline. • Possible source: Clinical record.	No/Yes (if yes, specify)	Extended

Variable description	Values and coding	Priority
Concurrent_Prevention • Definition: Use of non-antimicrobial STI or HIV prevention. • Timing: Baseline. • Possible source: Participant self-report. Possible selections: consistent condom use with non-steady partners; HAV vaccination; HBV vaccination; HPV vaccination; mpox vaccination; other	Multi-select	Extended

A3. Provider prescribing practices

Overview

Monitoring provider prescribing practices is important for understanding how doxycycline prophylaxis is being implemented in clinical settings and for assessing alignment with national or local guidance, antimicrobial stewardship principles, and emerging evidence. Prescribing practices influence access to doxycycline prophylaxis, patterns of use, clinical follow-up and overall antimicrobial exposure, and may therefore impact outcomes at both the individual-level and the population-level.

Relevant domains include the eligibility criteria applied in practice, the STI targeted by prescribing (e.g. syphilis, chlamydia), indications documented at the time of prescribing, dosing instructions provided, quantities dispensed, refill and follow-up arrangements, and the extent to which counselling and clinical monitoring are integrated into routine care. Systematic documentation of these elements supports interpretation of uptake and continuation patterns observed at the user level and helps distinguish between programme design factors and individual decision-making.

Variation in prescribing practices across providers, clinics or service models may reflect differences in experience with doxycycline prophylaxis, local implementation strategies, regulatory or reimbursement frameworks, and uncertainty related to an evolving evidence base. Understanding such variation can support quality assurance, identify training and support needs, and inform refinement of clinical guidance and implementation approaches, while contributing to responsible antimicrobial stewardship.

Objectives

The objectives of this sub-module are to:

- Document prescribing practices for doxycycline prophylaxis in participating settings, including eligibility criteria applied, indications recorded at the time of prescribing, and the STI targeted by prescribing (e.g. syphilis, chlamydia).
- Characterise dosing instructions and any provider-recommended limits on frequency of use, in relation to national or local guidance.
- Monitor quantities dispensed, refill policies and supply continuity to assess practical implementation and accessibility.
- Assess whether counselling is provided on adherence, STI testing, potential adverse effects and antimicrobial stewardship considerations.
- Document follow-up requirements linked to prescribing, such as clinical review intervals or planned laboratory monitoring.
- Describe provider- and facility-level characteristics (e.g. prescriber role, service type or clinical setting) to explore variation across contexts where feasible.

Note: *This section focuses on provider- and system-level practices that contextualise user-level data captured in Section A1. Variable selection and prioritisation aim to minimise redundancy while preserving the information needed to interpret variation in uptake, access and antimicrobial exposure.*

Existing data

While comprehensive comparable data remain limited, recent surveys and implementation studies have begun to characterise provider attitudes and prescribing practices. Clinical guidance from outside the EU/EEA, as well as emerging European guidance, has generally included recommendations on structured eligibility assessment, clear dosing instructions, counselling on adherence and risk reduction, specific education regarding potential side effects and mitigation strategies, clear communication that doxycycline prophylaxis is unlikely to prevent gonorrhoea in many regions, and periodic clinical review as part of doxycycline prophylaxis provision [1,40]. Early implementation experiences, largely reported from settings outside the EU/EEA, describe protocols that include initial clinical assessment, provision of written dosing instructions, dispensing of defined quantities of doxycycline and scheduled follow-up visits [1].

Comparative quantitative data on prescribing practices across providers, clinics or health systems are not yet available. Within the EU/EEA, approaches to prescribing doxycycline prophylaxis are likely to vary significantly due to diverging national guidelines [1]. These variations intersect with differences in service model (e.g. sexual health clinics versus primary care), regulatory and reimbursement frameworks, availability of national guidance, and provider familiarity with the use of doxycycline for prophylactic purposes. As implementation expands, harmonised documentation of prescribing practices will be important to characterise this variation, support antimicrobial stewardship and inform quality improvement, training, and implementation strategies.

In this context, documentation of provider prescribing practices contributes directly to priority research questions on comparative implementation models, legal or policy barriers, and the influence of health-system factors on doxy-PEP use. Harmonised data on eligibility assessment, prescribing criteria, dosing instructions and follow-up requirements can support comparative analyses across countries and settings, helping to identify approaches that best balance clinical feasibility, antimicrobial stewardship and public health objectives.

Proposed variables

Table 3. Provider prescribing practices variables

Variable description	Values and coding	Priority
Indication_Documented • Definition: Primary indication recorded by the provider for prescribing doxycycline prophylaxis. • Timing: At initiation. • Possible source: Medical record or provider questionnaire. Possible categories: ≥1 STI in past 12 months; ≥2 STIs in past 12 months; partner STI risk; HIV-PrEP use with elevated STI risk; request after counselling; enrolment in a programme with regular STI screening; other	Categories	Core
STI_Target • Definition: Primary STI outcome the provider intended to prevent when prescribing doxycycline prophylaxis. • Timing: At initiation. • Possible source: Medical record or provider questionnaire. Possible categories: syphilis; chlamydia; gonorrhoea; broad bacterial STI risk reduction (non-specific); other (specify)	Categories	Extended
STI_LevelOfImpact • Definition: Level of intended impact on the STI targeted the provider aimed to achieve when prescribing doxycycline prophylaxis. • Timing: At initiation. • Possible source: Medical record or provider questionnaire. Possible categories: individual-level (intended primarily to benefit the patient); population-level (intended primarily to benefit the community); both individual and population-level; unknown (not recorded)	Categories	Extended
Doxy_Dose_Regimen • Definition: Dosing regimen and instructions provided at prescribing. • Timing: At initiation. • Possible source: Prescription or provider record. Possible categories: standard regimen (200 mg after sex within 24–72 hours); daily regimen (100 mg daily); modified regimen (specify)	Categories	Core
Max_Doses_Advised • Definition: Any provider-advised limit on frequency of doxycycline prophylaxis use. • Timing: At initiation. • Possible source: Provider record or questionnaire. Possible categories: no specific limit; max 1 dose per 24 hours; max 3 doses per week; other	Categories	Extended
Initial_Doses_Dispensed • Definition: Number of doxycycline doses supplied at initiation for prophylactic use. • Timing: At initiation. • Possible source: Prescription or dispensing record.	Numeric (number of doses)	Core

Variable description	Values and coding	Priority
STI_Testing_Plan • Definition: Planned approach to ongoing STI screening as part of doxycycline prophylaxis use. • Timing: At initiation. • Possible source: Provider record. Possible categories: every three months; every six months; symptom-driven only; other	Categories	Core
FollowUp_Interval • Definition: Planned interval for clinical review following initiation. • Timing: At initiation. • Possible source: Appointment record or provider entry. Possible categories: three months; six months; other; no follow-up scheduled	Categories	Extended
Counselling_Provided • Definition: Whether counselling or structured information was provided at prescribing. • Timing: At initiation. • Possible source: Provider record or questionnaire. Additional information: duration of counselling (<5 min, 5–10 min, 10–15 min, >15 min)	No/Yes (if yes, record duration)	Extended
Counselling_Topics • Definition: Topics covered during counselling or information provision. • Timing: At initiation. • Possible source: Provider record or questionnaire. Possible selections: dosing and timing; adherence; STI testing; adverse effects; antimicrobial resistance; condom use; none; other	Multi-select	Extended
Refill_Policy • Definition: Policy regarding prescription refills without in-person review. • Timing: At initiation. • Possible source: Provider record or questionnaire. Possible categories: no refills without review; limited refills allowed; unrestricted refills; other	Categories	Extended
Provider_Barriers • Definition: Barriers encountered by the provider when prescribing doxycycline prophylaxis. • Timing: At initiation. • Possible source: Provider questionnaire. Possible categories: none; conflicting guidelines; legislative restriction; pharmacy refusal; medication unavailable; other	Categories	Extended
User_Barriers • Definition: User-level barriers noted at prescribing that may affect access. • Timing: At initiation. • Possible source: Provider or participant report. Possible categories: none; cost; stigma or confidentiality concerns; limited service access; difficulty attending follow-up; concerns about adverse effects; concerns about AMR; other	Categories	Extended
Cost_Coverage • Definition: Primary mode of payment for doxycycline prophylaxis. • Timing: At initiation. • Possible source: Provider or participant report. Possible categories: public insurance; private insurance; out-of-pocket; mixed; unknown	Categories	Extended
Prescriber_Type • Definition: Role of the prescriber. • Timing: At initiation. • Possible source: Provider questionnaire. Possible categories: sexual health physician; general practitioner; nurse practitioner; pharmacist prescriber; other	Categories	Extended

Variable description	Values and coding	Priority
Prescriber_Experience • Definition: Prescriber's level of experience with STI/HIV care. • Timing: At initiation. • Possible source: Provider questionnaire. Possible categories: high (STI/HIV specialist); moderate; low (generalist)	Categories	Extended
Facility_Type • Definition: Type of health-care setting where doxycycline prophylaxis was prescribed. • Timing: At initiation. • Possible source: Provider questionnaire or administrative data. Possible categories: sexual health clinic; primary care; hospital outpatient clinic; community-based service; private practice	Categories	Extended

A4. Clinical effectiveness outcomes

Overview

Assessing of clinical effectiveness is central to understanding the impact of doxycycline prophylaxis on bacterial STI outcomes in real-world settings. Monitoring should focus on incident, laboratory-confirmed infections among users of doxycycline prophylaxis, with attention to pathogen-specific outcomes and anatomical sites of infection, as clinical data indicate that efficacy can vary by site. Where feasible, linkage to patterns of use, including frequency and recency of use, can support interpretation of observed effectiveness in routine care, including the identification of breakthrough infections (defined here as laboratory-confirmed infections occurring despite reported doxy-PEP use according to recommended dosing and timing).

Characterising whether infections are symptomatic or detected through routine screening is important for interpreting clinical relevance, potential changes in presentation and implications for service delivery. Changes in testing practices or screening intensity following implementation of doxycycline prophylaxis may influence observed incidence and should be considered when interpreting trends.

For syphilis, emerging evidence suggests that doxy-PEP use may affect both the likelihood of diagnosis and aspects of clinical or serological presentation, including altered staging, milder or atypical symptoms, or delayed seroconversion and changes in non-treponemal antibody titres. Comprehensive documentation of incident syphilis cases, including stage, symptom status and relevant serological results, is therefore important for assessing potential effects of doxycycline prophylaxis on early detection, diagnosis and clinical outcomes.

Overall, systematic and harmonised collection of clinical effectiveness outcomes will support evaluation of both individual-level and population-level effects of doxycycline prophylaxis, including reductions in STI incidence, pathogen-specific differences in effectiveness, and potential shifts in clinical presentation or testing patterns following implementation.

Objectives

The objectives of this sub-module are to:

- Measure the incidence of laboratory-confirmed bacterial STIs among users of doxycycline prophylaxis, including *Chlamydia trachomatis*, *Treponema pallidum* and *Neisseria gonorrhoeae*.
- Characterise incident infections by anatomical site and clinical presentation (symptomatic versus asymptomatic).
- Assess time-to-event outcomes, including time to first diagnosed STI following initiation of doxycycline prophylaxis and the cumulative number of infections per individual during follow-up.
- Compare STI incidence among users of doxycycline prophylaxis with appropriate reference groups or time periods, including non-users within the same clinical setting and relevant population-level surveillance data, where available.
- Describe clinical and diagnostic characteristics of incident STIs occurring during periods of reported use of doxycycline prophylaxis, recognising limitations in attributing causality in the context of event-driven prophylaxis.
- Document treatment provided for diagnosed STIs, including the regimen used and follow-up requirements, to support interpretation of clinical outcomes and service impacts.
- For syphilis, record detailed diagnostic and serological information to explore potential effects of doxycycline prophylaxis on clinical presentation, diagnostic performance and serological responses.

Existing data

Randomised clinical trials have demonstrated reductions in incident *C. trachomatis* and *T. pallidum* infections among cisgender men who have sex with men and transgender women using doxy-PEP, with more variable effects observed for *N. gonorrhoeae*, reflecting underlying patterns of tetracycline resistance [3,5-7]. In contrast, a randomised clinical trial among cisgender women in Kenya did not demonstrate a significant reduction in STI incidence, highlighting the need for population-specific effectiveness data [8]. Early observational data from implementation settings outside the EU/EEA similarly suggest declines in syphilis and chlamydia diagnoses following increased doxy-PEP uptake, alongside limited or inconsistent reductions in gonorrhoea incidence [10,12,13,29]. Recent cohort studies within the EU/EEA have begun to report findings consistent with these observations, including reductions in chlamydia and syphilis incidence [13,41].

Recent reports have raised the possibility that doxy-PEP use may alter the clinical or serological presentation of early syphilis, including delayed seroconversion, delayed rises in non-treponemal titres or atypical manifestations [42,43]. The available evidence remains limited, and interpretation is complicated by concurrent changes in testing frequency, screening practices, case definitions and background epidemiology.

Within the EU/EEA, large-scale and systematic data on clinical effectiveness outcomes associated with doxycycline prophylaxis remain scarce. Expanded real-world monitoring will therefore be essential to strengthen understanding of effectiveness across diverse settings. Such monitoring should incorporate pathogen-specific diagnoses, anatomical site information, symptom status and standardised case definitions, and support assessment of contextual variability and downstream impacts on clinical care, antimicrobial resistance and health service utilisation.

In this context, monitoring clinical effectiveness outcomes directly addresses priority research questions, including the impact of doxy-PEP on incident STIs among users and their sexual contacts, potential implications for STI testing strategies, and effects on the clinical presentation and diagnosis of syphilis. Harmonised outcome definitions and longitudinal follow-up are essential for assessing time-to-event outcomes, for interpreting recurrent or breakthrough infections, and for evaluating whether current surveillance and diagnostic approaches remain fit for purpose in the context of doxycycline prophylaxis use.

