Cabotegravir for preventing HIV-1 in adults and young people [ID6255] Part 1

Confidential information redacted

Technology appraisal committee C [8th July 2025]

Chair: Stephen O'Brien

External assessment group: Birmingham Centre for Evidence and Implementation Science

Technical team: Emma McCarthy, Caron Jones, Ian Watson

Company: ViiV Healthcare

Cabotegravir for preventing HIV-1 in adults and young people [ID6255]

- ✓ **Background and recap of committee conclusions and remaining uncertainties**
- ❑ Key issues
- ❑ Additional issue raised after ACM2
- ❑ Summary of cost-effectiveness results
- ❑ Other considerations
- ❑ Summary

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Background on HIV and cabotegravir

ACM1 recap

- HIV is a retrovirus that infects and destroys immune cells that play a key role in fighting infections
- Estimated 106,890 people were living with HIV in the UK in 2020 - 4,040 newly diagnosed in 2022
- Untreated HIV progresses to late-stage infection, called acquired immunodeficiency syndrome (AIDS)

Technology details: cabotegravir (Apretude, ViiV Healthcare)

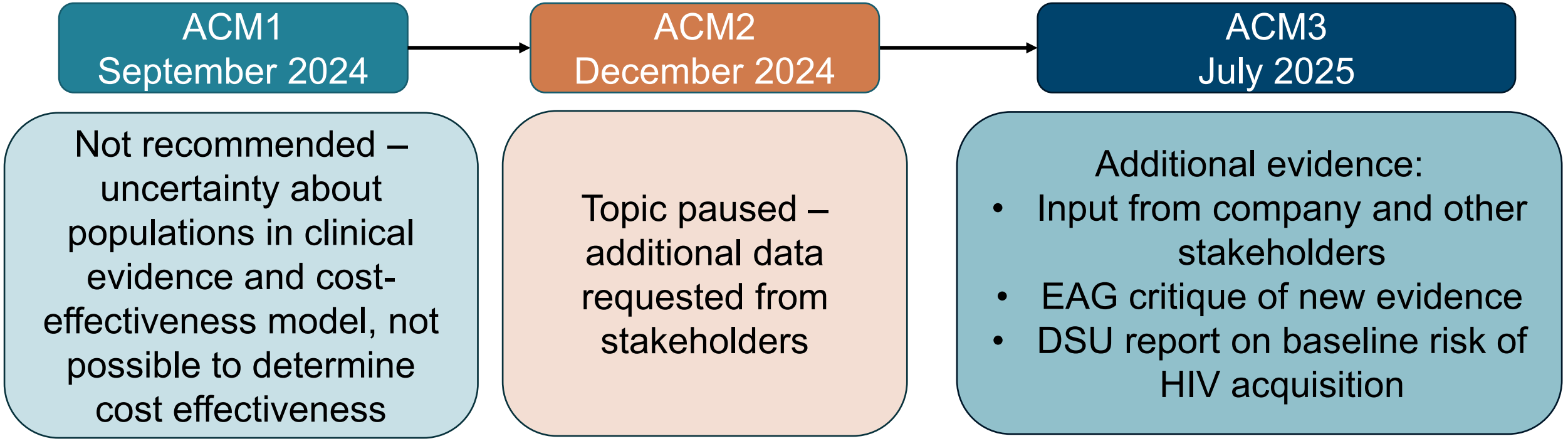
Marketing authorisation	Apretude is indicated in combination with safer sex practices for pre-exposure prophylaxis (PrEP) to reduce the risk of sexually acquired HIV-1 infection in high-risk adults and adolescents, weighing at least 35 kg
Mechanism of action	Second-generation INSTI that inhibits HIV integrase by binding to the integrase active site and blocking the strand transfer step of retroviral DNA integration
Administration	• Intramuscular injection every 2 months administered by healthcare professional experienced in the management of HIV PrEP • Daily tablets for approximately 1 month (at least 28 days) can be used as optional oral lead-in to assess tolerability to cabotegravir
Price	• List prices – cabotegravir injections: £1,197.02; oral cabotegravir tablets: £638.57 • Approximate annual cost: £7,820.69 (including 1-month optional oral lead in) • Existing simple PAS discounts in place for both cabotegravir intramuscular injections and oral cabotegravir tablets due to existing technology appraisal (TA757)

Abbreviations: CD4, cluster of differentiation 4; HIV, human immunodeficiency virus; INSTI, integrase strand transfer inhibitor

Appraisal history

DG post ACM1 - *Cabotegravir is not recommended, within its marketing authorisation, for pre-exposure prophylaxis (PrEP) alongside safer sex practices to reduce the risk of sexually acquired HIV-1 infection in adults and young people who have a high risk of HIV and weigh at least 35 kg.*

Post ACM2: *the committee were unable to make a recommendation, further evidence needed.*



Abbreviations: ACM, appraisal committee meeting; DG, draft guidance; HIV, human immunodeficiency virus; DSU, Decision Support Unit

Latest committee preferred assumptions

Issues discussed	Committee conclusion
Population	Cost-utility analysis using the whole population eligible for cabotegravir, including those who take oral PrEP exactly as prescribed, should be presented. Uncertainty around which specific population groups would engage with SHS to access cabotegravir if it were available
Comparators	TDF/FTC as the comparator for people who do and do not take oral PrEP exactly as prescribed. No PrEP as the comparator for people who cannot take PrEP
Baseline HIV acquisition	Significant uncertainty. Further information requested after ACM2 on population groups accessing cabotegravir, and impact on baseline risk
Duration of risk period	10 years, but uncertainty noted
Transition from cabotegravir to TDF/FTC	Uncertainty around exact proportion who should transition to TDF/FTC after stopping cabotegravir
Improved persistence with cabotegravir	Uncertainty around percentage improved persistence applied to cabotegravir compared with TDF/FTC

Committee established preferred assumptions for adherence, starting age, administration costs and frequency and HIV disutility – see appendix.

Abbreviations: PrEP, pre-exposure prophylaxis; SHS, sexual health services; TDF/FTC, tenofovir disoproxil/emtricitabine

Equality considerations

Summary of equality considerations raised at ACM1 and ACM2:

- HIV disproportionately affects – people of Black African family background; people of certain sexual orientation such as gay or bisexual men
- Key populations who are most at risk of HIV acquisition may be reluctant to engage in healthcare systems or to access sexual health services. Cultural concerns or stigma may exacerbate health inequity
- Deepening inequality in HIV outcomes, with increasing rates being seen in key populations, such as Black women, whose needs are not currently being met with available oral PrEP regimens
- Acknowledged inequity of access to PrEP in the UK for cisgender women

PrEP, pre-exposure prophylaxis; TDF/FTC, tenofovir disoproxil/emtricitabine

See appendix for equalities considerations at ACM1 and ACM2

Equality considerations

Equality issues included or raised in previous meetings or new evidence:

- Concern that current recommendation does not promote equality of opportunity by denying access to people who may benefit from cabotegravir where current PrEP options are not appropriate (e.g. cisgender women)
- Long-acting injectable PrEP would be beneficial to groups underserved by current treatments and reduce inequities in uptake
    - Underserved groups include: people from trans and non-binary communities, people who inject drugs, those who struggle with adherence, oral meds or those in whom the current standard of care agents are contraindicated, people who are homeless and/or and in unstable housing, those experiencing intimate partner violence

What are the committee's views on the equalities issues raised?
Are there any further equality considerations the committee should consider?
Are there any additional considerations, adjustments or recommendations required based on equality considerations?

PrEP, pre-exposure prophylaxis;

See appendix for equalities considerations at ACM1 and ACM2

Issues for discussion

Key issue	Questions for committee	ICER impact
Baseline risk of HIV acquisition	• What is the most appropriate baseline risk of HIV acquisition in MSM/TGW? • What is the most appropriate baseline risk of HIV acquisition in CGW?	Very large 
Population groups accessing cabotegravir	• Which population groups would access cabotegravir in practice? • How do the population groups accessing cabotegravir affect baseline risk?	Unknown 

Abbreviations: HIV, human immunodeficiency virus; TDF/FTC, tenofovir disoproxil/emtricitabine; MSM, men who have sex with men; CGW, cisgender women; TGW, transgender women

Issues for discussion

Key issue	Questions for committee	ICER impact
Duration of HIV risk period	• What is the most appropriate at-risk period?	Large
Transition from cabotegravir to TDF/FTC	• Is it appropriate to allow participants to transition to TDF/FTC after discontinuing cabotegravir? • What proportion of people transitioning to TDF/FTC should be used?	Large
Improved persistence with cabotegravir	• Is it plausible to assume that cabotegravir injections will improve persistence compared to oral PrEP? • If yes, what percentage improvement should be used in the model?	Large
Rate of discontinuation	• How should the rate of discontinuation be applied in the model?	Large

Other issue	Questions for committee	ICER impact
Efficacy data without oral lead-in	• Is it appropriate to use the efficacy data without oral lead in for decision making?	Small

Abbreviations: HIV, human immunodeficiency virus; TDF/FTC, tenofovir disoproxil/emtricitabine; PrEP, pre-exposure prophylaxis

