



UK Health
Security
Agency

Viral load of people living with HIV on effective anti-retroviral treatment (ART)

A rapid systematic review

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Main messages

1. This rapid systematic review (search up to 8 September 2025) identified and summarised evidence of variations in viral load in people living with human immunodeficiency virus (HIV) who were on stable anti-retroviral treatment (ART), and factors that may be related to those variations. Someone on stable ART was defined as having taken ART for at least 6 months and having had a viral load of less than 50 copies/mL for at least 6 months. The review included evidence of variation in viral load detected by different frequencies of testing and viral load levels over time.
2. Two randomised controlled trials (RCTs) ([1](#), [2](#)) and 4 cohort studies ([3 to 6](#)) were included.
3. Two studies compared different viral load testing frequencies ([2](#), [6](#)). A small proportion of people experienced a single viral load greater than 200 copies per millilitre (copies/mL) in both studies. In the RCT, no people reported 2 successive viral loads greater than 200 copies/mL in the 4-month testing group, but 2 out of 76 (2.6%) people in the 6-month testing group did (both had viral load levels greater than 1,000 copies/mL) ([2](#)). However, there were no significant differences in viral loads greater than or equal to 200 copies/mL (either single or 2 successive viral loads) between more frequent and less frequent viral load testing in either study.
4. Four studies reported viral load over time in people on stable ART, one RCT ([1](#)) and 3 cohort studies ([3 to 5](#)). The studies reported that among people on stable ART, most maintained viral load below 50 copies/mL throughout follow-up, regardless of whether they continued standard of care ART or switched to different regimens such as dual therapy or single-tablet options. Viral load greater than 200 copies/mL was only reported by one study ([1](#)).
5. Factors coinciding with a viral load greater than 200 copies/mL were only reported by one study ([1](#)) and related to one person out of 44 (2.2%) people who continued their stable ART. Factors included poor adherence to ART regimen and voluntary ART interruption. Viral load was reported to return to less than 50 copies/mL 12 weeks later after ART counselling. Studies that involved a change in ART reported some occurrences of viral loads above 50 copies/mL. These fluctuations may have been due to the change in ART, but this was not explored by these studies ([1](#), [3](#), [4](#)).
6. Risk of bias assessment highlighted that both RCTs were at moderate risk of bias. Allocation concealment and blinding of analysts were not reported in the RCTs. One RCT reported that a higher proportion of people in the 4-month (more frequent) testing group changed their ART regimen as compared to the 6-month (less frequent) testing group which could have introduced post randomisation bias affecting viral load levels ([2](#)).

7. The observational cohort studies were at moderate to high risk of bias due to limited adjustment for confounding factors, incomplete follow-up analysis, and inconsistent reporting of viral load measurement method.
8. In summary, the review looked for evidence on changes in viral load identified in people who were on stable ART (with viral loads less than 50 copies/mL for at least 6 months at the beginning of the study periods) and had viral load measured at 6 monthly intervals or less. The majority of people maintained viral loads less than 50 copies/mL throughout study follow-up periods. In the 2 studies reporting on testing frequencies, different testing frequencies did not identify significant differences in variations in viral load when comparing more frequent and less frequent viral load testing groups. There was limited information on factors contributing to viral loads greater than 200 copies/mL but one study reported poor adherence to ART and voluntary ART interruption as coinciding factors. The available evidence was limited in quantity and was at moderate to high risk of bias. This should be considered when interpreting the results, further evidence at low risk of bias may give a better estimate for the review question.

Purpose

The purpose of this rapid systematic review was to identify and summarise the available evidence that reported variations in viral load of people living with HIV who were on stable ART. In this review, stable ART was defined as having taken ART for at least 6 months and having had a viral load of less than 50 copies/mL for at least 6 months before beginning of the study period. Viral load had to be tested at a frequency of 6 monthly intervals or less. The rapid review also aimed to identify any evidence of factors that may contribute to variations in viral load.

The review questions were:

1. What is the viral load of people who are living with HIV on ART, measured at 6 monthly intervals or less?
2. What factors contribute to virological failure defined as a viral load greater than 200 copies/mL in people on ART?

The second review question was only explored in studies that answered the primary review question.