Proposed variables

Table 4. Clinical effectiveness outcome variables

Variable description	Values and coding	Priority
Incident_Syphilis • Definition: New, active syphilis infection meeting national diagnostic guidelines or European/WHO case definitions (direct detection and/or compatible serology with rising non-treponemal titres). • Timing: At diagnosis. • Possible source: Laboratory result (serology, NAAT where available) and/or clinical assessment. Additional information: stage (primary; secondary; early latent; late latent; unknown); symptomatic (No / Yes); non-treponemal titre at diagnosis (RPR/VDRL); treponemal test (Negative / Positive); NAAT technique, if applicable (manufacturer; cycle threshold (Ct) value)	No/Yes (if yes, record date) Additional	Core
Incident_Gonorrhoea • Definition: Laboratory-confirmed *Neisseria gonorrhoeae* infection. • Timing: At diagnosis. • Possible source: Laboratory result (NAAT and/or culture). Additional information: anatomical site (urethral; anorectal; oropharyngeal; vaginal; other); symptomatic (No / Yes); diagnostic method (NAAT; culture; both); NAAT technique, if applicable (manufacturer; Ct value)	No/Yes (if yes, record date) Additional	Core
Incident_Chlamydia • Definition: Laboratory-confirmed *Chlamydia trachomatis* infection. • Timing: At diagnosis. • Possible source: Laboratory result (NAAT). Additional information: anatomical site (urethral; anorectal; oropharyngeal; vaginal; other); symptomatic (No / Yes); NAAT technique, if applicable (manufacturer; Ct value)	No/Yes (if yes, record date) Additional	Core
Incident_LGV • Definition: Laboratory-confirmed lymphogranuloma venereum caused by *C. trachomatis* L-genotypes. • Timing: At diagnosis. • Possible source: Laboratory result (NAAT with genotyping). Additional information: anatomical site (urethral; anorectal; oropharyngeal; vaginal; other); symptomatic (No / Yes); L-genotype, if available (L1; L2; L3); NAAT technique, if applicable (manufacturer; Ct value)	No/Yes (if yes, record date) Additional	Extended
Incident_MG • Definition: Laboratory-confirmed *Mycoplasma genitalium* infection. • Timing: At diagnosis. • Possible source: Laboratory result (NAAT). Additional information: anatomical site (urethral; anorectal; oropharyngeal; vaginal; other); symptomatic (No / Yes); NAAT technique, if applicable (manufacturer; Ct value) *Note:* Regular asymptomatic screening for *M. genitalium* is not recommended. Interpretation of incident cases should consider prior infection or treatment history where available.	No/Yes (if yes, record date) Additional	Extended

Variable description	Values and coding	Priority
Incident_Enteric_STI • Definition: Laboratory-confirmed enteric bacterial infection associated with sexual transmission and relevant in the context of doxycycline exposure (e.g. *Shigella* spp.). • Timing: At diagnosis. • Possible source: Laboratory result. Additional information: pathogen (specify); symptomatic (No/Yes)	No/Yes (if yes, record date) Additional	Extended
Detection_Reason • Definition: Reason the STI was identified. • Timing: At diagnosis. • Possible source: Clinical record. Possible categories: routine screening (asymptomatic); symptomatic presentation; partner notification; other (specify)	Categories	Core
Treatment_Provided • Definition: Treatment regimen given for the diagnosed STI episode. • Timing: At diagnosis. • Possible source: Clinical record. Additional information: drug name; dose; duration; route; guideline concordant (No / Yes)	Additional	Core *(where feasible)*
Test_Cure_Performed • Definition: Test of cure performed for the diagnosed STI episode, when clinically indicated according to applicable guidelines. • Timing: At follow-up. • Possible source: Laboratory result. Additional information: pathogen (specify); anatomical site (urethral; anorectal; oropharyngeal; vaginal; other)	No/Yes (if yes, record date) Additional	Extended
Other_Antimicrobial_Use • Definition: Concurrent use of other antimicrobials for reasons other than for STI prevention. • Timing: At diagnosis or follow-up. • Possible source: Clinical record. Additional information: azithromycin; ceftriaxone; penicillin; moxifloxacin; erythromycin; ciprofloxacin; amoxicillin; cefixime; other (specify)	No/Yes/Unknown Additional	Extended
Complicated_Outcome • Definition: Whether clinical complications were present in association with the STI episode. • Timing: At diagnosis or follow-up. • Possible source: Clinical record. Additional information: epididymitis; disseminated gonococcal infection; neurosyphilis; pelvic inflammatory disease; other (specify)	No/Yes/Unknown Additional	Extended
Reinfection_Flag • Definition: Whether the infection represents a repeat infection with the same pathogen during follow-up. • Timing: At diagnosis. • Possible source: Derived from prior clinical records.	No/Yes/Unknown	Extended
Breakthrough_Flag • Definition: Infection occurring during a period of reported doxycycline prophylaxis use consistent with recommended dosing and timing. • Timing: At diagnosis. • Possible source: Derived variable (use history + infection event). *Note: This variable should be interpreted cautiously.*	No/Yes/Indeterminate	Extended (derived)

A5. Safety and adverse events

Overview

Monitoring safety and adverse events associated with the use of doxycycline prophylaxis in real-world settings is essential to assess tolerability, inform risk-benefit evaluations and support responsible antimicrobial stewardship. While randomised clinical trials have reported generally favourable safety profiles, broader implementation may reveal differences in the frequency, type or severity of adverse events due to variation in user characteristics, patterns of intermittent use, concurrent medication use, the use of specific psychoactive substances to enhance sexual experience(i.e. chemsex) and levels of clinical oversight.

Systematic recording of adverse events, including those that are mild, transient or of uncertain causality, supports early signal detection and allows comparison across settings and populations. Classification of adverse events by type and severity enables assessment of clinical relevance and supports alignment with recognised pharmacovigilance standards. Monitoring serious adverse events, including those requiring medical intervention or leading to interruption or discontinuation of doxycycline prophylaxis, is particularly important, as implementation expands beyond controlled trial environments.

Documentation of discontinuation and temporary interruption related to adverse events provides additional insight into tolerability and user experience. Recording mitigation strategies, such as counselling on dosing practices, food intake or sun protection, can inform refinements to clinical guidance and user support, with potential benefits for adherence and acceptability.

Objectives

The objectives of this sub-module are to:

- Collect and describe adverse events reported during use of doxycycline prophylaxis, including known reactions (e.g. gastrointestinal symptoms, photosensitivity) and less common or emerging events.
- Classify adverse events by type and severity using a recognised grading system (e.g. Common Terminology Criteria for Adverse Events [CTCAE] or comparable local scales).
- Monitor serious adverse events, including those requiring clinical intervention, hospitalisation or interruption of doxycycline prophylaxis, regardless of assessed causality.
- Document discontinuation or temporary cessation of doxycycline prophylaxis due to adverse events and characterise reasons where available.
- Record management or mitigation strategies used in response to adverse events to support interpretation of tolerability and inform clinical practice.
- Monitor pregnancy occurrence during doxycycline prophylaxis use and document related management decisions where applicable.

Existing data

Randomised clinical trials of doxy-PEP have generally reported good tolerability, with most adverse events being mild to moderate in severity and transient in nature, and only a small proportion of participants discontinuing due to gastrointestinal discomfort (most commonly nausea, vomiting, diarrhoea and abdominal pain) or photosensitivity [5-7]. While severe events are rare, one drug-related serious adverse event, a fixed-drug eruption, was reported in one trial [7].

However, real-world safety profiles remain incompletely characterised, particularly for populations under-represented in trials, for longer periods of intermittent or repeated use, and for contexts involving informal or unmonitored use. Although systematic reviews of long-term daily doxycycline use for other indications (such as acne treatment or malaria prophylaxis) demonstrate a generally safe profile with rare, serious side effects, safety data specifically on long-term, intermittent use for STI prevention remain limited [2]. Safety data are also limited for individuals using doxy-PEP alongside concurrent medications or in settings involving sexualised substance use. Emerging implementation experiences suggest that tolerability, reporting patterns and reasons for discontinuation may differ from those observed in controlled trial environments.

In this context, harmonised prospective monitoring across EU/EEA settings is needed to better characterise adverse events, identify rare or context-specific safety signals, and inform prescribing guidance, counselling messages and follow-up strategies as doxycycline prophylaxis use expands. Systematic documentation of adverse events, discontinuation and tolerability directly supports priority research questions on the benefits and risks of doxycycline prophylaxis at both individual and population levels, contributes to pharmacovigilance and antimicrobial stewardship considerations, and provides evidence to inform decisions on whether, and under what conditions, continued or expanded use of doxycycline prophylaxis may be appropriate.

Proposed variables

Table 5. Safety and adverse event variables

Variable description	Values and coding	Priority
Any_Adverse_Event • Definition: Occurrence of any adverse event during use of doxycycline prophylaxis since the last visit. • Timing: Each follow-up visit. • Possible source: Participant report or provider assessment.	No/Yes	Core
AE_Type • Definition: Type of adverse event experienced. • Timing: At event occurrence. • Possible source: Participant report and/or provider diagnosis. Possible selections: nausea/vomiting; diarrhoea; abdominal pain; photosensitivity or sunburn-like reaction; other rash; fixed drug eruption; headache; oesophagitis or pain on swallowing; oral or vaginal candidiasis; symptoms of increased intracranial pressure; weight gain; other (specify) *Note: Where feasible, this information can be coded to CTCAE categories for analytical or reporting purposes.*	Multi-select	Core
AE_Onset_Date • Definition: Date on which the adverse event began. • Timing: At event reporting. • Possible source: Participant report or clinical record.	Date (dd-mm-yyyy)	Extended
AE_Severity • Definition: Severity of the adverse event using a recognised grading system. • Timing: At event reporting. • Possible source: Provider assessment. Possible categories: CTCAE Grade 1 (mild); Grade 2 (moderate); Grade 3 (severe); Grade 4 (life-threatening); Grade 5 (death) *Note:* If a serious adverse event occurs, provide an additional description.	CTCAE Grade 1–5 (or local equivalent)	Core
AE_Relatedness • Definition: Provider assessment of the likelihood that the adverse event is related to doxycycline prophylaxis. • Timing: At event reporting. • Possible source: Provider assessment. Possible categories: related; possibly related; unrelated; unknown	Categories	Core
AE_ActionTaken • Definition: Action taken in response to the adverse event. • Timing: At event reporting. • Possible source: Participant report or provider record. Possible categories: none; self-managed; dose skipped; doxy-PEP temporarily stopped; doxy-PEP permanently discontinued; medical treatment provided; other (specify)	Categories	Core
AE_Outcome • Definition: Clinical outcome of the adverse event. • Timing: At event reporting or follow-up. • Possible source: Participant report or provider record. Possible categories: resolved; unresolved; recurrent; led to hospitalisation; other (specify)	Categories	Core
AE_Mitigation_Strategy • Definition: Measures advised or adopted to reduce recurrence or severity of adverse events. • Timing: At event reporting or follow-up. • Possible source: Participant report or provider advice. Possible categories: took with food; increased water intake; avoided sun exposure; adjusted timing; other (specify)	Categories	Extended
Pregnancy_Occurrence • Definition: Pregnancy occurring during doxycycline prophylaxis use (for individuals who can become pregnant). • Timing: At pregnancy identification. • Possible source: Participant report or pregnancy test result.	No/Yes/Not applicable	Core *(if applicable)*

Variable description	Values and coding	Priority
Pregnancy_Management • Definition: Action taken following pregnancy identification during doxycycline prophylaxis use. • Timing: At follow-up. • Possible source: Clinical record. Possible categories: doxycycline use stopped; doxycycline use continued; outcome unknown; other	Categories	Extended *(if applicable)*
Doxy_Discontinue_AE • Definition: Whether doxycycline prophylaxis was permanently discontinued due to an adverse event. • Timing: At discontinuation. • Possible source: Participant report or provider record.	No/Yes	Core
Discontinue_AE_Reason • Definition: Primary adverse-event reason for discontinuation, if applicable. • Timing: At discontinuation. • Possible source: Participant report or provider record. Possible categories: gastrointestinal; skin/photosensitivity; fixed drug eruption; other AE; participant preference; unknown	Categories	Extended

A6. Antimicrobial resistance (AMR) impacts

Overview

Monitoring potential AMR impacts associated with the use of doxycycline prophylaxis is a critical component of antimicrobial stewardship, clinical guidance development and public health evaluation. Potential impacts include changes in resistance patterns among bacterial STI pathogens, especially *Neisseria gonorrhoeae*, where tetracycline resistance is already common in many EU/EEA settings, as well as broader effects on commensal or bystander organisms (such as *Staphylococcus aureus,* Group A *Streptococcus* and commensal *Neisseria* species) that may act as reservoirs for resistance determinants.

In addition to direct selection for tetracycline-resistant strains, doxycycline prophylaxis may contribute to co-selection of resistance determinants when multiple genes are located on shared genetic elements (e.g. plasmids or other mobile genetic elements). Such mechanisms are relevant for *N. gonorrhoeae* (for example, co-selection involving the *tetM* gene alongside mosaic *penA* alleles, which confer decreased susceptibility to third-generation cephalosporins such as ceftriaxone and cefixime). However, the physical linkage between *tetM* and mosaic *penA* alleles is not consistent and may vary by strain and genetic context. Similar processes may occur in commensal organisms, where horizontal gene transfer can facilitate the spread of resistance determinants, with potential downstream implications for treatment of infections beyond STIs. Interpretation of AMR data therefore requires careful contextualisation using background surveillance data and awareness of underlying resistance trends and antibiotic consumption patterns.

Approaches to AMR data collection vary across EU/EEA settings. In some clinical contexts, routine culture and antimicrobial susceptibility testing are feasible and already embedded in surveillance systems, while more advanced microbiological or genomic methods (e.g. molecular detection of resistance markers, whole-genome sequencing, resistome or microbiome profiling) may be limited to research or sentinel laboratory networks.

Monitoring AMR in individuals using doxycycline prophylaxis informally or outside clinical pathways presents additional challenges, as such use may occur without routine testing or follow-up. While difficult to capture systematically, understanding resistance dynamics in these contexts is relevant, as unsupervised or frequent antibiotic exposure in the presence of undiagnosed infection or colonisation may have distinct implications for AMR development. Where feasible, indirect indicators or sentinel studies may help to contextualise these risks.

Objectives

The objectives of this sub-module are to:

- Characterise antimicrobial susceptibility patterns of *N. gonorrhoeae* isolates among users of doxycycline prophylaxis, with a focus on tetracycline resistance and other antibiotics routinely monitored through national and EU/EEA surveillance systems.
- Compare AMR findings among users of doxycycline prophylaxis with background population-level trends using established surveillance platforms (e.g. Euro-GASP and national laboratory reporting systems).
- Document molecular resistance determinants in *N. gonorrhoeae*, where feasible, to support understanding of resistance mechanisms and potential co-selection.

- Monitor resistance markers in other STI pathogens (e.g. *M. genitalium*) only where testing is clinically indicated and aligned with current guidelines.
- Explore potential impacts on commensal or bystander organisms (i.e. non-target bacteria exposed incidentally to doxycycline) in sentinel or research settings, recognising their role as potential reservoirs of resistance genes.
- Facilitate archiving of isolates or specimens for future AMR or genomic analyses as scientific questions and methodologies evolve.

Existing data

Surveillance data indicate a high baseline prevalence of tetracycline resistance in *N. gonorrhoeae* across many EU/EEA countries [44]. Emerging evidence suggests that doxycycline exposure may preferentially select for tetracycline-resistant gonococcal strains and may contribute to the co-selection of genetically linked resistance determinants [3,21,26,45]. To date, there is no evidence of clinically relevant doxycycline resistance in *T. pallidum* or *C. trachomatis*, and routine antimicrobial susceptibility testing is not available for either organism.

For *M. genitalium*, AMR monitoring remains focused on macrolide and fluoroquinolone resistance, reflecting current treatment pathways, while data on tetracycline-associated resistance mechanisms remain limited (although 16S rRNA mutations potentially associated with tetracycline resistance have been reported) [46]. A small number of observational and clinical studies suggest that doxycycline exposure may influence colonisation patterns or resistance gene carriage among commensal organisms, including *Neisseria* species, *Staphylococcus aureus*, Group A *Streptococcus* and enteric bacteria [15,23,26,47]. However, the clinical and epidemiological significance of these findings remains uncertain.

At present, no harmonised EU/EEA datasets directly link doxycycline prophylaxis use with AMR outcomes. Integrating AMR monitoring into doxy-PEP implementation studies, sentinel laboratory networks and existing surveillance systems will therefore be essential to assess potential impacts over time and to inform antimicrobial stewardship, clinical guidance and public health risk assessments.