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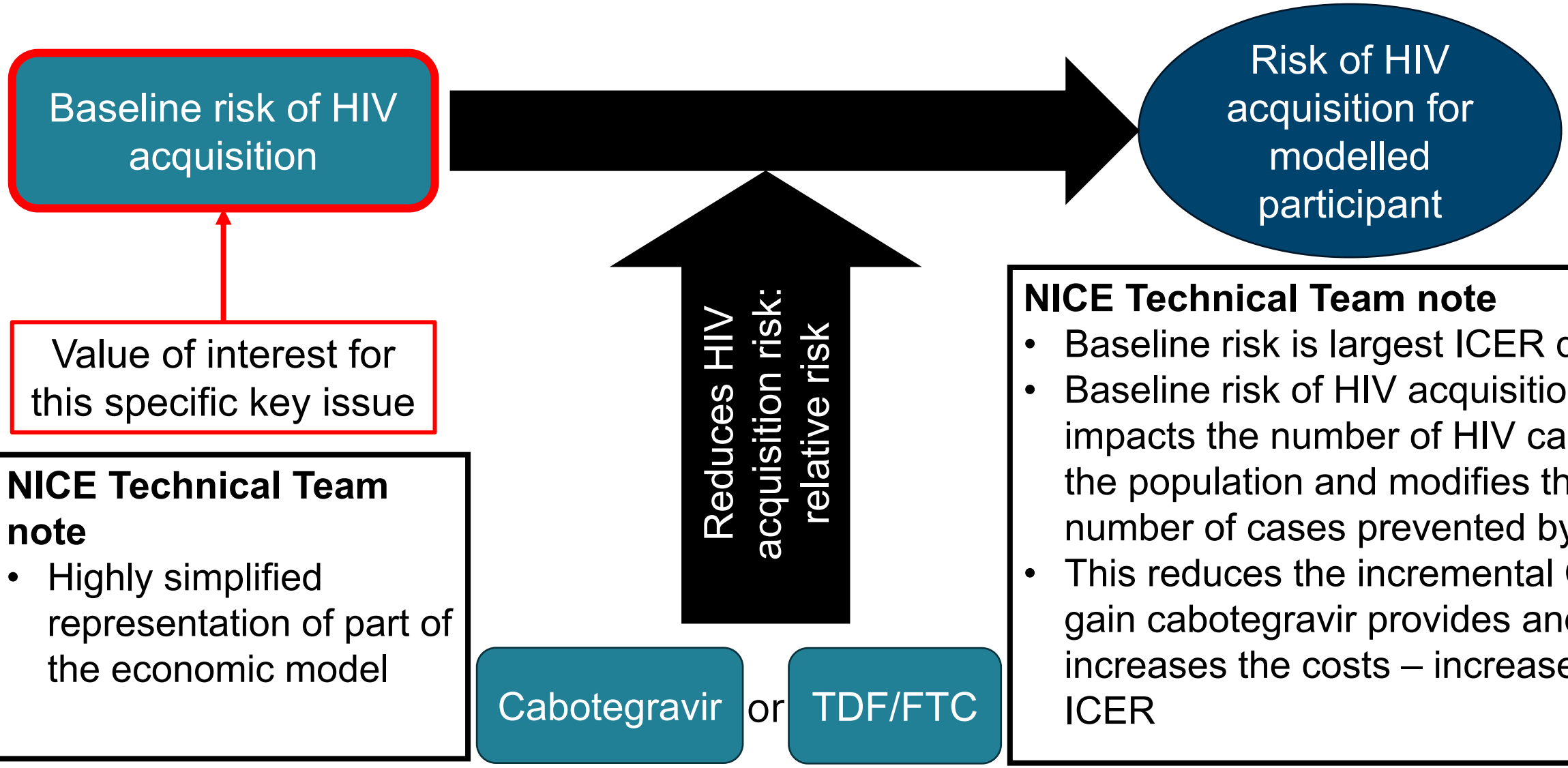
Key issue: Baseline risk of HIV acquisition



NICE Technical Team note

- Highly simplified representation of part of the economic model

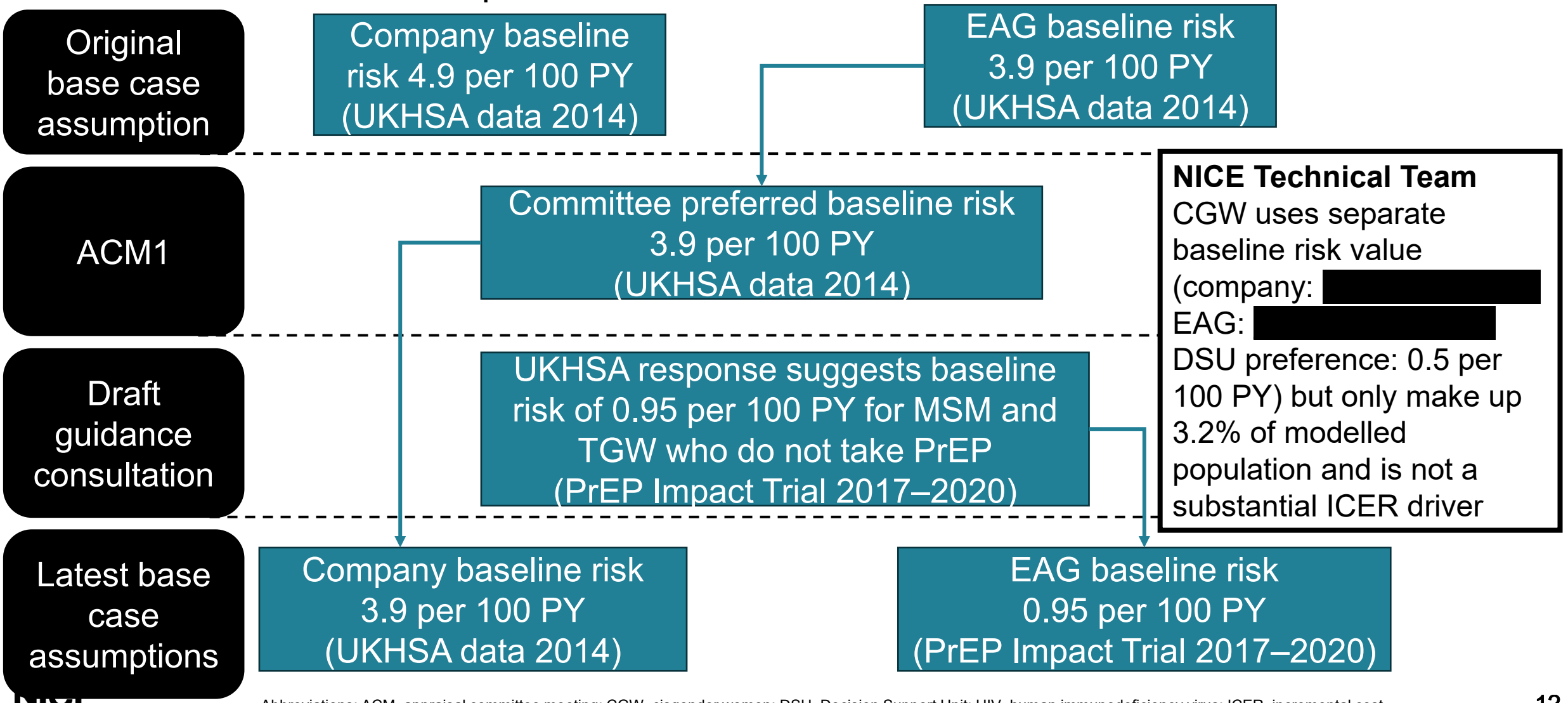
NICE Technical Team note

- Baseline risk is largest ICER driver
- Baseline risk of HIV acquisition impacts the number of HIV cases in the population and modifies the number of cases prevented by PrEP
- This reduces the incremental QALY gain cabotegravir provides and increases the costs – increases the ICER

Abbreviations: ACM, appraisal committee meeting; HIV, human immunodeficiency virus; ICER, incremental cost-effectiveness ratio; PY, person-years; QALY, quality-adjusted life year; TDF/FTC, tenofovir disoproxil/emtricitabine

Key issue: Baseline risk of HIV acquisition – MSM and TGW

ACM2 – committee were highly uncertain on the value that should be used in the model for baseline risk of HIV acquisition



Abbreviations: ACM, appraisal committee meeting; CGW, cisgender women; DSU, Decision Support Unit; HIV, human immunodeficiency virus; ICER, incremental cost-effectiveness ratio; MSM, men who have sex with men; PrEP, pre-exposure prophylaxis; PY, person-years; TGW, transgender women; UKHSA, UK Health Security Agency

Baseline risk of HIV acquisition – overview

MSM and TGW		
Company: 3.9	EAG/DSU: 0.95	GUMCAD: 0.43

CGW		
Company: [redacted]	EAG: [redacted]	DSU: 0.5

Stakeholder comments included:

- Appropriateness of IMPACT trial estimate
- Updated analyses from GUMCAD data
- Range of alternative baseline risk estimates
- Incidence in high-risk individuals; potential for scenario-based approach for subpopulations
- Review of evidence by DSU

Stakeholder comments included:

- HIV incidence estimates from recent Africa-based RCTs in women using oral PrEP
- Information on new HIV diagnoses made in England

Further comments from company, stakeholders and DSU

Abbreviations: HIV, human immunodeficiency virus; GUMCAD, Genitourinary Medicine Clinic Activity Dataset ; DSU, Decision Support Unit; MSM, men who have sex with men; CGW, cisgender women; TGW, transgender women; PrEP, pre-exposure prophylaxis

Key issue: Baseline risk of HIV acquisition – MSM and TGW (IMPACT)