This rapid systematic review was commissioned to help inform an update of the UK Advisory Panel for Healthcare Workers Living with Bloodborne Viruses (UKAP) guidance.

Methods

A rapid systematic review was conducted, following streamlined systematic methods to accelerate the review process and provide a timely, evidence-informed answer to the review question without compromising the rigour of the review process.

A literature search was undertaken to look for relevant randomised controlled trials, quasi-experimental studies, cohort studies, and mixed methods studies, published since 2015 up to 8 September 2025. The search was limited to studies published since 2015, as guided by subject matter experts, because the latest British HIV Association (BHIVA) ART guidance was published in 2015 ([7](#)). Two databases were searched: Medline and Embase.

A protocol was produced before the literature search was conducted, including the review question, the eligibility criteria, and all other methods. Full details of the methodology are provided in the protocol in [Annexe A](#). There were no deviations from the protocol.

1. Population: adults (18 years old or over) on ART for at least 6 months, with a viral load less than 50 copies/mL for at least 6 months before the beginning of the study period. ART was defined as treatment for people living with HIV that used one or more drugs to suppress the virus and reduce the risk of transmission. ART regimens that were of interest for this review were specified by subject matter experts and are provided in [Annexe B](#).
2. Settings: studies conducted in European countries, Australia, Canada, New Zealand and United States were of interest for this review.
3. Intervention: viral load testing (less than 6 month intervals reporting in copies/mL or international units/mL, and follow-up for a minimum of 12 months) to detect fluctuations in viral load.
4. Comparator: different viral load testing frequencies, or no comparator. Studies without a comparator group were included if they reported viral load over time.
5. Outcome: viral load levels. UKAP cut-offs for viral load were used: less than 50 copies/mL, 50 to 199 copies/mL, greater than or equal to 200 to 1000 copies/mL, and greater than 1000 copies/mL ([8](#)). The secondary outcome of interest was factors coinciding with increased viral load (only extracted if studies had the primary outcomes).

Viral load was defined as the amount of HIV-RNA (ribonucleic acid) in a person's blood, reported in copies/mL or international units/mL. Viral suppression referred to reducing the amount of HIV viral load in the blood to very low or undetectable levels as a result of effective ART, indicating good treatment response and minimal risk of transmission. In this review, stable ART was defined as having taken ART for at least 6 months and having had a viral load of less than 50 copies/mL for at least 6 months.

Screening on title and abstract was undertaken in duplicate by 2 reviewers for 20% of the eligible studies, with the remainder completed by one reviewer. Screening on full text was undertaken by one reviewer and checked by a second. Data extraction was performed by one reviewer and checked by a second. Any disagreements were resolved through discussion. Studies reporting the natural history of viral load were included only if viral load testing was conducted at intervals of less than 6 months (for a minimum of 12 months) with at least one reported result within this interval.

Risk of bias assessment was conducted in duplicate by 2 reviewers. The JBI tools for randomised controlled trials and cohort studies were used for critical appraisal of included studies ([9](#)).

Evidence

In total, 2,833 studies were screened at title and abstract and 54 studies were screened at full text. Of these, 6 studies met the inclusion criteria. A PRISMA diagram showing the flow of studies through the review is shown in [Annexe C](#), and studies excluded on full text screening, along with the reasons for their exclusion are available in [Annexe D](#). Study characteristics are available in [Annex E](#), and risk of bias assessments are available in [Annexe F](#).

Viral load testing frequencies

There was one RCT and one cohort study comparing viral loads tested at different frequencies to identify variations in viral load.

Weissman and others conducted an RCT in the United States of America (USA) (time period not reported) comparing follow-up care for people with HIV at 4-month and 6-month testing intervals ([2](#)). A total of 142 people (71.8% males) were randomised to one of the 2 testing intervals: testing every 4 months (46.5%) or testing every 6 months (53.5%). The median age was approximately 46 years. People included in the study were adults who had been on ART and had an undetectable viral load (less than 50 copies/mL) for at least one year prior to enrolment in the study. Median length of viral suppression (viral loads less than 50 copies/mL through effective ART) period prior to enrolment was 51 months. Most people were on protease inhibitor-based regimens (4-month testing: 48.5%, 6-month testing: 44.7%), with others on non-nucleoside reverse transcriptase inhibitors-based (4-month testing: 18.2%, 6-month testing: 13.2%) or alternative regimens (4-month testing: 3.3% and 6-month testing: 42.1%). Specific drugs and dosage were not reported.