In this context, data on AMR outcomes directly address a central priority research question: understanding the population-level impact of doxy-PEP on resistance patterns in STI pathogens and commensal organisms. Harmonised microbiological and genomic data are critical for assessing selection and co-selection mechanisms, contextualising findings against background resistance trends, and supporting future decision-making on thresholds at which doxy-PEP use may need to be reconsidered in light of emerging resistance patterns.

Proposed variables

Table 6. Antimicrobial resistance and microbiological variables

Variable description	Values and coding	Priority
A. *Neisseria gonorrhoeae* (primary AMR focus)		
NG_Culture_Performed • Definition: Whether culture was performed for gonorrhoea at diagnosis. • Timing: At diagnosis. • Possible source: Laboratory record. Additional information: anatomical site of cultured isolate (urethral; anorectal; oropharyngeal; vaginal; cervical; other); culture success (not successful / successful); pooled sample (No / Yes)	No/Yes Additional	Core
NG_AST_Method • Definition: Antimicrobial susceptibility testing (AST) method used. • Timing: With AST result. • Possible source: Laboratory record. Possible categories: MIC; disc diffusion; other	Categories	Core
NG_AST_Standard • Definition: Interpretive standard applied to AST. • Timing: With AST result. • Possible source: Laboratory record. *Note: Preference is given to EUCAST thresholds.*	EUCAST/CLSI/Other	Core

Variable description	Values and coding	Priority
NG_Tetracycline_Result • Definition: Phenotypic tetracycline susceptibility result. • Timing: With AST result. • Possible source: Laboratory record. Possible categories: susceptible; low-level resistance (>0.5 to <8 mg/L); high-level resistance (≥8 mg/L); not tested	Categories	Core
NG_Tetracycline_Value • Definition: Quantitative tetracycline AST value. • Timing: With AST result. • Possible source: Laboratory record. *Note: Preference is given to MIC (mg/L).*	MIC (mg/L) *or* zone diameter (mm)	Core
NG_Ceftriaxone_Result • Definition: Phenotypic ceftriaxone susceptibility result. • Timing: With AST result. • Possible source: Laboratory record. Possible categories: susceptible (<0.032 mg/L); decreased susceptibility (≥0.032 to ≤0.125 mg/L); resistant (>0.125 mg/L); not tested	Categories	Extended
NG_Ceftriaxone_Value • Definition: Quantitative ceftriaxone AST value. • Timing: With AST result. • Possible source: Laboratory record. *Note: Preference is given to MIC (mg/L).*	MIC (mg/L) *or* zone diameter (mm)	Extended
NG_Cefixime_Result • Definition: Phenotypic cefixime susceptibility result. • Timing: With AST result. • Possible source: Laboratory record. Possible categories: susceptible (<0.032 mg/L); decreased susceptibility (≥0.032 to ≤0.125 mg/L); resistant (>0.125 mg/L); not tested	Categories	Extended
NG_Cefixime_Value • Definition: Quantitative cefixime AST value. • Timing: With AST result. • Possible source: Laboratory record. *Note: Preference is given to MIC (mg/L).*	MIC (mg/L) *or* zone diameter (mm)	Extended
NG_Azithromycin_Result • Definition: Phenotypic azithromycin susceptibility result. • Timing: With AST result. • Possible source: Laboratory record. Possible categories: susceptible; resistant (>1 mg/L); high-level resistant (≥8 mg/L); not tested	Categories	Extended
NG_Azithromycin_Value • Definition: Quantitative azithromycin AST value. • Timing: With AST result. • Possible source: Laboratory record. *Note: Preference is given to MIC (mg/L).*	MIC (mg/L) *or* zone diameter (mm)	Extended
NG_AST_Other • Definition: Phenotypic AST results for other routinely tested antibiotics. • Timing: With AST result. • Possible source: Laboratory record. Possible selections: ciprofloxacin; spectinomycin; gentamicin; for each selected antibiotic, record result (susceptible; decreased susceptibility; resistant; high-level resistant); and value, where available	Multi-select with result	Extended
NG_tetM_Present • Definition: Presence of the *tetM* determinant. • Timing: If molecular testing is performed. • Possible source: WGS or PCR.	No/Yes/Not tested	Extended

Variable description	Values and coding	Priority
NG_penA_Mutation • Definition: Presence of a resistance-associated *penA* allele. • Timing: If molecular testing is performed. • Possible source: WGS or PCR. Additional information: if yes, include mutation pattern or type	No/Yes/Not tested Additional	Extended
NG_mtr_Mosaic • Definition: Presence of a mosaic *mtr* operon. • Timing: If molecular testing is performed. • Possible source: WGS or PCR. Additional information: if yes, include mutation pattern or type	No/Yes/Not tested Additional	Extended
NG_Sequence_Type • Definition: Gonococcal sequence type if genotyping is performed. • Timing: If genotyping is performed. • Possible source: WGS.	NG-STAR/NG-MAST/MLST (specify scheme)	Extended
NG_Population_AMR • Definition: Proportion of gonococcal isolates resistant to tetracycline at national or regional level. • Timing: Annual. • Possible source: Euro-GASP or national surveillance. Additional information: stratified by sex/key population; interpretation standard used (EUCAST; CLSI; other (specify))	Percentage (%) Additional	Core
B. Other STI pathogens		
MG_Macrolide_RAM • Definition: Presence of a macrolide resistance mutation in *M. genitalium* (23S rRNA). • Timing: If tested. • Possible source: Resistance assay or sequencing.	Detected/Not detected/Not tested	Extended
MG_Fluoroquinolone_RAM • Definition: Presence of a fluoroquinolone resistance mutation in *M. genitalium* (parC/gyrA). • Timing: If tested. • Possible source: Resistance assay or sequencing.	Detected/Not detected/Not tested	Extended
MG_Tetracycline_RAM • Definition: Presence of a tetracycline-associated 16S rRNA mutation in *M. genitalium*. • Timing: If tested. • Possible source: Resistance assay or sequencing.	Detected/Not detected/Not tested	Extended
CT_Tetracycline_RAM • Definition: Detection of tetracycline resistance determinants or relevant 16S rRNA mutations in *C. trachomatis*. • Timing: If tested. • Possible source: Resistance assay or sequencing.	Detected/Not detected/Not tested	Extended
C. Commensal and other pathogenic organisms		
Commensal_AMR • Definition: Whether AMR was assessed in commensal or bystander organisms. • Timing: If tested. • Possible source: Laboratory result.	No/Yes/Not tested	Extended
Commensal_Species • Definition: Commensal or bystander organisms tested. • Timing: If tested. • Possible source: Laboratory result. Possible selections: Non-pathogenic *Neisseria* species (e.g. *N. subflava*; *N. flavescens*; *N. lactamica*); *N. meningitidis*; *Staphylococcus aureus* (including MRSA); *Streptococcus pneumoniae*; enteric bacteria (e.g. *E. coli*); *Helicobacter pylori*; other (specify)	Multi-select	Extended

Variable description	Values and coding	Priority
Commensal_AMR_Result • Definition: Antimicrobial susceptibility result for the commensal organism. • Timing: If tested. • Possible source: Laboratory result. Possible categories: susceptible; intermediate; resistant; not tested (additional information: if tested, specify antibiotic)	Categories	Extended
Shigella_AMR_Result • Definition: Antimicrobial susceptibility result for *Shigella* spp. • Timing: If tested. • Possible source: Laboratory result. Possible categories: susceptible; intermediate; resistant; not tested (additional information: if tested, specify antibiotic)	Categories	Extended

Note: *As this is a living document, additional genetic markers associated with tetracycline or other antimicrobial resistance should be added as evidence evolves. No routine AMR variable is proposed for T. pallidum at present, as phenotypic susceptibility testing is not available and clinically relevant doxycycline resistance has not been established.*

A7. Microbiome impacts

Overview

Monitoring potential effects of doxycycline prophylaxis on the human microbiome may contribute to longer-term safety assessments and antimicrobial stewardship considerations. Repeated, intermittent exposure to doxycycline has the potential to influence the composition, diversity and functional characteristics of microbial communities at relevant anatomical sites. Such changes may include shifts in dominant taxa, alterations in microbial diversity or changes in the prevalence of antimicrobial resistance-associated genes through selection or co-selection mechanisms.

Evidence from studies of other antibiotic exposures indicates that even relatively short courses can result in long-lasting alterations to the gut microbiome, including reduced diversity and increased abundance of resistance-associated genes, with effects persisting for months or years in some individuals. The magnitude and persistence of these effects vary substantially depending on the antimicrobial spectrum, dose, duration of exposure and inter-individual baseline microbiome composition.

Microbiome monitoring is not required for routine implementation of doxycycline prophylaxis and will not be feasible in most clinical or surveillance settings. However, targeted microbiome studies may be appropriate in selected research or sentinel sites with access to appropriate laboratory infrastructure, sequencing capacity and bioinformatic expertise. In these contexts, harmonised and standardised approaches to sampling, storage, sequencing and data analysis are essential to ensure interpretability and comparability across sites and over time.

Given the complexity of microbiome data and the current uncertainty regarding clinical relevance, findings should be interpreted cautiously and in conjunction with clinical outcomes, antimicrobial resistance data and doxycycline exposure patterns. Microbiome monitoring is intended to inform research priorities, longer-term risk-benefit assessments and stewardship discussions, rather than to guide individual-level clinical decision-making at this stage.

Objectives

The objectives of this sub-module are to:

- Assess whether use of doxycycline prophylaxis is associated with measurable changes in microbiome composition, diversity or functional gene profiles over time.
- Characterise site-specific microbiome changes, where feasible, in anatomical locations relevant to doxycycline exposure (e.g. gastrointestinal, anorectal, oropharyngeal or vaginal, as applicable).
- Evaluate the presence or relative abundance of antimicrobial resistance-associated genes and point mutations, including tetracycline resistance determinants and resistance markers that may increase through co-selection.
- Determine whether observed microbiome changes are transient or persistent, including whether they reverse following interruption or discontinuation of doxycycline prophylaxis.
- Generate evidence to inform longer-term safety assessments, antimicrobial stewardship considerations and priorities for future research.

Existing data

Evidence on microbiome effects specifically associated with doxycycline prophylaxis remains limited. Data from other contexts involving intermittent or repeated doxycycline exposure suggest that antibiotic use can alter microbial community composition and increase detection of certain resistance-associated genes, particularly within the gut microbiome [15,47-49]. Emerging studies of doxy-PEP and doxy-PrEP suggest limited overall changes in microbial composition in some settings, although dose-dependent effects on the gut resistome, including increases in tetracycline antimicrobial resistance-associated genes, have also been observed [15,49,50]. However, available studies are heterogeneous in design, sampling strategies, sequencing methods and analytical approaches, and the magnitude, duration and clinical relevance of observed changes remain uncertain.

To date, no harmonised datasets exist on microbiome outcomes among users of doxycycline prophylaxis in the EU/EEA. Where microbiome monitoring is undertaken, standardised protocols for sample collection, storage (including temperature and timing), sequencing methodology (e.g. 16S rRNA gene sequencing, metagenomic sequencing or metatranscriptomic sequencing) and bioinformatic analysis are essential to support meaningful comparison across studies and over time. As evidence evolves, microbiome data may help contextualise AMR findings and inform future guidance and stewardship considerations related to doxycycline prophylaxis.

In this context, microbiome data collection, where feasible, supports priority research questions on colonisation resistance, resistome dynamics and the longer-term safety implications of intermittent doxycycline exposure. Although not required for routine implementation, harmonised microbiome studies conducted in selected research or sentinel settings can provide important contextual evidence on the persistence or reversibility of microbial changes and inform broader assessments of population-level risks and benefits associated with doxy-PEP use.

Proposed variables

Table 7. Microbiome variables

Variable description	Values and coding	Priority
Microbiome_Sample_Collected • Definition: Whether a microbiome sample was collected at the specified time point. • Timing: Baseline and predefined follow-up time points (e.g. 3, 6, 12 months). • Possible source: Sample collection logs. Additional information: anatomical site and sample type (stool; anorectal swab; oropharyngeal swab; vaginal swab; other); storage condition (frozen at -80°C; frozen at -20°C; other)	No/Yes (if yes, record date) Additional	Extended
Microbiome_Sequencing_Method • Definition: Primary sequencing approach used for microbiome analysis. • Timing: When analysis is performed. • Possible source: Laboratory record. Possible categories: 16S rRNA gene sequencing; metagenomic sequencing; metatranscriptomic sequencing; other (specify)	Categories	Extended
Microbiome_Composition • Definition: High-level description of microbiome composition. • Timing: When results are available. • Possible source: Laboratory record. Additional information: dominant taxa reported (No / Yes); taxonomic level (phylum; genus; species)	Additional	Extended
Microbiome_AMR_Assessed • Definition: Whether antimicrobial resistance gene profiling was performed. • Timing: When analysis is performed. • Possible source: Laboratory record.	No/Yes	Extended
Microbiome_Tetracycline_Result • Definition: Detection of tetracycline resistance-associated genes in a microbiome sample. • Timing: When results are available. • Possible source: Laboratory record.	Detected/Not detected/Not tested	Extended
Microbiome_AMR_Detected • Definition: Detection of non-tetracycline antimicrobial resistance genes. • Timing: When results are available. • Possible source: Laboratory record.	Detected (specify class)/Not detected/Not tested	Extended

Variable description	Values and coding	Priority
Microbiome_Pathogen_Detected • Definition: Identification of taxa of potential clinical relevance within the microbiome sample. • Timing: When results are available. • Possible source: Laboratory record.	Yes (specify)/No	Extended

Module B. Psychosocial and behavioural variables

This module provides guidance on the collection of psychosocial and behavioural variables relevant to doxycycline prophylaxis. Covered domains include sexual behaviour and exposure patterns, acceptability and adherence, provider attitudes and awareness, and sexualised substance use. For each domain, the module outlines: (i) relevance for monitoring and evaluation; (ii) key objectives; (iii) existing evidence or available data sources; and (iv) proposed variables with operational definitions and suggested coding schemes.

Behavioural and psychosocial data are essential for interpreting the clinical and epidemiological outcomes captured in Module A. Several variables presented here, including partner numbers, condom use, adherence and the use of specific psychoactive substances to enhance sexual experience, function as key covariates for measuring exposure, controlling for confounding and contextualising STI incidence and AMR outcomes. These variables are therefore relevant across study designs, including clinical monitoring, surveillance activities and research projects where psychosocial analysis is not the primary focus.

In addition, behavioural and psychosocial data support monitoring of acceptability, feasibility and potential unintended effects (e.g. changes in sexual practices or health-seeking behaviour). They also inform the design and adaptation of user support strategies, service delivery models and communication materials, contributing to equitable, user-centred and responsible implementation of doxy-PEP across EU/EEA settings.

B1. Sexual behaviour and exposure patterns

Overview

Monitoring sexual behaviour and sexual exposure patterns among individuals using doxycycline prophylaxis provides important context for interpreting clinical and microbiological outcomes. Variables describing partner numbers, frequency of condomless sexual contact, types of partners, engagement in chemsex (the use of specific psychoactive substances to enhance sexual experience), and sexual practices help characterise exposure to bacterial STIs and support adjustment for differences in exposure intensity across individuals and over time. Monitoring should assess whether users consistently apply prophylaxis across all indicated sexual exposures.