0.95 per 100 PY based on figure from non-trial SHS attendees in IMPACT study

Attendees of 157 SHS clinics across England (enrolled 2017-2020)

↓ Non-trial participants

Risk of HIV acquisition assessed in SHS attendees (>2 visits), with recorded negative HIV test and no evidence of obtaining PrEP from another source

↓ MSM only (n=85,072)

587 seroconversions in MSM non-trial attendees (61,605 PY follow-up)

HIV incidence estimate: **0.95 per 100 PY**

Abbreviations: HIV, human immunodeficiency virus; MSM, men who have sex with men; PrEP, pre-exposure prophylaxis; PY, person-years; TGW, transgender women; SHS, sexual health services; GBMSM, gay and bisexual men who have sex with men; BHIVA, British HIV Association; AIDS, acquired immunodeficiency syndrome; DSU, Decision Support Unit

Comments from stakeholders (BHIVA, National AIDS Trust, clinical expert)

- IMPACT study not designed to inform HIV incidence - 0.95 figure may underestimate risk
- At time of IMPACT, PrEP was unavailable on NHS – SHS attendees who are not high-risk or chose not to be in trial will have different risk profile to those eligible for cabotegravir
- IMPACT trial protocol – HIV incidence in GBMSM at higher risk of HIV ~ 3 per 100 PY

DSU comments on estimate

- Using baseline estimates based on populations most at risk with available estimates (i.e. MSM/TGW and CGW) is pragmatic
- 0.95 per 100 PY is reasonable for MSM (and as proxy for TGW)

Further comments from company, stakeholders and DSU

Key issue: Baseline risk of HIV acquisition – MSM and TGW (UKHSA)

Additional UKHSA analysis of STI surveillance system data from GUMCAD used to estimate HIV incidence rates from 2014-2023

GUMCAD data from GBMSM attending SHS between 2014 and 2023

↓ GBMSM with >2 HIV tests in follow up period

HIV incidence estimated with Kaplan–Meier analysis (follow up from 1st HIV test until last attendance or new diagnosis of HIV)

UKHSA comments on analysis

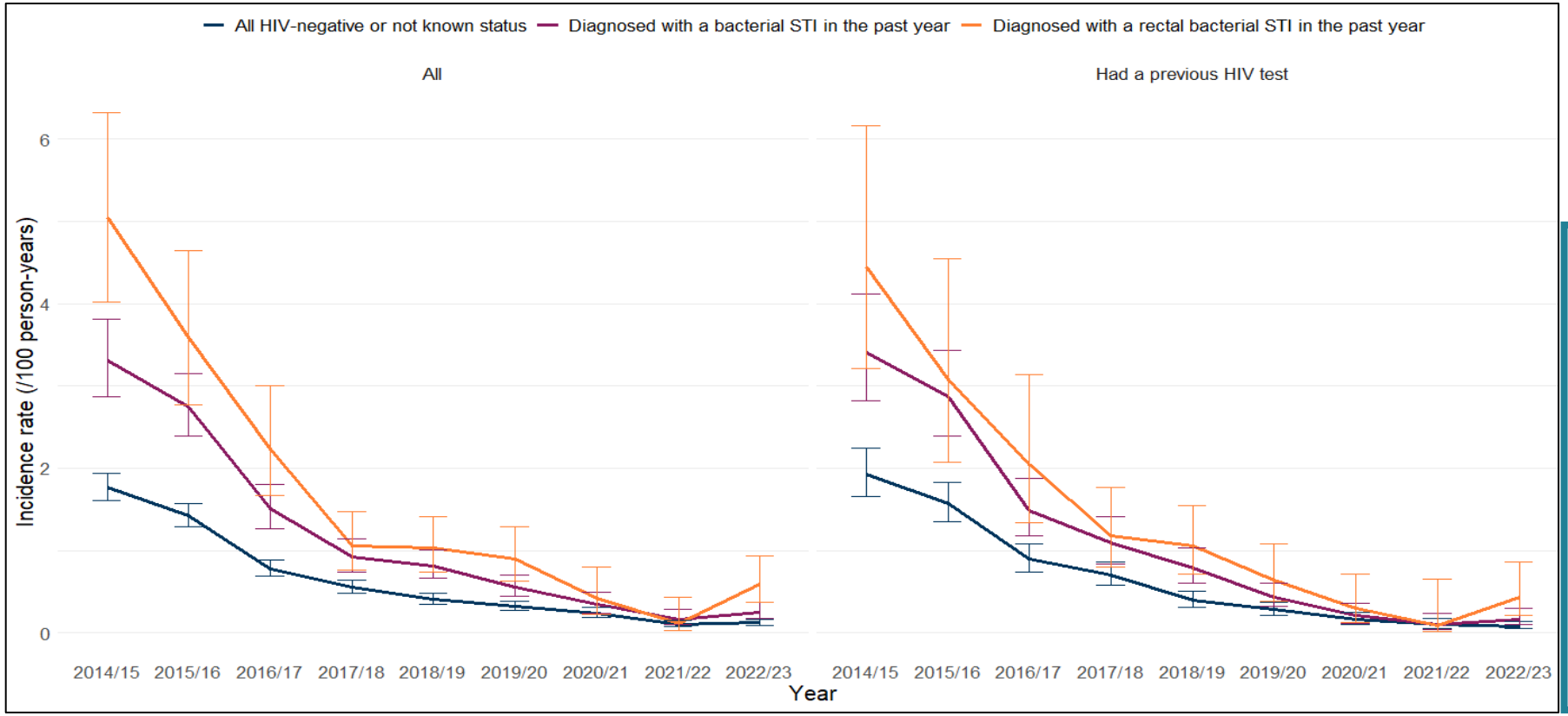
- New analysis replicates previous analyses from 2012-2014 using current surveillance data
- Introduction of PrEP, more widespread/frequent testing and increased coverage of antiretrovirals since 2014 may have influenced HIV incidence
- Data from GUMCAD used to estimate HIV incidence rates in GBMSM attending SHS between 2014/15 and 2022/23 (stratified by clinical markers of risk and PrEP use) shows marked decline in HIV incidence in GBMSM during this period
- Rise in HIV incidence rates in 2023 vs 2022 is not statistically significant

Abbreviations: HIV, human immunodeficiency virus; GBMSM, gay and bisexual men who have sex with men; PrEP, pre-exposure prophylaxis; GUMCAD, Genitourinary Medicine Clinic Activity Dataset ; SHS, sexual health services; UKHSA, UK Health Security Agency

Key issue: Baseline risk of HIV acquisition - MSM and TGW (UKHSA)

UKHSA further analysis shows marked decline in HIV incidence in GBMSM

HIV incidence rates in GBMSM attending SHS:



UKHSA data include incidence for different risk markers in people on PrEP (0.04-0.26) or not on PrEP (0.31-1.90)

HIV incidence tables in GBMSM

UKHSA

- Decline in HIV incidence in GBMSM during this period persists when stratified by PrEP status
- Supported by CD4 back-calculation estimations from HANDD

Year	HIV incidence in GBMSM with rectal bacterial STI in previous year (95% CI)	HIV incidence in GBMSM with rectal bacterial STI and HIV test in previous year (95% CI)
2014/15	4.9 per 100 PY (3.9-6.2)	3.9 per 100 PY (2.8-5.6)
2022/23	0.59 per 100 PY (0.37-0.94)	0.43 per 100 PY (0.22-0.87)

Abbreviations: HIV, human immunodeficiency virus; PYs, person years; GBMSM, gay and bisexual men who have sex with men; PrEP, pre-exposure prophylaxis; GUMCAD, Genitourinary Medicine Clinic Activity Dataset ; SHS, sexual health services; CI, confidence interval; CD4, cluster of differentiation 4; HANDD, HIV and AIDS New Diagnoses and Deaths Database

Key issue: Baseline risk of HIV acquisition – MSM and TGW

	Preferred risk per 100 PY	Source
Company base case	3.9, but literature search showed rates up to 17.4	GUMCAD (UKHSA) data, England and Wales, 2014
EAG base case, DSU preference	0.95	PrEP IMPACT study (UK)
Clinical expert at ACM2	2.41	PURPOSE 1 trial (non-UK)
BHIVA, National AIDS Trust stakeholder comments	2–3 (as minimum)	Multiple studies
Clinical expert stakeholder comments	3.9 or 9	3.9 – GUMCAD data (2014) 9 – PROUD study (2012-14)
HIV incidence in GBMSM with rectal bacterial STI and HIV test in previous year	0.43 (includes people on and not on PrEP)	UKHSA updated analysis from GUMCAD (2022/23)

What is the most plausible estimate of baseline HIV acquisition in MSM and TGW?

HIV, human immunodeficiency virus; PYs, person years; PrEP, pre-exposure prophylaxis; GUMCAD, Genitourinary Medicine Clinic Activity Dataset; BHIVA, British HIV Association; AIDS, acquired immunodeficiency syndrome; UKHSA, UK Health Security Agency; MSM, men who have sex with men; TGW, transgender women

Key issue: Baseline risk of HIV acquisition - CGW

UKHSA comments

Background

- At ACM2, company assumed baseline risk of HIV acquisition in CGW = [redacted] - EAG preference = [redacted]
- Newest company base case [redacted] assumes baseline risk for CGW = [redacted]

Stakeholder comments (BHIVA, National AIDS Trust, clinical expert)

- Recent Africa-based RCTs for women using oral PrEP give background HIV incidence of 2.41 per 100 PY (PURPOSE-1) and incidence on oral PrEP of 1.69-1.85/100PY. May be generalisable to UK since HIV disproportionately affects heterosexual men and women of African origin
- UKHSA data indicates rise in new HIV diagnoses in 2022/23 highest in heterosexual men and women with additional impact on Black African communities (a 64% increase).