A small proportion of people experienced a single viral load greater than 200 copies/mL in both testing interval groups over the follow-up period (the median length of follow-up was 766 days in the 4-month testing group and 696 days in the 6-month testing group). Seven out of 66 people (10.6%) tested every 4 months and 5 out of 76 people (6.6%) tested every 6 months recorded a

single detectable viral load above 200 copies/mL. There was no significant difference between the testing groups (p value 0.39).

No people reported 2 successive viral loads greater than 200 copies/mL in the 4-month testing group. In the 6-month testing group, 2 successive viral loads greater than 200 copies/mL were observed in 2 people (2.6%) (both had viral load levels greater than 1000 copies/mL). The difference between groups was not statistically significant (p value 0.50). The first person in the 6-month testing group had a viral load of 2,207 copies/mL at 21 months post enrolment with a subsequent viral load of 204 copies/mL 6 months after. The second person had a viral load of 19,307 copies/mL at 7 months with a subsequent viral load of 17,198 copies/mL 7 months after. Factors coinciding with the increased viral load levels were not reported.

The authors reported that the study was underpowered (lacked enough participants to detect true differences between groups). The very low rates of increased viral loads (zero people reporting 2 successive viral loads greater than 200 copies/mL in the 4-month testing group and 2 people reporting 2 successive viral loads greater than 200 copies/mL in the 6-month testing group) may limit the ability to detect true differences between groups.

One prospective cohort study conducted in the USA between 1999 and 2013 reported on 573 adults (80.6% males, median age 46 years) on ART who had maintained plasma viral load levels of less than 50 copies/mL for at least 2 years (minimum of at least 3 tests per year) while receiving a stable combination ART (cART) regimen (6). The cART regimen included combinations of non-nucleoside reverse transcriptase inhibitors (NNRTIs), nucleoside reverse transcriptase inhibitors (NRTIs), protease inhibitors, enhancers and integrase inhibitors. Specific drugs and dosage within these classes were not reported.

Two hundred and fifty-two out of 573 people who had at least 3 viral load tests performed in the year after observation began (with at least 6 months between first and last) were classified as frequent testers, while 321 out of 573 people who had 2 viral load tests performed during the year after observation began were classified as less frequent testers (people with only one viral load were omitted from further analyses). Those with frequent testing and less frequent testing did not differ significantly by age, sex at birth, race or ethnicity, HIV risk category, AIDS status, lowest or baseline cluster of differentiation 4 (CD4) count, cART classification, history of smoking, or hepatitis C coinfection.

People were followed up for 2 years. Fifty-three frequent testers (21%) and 63 less frequent testers (19.6%) experienced at least one viral load greater than or equal to 200 copies/mL. However, the difference between testing interval groups was not significant (p value 0.71). Factors coinciding with increased viral load levels were not reported.

Critical appraisal of evidence on viral load testing frequencies

The RCT (2) was at moderate risk of bias. It was an un-blinded trial, however knowledge of group allocation was considered unlikely to affect people's viral load measurements. The study

did not explicitly report blinding of laboratory analysts. Lack of blinding of laboratory analysts may have influenced their interpretation of viral load measurements. The RCT reported that although the reasons for ART changes were similar between groups, a higher proportion of people in the 4-month testing group changed their ART regimen as compared to the 6-month testing group. This could have introduced post randomisation bias affecting viral load levels.

There were a number of concerns relating to risk of bias in the observational cohort study (6). The study reported that both groups were well balanced demographically, however, bias may have been introduced as people who were perceived as more adherent to ART may have had their viral load tested less frequently. The study could not assess the extent to which less frequent viral load monitoring was an intentional choice from clinicians, people missing their clinical appointments or peoples' preference. The study did not report any statistical methods to account for participants who dropped out or were lost during follow-up. In addition, the study did not report the specific laboratory test used to measure viral loads.