Behavioural data also contribute to assessing whether sexual practices remain stable or change following initiation of doxycycline prophylaxis, and to contextualising outcomes such as STI incidence, adherence patterns and overall antimicrobial consumption. Information on partner types and testing practices may further support interpretation of eligibility criteria where these exist and inform service planning and targeted prevention strategies.

It is recognised that increased awareness and availability of doxycycline prophylaxis may lead to use beyond formally monitored or clinically indicated populations, including informal or non-prescribed use. While such use may not be fully captured within structured cohorts, harmonised behavioural data collection within studies and programmes remain important for interpreting observed outcomes and informing broader public health and antimicrobial stewardship considerations.

Objectives

The objectives of this sub-module are to:

- Describe sexual behaviour and sexual exposure patterns among users of doxycycline prophylaxis, including partner numbers, partner types and frequency of condomless sexual contact over defined recall periods.
- Assess whether sexual behaviour changes over time following initiation of doxycycline prophylaxis.
- Characterise contexts of sexual exposure, including types of partners and concurrency, where feasible.
- Document ongoing protective practices, such as condom use and routine STI testing, to contextualise use of doxycycline prophylaxis.
- Provide behavioural context to support interpretation of clinical outcomes, including incident STIs, adherence patterns and overall antimicrobial consumption.

Existing data

Randomised clinical trials of doxy-PEP have not demonstrated substantial differences in sexual behaviour between intervention and control groups; however, follow-up periods were relatively short, and the studies were conducted within structured clinical settings that included counselling and regular monitoring [10,12,13]. As a result, trial findings may not fully capture behavioural dynamics in routine care or broader community contexts.

Observational studies and early implementation data suggest that many doxy-PEP users were already participating in sexual networks associated with higher STI exposure before initiation [11,31]. Nevertheless, available evidence remains limited, context-specific and subject to reporting and selection biases. Longer-term behavioural trends following wider implementation, including potential changes in sexual practices and partner communication, are not yet well characterised.

Within the EU/EEA, routine monitoring of sexual behaviour indicators in relation to doxycycline prophylaxis remains limited. Existing European behavioural surveillance instruments (e.g. EMIS-2024) collect harmonised data on partner numbers, condom use and testing behaviours, and may serve as useful reference frameworks for aligning behavioural data collection within doxycycline prophylaxis studies and programmes [34].

In this context, behavioural data are central to several priority research questions, including how doxy-PEP may influence STI transmission dynamics, testing strategies and interpretation of clinical effectiveness outcomes. Harmonised measurement of sexual exposure patterns enables adjustment for differences in sexual behaviour when assessing effectiveness, supports evaluation of whether current testing approaches identify clinically meaningful infections, and informs methods to assess the population-level impact of doxycycline prophylaxis.

Proposed variables

Table 8. Sexual behaviour and exposure variables

Variable description	Values and coding	Priority
Num_Partners_12m • Definition: Number of sexual partners in the past 12 months (or other defined recall period). • Timing: Baseline and follow-up. • Possible source: Participant self-report (questionnaire). Suggested intervals: 0; 1–5; 6–10; 11–20; 21–50; >50	Numerical (or intervals)	Core
NS_Partners_12m • Definition: Number of non-steady sexual partners in the past 12 months (or other defined recall period). • Timing: Baseline and follow-up. • Possible source: Participant self-report (questionnaire). Suggested intervals: 0; 1–5; 6–10; 11–20; 21–50; >50	Numerical (or intervals)	Core
Sex_Acts_Types_12m • Definition: Types of sexual acts engaged in during the past 12 months (or other defined recall period). • Timing: Baseline and follow-up. • Possible source: Participant self-report (questionnaire). Possible selections: insertive anal sex; receptive anal sex; oral sex; vaginal or frontal sex; other (specify); prefer not to say	Multi-select	Core
Condomless_Sex_12m • Definition: Frequency of condomless sex with non-steady partners in the past 12 months (or other defined recall period). • Timing: Baseline and follow-up. • Possible source: Participant self-report (questionnaire). Possible categories: never; rarely; sometimes; mostly; always	Categories	Core
Group_Sex_12m • Definition: Sexual activity involving three or more people during a single sexual encounter (group sex) in the past 12 months (or other defined recall period). • Timing: Baseline and follow-up. • Possible source: Participant self-report (questionnaire).	No/Yes (optionally record frequency)	Extended

Variable description	Values and coding	Priority
STI_Testing_12m • Definition: Frequency of STI testing in the past 12 months (or other defined recall period).. • Timing: Baseline and follow-up. • Possible source: Participant self-report (questionnaire). Possible categories: not tested; once; more than once	Categories	Core
STI_Testing_Reason • Definition: Reason for the most recent STI test. • Timing: Baseline and follow-up. • Possible source: Participant self-report (questionnaire). Possible categories: routine screening; symptoms; partner notification; HIV-PrEP-related; other (specify)	Categories	Extended
Doxy_Use_Recency • Definition: Recency of self-reported doxycycline prophylaxis use. • Timing: Baseline and follow-up. • Possible source: Participant self-report (questionnaire). Possible categories: within the last 24 hours; within the last seven days; within the last four weeks; within the last three months; within the last six months; within the last 12 months; within the last five years; longer ago; never *Note: This variable is also included in A1. In B1, it is used to contextualise use in relation to sexual exposure and prevention behaviour.*	Categories	Core
Other_Antibiotic_Prophylaxis • Definition: Use of antibiotics other than doxycycline before or after sex to reduce STI risk. • Timing: Baseline and follow-up. • Possible source: Participant self-report (questionnaire).	No / Yes (specify antibiotic, if known)	Extended
Doxy_Source • Definition: Source of doxycycline used for STI prevention. • Timing: Baseline and follow-up. • Possible source: Participant self-report (questionnaire). Possible categories: prescribed; pharmacy without prescription; leftover medication; partner/friend; online/from abroad; other (specify)	Categories	Core
Doxy_Timing_Last • Definition: Timing of doxycycline intake relative to the last sexual exposure where used. • Timing: Baseline and follow-up. • Possible source: Participant self-report (questionnaire). Possible categories: within 24 hours before sex; ≤24 hours after sex; 24–48 hours after sex; 48–72 hours after sex; >72 hours after sex; daily use; not taken	Categories	Extended
Perceived_Behaviour_Change • Definition: Self-perceived change in behaviour since starting doxycycline prophylaxis. • Timing: Baseline and follow-up. • Possible source: Participant self-report (questionnaire). Additional information: partner number (more; same; fewer); condom use (more; same; less); substance use (more; same; less)	No / Yes Additional	Extended
Doxy_NS_Indicator • Definition: Doxycycline prophylaxis use among individuals reporting non-steady partners. • Timing: Baseline and follow-up. • Possible source: Derived from other variables. Suggested derived variable: Doxy_Use_Recency / NS_Partners_12m (ECDC indicator: Doxy_Use_Recency_12m / NS_Partners_12m)	Numerical (derived)	Core (derived)

***Note**: recall period of variables describing a behaviour over a specific period such as the last 12 months should be adapted to the routine follow-up of the specific study (e.g. Num_Partners_12m should be adapted to 3 months).*

B2. Acceptance, adherence and perceptions

Overview

Understanding the acceptability, adherence and user perceptions related to doxycycline prophylaxis is important for evaluating feasibility, sustained use and real-world effectiveness. Psychosocial perceptions, including motivation, perceived benefits, concerns about side effects or repeated antimicrobial use, and perceived social acceptability, may influence initiation, correct use and continuation over time.

Experiences of stigma related to sexual health, antibiotic use or doxycycline prophylaxis specifically (often resembling the stigma previously observed during early HIV-PrEP implementation) may further affect individual's willingness to access services, disclose use or adhere consistently. Collecting these data supports interpretation of adherence patterns, identification of psychosocial or structural barriers and adaptation of implementation approaches. Such insights can inform user-support strategies, clinical counselling, health communication and programme design to promote equitable, acceptable and responsible use.

Objectives

The objectives of this sub-module are to:

- Assess perceived acceptability of doxycycline prophylaxis among current and potential users, including perceived usefulness, willingness to continue use and likelihood of recommending doxycycline prophylaxis to others.
- Measure self-reported adherence to recommended doxycycline prophylaxis dosing and identify reasons for missed, delayed or non-indicated doses.
- Identify motivations for doxycycline prophylaxis use, including perceived benefits related to STI prevention, anxiety reduction or treatment avoidance.
- Document concerns or hesitations related to doxycycline prophylaxis use, including antimicrobial resistance, side effects, long-term antibiotic exposure, stigma or cost.
- Explore facilitators and barriers to initiation and continued use, including access, convenience, prescribing conditions, tolerability, dosing burden and psychosocial influences.
- Assess experiences of stigma and perceptions of social judgement related to doxycycline prophylaxis use or STI prevention behaviours, and how these influence use.

Existing data

Survey and qualitative studies suggest that doxycycline prophylaxis is generally perceived as acceptable among individuals at elevated risk of bacterial STIs. Commonly reported motivations include perceived effectiveness, reduced anxiety about STI acquisition and increased sense of control over sexual health [30,39,51,52]. At the same time, concerns related to AMR, the use of antibiotics in asymptomatic contexts, and potential social judgement or stigma have been identified as important sources of hesitancy [30,39,52,53]. Furthermore, recent survey data demonstrate that explicitly providing potential users with information about the risks of AMR decreased willingness to use and increased concerns regarding side effects, highlighting the role of balanced health communication [39].

Randomised clinical trials have reported high self-reported adherence in structured research settings with regular counselling and follow-up; however, where pharmacological measures were used, these sometimes indicated lower adherence than participants reported [8,10,12,13]. Emerging implementation data from real-world settings indicate greater variability, with reported barriers including uncertainty or misunderstanding of dosing instructions, concerns about tolerability and side effects (most notably nausea), challenges related to access or timing of doses, fears of negative partner reactions, worries about potential interactions with existing daily medications, and worries about social stigma associated with antibiotic use [52,54,55]. Systematic data from EU/EEA settings remain limited, particularly with respect to longer-term adherence and patterns of intermittent use.

In this context, monitoring acceptability and adherence directly supports priority research questions on willingness to use doxycycline prophylaxis, barriers and facilitators to initiation and continuation, and community preferences for dosing schedules and delivery models. Harmonised psychosocial data are essential to interpret real-world effectiveness, identify modifiable barriers to appropriate use, and inform user-centred implementation strategies that align with antimicrobial stewardship principles.

Proposed variables

Table 9. Acceptance, adherence and psychosocial variables

Variable description	Values and coding	Priority
Doxy_Use_Adherence • Definition: Self-reported adherence to recommended doxycycline prophylaxis dosing and timing when used. • Timing: Follow-up. • Possible source: Participant self-report (questionnaire). Possible categories: always; often; sometimes; rarely; never	Categories	Core
Doxy_Missed_Reasons • Definition: Reasons for missed or delayed doses of doxycycline prophylaxis. • Timing: Follow-up. • Possible source: Participant self-report (questionnaire). Possible selections: forgot medication; unsure whether use was indicated; intoxicated/substance use; side effects; ran out; access barriers; concern about frequent antibiotic use/AMR; missed recommended dosing window; other (specify)	Multi-select	Core
Doxy_Acceptability • Definition: Perceived acceptability of doxycycline prophylaxis. • Timing: Follow-up. • Possible source: Participant self-report (questionnaire). Possible categories: very acceptable; somewhat acceptable; neutral; somewhat unacceptable; very unacceptable	Categories	Core
Doxy_Willingness_Continue • Definition: Likelihood of continuing doxycycline prophylaxis use. • Timing: Follow-up. • Possible source: Participant self-report (questionnaire). Possible categories: very likely; likely; unsure; unlikely; very unlikely	Categories	Core
Doxy_Motivation • Definition: Perceived benefits or motivations for doxycycline prophylaxis use. • Timing: Follow-up. • Possible source: Participant self-report (questionnaire). Possible selections: reduce STI risk; reduce anxiety; avoid injectable treatment; reduce downtime due to STIs; protect partners' health; convenience; provider recommendation; partners or peers use doxycycline prophylaxis; other (specify)	Multi-select	Core
Doxy_Concerns • Definition: Specific concerns or hesitations regarding doxycycline prophylaxis. • Timing: Follow-up. • Possible source: Participant self-report (questionnaire). Possible selections: AMR; side effects; long-term antibiotic exposure; stigma/social judgement; substance interactions; cost; concern that use may encourage risk-taking; no concerns; other (specify)	Multi-select	Core
Doxy_Stigma_Experience • Definition: Experience of stigma or negative judgement related to doxycycline prophylaxis use. • Timing: Follow-up. • Possible source: Participant self-report (questionnaire). Possible categories: none; mild; moderate; severe	Categories	Extended
Doxy_Stigma_Source • Definition: Source of stigma or negative judgement related to doxycycline prophylaxis use. • Timing: Follow-up. • Possible source: Participant self-report (questionnaire). Possible selections: health-care providers (e.g. physicians, nurses); sexual partners; social or community environment; online or social media contexts; other (specify)	Multi-select	Extended

Variable description	Values and coding	Priority
Doxy_Willingness_Stop • Definition: Willingness to stop doxycycline prophylaxis if recommended due to safety or AMR concerns. • Timing: Follow-up. • Possible source: Participant self-report (questionnaire). Possible categories: very willing; willing; unsure; unwilling; very unwilling	Categories	Extended

B3. Provider attitudes and awareness

Overview

Healthcare providers play a central role in the implementation, accessibility and appropriate use of doxycycline prophylaxis. Provider knowledge, confidence and perceptions influence whether doxycycline prophylaxis is discussed, how eligibility criteria are applied, the quality of counselling provided and the extent to which antimicrobial stewardship principles are integrated into practice.

Understanding provider attitudes helps to interpret variation in access and user experience across settings and may explain differences in uptake, prescribing thresholds and follow-up practices. Monitoring provider perspectives over time can also inform assessments of system readiness, identify training and support needs, and guide the development of clinical pathways, tools to support decision making and communication materials as evidence and guidance evolve.

Objectives

The objectives of this sub-module are to:

- Assess provider awareness of doxycycline prophylaxis evidence, national or regional guidance and organisational policies.
- Distinguish between provider knowledge, confidence and comfort in prescribing and counselling on doxycycline prophylaxis.
- Characterise provider perceptions of potential benefits and risks, including antimicrobial resistance, adverse effects, behavioural impacts, antibiotic stewardship and implications for clinical workload.
- Document routine clinical practices related to doxycycline prophylaxis, including whether discussion is proactive or user-initiated, and whether structured follow-up is implemented.
- Identify provider- and setting-level factors associated with variation in attitudes and practices, including service type and experience.
- Inform training, implementation support and communication strategies.

Existing data

Published data on healthcare provider attitudes toward doxycycline prophylaxis in EU/EEA settings remain limited. Evidence from expert consultations, guidance development processes and institutional statements suggest a wide spectrum of views, ranging from strong support for targeted doxy-PEP use to more cautious positions driven by concerns about AMR, uncertainty regarding long-term population-level effects, regulatory or legal considerations and implications for clinical workload [1].