DSU comments

- HIV new diagnoses in 2023 in heterosexuals exceeds MSM diagnoses – and most of these are from people first diagnosed abroad
- Using data from all heterosexuals (0.05% in 2013) and Black African heterosexual men and women as proxy for CGW, crude estimate of 0.5 per 100 PY recommended for CGW

Abbreviations: CGW, cisgender women; HIV, human immunodeficiency virus; [redacted]; PYs, person years; PrEP, pre-exposure prophylaxis; GUMCAD, Genitourinary Medicine Clinic Activity Dataset; BHIVA, British HIV Association; AIDS, acquired immunodeficiency syndrome; UKHSA, UK Health Security Agency; TDF/FTC, tenofovir disoproxil/emtricitabine; RCT, randomised controlled trial; MSM, men who have sex with men

What is the most plausible estimate of baseline HIV acquisition for CGW?

Key issue: Population groups accessing cabotegravir

Background

- At ACM2, committee were highly uncertain about which specific population groups would engage with SHS to access cabotegravir if it were available – requested that stakeholders provide information on this and the effect on baseline risk of HIV acquisition

Company

- Cabotegravir will mainly be offered in clinical practice by people at high risk of HIV acquisition for whom oral PrEP is not appropriate – incidence in this population will be higher than for those for whom oral PrEP is suitable
  - Analyses based on mixed population of people not on PrEP may underestimate incidence in high-risk individuals (i.e. people for whom oral PrEP is not appropriate)
- Experts from 2025 company advisory board – [redacted]
- Baseline risk in subpopulations (e.g. those unable to take oral PrEP and those with suboptimal/optimal adherence to oral PrEP) difficult to quantify because of limited data granularity

Abbreviations: HIV, human immunodeficiency virus; SHS, sexual health services; PrEP, pre-exposure prophylaxis

Key issue: Population groups accessing cabotegravir

Stakeholders (BHIVA, National AIDS Trust, clinical expert)

- Cabotegravir expected to serve groups for whom oral PrEP is unsuitable, inaccessible, or unsustainable (and are expected to be at higher risk). RWE shows increased uptake and adherence of PrEP where injectable PrEP is available, and preference for injectable PrEP in underserved groups
  - Study of PrEP naïve population in Brazil (ImPrEP) - 83% chose cabotegravir vs 58% oral PrEP

EAG

- Most of the supporting evidence provided is not UK-based and has low generalisability to UK clinical practice, or does not provide information on who might benefit from cabotegravir – so uncertain who might have cabotegravir in UK clinical practice
- ImPrEP study was a selected group and does not offer information about who might have cabotegravir in clinical practice

Key groups highlighted by stakeholders

Which population groups would access cabotegravir in practice? How do the population groups accessing cabotegravir affect baseline risk?

Abbreviations: HIV, human immunodeficiency virus; GBMSM, gay and bisexual men who have sex with men; PrEP, pre-exposure prophylaxis; RWE, real world evidence

Key issues: Duration of risk period

EAG and further DSU comments

Background

- ACM1 – committee concluded 10-year duration of risk period is appropriate
- Committee noted that although RWE showed high discontinuation of PrEP over 12 months, it was not clear how many people restart PrEP

Company

- 5-year duration is appropriate despite uncertainty based on ACM1 clinical expert opinion and RWE showing high rates of discontinuation of TDF/FTC (66% from ImPrEP)
- UK advisory board – [redacted]

Stakeholders (comments from National AIDS Trust)

- 5-year period better aligns with RWE and clinical practice → 10 years overestimates duration of continuous PrEP use

DSU analysis

- Recent systematic reviews and meta-analyses show consistent restarting of PrEP (see details)
- Ongoing risk may persist in high-risk groups → shown in study of women selling sex in Zimbabwe for 6-15 years (risk = 2.1 per 100 PY – DSU acknowledges lack of generalisability)
- Evidence appears to support 10-year risk period more than 5 years

Abbreviations: RWE, real world evidence; PrEP, pre-exposure prophylaxis; TDF/FTC, tenofovir disoproxil/emtricitabine; MSM, men having sex with men; TGW, transgender women; PY, person years

What is the most appropriate duration of risk period?

Key issue: Transition from cabotegravir to TDF/FTC

Background

- ACM1 – committee concluded it was appropriate to allow some people to transition from cabotegravir to TDF/FTC, but there was uncertainty around the exact proportion

Company

- Maintains that [redacted] of people will take TDF/FTC after discontinuation of cabotegravir
- RWE has shown that some individuals transition from cabotegravir to oral PrEP - though numbers in UK uncertain due to low use in current practice

Stakeholders (National AIDS Trust)

- Limited transitions between oral and injectable PrEP (managed via clinical discretion) and most cabotegravir users will be individuals who cannot or will not use oral PrEP

EAG comments

- Evidence cited by company from Zambia (Paxon 2025) and USA (Dieterich 2025, Traeger 2025) is either not verifiable from published abstract or not generalisable to UK practice
- Study cited by National AIDS Trust does not provide commentary or evidence of rates of switching from cabotegravir to oral PrEP

- Is it appropriate to allow people to transition to TDF/FTC after discontinuing cabotegravir?
- What proportion of people transitioning to TDF/FTC should be used?

PrEP, post exposure prophylaxis; TDF/FTC, tenofovir disoproxil/emtricitabine;

Key issues: Persistence

Further company, EAG, stakeholder comments

Background

- Committee concluded there would potentially be an improvement in persistence (willingness to continue taking cabotegravir vs oral PrEP) but uncertainty around the % improvement

Company

- Additional evidence based on [redacted] shows [redacted] with [redacted] at 12 months ([redacted]) – 20% improvement is conservative
- Additional evidence from 7 studies with maximum follow-up of 60 weeks supports high levels of persistence with cabotegravir

EAG comments

- Company cited evidence on oral PrEP persistence from French healthcare system (n=42,159) which shows 80-90% of users renewing oral PrEP between semesters (6-month periods)
- Persistence definitions vary across studies: data from largest study (OPERA) cited by company that shows 81% persistence after 10 months is based on 646 complete initiators (≥2 injections) instead of full population that started cabotegravir (n=784)
- In company advisory board, [redacted]

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PrEP, pre-exposure prophylaxis; TDF/FTC, tenofovir disoproxil/ emtricitabine;

Should an improvement in persistence be included in the model? If yes, what percentage improvement should be used?

Key issue: Discontinuation rate correction

Background

- Company identified an error in the implementation of discontinuation rates in its cost-effectiveness model, but EAG do not believe it is an error that needs correcting

Company

- Discontinuation rates for oral PrEP and cabotegravir (estimated from data to 6 months) were erroneously applied for 5 monthly cycles instead of 6
- This implementation error has been corrected in the updated base-case analysis

EAG comments

- Company's claim that discontinuation rates were applied for 5 monthly cycles is factually inaccurate
- Discontinuation rates were applied for 6 monthly cycles in the previous implementation and 7 monthly cycles in the current implementation
- Cycle begins from Month 1 and not 0, so the cohort would have spent 6 months in the various health states at the end of the 6th cycle

What is the committee's preferred method for applying discontinuation rates in the model?

Abbreviations: PrEP, pre-exposure prophylaxis

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Other issues: Efficacy data without oral lead-in

Background

- Cabotegravir SmPC allows for optional OLI - previous company base case assumes 50% of people receive OLI

Company

- RWE study (Hazra 2024) from USA (n=270) found that 97.8% of people having cabotegravir for PrEP do not receive the OLI – remaining 2.2% not significant driver of cost-effectiveness
- Company's updated base case assumes 0% of people in the model receive the OLI – based on injection phase only efficacy data from an updated ITC (see appendix)
- HIV acquisition risk during OLI period due to sub-optimal adherence to oral PrEP. Appropriate to consider cabotegravir efficacy using injection phase only based on SmPC and RWE

EAG comments

- Sub-optimal adherence to oral PrEP may not be linked to all HIV acquisitions – excluding people in the OLI phase may bias analysis
- Minimal difference in cost effectiveness estimates

PrEP, pre-exposure prophylaxis; HIV, human immunodeficiency virus; SmPC summary of product characteristics; OLI, oral lead-in; RWE, real world evidence

Is it appropriate to use the efficacy data without oral lead-in for decision making?