Viral load testing frequencies summary

Both the RCT and cohort study did not report significant differences in variations in viral load levels (either a single viral load greater than 200 copies/mL or 2 successive, viral loads greater than 200 copies/mL). More frequent viral load testing among people on stable ART did not affect detection of variation in viral load. The available evidence was limited in quantity and was at moderate to high risk of bias due to key details on randomisation and blinding being unclear in the RCT, and because differences in treatment changes between groups may have influenced results. The observational study also had some limitations, including possible bias in who received less frequent testing and missing information on follow-up and laboratory methods.

Viral load over time

There was one RCT and 3 cohort studies reporting viral load over time in people on ART. For the purposes of this review, we were interested in viral load over time and factors associated with increased viral loads only, and therefore only those results are presented below.

One RCT conducted in Spain between December 2018 and January 2021 evaluated people on ART with viral loads less than 50 copies/mL for at least 6 months (1). Eligible people were on at least 3 antiretroviral drugs and had evidence of results showing that the virus was resistant to at least 2 antiretroviral drug classes. The purpose of the RCT was to evaluate the effectiveness and the safety of dolutegravir plus darunavir/cobicistat as a once-daily treatment compared to continuation of current stable ART.

People included in the study had a median age of 55 years, with 76.4% males. Before the study started, 68.0% of people were on boosted darunavir (taken with other ART drugs) and 66.0% on integrase inhibitors, with 37.1% on twice-daily regimens and a median prior exposure to 13 antiretroviral drugs. Viral load was monitored at baseline, week 12, 24, 36, and 48.

A total of 89 people were randomised, with 44 (49.4%) assigned to continue their current stable ART and 45 (50.5%) assigned to switch to dual therapy with dolutegravir (50mg) and darunavir/cobicistat (800/150mg) once daily.

Baseline ART regimens in the current stable ART group included darunavir/cobicistat with raltegravir and etravirine or darunavir/cobicistat with emtricitabine/tenofovir alafenamide.

Three (6.7%) people in the dolutegravir plus darunavir/cobicistat group experienced a single viral load greater than or equal to 50 copies/mL during the follow-up period. No people in the dolutegravir plus darunavir/cobicistat group had a viral load greater than or equal to 50 copies/mL at 2 consecutive visits measured within 2 to 4 weeks. At week 48, 6 people in the dolutegravir plus darunavir/cobicistat group had no data: 3 due to discontinuation due to adverse events and 3 due to being lost to follow-up.

Five (11.4%) people in the group who continued their current stable ART experienced a single viral load measurement greater than or equal to 50 copies/mL during the follow-up period. Two people (4.5%) in the group who continued their current stable ART had detection of viral load greater than or equal to 50 copies/mL at 2 consecutive visits measured within 2 to 4 weeks. The first person recorded viral loads of 83 copies/mL and confirmed as 89 copies/mL at week 12. The second recorded viral loads of 74 copies/mL and confirmed 2,115 copies/mL at week 24. Changes in ART were not performed for either person. Factors coinciding with increased viral load levels for the second person were poor adherence to ART regimen (43%) and voluntary ART interruption at week 24. Re-suppression of HIV-1 (a viral load less than 50 copies/mL) was achieved by the second person at week 36 after ART counselling in the form of help and education to support adherence to ART.

Three cohort studies reported viral load over time in people on ART ([3 to 5](#)).

Charpentier and others conducted a single-centre cohort study in France between September 2012 and February 2013 including 116 adults (67% males, median age 43 years) on cART with viral loads less than 50 copies/mL for a median of 17 months ([3](#)). People were switched to a single-tablet regimen of tenofovir disoproxil fumarate, emtricitabine and rilpivirine (once daily). Viral load was monitored at baseline, week 4, 12, 24, 36 and 48 over a 96-week follow-up period.

Blood samples were available for 107 people at week 12, 86 people at week 24, 66 people at week 36, 81 people at week 48, 88 people at weeks 72 and 77 people at week 96. During follow-up, 17 people (15%) discontinued treatment due to adverse events. Most people maintained viral loads less than 50 copies/mL throughout the follow-up.