Early programme experiences indicate that some providers defer prescribing until national or institutional guidance is available, whereas others adopt doxycycline prophylaxis earlier in settings with high STI burden or strong community demand. In EU/EEA countries that lack formal national guidance, there is evidence of off-label prescribing of doxycycline prophylaxis by healthcare providers [1]. Provider awareness, confidence and familiarity with doxycycline prophylaxis may vary across service types and levels of STI expertise, with potential implications for prescribing practices and equitable access [56]. As awareness and implementation expand, systematic monitoring of provider attitudes, experiences and decision-making will be important to support consistent, evidence-aligned and stewardship-informed practice across EU/EEA settings.

In this context, provider perspectives are directly relevant to priority research questions concerning legal, policy and implementation barriers to doxy-PEP, as well as comparative analyses of national guidance and service delivery models. Harmonised assessment of provider awareness, confidence and concerns can help explain variation in access and prescribing practices, identify training and support needs, and support more consistent implementation aligned with evolving evidence and public health objectives.

Proposed variables

Table 10. Provider attitudes and awareness variables

Variable description	Values and coding	Priority
Doxy_Guideline_Awareness • Definition: Awareness of national, regional or organisational doxycycline prophylaxis guidance. • Timing: Baseline and periodic reassessment. • Possible source: Provider survey. Possible categories: fully aware; somewhat aware; aware that guidance exists but not familiar; no guidance exists; not aware	Categories	Core
Doxy_Evidence_Knowledge • Definition: Self-assessed knowledge of the doxycycline prophylaxis evidence base. • Timing: Baseline and periodic reassessment. • Possible source: Provider survey. Possible categories: very good; good; moderate; limited; none	Categories	Core
Doxy_Confidence_Prescribing • Definition: Confidence in making an informed decision about whether to prescribe doxycycline prophylaxis. • Timing: Baseline and periodic reassessment. • Possible source: Provider survey. Possible categories: very confident; confident; unsure; not confident; not at all confident	Categories	Core
Doxy_Comfort_Prescribing • Definition: Comfort level with prescribing doxycycline prophylaxis in clinical practice. • Timing: Baseline and periodic reassessment. • Possible source: Provider survey. Possible categories: very comfortable; comfortable; neutral; uncomfortable; very uncomfortable	Categories	Core
Doxy_Confidence_Counselling • Definition: Confidence in discussing doxycycline prophylaxis proactively with eligible individuals. • Timing: Baseline and periodic reassessment. • Possible source: Provider survey. Possible categories: very confident; confident; unsure; not confident; not at all confident	Categories	Core
Doxy_Comfort_Counselling • Definition: Comfort with discussing doxycycline prophylaxis proactively with eligible individuals. • Timing: Baseline and periodic reassessment. • Possible source: Provider survey. Possible categories: very comfortable; comfortable; neutral; uncomfortable; very uncomfortable	Categories	Core
Doxy_Provider_Role • Definition: Professional role of the provider. • Timing: Baseline and periodic reassessment. • Possible source: Provider survey. Possible categories: physician; nurse; pharmacist; other (specify)	Categories	Core
Doxy_Service_Setting • Definition: Clinical setting in which doxycycline prophylaxis is provided or considered. • Timing: Baseline and periodic reassessment. • Possible source: Provider survey. Possible categories: sexual health clinic; HIV clinic; primary care; hospital outpatient; community service; other (specify)	Categories	Core

Variable description	Values and coding	Priority
Doxy_Provider_Benefits • Definition: Provider-perceived benefits of doxycycline prophylaxis. • Timing: Baseline and periodic reassessment. • Possible source: Provider survey. Possible selections: reduction in syphilis; reduction in chlamydia; reduced user anxiety; improved user wellbeing; reduced STI-related visits; other (specify)	Multi-select	Extended
Doxy_Provider_Risks • Definition: Provider-perceived risks of doxycycline prophylaxis. • Timing: Baseline and periodic reassessment. • Possible source: Provider survey. Possible selections: AMR in *N. gonorrhoeae*; broader AMR; adverse effects; behavioural risk compensation; long-term uncertainty; workload impact; regulatory concerns; other (specify)	Multi-select	Extended
Doxy_Prescribing_Approach • Definition: Typical approach to doxycycline prophylaxis discussion and prescribing. • Timing: Baseline and periodic reassessment. • Possible source: Provider survey. Possible categories: proactively offered; mainly user-requested; case-by-case; generally avoided	Categories	Extended
Doxy_FollowUp_Practice • Definition: Use of structured follow-up for users of doxycycline prophylaxis. • Timing: Baseline and periodic reassessment. • Possible source: Provider survey. Possible categories: always; often; sometimes; never; not applicable	Categories (specify practices, if applicable)	Extended
Doxy_Case_Volume • Definition: Approximate number of individuals prescribed doxycycline prophylaxis relative to overall caseload. • Timing: Baseline and periodic reassessment. • Possible source: Provider survey. Possible categories: none; few; some; many	Categories	Extended
Doxy_Support_Needs • Definition: Areas where additional support or training is desired. • Timing: Baseline and periodic reassessment. • Possible source: Provider survey. Possible selections: eligibility criteria; AMR evidence; counselling tools; monitoring templates; participant materials; other (specify)	Multi-select	Extended

B4. Use of specific psychoactive substances to enhance sexual experience ('chemsex')

Overview

The use of specific psychoactive substances to enhance sexual experience, commonly referred to as 'chemsex', describes the use of synthetic stimulants and various other substances to facilitate and enhance sex, and is distinct from general recreational substance use. Substances used can range from stimulants, such as methamphetamine and synthetic cathinones, to depressants such as GHB/GBL and dissociatives such as ketamine, although patterns vary by setting and over time. 'Chemsex' practices may involve prolonged sexual activity, multiple or anonymous partners, and reduced use of barrier protection, contributing to elevated exposure to bacterial STIs.

'Chemsex' may also affect the feasibility of timely doxycycline prophylaxis dosing through delayed or missed doses, difficulty estimating exposure windows or reduced engagement with routine sexual healthcare. In these contexts, doxycycline prophylaxis may be used as an additional prevention approach when substance use reduces engagement with other sexual health prevention practices. Monitoring 'chemsex' involvement therefore provides important context for interpreting STI outcomes, adherence patterns and antimicrobial consumption, and may help identify opportunities for tailored support, including harm reduction, psychosocial or adherence support interventions where relevant.

Objectives

The objectives of this sub-module are to:

- Estimate the proportion of doxycycline prophylaxis users reporting 'chemsex' and describe the substances most commonly used.
- Characterise the recency, frequency and context of 'chemsex' episodes, including group settings and session duration, where feasible.
- Assess associations between 'chemsex' and key outcomes, including doxycycline prophylaxis adherence, STI incidence and engagement with testing or follow-up.
- Monitor changes in 'chemsex' behaviour over time following initiation of doxycycline prophylaxis.
- Identify support needs, including harm reduction, psychosocial or mental health services, and adherence support strategies tailored to individuals who engage in 'chemsex'.

Existing data

Behavioural surveillance data and cohort studies indicate that 'chemsex' occurs among gay, bisexual and other men who have sex with men in Europe, with prevalence varying by country, community norms, substance availability and access to harm reduction and support services [57-59]. 'Chemsex' has been associated with higher STI exposure and more complex prevention needs, particularly among individuals already engaged in HIV-PrEP or sexual health services [60,61].

While data specifically examining 'chemsex' in the context of doxycycline prophylaxis remain limited, recent evidence from EU/EEA settings suggests an association between 'chemsex' and current or past doxy-PEP use and indicates that doxy-PEP may be perceived as particularly useful by some individuals who frequently engage in this practice [30,39]. At the same time, real-world contexts of substance use pose practical challenges for timely dosing and adherence, highlighting the need for further quantitative and qualitative investigation.

In this context, data on 'chemsex' contribute directly to priority research questions on barriers and facilitators to adherence, contextual factors influencing use of doxycycline prophylaxis and community support needs. Harmonised monitoring of 'chemsex'-related behaviours helps contextualise STI exposure and adherence challenges, supports the development of tailored harm reduction strategies and informs evaluation of how doxycycline prophylaxis interacts with broader sexual health and substance use patterns.

Proposed variables

Table 11. Sexualised substance use (chemsex) variables

Variable description	Values and coding	Priority
Chemsex_Use • Definition: Use of specific psychoactive substances to enhance sexual experience (chemsex), including substances such as methamphetamine, mephedrone, GHB/GBL, ketamine or related stimulants. • Timing: Baseline and follow-up. • Possible source: Participant self-report (questionnaire).	No/Yes/Prefer not to say	Core
Chemsex_Recency • Definition: Recency of using specific psychoactive substances to enhance sexual experience (as defined above). • Timing: Baseline and follow-up. • Possible source: Participant self-report (questionnaire). Possible categories: within the last 24 hours; within the last 7 days; within the last 4 weeks; within the last 6 months; within the last 12 months; within the last 5 years; longer ago	Categories	Core
Chemsex_Substances • Definition: Substances used for sexualised purposes at the last or most recent 'chemsex' episode. • Timing: Baseline and follow-up. • Possible source: Participant self-report (questionnaire). Possible selections: ecstasy/MDMA; cocaine; amphetamine (speed); crystal methamphetamine (Tina, Pervitin); mephedrone; ketamine; GHB/GBL; other (specify)	Multi-select	Core
Chemsex_4w • Definition: Any use of specific psychoactive substances to enhance sexual experience in the past four weeks. • Timing: Baseline and follow-up. • Possible source: Participant self-report (questionnaire). *Note: Variable based on an EMIS-2024 measure developed for ECDC monitoring purposes.*	No/Yes	Core
Chemsex_Substances_4w • Definition: Use of any of the following four substances (GHB/GBL, mephedrone, ketamine or crystal methamphetamine) for sexual purposes in the past four weeks. • Timing: Baseline and follow-up. • Possible source: Derived variable from Chemsex_Substances and Chemsex_4w. *Note: Derived variable based on EMIS-2024 measures.*	No/Yes	Extended (derived)
Chemsex_Frequency • Definition: Proportion of sexual encounters involving substance use. • Timing: Baseline and follow-up. • Possible source: Participant self-report (questionnaire). Possible categories: none; <50%; ≥50%; nearly all	Categories	Core
Chemsex_Impact_Doxy • Definition: Self-reported impact of the use of specific psychoactive substances to enhance sexual experience on ability to follow doxycycline prophylaxis dosing recommendations. • Timing: Baseline and follow-up. • Possible source: Participant self-report (questionnaire). Possible selections: no impact; delayed dose (more than 72 hours); missed dose; uncertain whether dosing was needed; other (specify)	Multi-select	Core
Chemsex_Group_Recency • Definition: Recency of using specific psychoactive substances to enhance sexual experience involving more than one partner at the same time. • Timing: Baseline and follow-up. • Possible source: Participant self-report (questionnaire). Possible categories: within the last 24 hours; within the last 7 days; within the last 4 weeks; within the last 6 months; within the last 12 months; within the last 5 years; longer ago; never	Categories	Extended

Variable description	Values and coding	Priority
Chemsex_Group_Location • Definition: Location of the most recent use of specific psychoactive substances to enhance sexual experience involving more than one partner at the same time. • Timing: Baseline and follow-up. • Possible source: Participant self-report (questionnaire). Possible categories: at home; someone else's home; hotel room; club or backroom of a bar; sauna; sex-on-premises venue; outdoor cruising location; other (specify)	Categories	Extended
Chemsex_Duration • Definition: Length of the most recent use of specific psychoactive substances to enhance sexual experience session or typical length of such sessions. • Timing: Baseline and follow-up. • Possible source: Participant self-report (questionnaire). Possible categories: <6 hours; 6–12 hours; 12–24 hours; 24–48 hours; >48 hours	Categories	Extended
Chemsex_Concern • Definition: Self-perceived level of concern about one's own use of specific psychoactive substances to enhance sexual experience Timing: Baseline and follow-up. • Possible source: Participant self-report (questionnaire). Possible categories: no concern; mild concern; moderate concern; high concern; prefer not to say	Categories	Extended
Chemsex_Support_Need • Definition: Self-reported need or interest in additional support related to 'chemsex'. • Timing: Baseline and follow-up. • Possible source: Participant self-report (questionnaire).	No/Yes (if yes, specify)	Extended

Module C. Cross-cutting considerations

Module C focuses on harmonisation, interoperability and interpretation of data generated using the proposed variables across different studies and EU/EEA settings. It outlines cross-cutting methodological, analytical and operational considerations that apply across the epidemiological, clinical, behavioural and psychosocial variables described in Modules A and B. Its purpose is to support consistent, proportionate and interpretable data collection across diverse EU/EEA settings, while recognising variation in health systems, surveillance capacity, regulatory frameworks and available resources.

This module does not introduce additional variables. Instead, it provides guiding principles to inform the selection, implementation and interpretation of the proposed datasets. The focus is on feasibility, data quality, ethical conduct and appropriate interpretation of findings. This module is intended as a framing and harmonisation resource rather than a detailed implementation or study design manual.

C1. Implementation contexts and use cases

The variables described in this guidance are designed to be applicable across multiple implementation contexts; however, regulatory requirements, laboratory capacity and ethical approvals may differ across settings. Therefore, not all modules or variables are expected to be implemented in every setting. Selection should be guided by study purpose, capacity, governance arrangements and the intended use of the data.

Three broad implementation contexts are described:

1. **Routine clinical monitoring**
   Use of the core minimum dataset in HIV care, HIV-PrEP, STI or sexual health services to support local monitoring of doxycycline prophylaxis use, safety and selected outcomes.

2. **Cross-sectional behavioural or provider surveys**
   Use of selected behavioural and psychosocial variables (Module B) in population-based or service-based surveys (e.g. EMIS-type instruments) to assess awareness, acceptability, behaviours and perceptions related to doxycycline prophylaxis.

3. **Prospective clinical, implementation or surveillance cohorts**
   Use of core and selected extended variables, including biological outcomes (e.g. STI incidence, AMR indicators), in settings where clinical follow-up and laboratory capacity permit.

Hybrid designs combining elements of these contexts may also be appropriate. Clear documentation of the implementation context is essential to support interpretation of findings and to enable alignment, comparison or pooling of data across studies and settings.

C2. Study design and analytical considerations

Data collected using this guidance may support descriptive monitoring, exploratory analyses or hypothesis-generating research. As most applications will rely on observational data, findings should be interpreted with caution, and causal inference should not be assumed without suitable study design and analytical approaches.

Key considerations include:

- Clear definition of denominators (e.g. eligible population, individuals offered doxycycline prophylaxis, individuals using doxycycline prophylaxis), using harmonised definitions consistent with Modules A and B.
- Eligibility criteria for doxycycline prophylaxis may differ across countries, settings and time periods, and should be documented clearly when comparing uptake, prescribing patterns or outcomes. This will enable cross-site comparisons.
- Distinction between eligibility criteria, prescribing practices and actual use, including informal or non-prescribed use where feasible.
- Where data include different prophylactic strategies, such as doxycycline post-exposure prophylaxis (doxy-PEP) and daily doxycycline pre-exposure prophylaxis (doxy-PrEP), these should be distinguished analytically where possible, given differences in dosing patterns and cumulative exposure.
- Explicit documentation of comparator or reference groups, including non-users, historical controls or within-person comparisons, depending on study design.
- Alignment of analytical methods and outcome definitions with study objectives, recognising that small effect sizes may require pooled analyses or coordinated analytical strategies across studies.
- Transparent reporting of data sources, assumptions and limitations, including recall bias in self-reported data and variation in testing or follow-up intensity.