Further EAG comments

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Summary of updated company and EAG base case assumptions

Differences in assumptions included in issues for discussion

Assumption	Company base case	EAG base case
Baseline risk of HIV acquisition (MSM/TGW)	3.9 per 100 PY	0.95 per 100 PY (DSU preference)
Baseline risk in CGW	[redacted]	[redacted]
Duration of risk period	5 years	10 years (DSU preference)
Transitioning from cabotegravir to oral PrEP	[redacted] of individuals transition from cabotegravir to oral PrEP	No transitioning from cabotegravir to oral PrEP
Persistence to cabotegravir	20% improved persistence for cabotegravir over oral PrEP	Persistence to cabotegravir equal to oral TDF/FTC
Source of efficacy data	Injection phase only	Injection phase with OLI
Rate of discontinuation	Discontinuation rate “error” corrected	Unchanged

Note: neither the company’s or EAG’s base case assumptions align with all of the latest committee’s preferred assumptions (see slide 5)

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HIV, human immunodeficiency virus; PrEP, pre-exposure prophylaxis; PY, person-yearsTDF/FTC, tenofovir disoproxil/emtricitabine; MSM, men having sex with men; TGW, transgender women; OLI, oral lead-in

Summary of updated company and EAG base cases

Exact cost-effectiveness results are reported in part 2 due to confidential discounts for cabotegravir and TDF/FTC

Company base case

- Cabotegravir is less costly and generated more QALYs than TDF/FTC
- ICER for cabotegravir remains dominant over TDF/FTC and over no PrEP
- Probabilistic results similar to deterministic results

EAG base case

- Cabotegravir is more costly and generated more QALYs than TDF/FTC
- ICER for cabotegravir vs TDF/FTC remains considerably higher than £30,000 per QALY gained
- ICER for cabotegravir vs no PrEP is higher than £30,000 per QALY gained
- Probabilistic results similar to deterministic results

Cost-effectiveness plane

Abbreviations: ICER, incremental cost-effectiveness ratio; PrEP, pre-exposure prophylaxis; QALY, quality-adjusted life year; TDF/FTC, tenofovir disoproxil/emtricitabine

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Managed access

Committee view on managed access

The committee explored the potential for managed access at ACM2. It identified key uncertainties including:

- Most appropriate value for baseline risk of HIV acquisition
- Whether persistence improves with cabotegravir compared to oral PrEP
- Whether populations with a PrEP need that historically do not engage with SHS would access cabotegravir if it became available in practice

Stakeholder views (BHIVA, National AIDS Trust, clinical expert)

- Routine recommendation preferred, but MA would offer access to cabotegravir while collecting data on whether injectable PrEP increases uptake and persistence among key populations or those for whom oral PrEP does not meet their needs
- Data that could be collected: demographics, past service use, coverage, discontinuation
- SHS commissioned by local authorities instead of NHS – complicates MA implementation
- Real world data on persistence, transitions, and cost assumptions can still be collected in routine commissioning and existing national surveillance mechanisms

Note: a managed access proposal has not been submitted

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Summary of issues

Key issue	ICER impact	Slide
Baseline risk of HIV acquisition	Very large	11-18
Population groups accessing cabotegravir	Unknown	19-20
Duration of HIV risk period	Large	21
Transition from cabotegravir to TDF/FTC	Large	22
Improved persistence with cabotegravir	Large	23
Rate of discontinuation	Large	24

Other issue	ICER impact	Slide
Efficacy data without oral lead-in	Small	26

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Abbreviations: HIV, human immunodeficiency virus;; TDF/FTC, tenofovir disoproxil/emtricitabine

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Supplementary appendix

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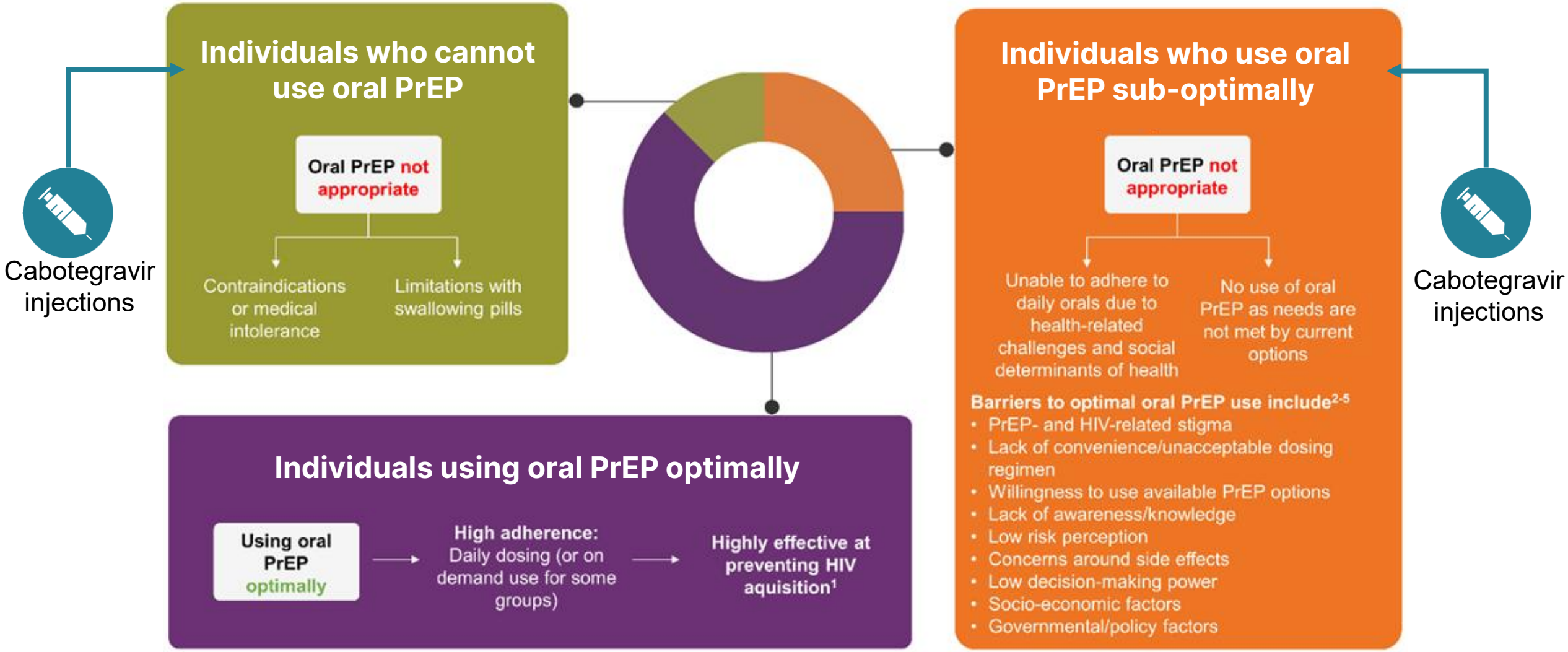
Populations with PrEP needs



Sources: 1. Sullivan et al, 2023; 2. Calabrese et al, 2020; 3. Coukan et al, 2023; 4. Sidebottom et al, 2018; 5. National AIDS Trust

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Abbreviations: HIV, human immunodeficiency virus; PrEP, pre-exposure prophylaxis

= proposed positioning of cabotegravir

Treatment pathway

= established treatment

= proposed positioning

People at risk of sexually acquired HIV-1 infection

Treatments delivered in Level 3 SHS

- Cabotegravir injections
- Oral TDF/FTC
- Oral TAF/FTC

HIV exposure

HIV acquisition

Treatments delivered in secondary care

- Antiretroviral treatment
- Cabotegravir with rilpivirine injections (NICE TA757)

- TDF/FTC and TAF/FTC are both forms of oral PrEP
- The majority of oral PrEP users in the UK will receive TDF/FTC
- TAF/FTC is used for individuals that are intolerant or contraindicated to TDF/FTC (NHS Clinical Commissioning Policy 2023)
- For the pre-exposure prophylaxis of HIV, TAF/FTC is only licensed in MSM

Abbreviations: HIV, human immunodeficiency virus; MSM, men who have sex with men; PrEP, pre-exposure prophylaxis; SHS, sexual health services; TAF/FTC, tenofovir alafenamide/emtricitabine; TDF/FTC, tenofovir disoproxil/emtricitabine

Decision problem population

	Final scope	Company	EAG comments
Population	People at risk of sexually acquired HIV-1 infection.	Adults and adolescents (weighing at least 35 kg) at risk of sexually acquired HIV for whom oral PrEP is not appropriate. Rationale: Current SoC meets the needs of the broad population of people likely to be exposed to HIV. However, there are still people who are likely to be exposed to HIV who are underserved by oral PrEP. A new drug class, modalities, and or dosing frequencies, such as cabotegravir, will help to address the unmet needs for these individuals	The EAG considers that 'Adults and adolescents (weighing at least 35 kg) at risk of sexually acquired HIV' is in line with the NICE scope. However, the main clinical evidence submitted by the company for the comparison of CAB-LA with TDF/FTC is limited to adults aged ≥18 years in specific populations, i.e. men who have sex with men/transgender women, or cisgender women <45 years.