Viral load levels greater than 50 copies/mL were observed in 3 people at week 12 or 24. The first person reported a viral load of 60 copies/mL, the second reported a viral load of 70 copies/mL and the third reported a viral load of 75 copies/mL. All 3 people had viral loads of less than 50 copies/mL at the next test (within at least 12 weeks). No viral loads of greater than

200 copies/mL were reported, and no factors coinciding with increased viral load levels were identified.

Another prospective cohort study conducted by Charpentier and others in France between September 2014 and March 2016 reported on 239 adults (median age 51 years) on cART with viral loads less than 50 copies/mL for at least 6 months with varied genotypic susceptibility scores (which indicate how effective a person’s HIV medications are likely to be based on the virus’s past resistance) (4). People were grouped into 3 categories according to their genotypic susceptibility scores. Group 1 included people whose treatment mainly depended on a single fully active drug, dolutegravir [28 people (12%)]. Group 2 included people whose treatment involved 2 drugs with partial effectiveness [70 people (29%)]. Group 3 included people receiving 3 fully active drugs, representing the highest level of treatment effectiveness against the virus [141 people (59%)].

A total of 229 people out of 239 (96%) were switched to a dolutegravir-based regimen (50mg) once daily with one year of follow-up. This regimen was combined with abacavir/lamivudine, rilpivirine or tenofovir/emtricitabine depending on genotypic susceptibility. Full details of dolutegravir-based ART regimen associated drugs and sample size are reported in [Table D.2](#).

Viral load was measured at baseline, week 4, 12, 24, 36, and 48, with each person having at least 2 measurements within the first year. During follow-up, most people maintained viral loads less than 50 copies/mL. Between baseline and week 48, 20 people (8.4%) discontinued treatment due to adverse events.

Sixteen out of 239 (6.7%) recorded a single viral load greater than 50 but less than 1000 copies/mL that subsequently returned to less than 50 copies/mL at the next measurement. Four out of 235 people (1.7%) recorded viral loads between 50 and 200 copies/mL during 2 consecutive measurements. Information on viral load levels for 4 people with 2 consecutive viral load levels between 50 to 200 copies/mL is provided in [Table 1](#).

Table 1. Viral load levels in 4 people with 2 consecutive viral loads between 50 to 200 copies/mL

Person	ART regimen	Viral load at elevated measurement (copies/mL)	Viral load at subsequent measurement (copies/mL)
1	dolutegravir (50mg) + darunavir/ritonavir (800/100mg)	200 (week 48)	89 (week 60)
2	dolutegravir + abacavir + lamivudine (once daily) + darunavir/ritonavir (600/100mg twice daily)	91 (week 48)	84 (week 52)

Person	ART regimen	Viral load at elevated measurement (copies/mL)	Viral load at subsequent measurement (copies/mL)
3	dolutegravir (50mg once daily) + tenofovir disoproxil fumarate + emtricitabine	91 (week 4)	64 (week 8)
4	dolutegravir (50mg once daily) + abacavir + lamivudine	101 (week 24)	73 (week 30)

Possible reasons for the increased viral load levels (2 consecutive viral loads between 50 and 200 copies/mL) in the 4 people include: 2 people had lower than expected levels of their ART drugs (dolutegravir or darunavir) in their bloodstream, 2 had prior exposure to another ART drug (raltegravir), and some had old drug resistance changes that might have made the virus harder to treat. Three out of 4 people had the common type of HIV (subtype B), and one had a rare type that was a mix of 2 strains. Some people also had drug-to-drug interactions between their ART drugs and other medication.

Maggiolo and others conducted a prospective cohort study in Italy including 94 adults (77.7% males, median age 52 years) on stable cART for more than 6 months who had a viral load less than 50 copies/mL for at least 6 months prior to the study (5). All people were switched to dual therapy with lamivudine (50mg once daily) and dolutegravir (300mg once daily). Viral load was monitored at baseline, 2, 4, and 6 months, and subsequently every 3 to 4 months, over a median follow-up period of 17.4 months. During the 6 month follow-up, 3 people were admitted to hospital because of causes judged unrelated to cART. One person was lost to follow-up and 2 people died between the 6 month of therapy and the end of follow-up. All remaining people (91 out of 94) maintained viral loads less than 50 copies/mL at baseline, 2 months, 6 months and throughout follow-up.