- Analyses should consider the extent and pattern of missing data, incomplete follow-up and differential ascertainment across variables or sites, as these may affect comparability and interpretation.
- Interpretation should consider the representativeness of participating sites and populations, particularly where data are derived from sentinel services, convenience samples or selected implementation settings.

C3. Data quality, governance and ethical considerations

High-quality and comparable data depend on consistent application of variable definitions, recall periods and coding schemes. Where deviations from the proposed definitions occur, these should be clearly documented.

Key principles include:

- Proportional data collection aligned with the stated objectives of monitoring or research.
- Usingnon-stigmatising, inclusive language, particularly for behavioural, psychosocial and population descriptors.
- Complying with applicable data protection and privacy regulations, including GDPR, with appropriate safeguards for sensitive health and behavioural data.
- Providing transparency regarding data ownership, access and potential secondary use, particularly in the context of pooled or cross-country analyses.
- Data derived from multiple sources should be documented clearly such as procedures for data linkage, de-duplication and validation.

In settings where informal or self-sourced doxycycline use is documented, particular care is required to avoid unintended stigmatisation or the punitive use of data. Ethical approval processes, consent requirements and governance arrangements are country- and context-specific and must be addressed in accordance with national regulations. Ethical oversight should be proportionate to the nature of the data collected and the setting in which collection occurs.

C4. Interpretation and unintended effects

Data generated using this guidance should be interpreted within a broader public health framework. Particular caution is required when interpreting short-term trends or findings related to antimicrobial resistance, behavioural change or informal use.

Key considerations include:

- Potential spillover effects associated with increased awareness or availability of doxycycline prophylaxis, including changes in expectations around antibiotic use beyond STI prevention.
- The importance of harm reduction framing in contexts where doxycycline prophylaxis is provided in response to user-initiated requests or informal use.
- Avoiding over-interpretation of early signals, particularly where background epidemiological trends, testing practices or surveillance sensitivity are changing.
- Recognition that questionnaire items or variable descriptions referring to recommended practices or time windows are measurement constructs used for data collection and interpretation, rather than clinical recommendations.

Findings from individual studies or settings should not be interpreted in isolation or used as sole triggers for policy change without triangulation with other data sources.

This guide supports evidence generation and monitoring. It does not promote or discourage the use of doxycycline prophylaxis, nor does it replace national clinical recommendations or antimicrobial stewardship policies.

C5. Harmonisation and data comparability

Harmonisation of data collection and reporting can enhance comparability across studies and settings, particularly where anticipated effect sizes are small. This guide supports harmonisation through shared variable definitions, coding schemes and core datasets, while recognising that implementation will necessarily vary across EU/EEA contexts.

To facilitate harmonised data use, studies applying this guidance are encouraged to document variable definitions, coding decisions, denominators, data sources and any deviations from the proposed variable specifications. Studies applying this guide should also document the version of the guide used, the date of implementation and any local adaptations to variable definitions, coding schemes, recall periods or follow-up intervals.

Where appropriate, alignment of study definitions, denominators and analytical approaches at an early stage may facilitate pooled or comparative analyses. Harmonisation does not imply centralised data collection, mandatory data sharing or uniform implementation across settings.

References

1. European Centre for Disease Prevention and Control (ECDC). Public health considerations on the use of doxycycline for post-exposure prophylaxis for bacterial sexually transmitted infections in the EU/EEA. Stockhom: ECDC; 2026. Available at: https://www.ecdc.europa.eu/en/publications-data/public-health-considerations-use-doxycycline-post-exposure-prophylaxis-bacterial
2. Bachmann LH, Barbee LA, Chan P, Reno H, Workowski KA, Hoover K, et al. CDC Clinical Guidelines on the Use of Doxycycline Postexposure Prophylaxis for Bacterial Sexually Transmitted Infection Prevention, United States, 2024. MMWR Recomm Rep. 2024 Jun 6;73(2):1-8. Available at: https://www.ncbi.nlm.nih.gov/pubmed/38833414
3. Unemo M, Cole MJ, Kodmon C, Day M, Jacobsson S, European Gonococcal Tetracycline-Resistance Study G. High tetracycline resistance percentages in Neisseria gonorrhoeae in Europe: is doxycycline post-exposure prophylaxis unlikely to reduce the incident gonorrhoea cases? Lancet Reg Health Eur. 2024 Mar;38:100871. Available at: https://www.ncbi.nlm.nih.gov/pubmed/38476738
4. CIHR Pan-Canadian Network for HIV and STBBI Clinical Trials Research. CTN 329: Doxycycline Intervention for bacterial STI ChemoprOphylaxis (DISCO). 2025. Available at: https://www.ctnplus.ca/study/ctn-329-doxycycline-intervention-for-bacterial-sti-chemoprophylaxis-disco/
5. Molina JM, Charreau I, Chidiac C, Pialoux G, Cua E, Delaugerre C, et al. Post-exposure prophylaxis with doxycycline to prevent sexually transmitted infections in men who have sex with men: an open-label randomised substudy of the ANRS IPERGAY trial. Lancet Infect Dis. 2018 Mar;18(3):308-17. Available at: https://www.ncbi.nlm.nih.gov/pubmed/29229440
6. Luetkemeyer AF, Donnell D, Dombrowski JC, Cohen S, Grabow C, Brown CE, et al. Postexposure Doxycycline to Prevent Bacterial Sexually Transmitted Infections. N Engl J Med. 2023 Apr 6;388(14):1296-306. Available at: https://www.ncbi.nlm.nih.gov/pubmed/37018493
7. Molina JM, Bercot B, Assoumou L, Rubenstein E, Algarte-Genin M, Pialoux G, et al. Doxycycline prophylaxis and meningococcal group B vaccine to prevent bacterial sexually transmitted infections in France (ANRS 174 DOXYVAC): a multicentre, open-label, randomised trial with a 2 x 2 factorial design. Lancet Infect Dis. 2024 Oct;24(10):1093-104. Available at: https://www.ncbi.nlm.nih.gov/pubmed/38797183
8. Stewart J, Oware K, Donnell D, Violette LR, Odoyo J, Soge OO, et al. Doxycycline Prophylaxis to Prevent Sexually Transmitted Infections in Women. N Engl J Med. 2023 Dec 21;389(25):2331-40. Available at: https://www.ncbi.nlm.nih.gov/pubmed/38118022
9. Abe S, Mizushima D, Ando N, Kawashima A, Uemura H, Shibata S, et al. Doxycycline pre-exposure prophylaxis prevents sexually transmitted infections without affecting vaginal bacterial flora in female sex workers. JAC Antimicrob Resist. 2025 Apr;7(2):dlaf054. Available at: https://www.ncbi.nlm.nih.gov/pubmed/40390838
10. Lewis FM, Cope AB, Clark K, Madera R, Asbel L, Newman DR, et al. Doxycycline post-exposure prophylaxis is effective and highly acceptable in an urban public sexually transmitted disease clinic: Philadelphia, 2019-2023. Sexually transmitted diseases. 2025:10.1097.
11. Traeger MW, Leyden WA, Volk JE, Silverberg MJ, Horberg MA, Davis TL, et al. Doxycycline Postexposure Prophylaxis and Bacterial Sexually Transmitted Infections Among Individuals Using HIV Preexposure Prophylaxis. JAMA Intern Med. 2025 Mar 1;185(3):273-81. Available at: https://www.ncbi.nlm.nih.gov/pubmed/39761062
12. Sankaran M, Glidden DV, Kohn RP, Nguyen TQ, Bacon O, Buchbinder SP, et al. Doxycycline Postexposure Prophylaxis and Sexually Transmitted Infection Trends. JAMA Intern Med. 2025 Mar 1;185(3):266-72. Available at: https://www.ncbi.nlm.nih.gov/pubmed/39761052
13. Palacios R, Gomez-Ayerbe C, Martin-Cortes S, Gonzalez-Jimenez A, Lopez-Jodar M, Perez-Hernandez IA, et al. Post-exposure prophylaxis with doxycycline (DoxyPEP) to prevent STIs in a real-world setting: the PRIDOX study. J Antimicrob Chemother. 2025 Dec 2;80(12):3306-10. Available at: https://www.ncbi.nlm.nih.gov/pubmed/41189494
14. Sokoll PR, Migliavaca CB, Doring S, Traub U, Stark K, Sardeli AV. Efficacy of postexposure prophylaxis with doxycycline (Doxy-PEP) in reducing sexually transmitted infections: a systematic review and meta-analysis. Sex Transm Infect. 2025 Jan 29;101(1):59-67. Available at: https://www.ncbi.nlm.nih.gov/pubmed/39097410
15. Chu VT, Glascock A, Donnell D, Grabow C, Brown CE, Ward R, et al. Impact of doxycycline post-exposure prophylaxis for sexually transmitted infections on the gut microbiome and antimicrobial resistome. Nat Med. 2025 Jan;31(1):207-17. Available at: https://www.ncbi.nlm.nih.gov/pubmed/39363100
16. Vanbaelen T, Manoharan-Basil SS, Kenyon C. Studies of post-exposure prophylaxis with doxycycline should consider population-level selection for antimicrobial resistance. Lancet Infect Dis. 2024 Oct;24(10):e606-e7. Available at: https://www.ncbi.nlm.nih.gov/pubmed/39181147
17. Roberts M, Davis P. Doxycycline post-exposure prophylaxis and off-target antimicrobial resistance: potential amplification within sexual networks. Oxford University Press US; 2025. p. jiaf439.
18. Luetkemeyer AF, Donnell D, Cohen SE, Dombrowski JC, Grabow C, Haser G, et al. Doxycycline to prevent bacterial sexually transmitted infections in the USA: final results from the DoxyPEP multicentre, open-label, randomised controlled trial and open-label extension. Lancet Infect Dis. 2025 Aug;25(8):873-83. Available at: https://www.ncbi.nlm.nih.gov/pubmed/40147465

19. Mortimer TD, Grad YH. A genomic perspective on the near-term impact of doxycycline post-exposure prophylaxis on Neisseria gonorrhoeae antimicrobial resistance. Clinical Infectious Diseases. 2023;77(5):788-91.

20. Vanbaelen T, Manoharan-Basil SS, Kenyon C. Doxycycline Postexposure Prophylaxis Could Induce Cross-Resistance to Other Classes of Antimicrobials in Neisseria gonorrhoeae : An In Silico Analysis. Sex Transm Dis. 2023 Aug 1;50(8):490-3. Available at: https://www.ncbi.nlm.nih.gov/pubmed/36952471

21. Berçot B, Assoumou L, Caméléna F, Voitichouk C, Mérimèche M, Ouattara M, et al. Antimicrobial-Resistant Neisseria gonorrhoeae Infections in Men Using Doxycycline Postexposure Prophylaxis: A Substudy of the ANRS 174 DOXYVAC Trial. Clinical Infectious Diseases. 2025:ciaf591.

22. Dallas SD, McGee L, Limbago B, Patel JB, McElmeel ML, Fulcher LC, et al. Development of doxycycline MIC and disk diffusion interpretive breakpoints and revision of tetracycline breakpoints for Streptococcus pneumoniae. J Clin Microbiol. 2013 Jun;51(6):1798-802. Available at: https://www.ncbi.nlm.nih.gov/pubmed/23554197

23. Kenyon C, Gestels Z, Vanbaelen T, Abdellati S, Van Den Bossche D, De Baetselier I, et al. Doxycycline PEP can induce doxycycline resistance in Klebsiella pneumoniae in a Galleria mellonella model of PEP. Front Microbiol. 2023;14:1208014. Available at: https://www.ncbi.nlm.nih.gov/pubmed/37711686

24. Whiley DM, Tickner JA, Kundu RL, Hogan TR, van Hal SJ, Lahra MM. Selection of Neisseria gonorrhoeae ceftriaxone resistance using doxycycline post-exposure prophylaxis. Lancet Infect Dis. 2023 Aug;23(8):e268-e9. Available at: https://www.ncbi.nlm.nih.gov/pubmed/37321241

25. Do K, Unemo M, Kenyon C, Hocking JS, Kong FYS. Tetracycline-resistant Neisseria gonorrhoeae global estimates-impacts on doxycycline post-exposure prophylaxis implementation and monitoring: a systematic review. JAC Antimicrob Resist. 2025 Aug;7(4):dlaf120. Available at: https://www.ncbi.nlm.nih.gov/pubmed/40636396

26. Soge OO, Thibault CS, Cannon CA, McLaughlin SE, Menza TW, Dombrowski JC, et al. Potential Impact of Doxycycline Post-Exposure Prophylaxis on Tetracycline Resistance in Neisseria gonorrhoeae and Colonization With Tetracycline-Resistant Staphylococcus aureus and Group A Streptococcus. Clin Infect Dis. 2025 Jul 18;80(6):1188-96. Available at: https://www.ncbi.nlm.nih.gov/pubmed/40036749

27. European Centre for Disease Prevention and Control (ECDC). Country support in diseases related to the Sustainable Development Goals. Stockholm: ECDC; 2026. Available at: https://www.ecdc.europa.eu/en/about-ecdc/partners-and-networks/support-and-services-eueea-countries/country-support-diseases

28. European Union. Regulation (EU) 2016/679 of the European Parliament and of the Council of 27 April 2016 on the protection of natural persons with regard to the processing of personal data and on the free movement of such data, and repealing Directive 95/46/EC (General Data Protection Regulation). 2016. Available at: https://eur-lex.europa.eu/eli/reg/2016/679/oj/eng

29. Scott HM, Roman J, Spinelli M, Bena J, Torres T, Glidden D, et al. Sexually transmitted infections after implementation of doxycycline postexposure prophylaxis. Sex Transm Infect. 2025 Dec 3 Available at: https://www.ncbi.nlm.nih.gov/pubmed/41339087

30. Teker B, Hoornenborg E, Schim van der Loeff MF, Boyd A, Heijne JC, Prins M, et al. Emergent informal use of doxycycline post- and pre-exposure prophylaxis among men who have sex with men and transgender and gender diverse people, the Netherlands, 2024. Euro Surveill. 2025 Jul;30(26):2400707. Available at: https://www.ncbi.nlm.nih.gov/pubmed/40613130

31. Villanueva Baselga S, Ruben M, Luis V. A practice already in use: a snapshot survey on the use of doxycycline as a preventive strategy (Doxy-PEP and Doxy-PrEP) in the GBMSM population in Spain. Infection. 2025;53(1):437-41.