Abbreviations: CAB-LA, cabotegravir injection; HIV, human immunodeficiency virus; PrEP, pre-exposure prophylaxis; SoC, standard of care; TDF/FTC, tenofovir disoproxil/emtricitabine

Latest committee preferred assumptions – other issues

Issues discussed	Committee conclusion
Adherence to TDF/FTC	Adherence to TDF/FTC lower for CGW compared with MSM and TGW
Starting age of model population	Starting age of 33 years
Cabotegravir administration costs	Administration costs based on 1 hour of clinic time
Cabotegravir injections administration frequency	Administration every 2 months
Disutility associated with living with HIV	Disutility of –0.11 associated with living with HIV

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HIV, human immunodeficiency virus; MSM, men who have sex with men; PrEP, pre-exposure prophylaxis; TDF/FTC, tenofovir disoproxil/emtricitabine; CGW, cisgender women; TGW, transgender women

Key issue: Baseline risk of HIV acquisition - MSM and TGW

Company

- Literature search of reported HIV incidence in the UK and Western Europe showed rates of 3.9–17.4/100 PYs in high-risk populations not receiving PrEP – so maintains that baseline risk of 3.9 per 100 PYs is conservative
  - UKHSA data shows HIV diagnoses first made in England rose 15% from 2022 to 2023
  - Potential risk of increasing UK incidence between 2025 and 2030
- Analyses based on mixed population of people not on PrEP may underestimate incidence in high-risk individuals, specifically in people for whom oral PrEP is not appropriate
  - HIV diagnoses reported in GUMCAD and HARS should be included
- Using single marker of high risk may not adequately stratify population and underestimates baseline risk – scenario analyses with a range of markers may mitigate this

Comments from stakeholders (BHIVA, National AIDS Trust, clinical expert)

- RCTs of oral PrEP (in people at higher risk of HIV) show PrEP reduces HIV incidence to figure comparable with IMPACT non-users of PrEP (~1 per 100 PY or lower)
- Scenario based approach (with range of risk markers and baseline risks for subpopulations) instead of single point estimate may be a more appropriate for cost effectiveness analysis
- Range of alternative baseline risk values suggested from 2-9 per 100 PY

HIV, human immunodeficiency virus; PYs, person years; PrEP, pre-exposure prophylaxis; GUMCAD, Genitourinary Medicine Clinic Activity Dataset; HARS, HIV and AIDS Reporting System

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Key issue: Baseline risk of HIV acquisition - MSM and TGW

DSU – EAG's baseline estimate of 0.95 per 100 PY is reasonable baseline risk in MSM

DSU analysis of baseline risk evidence

- Sustained year-on-year decline in new HIV infections in England before increase in 2022/23 suggests current incidence lower than 3.9 per 100 PY estimate from GUMCAD 2014
  - Most new diagnoses in England in 2023 among people exposed through sex between men and women (60% where probable route of exposure recorded)
  - Increase in people previously diagnosed abroad (53%, 3198/6008) also drives 2022/23 new diagnoses
- Specific data informing subpopulation risk (i.e. ability to take oral PrEP, risk behaviours, partner information) not routinely available, timely and robust
  - Using baseline estimates based on populations most at risk with available estimates (i.e. MSM/TGW and CGW) is pragmatic instead of scenario-based approach
- Estimate of 0.95 per 100 PY is reasonable – and higher than 2022/23 GUMCAD estimates (0.43 per 100 PY) or 2019 MSM clinic data (0.25 per 100 PY)
  - Incidence estimates from studies in sub-Saharan Africa (PURPOSE-1, HPTN-084) not considered generalisable to UK setting

What is the most plausible estimate of baseline HIV acquisition in MSM and TGW?

HIV, human immunodeficiency virus; PYs, person years; PrEP, pre-exposure prophylaxis; GUMCAD, Genitourinary Medicine Clinic Activity Dataset; HARS, HIV and AIDS Reporting System

Graphs of diagnosis figures by route of exposure and location of diagnosis

Key issue: Baseline risk of HIV acquisition

UKHSA further analysis shows marked decline in HIV incidence in GBMSM

HIV incidence rates among GBMSM attending SHS who were repeat HIV testers, by clinical markers of HIV risk

Clinical markers of risk	2014/15		2022/23	
	Repeat testers	Rates per 100 PY (95%CI)	Repeat testers	Rates per 100 PY (95%CI)
HIV negative or unknown (Total)	37,576	1.77 (1.61-1.94)	56,900	0.11 (0.08-0.15)
[a] Bacterial STI diagnoses in the previous year	8,704	3.31 (2.87-3.81)	15,326	0.16 (0.10-0.28)
[b] Recent rectal bacterial STI in the previous year (subset of [a])	2,313	5.04 (4.02-6.32)	4,179	0.11 (0.03-0.43)
[c] history of HIV test in the previous 42-365 days (including [a] and [b] within this group)	12,921	1.93 (1.66-2.24)	24,123	0.10 (0.06-0.17)
Subset of [c] with bacterial STI diagnoses in the previous year	4,553	3.40 (2.81-4.12)	9,625	0.10 (0.04-0.23)
Subset of [c] with rectal bacterial STI in the previous year	1,203	4.44 (3.21-6.16)	2,430	0.09 (0.01-0.65)

HIV, human immunodeficiency virus; PYs, person years; GBMSM, gay and bisexual men who have sex with men;; SHS, sexual health services; UKHSA, UK Health Security Agency; STI, sexually transmitted infection; CI, confidence interval

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Key issue: Baseline risk of HIV acquisition

UKHSA further analysis shows marked decline in HIV incidence in GBMSM

HIV incidence rates among GBMSM attending SHS who were repeat testers, by clinical markers of HIV risk and PrEP use, 2022/23

Clinical markers of risk	Repeat testers	HIV risk reduction in PrEP users	Rates per 100 PY, Not On PrEP	Rates per 100 PY- using PrEP
HIV negative or unknown (Total)	56,900	-86%	0.36 (0.26-0.50)	0.05 (0.03-0.08)
[a] Bacterial STI diagnoses in previous year	15,326	-91%	0.94 (0.62-1.45)	0.08 (0.04-0.17)
[b] Recent rectal bacterial STI in previous year (subset of [a])	4,179	-91%	1.90 (1.13-3.21)	0.17 (0.06-0.46)
[c] history of HIV test in previous 42-365 days including [a] and [b] within this group	24,123	-87%	0.31 (0.15-0.61)	0.04 (0.02-0.09)
Subset of [c] with bacterial STI diagnoses in previous year	9,625	-89%	0.75 (0.36-1.58)	0.08 (0.03-0.19)
Subset of [c] with rectal bacterial STI in previous year	2,430	-79%	1.22 (0.46-3.25)	0.26 (0.10-0.70)

HIV, human immunodeficiency virus; PYs, person years; GBMSM, gay and bisexual men who have sex with men;; SHS, sexual health services; UKHSA, UK Health Security Agency; STI, sexually transmitted infection; CI, confidence interval; PrEP, pre-exposure prophylaxis

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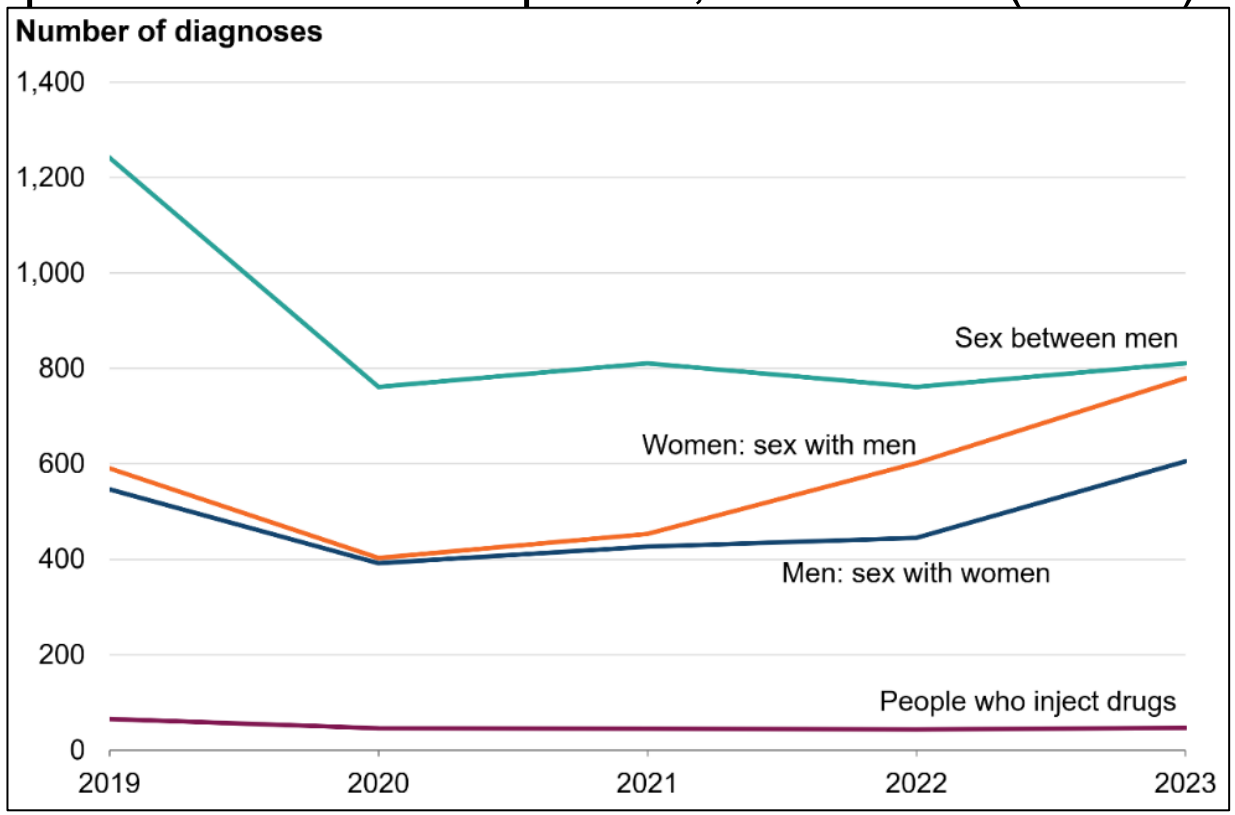
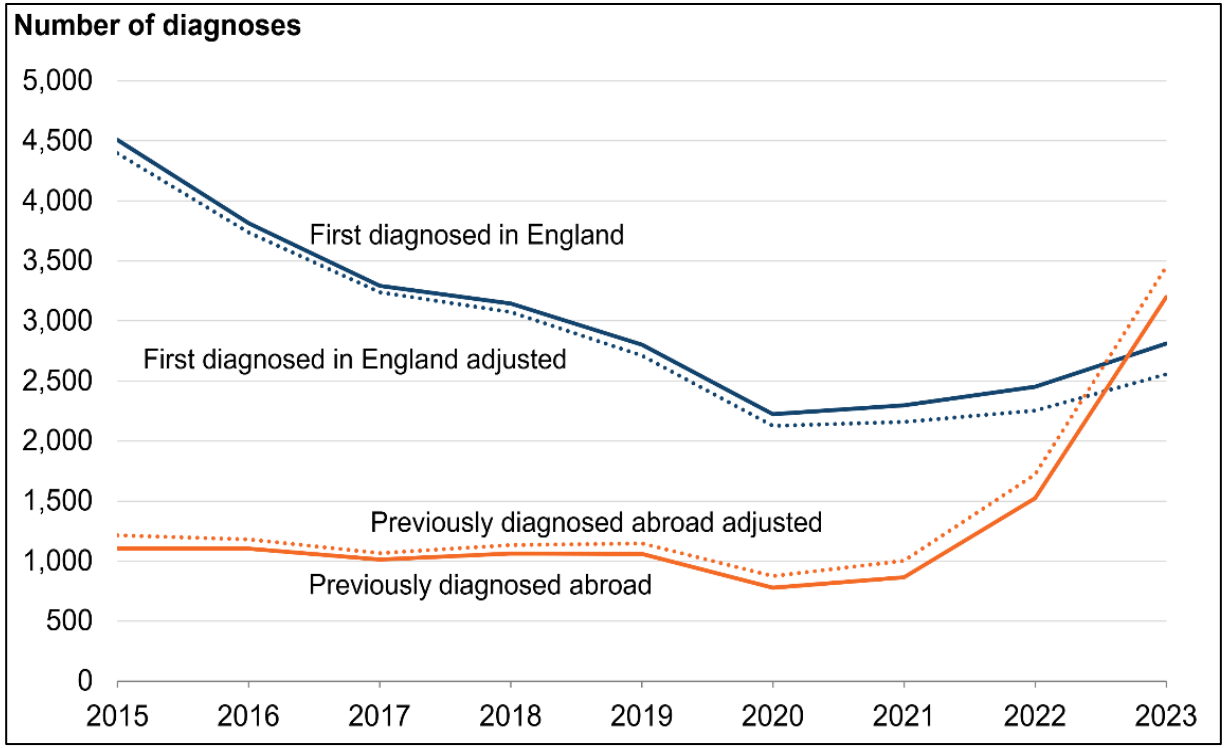
Key issue: Baseline risk of HIV acquisition