Critical appraisal of evidence on viral load over time

The RCT (1) was at moderate risk of bias. It was an un-blinded trial, however knowledge of treatment received was considered unlikely to affect people's viral load measurements. Blinding of laboratory analysts was not reported. Lack of blinding of analysts may have influenced the interpretation of viral load measurements. The study reported that good ART adherence prior to the study was assumed and not measured. The study did not report the laboratory test used to measure viral load.

The cohort studies were at moderate to high risk of bias. One of the cohort studies did not report the laboratory test used to measure viral loads (5). Strategies to deal with confounding factors were not reported by 2 studies (3, 4). None of the cohort studies reported any statistical analyses to account for loss to follow-up.

Viral load over time summary

Across the one RCT and 3 cohort studies, viral load remained well controlled over time among people on stable ART. Most people maintained viral load below 50 copies/mL throughout follow-up, regardless of whether they continued standard of care ART or switched to simplified regimens such as dual therapy or single-tablet options. Some occurrences of viral load above 50 copies/mL were observed in a few people across 3 studies (1, 3, 4). Viral load greater than 200 copies/mL was only reported by one study (1). Higher viral load was linked to poor adherence to ART, voluntary ART interruption or drug-to-drug interactions. The evidence was at moderate to high risk of bias because blinding of analysts and laboratory tests for measurement of viral load were not reported in the RCT. The cohort studies had some limitations including minimal adjustment for confounding factors, inconsistent reporting of laboratory tests to measure viral load, and no analyses to address loss to follow-up.

Health inequalities

All the included studies focused on people who were on stable ART with viral load less than 50 copies/mL for at least 6 months. Only one RCT (2) reported participant recruitment from a clinical site, where most people were from racial and ethnic minority groups, had low income, and were under or not insured. The authors reported that limited access to care may lead HIV providers to act as primary care providers, potentially resulting in unintended negative health outcomes. One cohort study reported that it was conducted in well-established urban HIV specialty clinics, therefore, aspects of care, engagement in care, and laboratory monitoring might be different from less experienced HIV care environments (6).

None of the included studies specifically examined differences in outcomes by demographic or socio-economic factors such as age, sex, ethnicity, migration status or social deprivation. No studies reported on any other factors that could influence viral load monitoring or virological outcomes.

Limitations

This rapid systematic review used streamlined systematic methods to accelerate the review process. Sources of evidence searched included databases of peer-reviewed and preprint research, but an extensive search of other sources was not conducted, restrictions were made to the search strategy and most article screening was completed without duplication, so it is possible relevant evidence may have been missed. Three studies recruited people from a single clinical site and only one study reported factors contributing to viral load levels greater than 200 copies/mL in people on ART with viral loads measured at least less than 6 month intervals, limiting generalisability of findings.

Both RCTs (1, 2) were conducted using an open-label design in which people and intervention providers were unblinded (although this is unlikely to affect viral load outcomes). The RCTs did not explicitly state allocation concealment and whether the outcome assessors were blinded. Both RCTs had small sample sizes limiting generalisability to wider population of people on ART. Cohort studies lacked comparison with a control group except one (6) and none of them accounted for loss to follow-up statistically. Cohort studies also had significant heterogeneity in people characteristics (including reasons for switching ART, associated drugs), therefore viral load measurements were not available for all the people at all study time points. Only 2 out of the 6 studies reported the laboratory tests used to measure viral load (3, 4). Five out of the 6 included studies (1 to 5) switched people from their stable ART at the beginning of the study to a new ART regimen or dosage, which may have affected their viral load.

Evidence gaps

There was limited evidence on studies comparing different viral load testing frequencies with only one RCT (2) and one cohort study (6) identified. Only 2 studies reported on factors contributing to increased viral load levels (1, 4). All included studies were conducted either in Europe or North America, with no evidence identified from Australia, Canada and New Zealand.