32. Wagner L, Boesecke C, Baumgarten A, Scholten S, Schellberg S, Hoffmann C, et al. Is doxycycline post-exposure prophylaxis being utilised in Germany? Insights from an online survey among German men who have sex with men. Infection. 2025 Feb;53(1):61-70. Available at: https://www.ncbi.nlm.nih.gov/pubmed/39042326

33. Chan PA, Malyuta Y, Parent H, Tao J, Erbe M, Salhaney P, et al. Early adopters of doxycycline as post-exposure prophylaxis to prevent bacterial sexually transmitted infections in a real-world clinical setting. Sex Transm Infect. 2024 Aug 19;100(6):339-42. Available at: https://www.ncbi.nlm.nih.gov/pubmed/38821877

34. Aphami L, Bereczky T, Casalini JL, Lunchenkov N, Jonas KJ, Marcus U, et al. European Men-Who-Have-Sex-With-Men and Trans People Internet Survey (EMIS-2024): Design and Methods. Sexuality Research and Social Policy. 2026:1-20.

35. Torres da Silva MS, Luz PM, A Konda K, Vega-Ramírez H, Coutinho C, Qquellon J, et al. Doxy-pep interest, awareness, and use among sexual and gender minorities in brazil, mexico, and peru: findings from a web-based survey. 2024

36. Barry MB, J; Roman, J; Scott, H. The Doxy-PEP continuum among patients receiving care at a sexual health clinic in San Francisco. Presented at: 32nd Conference on Retroviruses and Opportunistic Infections (CROI 2025); San Francisco, USA.

37. Scott HR, J; Spinelli, A; Bena, J; Barry, M; Heise, M; Buchbinder, S. High sustained effectiveness of Doxycycline PEP for STI prevention after clinical implementation. Presented at: 32nd Conference on Retroviruses and Opportunistic Infections (CROI 2025); San Francisco, USA.

38. Hazra A, McNulty MC, Pyra M, Pagkas-Bather J, Gutierrez JI, Pickett J, et al. Filling in the Gaps: Updates on Doxycycline Prophylaxis for Bacterial Sexually Transmitted Infections. Clin Infect Dis. 2024 Feb 9 Available at: https://www.ncbi.nlm.nih.gov/pubmed/38332660

39. Vanbaelen T, Rotsaert A, De Baetselier I, Platteau T, Hensen B, Reyniers T, et al. Doxycycline post-exposure prophylaxis among men who have sex with men and transgender women in Belgium: awareness, use and antimicrobial resistance concerns in a cross-sectional online survey. Sex Transm Infect. 2025 Jan 29;101(1):34-40. Available at: https://www.ncbi.nlm.nih.gov/pubmed/39209541

40. Saunders J, Deering J, Dewsnap C, Drayton R, Gilmore J, Grant A, et al. British Association for Sexual Health and HIV (BASHH) UK national guideline for the use of doxycycline post-exposure prophylaxis (DoxyPEP) for the prevention of syphilis, 2025. Int J STD AIDS. 2025 Sep;36(10):756-64. Available at: https://www.ncbi.nlm.nih.gov/pubmed/40505019

41. Raccagni AR, Diotallevi S, Lolatto R, Bruzzesi E, Catalano G, Mainardi I, et al. DoxyPEP: real-life effectiveness in a cohort of men who have sex with men in Milan, Italy. Lancet Infect Dis. 2025 Jan;25(1):e1-e3. Available at: https://www.ncbi.nlm.nih.gov/pubmed/39577454

42. Raccagni AR, Bruzzesi E, Castagna A, Nozza S. Doxycycline postexposure prophylaxis may delay seroconversion in incident syphilis. Sex Transm Infect. 2024 Aug 19;100(6):397. Available at: https://www.ncbi.nlm.nih.gov/pubmed/38886053

43. Chircop O, Jaggers C, Spiteri M, Schembri A, Padovese V. DOXY do, or DOXY Don't? Syphilis and doxycycline post-exposure prophylaxis: A case report. Int J STD AIDS. 2025 Mar;36(4):324-6. Available at: https://www.ncbi.nlm.nih.gov/pubmed/39689342

44. Jacobsson S, Cole MJ, Jansen van Rensburg M, Schroder D, Mardh O, Kodmon C, et al. High prevalence of tetracycline resistance in Neisseria gonorrhoeae across 22 European countries, 2024. Euro Surveill. 2026 Jan;31(2):2500965. Available at: https://www.ncbi.nlm.nih.gov/pubmed/41540930

45. Reichert E, Grad YH. Effects of doxycycline post-exposure prophylaxis for prevention of sexually transmitted infections on gonorrhoea prevalence and antimicrobial resistance among men who have sex with men in the USA: a modelling study. Lancet Microbe. 2024 Nov;5(11):100926. Available at: https://www.ncbi.nlm.nih.gov/pubmed/39374606

46. Bercot B, Charreau I, Rousseau C, Delaugerre C, Chidiac C, Pialoux G, et al. High Prevalence and High Rate of Antibiotic Resistance of Mycoplasma genitalium Infections in Men Who Have Sex With Men: A Substudy of the ANRS IPERGAY Pre-exposure Prophylaxis Trial. Clin Infect Dis. 2021 Oct 5;73(7):e2127-e33. Available at: https://www.ncbi.nlm.nih.gov/pubmed/33305785

47. Fernandez-Ibanez R, Moreno S, Fernandez M. A Review of Doxycycline Post-Exposure Prophylaxis and Its Implications for Antimicrobial Resistance and the Human Microbiome. Infect Dis Ther. 2026 Jan;15(1):57-84. Available at: https://www.ncbi.nlm.nih.gov/pubmed/41366180

48. Carpenter L, Miller S, Flynn E, Choo JM, Collins J, Shoubridge AP, et al. Exposure to doxycycline increases risk of carrying a broad range of enteric antimicrobial resistance determinants in an elderly cohort. J Infect. 2024 Oct;89(4):106243. Available at: https://www.ncbi.nlm.nih.gov/pubmed/39142392

49. Knodel S, Main L, DeLeon M, Lamont A, Edward J, Gupta AK, et al. Impact of doxycycline pre-exposure prophylaxis (doxyPrEP) for sexually transmitted infections on the microbiome of men who have sex with men on HIV PrEP. Nat Commun. 2025 Jul 3;16(1):6143. Available at: https://www.ncbi.nlm.nih.gov/pubmed/40610420

50. Manoharan-Basil SS, Vanbaelen T, Kenyon C. Threshold effects of doxycycline postexposure prophylaxis (PEP) on the gut resistome and microbiome: Evidence from change-point analyses. Int J Infect Dis. 2026 Feb;163:108322. Available at: https://www.ncbi.nlm.nih.gov/pubmed/41422940

51. Fredericksen RJ, Perkins R, Brown CE, Cannon C, Lopez C, Cohee A, et al. Doxycycline as Postsexual Exposure Prophylaxis: Use, Acceptability, and Associated Sexual Health Behaviors Among a Multi-Site Sample of Clinical Trial Participants. AIDS Patient Care STDS. 2024 Apr;38(4):155-67. Available at: https://www.ncbi.nlm.nih.gov/pubmed/38656217

52. Ehsan R, D'Angelo AB, Westmoreland DA, Grov C. Perceptions about doxycycline post-exposure prophylaxis (Doxy-PEP) as an STI-prevention strategy among gay and bisexual men (GBM) in the United States: Results from a qualitative study. Prev Med. 2024 Jun;183:107977. Available at: https://www.ncbi.nlm.nih.gov/pubmed/38692309

53. Holt M, Bavinton BR, Calabrese SK, Broady TR, Clackett S, Cornelisse VJ, et al. Acceptability of doxycycline prophylaxis, prior antibiotic use, and knowledge of antimicrobial resistance among Australian gay and bisexual men and non-binary people. Sexually Transmitted Diseases. 2024:10.1097.

54. Mogaka FO, Kwach B, Odira A, O'Malley G, Hearst M, Bukusi EA, et al. Stakeholder perspectives on integrating doxycycline postexposure prophylaxis into Kenyan HIV PrEP programmes. Sex Transm Infect. 2025 Jul 8 Available at: https://www.ncbi.nlm.nih.gov/pubmed/40628421

55. Bird J, Alawyia B, Spernovasilis N, Alon-Ellenbogen D. From Cure to Prevention: Doxycycline's Potential in Prophylaxis for Sexually Transmitted Infections. Antibiotics (Basel). 2024 Dec 5;13(12):1183. Available at: https://www.ncbi.nlm.nih.gov/pubmed/39766573

56. Allan-Blitz L-T, Mayer KH. Doxycycline post-exposure prophylaxis for bacterial sexually transmitted infections: the current landscape and future directions. Current HIV/AIDS Reports. 2025;22(1):1.

57. Coronado-Munoz M, Garcia-Cabrera E, Quintero-Florez A, Roman E, Vilches-Arenas A. Sexualized Drug Use and Chemsex among Men Who Have Sex with Men in Europe: A Systematic Review and Meta-Analysis. J Clin Med. 2024 Mar 21;13(6):1812. Available at: https://www.ncbi.nlm.nih.gov/pubmed/38542036

58. Whitlock GG, Protopapas K, Bernardino JI, Imaz A, Curran A, Stingone C, et al. Chems4EU: chemsex use and its impacts across four European countries in HIV-positive men who have sex with men attending HIV services. HIV Med. 2021 Nov;22(10):944-57. Available at: https://www.ncbi.nlm.nih.gov/pubmed/34432363

59. Evers YJ, Van Liere G, Hoebe C, Dukers-Muijrers N. Chemsex among men who have sex with men living outside major cities and associations with sexually transmitted infections: A cross-sectional study in the Netherlands. PLoS One. 2019;14(5):e0216732. Available at: https://www.ncbi.nlm.nih.gov/pubmed/31086390

60. JL FA, Panagiotoglou D, Greenwald ZR, Blanchette M, Trottier C, Vaziri M, et al. Chemsex and incidence of sexually transmitted infections among Canadian pre-exposure prophylaxis (PrEP) users in the l'Actuel PrEP Cohort (2013-2020). Sexually Transmitted Infections. 2022;98(8):549-56.

61. Druckler S, van Rooijen MS, de Vries HJC. Chemsex Among Men Who Have Sex With Men: a Sexualized Drug Use Survey Among Clients of the Sexually Transmitted Infection Outpatient Clinic and Users of a Gay Dating App in Amsterdam, the Netherlands. Sex Transm Dis. 2018 May;45(5):325-31. Available at: https://www.ncbi.nlm.nih.gov/pubmed/29465683

Annex 1. Group of Experts

Name	Affiliation	Country	Competency areas
Axel J. Schmidt	London School of Hygiene and Tropical Medicine (LSHTM), The European MSM Internet Survey (EMIS)	Germany	Civil society, HIV/STI physician, epidemiologist
Béatrice Bercot	Saint-Louis Hospital, Paris	France	AMR in bacterial STIs, clinical trials of doxy-PEP, public health – STI network
Christopher Kenyon	STI Unit, Institute of Tropical Medicine, Antwerp	Belgium	AMR in bacterial STIs, human microbiome, sexual health care/clinician
Dagmar Heuer	Robert Koch Institute	Germany	Microbiologist
David Chromy	Medical University of Vienna, Department of Dermatology	Austria	Dermatologist
Emma Rubenstein	Université Paris Cité	France	Infectious diseases, clinical trials of doxy-PEP
Finn Filén	Södersjukhuset, Stockholm	Sweden	Clinician in infectious diseases and dermato-venerology
Giovanni Villa	St. James's Hospital, Dublin	Ireland	Clinical trials of doxy-PEP, sexual health care/clinician
Gyde Steffen	Robert Koch Institute	Germany	Public health epidemiology
Henry J. C. de Vries	Amsterdam University Medical Centres and Public Health Service of Amsterdam	Netherlands	Sexual health care/clinician, clinical trials of doxy-PEP
Jean-Michel Molina	Université Paris Cité	France	Clinical trials of doxy-PEP, head the of Infectious Diseases Department, professor of infectious diseases
Klaus Jansen	Department for Infectious Disease Epidemiology, Robert Koch Institute	Germany	Public health – STI network epidemiology, chair of the ECDC STI Network Coordination Committee
Magnus Unemo	WHO Collaborating Centre for Gonorrhoea and Other STIs, National Reference Laboratory for STIs, Department of Laboratory Medicine, Microbiology, Örebro University Hospital, Örebro	Sweden	AMR in bacterial STIs, human microbiome, ECDC Euro-GASP consultant
Regina Selb	Robert Koch Institute	Germany	Public health microbiology, epidemiology, immunology, STIs
Ricardo Werner	Division of Evidence-Based Medicine (dEBM) and consultant physician at Charité – Universitätsmedizin Berlin, Department of Dermatology, Venereology and Allergology	Germany	Clinical trials of doxy-PEP, sexual health care/clinician
Robert Hejzák	The European AIDS Treatment Group (EATG), Czech AIDS Help	Czechia	Civil society, observer on the ECDC STI Network Coordination Committee
Sorin Tiplica	International Union Against Sexually Transmitted Infection (IUSTI) Europe	Romania	Sexual health care/clinician
Thibaut Vanbaelen	STI Clinic, Institute of Tropical Medicine, Antwerp	Belgium	Clinical trials of doxy-PEP, sexual health care/clinician, AMR in bacterial STIs
Viviane Bremer	Robert Koch Institute	Germany	Head of Unit for HIV, STI and hepatitis

Annex 2. Core minimum dataset for harmonised data collection on doxycycline prophylaxis

This annex summarises the core minimum dataset proposed across Modules A and B to support harmonised data collection on doxycycline prophylaxis in EU/EEA settings. It is intended as a practical implementation aid for developing data collection tools or aligning existing systems. Full variable definitions, coding details and implementation notes are provided in the corresponding module tables.

Sites with limited capacity are encouraged to prioritise this core minimum dataset as the standard foundation for harmonised data collection, with extended variables added according to feasibility, infrastructure and specific research or surveillance objectives.