DSU - HARS data highlights that rise in recent HIV diagnoses is driven by exposure via sex between men and women, and people previously diagnosed abroad

New HIV diagnoses by gender identity and probable route of exposure, 2019-2023 (HARS)



New HIV diagnoses by country of diagnosis (including adjustments for misallocation), 2015-2023 (HARS)



HIV, human immunodeficiency virus; HARS; HIV and AIDS Reporting System GBMSM, gay and bisexual men who have sex with men;; SHS, sexual health services; UKHSA, UK Health Security Agency; STI, s

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Key issue: Baseline risk of HIV acquisition - CGW

UKHSA analysis

- Less current evidence for HIV incidence in women in England – incidence rates estimated as 0.03-0.05 per 100 PY in 2009-2013
  - Incidence in black African heterosexuals significantly higher – increased from 0.15 per 100 PY in 2009 to 0.19 per 100 PY in 2013)
- Total new HIV diagnoses made in England in women likely exposed through sex with men has remained stable – suggests HIV transmission in this group not declining

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What is the most plausible estimate of baseline HIV acquisition for CGW?

CGW, cisgender women; HIV, human immunodeficiency virus; PYs, person years; PrEP, pre-exposure prophylaxis; GUMCAD, Genitourinary Medicine Clinic Activity Dataset; BHIVA, British HIV Association; AIDS, acquired immunodeficiency syndrome; UKHSA, UK Health Security Agency; TDF/FTC, tenofovir disoproxil/emtricitabine; RCT, randomised controlled trial

Key issue: Population groups accessing cabotegravir

Underserved groups highlighted in stakeholder comments:

- Racially minoritised GBMSM
- People from trans and non-binary communities
- Women from Black African and other high-prevalence communities
- Migrants, people who inject drugs
- People who are homeless and/or and in unstable housing
- Those experiencing intimate partner violence

Key issues: Duration of risk period

EAG comments

- Acknowledges that 1 study showing over 40% of people discontinuing TDF/FTC at 12 months supports shorter risk period, but other company statements relating to 5-year risk period are based on extrapolations of this data
- Company cited studies examining persistence – relationship to risk is unclear
- Insufficient evidence and inconsistent expert opinion about duration of risk period

DSU analysis

- 2024 systematic review and meta-analysis → higher restarting of PrEP in studies in heterosexual populations vs MSM or TGW (aOR 1.50; 95%CI 1.25-1.81) – ~25% of people who stopped PrEP restarted (with wide variation by country and population)
- 2022 global systematic review and meta-analysis of oral PrEP→ among people who discontinued PrEP, nearly half (47.3%; 95%CI 31.5-63.2) reinitiated PrEP within 1 year of PrEP initiation
- Age stratified incidence estimates → do not show length of period at risk but can show whether risk is present across all age groups
- Ongoing risk may persist in high-risk groups → shown in study of women selling sex in Zimbabwe for 6-15 years (with risk of 2.1 per 100 PY) – DSU acknowledges lack of generalisability to wider population
- Evidence appears to support 10-year risk period more than 5-year period

RWE, real world evidence; PrEP, post exposure prophylaxis; TDF/FTC, tenofovir disoproxil/emtricitabine; MSM, men having sex with men; TGW, transgender women; PY, person years

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Updated efficacy data – injection phase only

Updated efficacy data with injection phase only further reduces risk of HIV acquisition

New HR estimates for HIV acquisition in revised company base case

Injection phase only – post hoc analysis of blinded study period	HPTN-083 (MSM/TGW)		HPTN-084 (CGW)	
	Cabotegravir	TDF/FTC	Cabotegravir	TDF/FTC
Number of HIV acquisitions	[redacted]	[redacted]	[redacted]	[redacted]
HR (95% CI)	[redacted]		[redacted]	

Indirect comparison % effectiveness for original submission and addendum

Indirect comparison % treatment effectiveness	Original submission	Addendum ([redacted])
Cabotegravir versus no PrEP (HPTN-083 population)	[redacted]	[redacted]
Cabotegravir versus no PrEP (HPTN-084 population)	[redacted]	[redacted]

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EAG: results presented in addendum for 'original submission' differ slightly to CS table 22 → reason is unclear

HR, hazard ratio; PrEP, pre-exposure prophylaxis; HIV, human immunodeficiency virus; MSM; men who have sex with men; TGW, transgender women; CGW, cisgender women

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Key issues: Persistence

Additional data presented from company on persistence

Persistence of cabotegravir [redacted] in individuals [redacted]

% Percentage of individuals persistent [redacted] with cabotegravir [redacted]

PrEP, post exposure prophylaxis; TDF/FTC, tenofovir disoproxil/ emtricitabine;

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Key issues: Persistence

Company (continued)

- Persistence studies cited by company include 6 studies from the USA (Mills 2024, Ramgopal 2024, Baker 2025, Traeger 2025, Pilgrim 2025, Altamirano 2023) and the ImPrEP study from Brazil (Grinsztejn 2025) – all studies except Baker 2025 reported as abstracts/posters only
- High rates of discontinuation of oral PrEP have been previously demonstrated in literature
- Company expert advisory board – [redacted]
- HIV treatment vs oral treatment options could be used
  - US based study (ABOVE) reported longer persistence in people living with HIV and receiving long-acting cabotegravir plus rilpivirine compared with oral antiretroviral therapy (274 vs 256 days, p<0.001)
- Increased persistence with injectable therapies vs oral therapies can be seen in other disease areas including type 2 diabetes and mental health conditions

Input from stakeholders (BHIVA, National AIDS Trust, clinical expert)

- Evidence from literature demonstrates that long-acting injectable PrEP would increase PrEP uptake and persistence
- US-based study (PILLAR) reported that 72% (144/201) of cabotegravir users remained on cabotegravir for 12 months with no HIV acquisition

PrEP, pre-exposure prophylaxis; HIV, human immunodeficiency virus

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Key issues: Persistence

EAG comments

- Evidence cited to support claims on persistence with cabotegravir is low in generalisability with short follow up – and persistence defined differently across studies
- Evidence on persistence of oral PrEP cited by company of data from French healthcare system (n=42,159) shows 80-90% of users renewing oral PrEP between semesters
  - EAG considers study reasonably representative of NHS population
- EAG has concerns about the appropriateness of using data from long-acting HIV treatment – ABOVE study has limited details available and does not report persistence as a proportion of people included in study
- EAG notes in company advisory board, [redacted]

Should an improvement in persistence be included in the model? If yes, what percentage improvement should be used?