Conclusion

In summary, the review documented evidence on variations in viral loads of people on stable ART who had viral loads less than 50 copies/mL for at least 6 months before the beginning of the study period. Viral load had to be measured at least less than 6 month intervals. Two studies compared different viral load testing frequencies to identify variations, and 4 studies reported viral load over time in people on ART. Most people maintained viral loads less than 50 copies/mL throughout study follow-up periods. Of the studies comparing different testing frequencies, one RCT reported that 2 out of 76 people (2.6%) in the 6-month testing group had 2 successive viral loads of greater than 200 copies/mL, while no people in the 4-month testing group had successive viral loads of greater than 200 copies/mL. The cohort study comparing viral loads levels in frequent testers and less frequent testers reported 53 frequent testers (21.0%), and 63 less frequent testers (19.6%) had at least one viral load greater than or equal to 200 copies/mL. Different testing frequencies did not lead to significant difference in detection of variations in viral load. Two out of the 4 studies reporting viral loads over time reported at least one viral load greater than or equal to 200 copies/mL.

Factors coinciding with increased viral load levels were reported by 2 studies, although only one study reported factors coinciding with viral loads greater than 200 copies/mL. Factors included poor adherence to ART regimen and voluntary ART interruption. However, it should be highlighted that the evidence was at moderate to high risk of bias and therefore may not provide a fully reliable indication of viral load levels in people on effective ART.

Acknowledgments

We would like to thank colleagues within the All Hazards Public Health Response division who either reviewed or input into aspects of the review.

Disclaimer

UKHSA's rapid systematic reviews and evidence summaries aim to provide the best available evidence to decision makers in a timely and accessible way, based on published peer-reviewed scientific papers, and papers on preprint servers. Note that the reviews:

- use accelerated methods and may not be representative of the whole body of evidence publicly available
- have undergone an internal independent peer review but not an external peer review
- are only valid as of the date stated on the review

In the event that this review is shared externally, note additionally, to the greatest extent possible under any applicable law, that UKHSA accepts no liability for any claim, loss or damage arising out of, or connected with the use of, this review by the recipient or any third party including that arising or resulting from any reliance placed on, or any conclusions drawn from, the review.

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Annexe A. Protocol

Review question

There are 2 review questions:

1. What is the viral load of people living with HIV who are on anti-retroviral treatment (ART), measured at 6 monthly intervals or less?
2. What factors contribute to virological failure defined as viral loads greater than 200 copies/mL in people on ART?

A search for primary evidence to answer this review question will be conducted up to 8 September 2025.

Eligibility criteria

Table A.1. Inclusion and exclusion criteria

	Included	Excluded
Population	Adults (18 years and above) living with HIV who: <ul style="list-style-type: none"> • are on ART see Annexe B, for at least 6 months [note 1] • have a viral load (less than 50 copies/mL) for at least 6 months 	<ul style="list-style-type: none"> • adults living with HIV who are able to maintain undetectable viral loads for at least 12 months despite not having started ART (elite controllers) • women starting ART at the time of pregnancy • people naïve to ART
Context	To inform guidance on monitoring healthcare workers on ART, but the review will not be limited to that population	
Settings	European countries, Australia, Canada, New Zealand and United States	Partial records (for example prison health if there is movement between provider)
Intervention or exposure	Testing intervals (less than 6 month intervals reporting in copies/mL or IU/mL, for a minimum of 12 months)	
Comparator	Different testing frequencies (viral load testing) Studies with no comparator but that report a natural history of viral load	

	Included	Excluded
Outcomes	<p>Primary outcomes:</p> <ul style="list-style-type: none"> viral load levels (UKAP cut offs): less than 50 copies/mL, 50 to 199 copies/mL, greater than or equal to 200 to 1000 copies/mL, greater than 1000 copies/mL (8) frequency of viral load testing (where no comparator) <p>Secondary outcome (to be extracted only from studies that report the primary outcome(s)):</p> <ul style="list-style-type: none"> factors [note 2] coinciding with viral load levels 	Dried blood spot tests measures of viral load
Language	English	Any other language
Date of publication	2015 to present	Studies published before 2015
Study design	<p>Experimental studies including randomised-controlled trials, quasi-experimental studies, cross-over designs</p> <p>Observational studies including cohort studies</p> <p>Mixed methods studies (quantitative group if they report viral load)</p>	<p>Reviews (all types)</p> <p>Descriptive studies including case series or case reports</p> <p>Qualitative studies</p> <p>Before and after studies</p> <p>Case control studies</p> <p>Cross sectional studies</p> <p>Modelling studies</p>
Publication type	Peer-reviewed published research	<p>Conference abstracts</p> <p>Editorials</p> <p>Letters</p> <p>News articles</p> <p>Grey literature</p> <p>Preprints</p>

Note 1: adults on long acting injectables will be reported as a sub-group.