Variable name	**Short description**	**Timing**	**Values and coding**
A1. Uptake and use patterns			
Doxy_Offered	Doxycycline prophylaxis offered or discussed	Baseline	No / Yes
Doxy_Received	Doxycycline prophylaxis received	Baseline or follow-up	No / Yes
Doxy_Regimen_Type	Type of prophylaxis regimen used	Baseline and updated during follow-up	Categories
Doxy_Use_Recency	Recency of self-reported doxycycline prophylaxis use	Each follow-up	Categories
Doxy_Use_Frequency	Number of uses in recall period	Each follow-up	Numeric
Doxy_Exposure_Coverage	Extent of use in relation to relevant sexual exposures	Each follow-up	Categories
Doxy_Doses_Distributed	Number of doses provided for prophylactic use	Baseline and refill/follow-up visits	Numeric
A2. User demographics and equity			
Age	Age at enrolment	Baseline	Numeric (years) or categorised
Gender_Identity	Self-identified current gender identity	Baseline	Categories
Gender_Partners	Gender identity or identities of sexual partners	Baseline	Categories
Key_Population	Behaviourally defined key population	Baseline	Categories
HIV_Diagnosis_Status	HIV diagnosis status	Baseline	No / Yes
HIV_PrEP_Status	HIV-PrEP use status	Baseline and follow-up	Categories
Prior_STI_History	History of diagnosed bacterial STIs in prior 12 months	Baseline	Multi-select
Baseline_STI_Status	Laboratory-confirmed STI at baseline screening (clinical cohorts only)	Baseline	Negative / Positive (by pathogen)
A3. Provider prescribing practices			
Indication_Documented	Main indication recorded for prescribing	At initiation	Categories
Doxy_Dose_Regimen	Dosing regimen and instructions provided	At initiation	Categories
Initial_Doses_Dispensed	Number of doses supplied at initiation	At initiation	Numeric
STI_Testing_Plan	Planned approach to ongoing STI screening	At initiation	Categories
A4. Clinical effectiveness outcomes			
Incident_Syphilis	New active syphilis infection	At diagnosis	No / Yes, with date and additional details
Incident_Gonorrhoea	Laboratory-confirmed gonorrhoea	At diagnosis	No / Yes, with date and additional details
Incident_Chlamydia	Laboratory-confirmed chlamydia	At diagnosis	No / Yes, with date and additional details
Detection_Reason	Reason the STI was identified	At diagnosis	Categories
Treatment_Provided	Treatment regimen given for the diagnosed STI episode	At diagnosis	Additional information
A5. Safety and adverse events			
Any_Adverse_Event	Any adverse event reported	Each follow-up	No / Yes

Variable name	Short description	Timing	Values and coding
AE_Type	Type of adverse event	At event occurrence	Multi-select
AE_Severity	Severity of adverse event	At event reporting	CTCAE Grade 1–5 or local equivalent
AE_Relatedness	Likelihood adverse event is related to doxycycline prophylaxis	At event reporting	Categories
AE_ActionTaken	Action taken in response to adverse event	At event reporting	Categories
AE_Outcome	Clinical outcome of adverse event	At event reporting or follow-up	Categories
Pregnancy_Occurrence	Pregnancy during doxycycline prophylaxis use, where applicable	At pregnancy identification	No / Yes / Not applicable
Doxy_Discontinue_AE	Permanent discontinuation due to adverse event	At discontinuation	No / Yes
A6. Antimicrobial resistance (AMR) impacts			
NG_Culture_Performed	Gonorrhoea culture performed at diagnosis	At diagnosis	No / Yes
NG_AST_Method	AST method used	With AST result	Categories
NG_AST_Standard	Interpretive standard applied to AST	With AST result	EUCAST / CLSI / Other
NG_Tetracycline_Result	Tetracycline susceptibility result	With AST result	Categories
NG_Tetracycline_Value	Quantitative tetracycline AST value	With AST result	MIC (mg/L) or zone diameter (mm)
NG_Population_AMR	Background proportion of gonococcal isolates resistant to tetracycline	Annual	Percentage (%)
A7. Microbiome impacts (no core variables)			
B1. Sexual behaviours and exposure patterns			
Num_Partners_12m	Number of sexual partners in recall period	Baseline and follow-up	Numeric or intervals
NS_Partners_12m	Number of non-steady sexual partners in recall period	Baseline and follow-up	Numeric or intervals
Sex_Acts_Types_12m	Types of sexual acts in recall period	Baseline and follow-up	Multi-select
Condomless_Sex_12m	Frequency of condomless sex with non-steady partners	Baseline and follow-up	Categories
STI_Testing_12m	Frequency of STI testing in past 12 months	Baseline and follow-up	Categories
Doxy_Use_Recency	Recency of self-reported doxycycline prophylaxis use	Baseline and follow-up	Categories
Doxy_Source	Source of doxycycline used for STI prevention	Baseline and follow-up	Categories
Doxy_NS_Indicator	Doxycycline prophylaxis use among individuals reporting non-steady partners	Baseline and follow-up	Numeric (derived)
B2. Acceptance, adherence and perceptions			
Doxy_Use_Adherence	Self-reported adherence to recommended dosing and timing	Follow-up	Categories
Doxy_Missed_Reasons	Reasons for missed or delayed doses	Follow-up	Multi-select
Doxy_Acceptability	Perceived acceptability of doxycycline prophylaxis	Follow-up	Categories
Doxy_Willingness_Continue	Likelihood of continuing use	Follow-up	Categories
Doxy_Motivation	Perceived benefits or motivations for use	Follow-up	Multi-select
Doxy_Concerns	Concerns or hesitations regarding use	Follow-up	Multi-select
B3. Provider attitudes and awareness			
Doxy_Guideline_Awareness	Awareness of relevant guidance	Baseline and periodic reassessment	Categories
Doxy_Evidence_Knowledge	Self-assessed knowledge of evidence base	Baseline and periodic reassessment	Categories
Doxy_Confidence_Prescribing	Confidence in deciding whether to prescribe	Baseline and periodic reassessment	Categories
Doxy_Comfort_Prescribing	Comfort with prescribing in clinical practice	Baseline and periodic reassessment	Categories
Doxy_Confidence_Counselling	Confidence in discussing doxycycline prophylaxis proactively	Baseline and periodic reassessment	Categories

Variable name	**Short description**	**Timing**	**Values and coding**
Doxy_Comfort_Counselling	Comfort with discussing doxycycline prophylaxis proactively	Baseline and periodic reassessment	Categories
Doxy_Provider_Role	Professional role of provider	Baseline and periodic reassessment	Categories
Doxy_Service_Setting	Clinical setting in which prophylaxis is provided or considered	Baseline and periodic reassessment	Categories
B4. Chemsex (use of specific psychoactive substances to enhance sexual experience**)**			
Chemsex_Use	Any sexualised substance use	Baseline and follow-up	No/Yes/Prefer not to say
Chemsex_Recency	Recency of sexualised substance use	Baseline and follow-up	Categories
Chemsex_Substances	Substances used for sexualised purposes	Baseline and follow-up	Multi-select
Chemsex_4w	Any sexualised substance use in past 4 weeks	Baseline and follow-up	No / Yes
Chemsex_Frequency	Proportion of sexual encounters involving substance use	Baseline and follow-up	Categories
Chemsex_Impact_Doxy	Impact of sexualised substance use on ability to follow dosing recommendations	Baseline and follow-up	Multi-select

Abbreviations: *AST, antimicrobial susceptibility testing; CLSI, Clinical and Laboratory Standards Institute; CTCAE, Common Terminology Criteria for Adverse Events; EUCAST, European Committee on Antimicrobial Susceptibility Testing; HIV-PrEP, HIV pre-exposure prophylaxis; MIC, minimum inhibitory concentration; STI, sexually transmitted infection.*

Annex 3. Practical example: monitoring doxy-PEP in a clinical cohort setting

1. Introduction

This practical example illustrates how the variables described in Modules A and B can be applied in a real-world clinical monitoring setting. It is intended to support sexual health clinics, HIV-PrEP programmes and other clinical services that wish to monitor the implementation and outcomes of doxy-PEP for the prevention of bacterial STIs. This practical example focuses on monitoring event-driven doxycycline post-exposure prophylaxis (doxy-PEP) in a clinical cohort setting. This example is based on available evidence and expert input at the time of writing and should be adapted to the local context and evolving evidence.

The example is illustrative and does not prescribe a single implementation model; sites should adapt the proposed approach according to local guidance, infrastructure and monitoring objectives.

Clinical services implementing doxycycline prophylaxis may benefit from practical guidance on:

- which variables to collect;
- how often data should be collected;
- how these data can support monitoring and evaluation of doxycycline prophylaxis programmes.

This example demonstrates how core variables, together with selected extended variables where relevant, can be integrated into a prospective clinical monitoring cohort.

2. Clinical setting and monitoring objectives

This section outlines the illustrative clinical setting for the worked example and the main monitoring objectives that guide data collection.

2.1 Clinical setting

This example is set in a sexual health clinic integrated with an HIV-PrEP programme.

The clinic provides:

- HIV- and STI-related counselling;
- routine STI screening;
- provision of HIV-PrEP services;
- treatment of bacterial STIs.

Individuals with an indication for doxy-PEP according to national, regional or local guidance, regulations and protocols may be offered doxycycline as prophylaxis following clinical consultation and shared decision-making.

2.2 Monitoring objectives

The clinic aims to monitor doxycycline prophylaxis use in order to:

- assess uptake and persistence of doxy-PEP use;
- evaluate changes in STI incidence;
- monitor antibiotic consumption;
- identify potential safety signals;
- assess potential AMR trends.

The objectives may, however, vary between settings, and data collection should be adapted accordingly.

3. Study design

This section describes the illustrative cohort design, population, inclusion criteria and key implementation characteristics. The monitoring programme is implemented as a prospective and retrospective observational cohort embedded within routine clinical care.

3.1 Population

Participants may include individuals among the clinic's attendees who:

- are living with HIV or using HIV-PrEP;
- have a recent history of bacterial STI;
- report behavioural indicators associated with an increased likelihood of STI acquisition.

3.2 Inclusion criteria

Individuals with an indication for doxy-PEP according to national, regional or local regulations and protocols who are offered doxycycline as STI prophylaxis are eligible for inclusion, regardless of whether they initiate doxy-PEP. This allows comparison of STI outcomes and other indicators between individuals who initiate doxy-PEP and those who do not. Eligibility criteria may vary according to local clinical guidance.

3.3 Study characteristics

Key study characteristics are summarised in Table 1A.

Table 1A. Study characteristics

Study characteristic	Description
Study design	Prospective observational cohort
Setting	Sexual health clinic with HIV-PrEP services
Population	Individuals eligible for or initiating doxy-PEP
Follow-up duration	24 months (or longer, adaptable to local context)
Visit frequency	Every three months (aligned with routine STI screening)
Data sources	Clinical records, laboratory test results, questionnaires

3.4 Ethical considerations

The implementation of a prospective monitoring cohort within routine clinical care may require approval from relevant local, regional or national ethics committees, depending on the regulatory context.

Participating clinics and centres should assess whether formal ethical approval is required for data collection and analysis, particularly when data are used for scientific or research purposes beyond routine care. In some settings, this may include submission of a study protocol and supporting documentation to an ethics review board.

In addition, clinics may be required to provide participants with a patient or participant information sheet outlining the purpose of data collection, the type of data collected and how these data will be used. Where applicable, informed consent procedures must be implemented in accordance with local regulations.

Data collection and management should comply with applicable data protection regulations, including the General Data Protection Regulation (GDPR), ensuring confidentiality, secure data handling and appropriate governance structures.

4. Data collection framework

Data collection in the cohort is organised around three types of time point:

- Baseline (enrolment);
- Routine follow-up visits;
- Event-based data collection (e.g. STI diagnosis).

These time points align with routine sexual health service workflows.

Table 2A. Time points for data collection

Time point	Data collected	Relevant modules
Baseline	Prior and current doxy-PEP uptake, demographics, STI history, HIV status, doxycycline regimen, behavioural indicators	A1, A2, B1, B4
Routine follow-up (e.g. every three months)	Doxycycline use patterns, STI screening results, behavioural indicators, safety monitoring, adverse events *Note*: recall period of variables describing a behaviour over a specific period such as the last 12 months should be adapted to the routine follow-up of the specific study (e.g. Num_Partners_12m should be adapted to 3 months)	A1, A5, B1, B4
STI diagnosis and laboratory analysis	Laboratory-confirmed STI diagnoses and microbiological outcomes, including culture and antimicrobial susceptibility testing	A4, A6

5. Baseline data collection

Baseline data collection establishes participant characteristics and clinical context at the time of eligibility assessment or the offer of doxy-PEP.

5.1 Uptake and use patterns

Table 3A. Variables for uptake and use of doxy-PEP at baseline

Variable description	Module
Doxy_Offered	A1
Doxy_Received	A1
Doxy_Regimen_Type	A1
Doxy_Initiation_Reason	A1

5.2 Demographic and equity indicators

Table 4A. Variables for demographic and equity characteristics

Variable description	Module
Age	A2
Gender_Identity	A2
Sex_Assigned_Birth	A2
Gender_Partners	A2
Key_Population	A2
Migrant_Status	A2
Country_of_Birth	A2
Education_Level	A2
Employment_Status	A2
Sex_Work_Offered	A2

5.3 HIV-related variables

Table 5A. Variables for HIV-related characteristics

Variable description	Module
HIV_Diagnosis_Status	A2
HIV_Diagnosis_Year	A2
HIV_PrEP_Status	A2

5.4 STI history-related variables

Table 6A. Variables for STI history

Variable description	Module
Prior_STI_History	A2
Baseline_STI_Status	A2
Baseline_STI_Symptom	A2
STI_Complications_History	A2

5.5 Behavioural variables

Table 7A. Variables for sexual behavioural characteristics

Variable description	Module
Num_Partners_12m	B1
NS_Partners_12m	B1
Sex_Acts_Types_12m	B1
Condomless_Sex_12m	B1
Group_Sex_12m	B1
STI_Testing_12m	B1
Concurrent_Prevention	A2
Chemsex_Use	B4
Chemsex_Recency	B4
Chemsex_Substances	B4

6. Follow-up data collection

Routine follow-up visits typically occur every three months, aligned with STI screening schedules in many sexual health services.

These visits allow monitoring of:

- doxy-PEP use
- clinical outcomes
- behavioural indicators
- adverse events.

6.1 Monitoring doxy-PEP use

Table 8A. Variables for monitoring doxy-PEP use at follow-up

Variable description	Module
Doxy_Use_Recency	A1
Doxy_Use_Frequency	A1
Doxy_Current_Use	A1
Doxy_Exposure_Coverage	A1
Other_Antimicrobial_Prophylaxis	A1
Doxy_SelfTreatment_STI	A1

6.2 Monitoring STI outcomes

Table 9A. Variables for monitoring STI outcomes at follow-up

Variable description	Module
Incident_Syphilis	A4
Incident_Gonorrhoea	A4
Incident_Chlamydia	A4
Incident_LGV	A4

6.3 Monitoring behavioural outcomes

Table 10A. Variables for monitoring behavioural outcomes at follow-up

Variable description	Module
Num_Partners_12m	B1
NS_Partners_12m	B1
Sex_Acts_Types_12m	B1
Condomless_Sex_12m	B1
Group_Sex_12m	B1
STI_Testing_12m	B1
Chemsex_4w	B4
Chemsex_Substances_4w	B4

Note: recall period of variables describing a behaviour over a specific period such as the last 12 months should be adapted to the routine follow-up of the specific study (e.g. Num_Partners_12m should be adapted to 3 months)

6.4 Monitoring safety outcomes

Table 11A. Variables for monitoring safety outcomes at follow-up

Variable description	Module
Any_Adverse_Event	A5
AE_Type	A5
AE_Onset_Date	A5
AE_Severity	A5
AE_Relatedness	A5
AE_ActionTaken	A5
AE_Outcome	A5
Doxy_Discontinue_AE	A5
Discontinue_AE_Reason	A5

6.5 Monitoring microbiological outcomes

Table 12A. Variables for monitoring *Neisseria gonorrhoeae* antimicrobial susceptibility at follow-up

Variable description	Module
NG_Culture_Performed	A6
NG_AST_Method	A6
NG_AST_Standard	A6
NG_Tetracycline_Result	A6
NG_Tetracycline_Value	A6
NG_Ceftriaxone_Result	A6
NG_Cefixime_Result	A6
NG_Azithromycin_Result	A6
NG_AST_Other	A6

7. Practical considerations for implementation

When implementing a cohort for monitoring, clinics should consider:

- integration with routine clinical workflows;
- alignment with existing STI screening schedules;
- standardised laboratory procedures;
- data governance and GDPR compliance;
- potential mechanisms for data sharing across sites.

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