PrEP, post exposure prophylaxis; HIV, human immunodeficiency virus

Other issues: Efficacy data without oral lead in

EAG comments on updated efficacy data

- Limited study details available from RWE study used to support injection-only analysis (published as abstract only) and generalisability of study to relevant UK population is unclear
- No information provided on current or anticipated use of the optional OLI in UK clinical practice – issue not raised at company advisory board
- Sub-optimal adherence to oral PrEP may not be linked to all HIV acquisitions – excluding people in the OLI phase may bias analysis
- When addendum inputs are applied to the previous version of the economic model there is a difference in cost effectiveness estimates

Is it appropriate to use the efficacy data without oral lead in for decision making?

PrEP, pre-exposure prophylaxis; HIV, human immunodeficiency virus; SmPC summary of product characteristics; OLI, oral lead in; RWE, real world evidence

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Equality considerations – ACM1

- HIV disproportionately affects: people of Black African family background; people of certain sexual orientation such as gay or bisexual men
- Key populations most at risk of HIV acquisition may be reluctant to engage in healthcare systems or to access sexual health services. Cultural concerns or stigma may exacerbate health inequity.
- Long-acting injections may not suit people who cannot easily access or schedule the necessary clinic appointments
- Long-acting injections may benefit some young people who struggle with managing oral therapies
- Acknowledged inequity of access to PrEP in the UK for cis-gender women
- Eligibility for key cabotegravir trials excluded current or planned pregnancy or breastfeeding status

Abbreviations: HIV, human immunodeficiency virus; PrEP, pre-exposure prophylaxis

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Equality considerations

Equality considerations raised during DG consultation

- If oral PrEP remains the sole option for women, this will reduce its acceptability and uptake among the most vulnerable, potentially leading to preventable new HIV transmissions
- For women with a PrEP need, the committee should consider the advantages of offering multiple administration routes in contraception and how these benefits could be applied to PrEP
- TAF/FTC is not licensed in CGW, creating inequity for women with contraindications to TDF/FTC
- UKHSA 2023 - only 40.9% of heterosexual and bisexual women with a PrEP need, initiated or continued PrEP
- Deepening inequality in HIV outcomes, with increasing rates being seen in key populations, such as Black women, whose needs are not currently being met with available oral PrEP regimens
    - Access to cabotegravir for PrEP is important to improve equity of access and to begin to address these disparities in outcomes for key populations.

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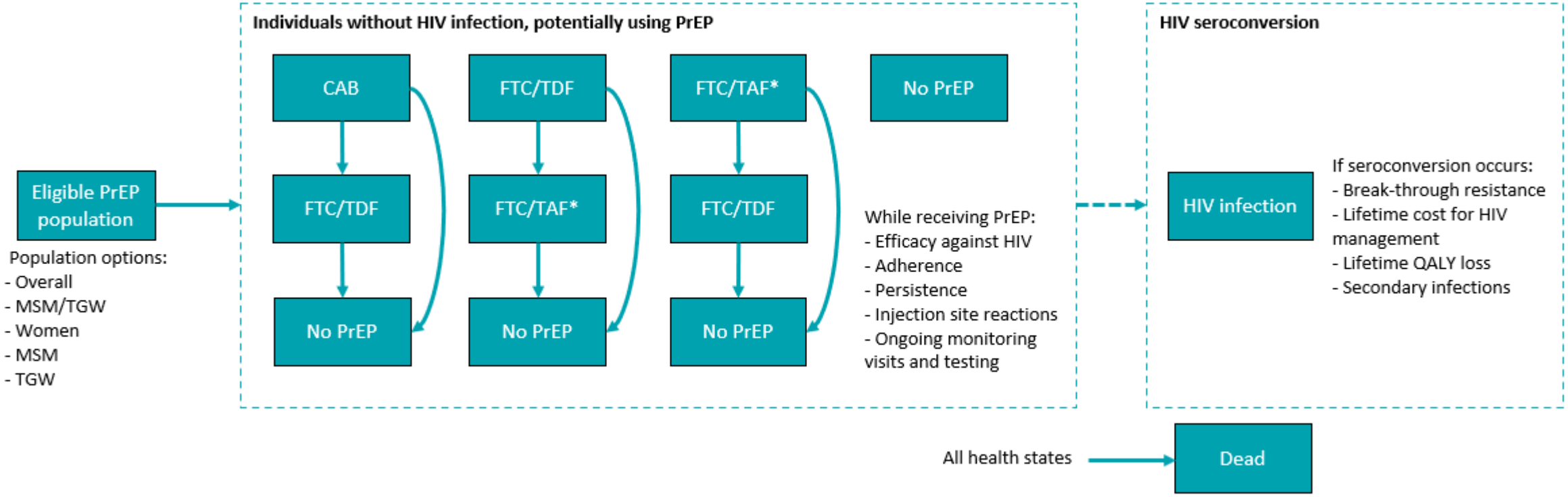
Abbreviations: ACM, appraisal committee meeting; CGW, cisgender women; HIV, human immunodeficiency virus; MSM, men who have sex with men; PrEP, pre-exposure prophylaxis; TAF/FTC, tenofovir alafenamide/emtricitabine; UKHSA, UK Health Security Agency

Company's model structure

Model structure

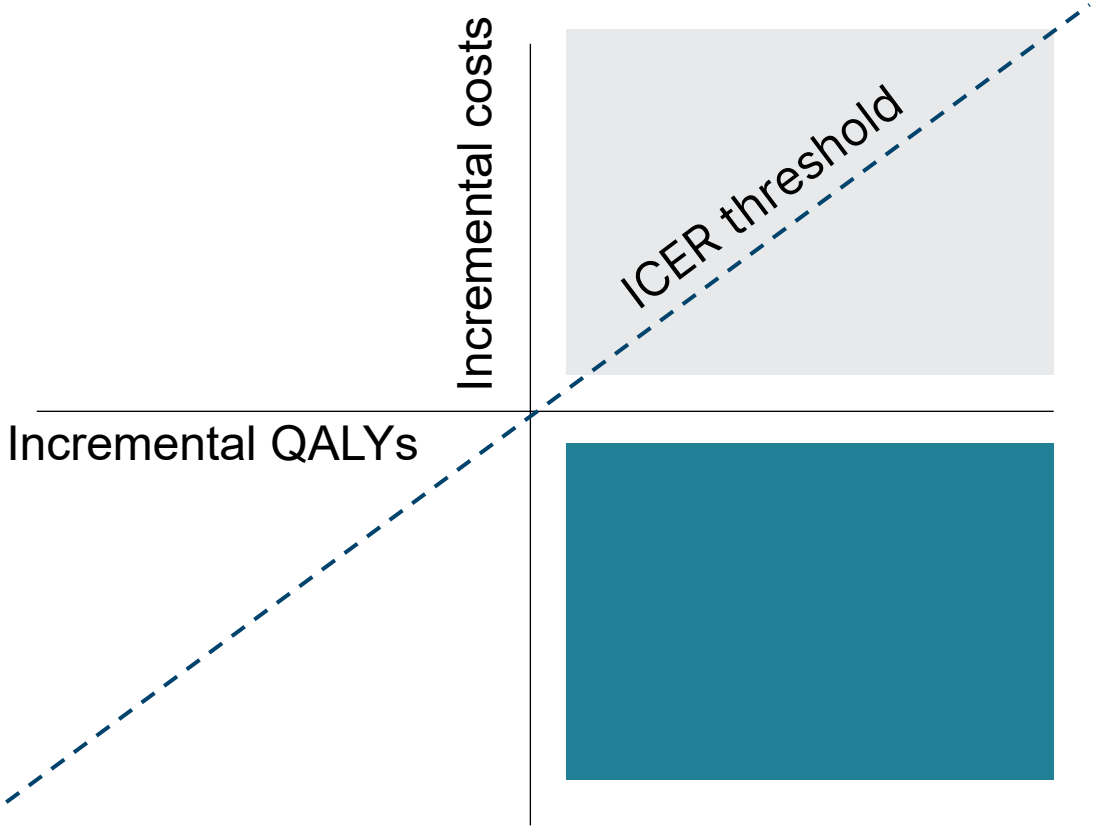


* FTC/TAF is only available for MSM and TGW subpopulations.

Abbreviations: CAB, cabotegravir; CGW, cisgender women; HIV, human immunodeficiency virus; MSM, men who have sex with men; PrEP, pre-exposure prophylaxis; FTC/ TAF, tenofovir alafenamide/emtricitabine; FTC/TDF, tenofovir disoproxil/emtricitabine; TGW, transgender women

Cost effectiveness - company and EAG base case

Exact cost effectiveness results are reported in part 2 due to confidential discounts for cabotegravir and TDF/FTC



EAG base case vs TDF/FTC and vs no PrEP:
Cabotegravir is more costly and generates more QALYs (ICERs >£30,000 per QALY gained)

Company base case vs TDF/FTC and vs no PrEP:
Cabotegravir is less costly and generates more QALYs

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Abbreviations: ICER, incremental cost-effectiveness ratio; PrEP, pre-exposure prophylaxis; QALY, quality-adjusted life year; TDF/FTC, tenofovir disoproxil/emtricitabine

Managed access

Company has not submitted a managed access proposal

The committee can make a recommendation with managed access if:

- the technology cannot be recommended for use because the evidence is too uncertain
- the technology has the **plausible potential** to be cost effective at the **currently agreed price**
- new evidence that could **sufficiently support the case for recommendation** is expected from ongoing or planned clinical trials, or could be collected from people having the technology in clinical practice
- data could feasibly be collected within a reasonable timeframe (up to a **maximum of 5 years**) without **undue burden**.