Note 2: examples of factors include (non-exhaustive): adherence, high baseline viral load level, low CD4+ T- cell counts, demographics and clinical history.

Identification of studies

The following databases and trial registries will be searched for studies published up to 8 September 2025: Medline and Embase. The search strategy presented in [Search strategy below](#).

Screening

Title and abstract screening will be undertaken in duplicate by 2 reviewers for at least 20% of the eligible studies, with the remainder completed by one reviewer. Disagreement will be resolved by discussion or with involvement of a third reviewer where necessary.

Screening on full text will be undertaken by one reviewer and checked by a second.

Data extraction

Summary information for each study will be extracted and reported in tabular form. Information to be extracted will include:

- country
- study period
- study design
- study participants
- ART regimen
- monitoring frequency (testing intervals)
- viral load laboratory testing assay (test)
- viral load levels (less than 50 copies/mL, 50 to 199 copies/mL, greater than or equal to 200 to 1,000 copies/mL, greater than 1,000 copies/mL)
- length of raised viral load
- number of consecutive readings of raised viral load thresholds and time between them
- factors coinciding with viral load levels
- other relevant contextual data

Data extraction will be undertaken by one reviewer and checked by a second.

Risk of bias assessment

Two reviewers will independently complete a risk of bias assessment for included studies, with disagreements resolved by discussion or with a third reviewer. Primary studies will be assessed using the relevant JBI checklist ([9](#)).

Synthesis

Where studies are similar enough to combine and present data in a consistent format, a narrative synthesis will be produced to interpret the findings. The number of studies, the number of people in each study, effect size and variance and a summary of the risk of bias across studies reporting each outcome will be summarised and presented. Alternatively, if studies present methodological differences that would make synthesis inappropriate, a narrative summary of each study will be provided.

Health inequalities

No health inequalities relating to this question, separate from the specific topic area it covers will be assessed.

Search strategy

Ovid MEDLINE(R) ALL <1946 to 5 September 2025>

1. exp HIV/ (111,123)
2. exp HIV Infections/ (332,254)
3. hiv.tw,kf. (383,862)
4. (hiv-1 or hiv1).tw,kf. (89,301)
5. (hiv-2 or hiv2).tw,kf. (5,168)
6. (hiv adj3 (postiv* or seropositiv* or sero-positiv*)).tw,kf. (54,638)
7. human immunodeficiency virus*.tw,kf. (103,928)
8. human immunodeficiency virus*.tw,kf. (8)
9. human immuno-deficiency virus*.tw,kf. (318)
10. human immune-deficiency virus*.tw,kf. (546)
11. ((people or person* or population*) adj3 (living or live*) adj3 (HIV or AIDS)).tw,kf. (20,871)
12. PLWH.tw,kf. (5,285)
13. PLWHA.tw,kf. (1,332)
14. PLWHIV.tw,kf. (377)
15. (AIDS adj virus*).tw,kf. (1,137)
16. acquired immunodeficiency syndrome*.tw,kf. (21,478)
17. acquired immunodeficiency syndrome*.tw,kf. (13)
18. acquired immuno-deficiency syndrome*.tw,kf. (146)
19. acquired immune-deficiency syndrome*.tw,kf. (6,601)
20. or/1-19 (481,322)
21. exp Anti-Retroviral Agents/ (92,341)
22. Antiretroviral Therapy, Highly Active/ (22,931)
23. (antiretrovir* adj2 (therap* or treat* or drug* or medication* or agent* or regime*)).tw,kf. (73,727)

24. (anti-retrovir* adj2 (therap* or treat* or drug* or medication* or agent* or regime*)).tw,kf. (4,448)
25. ART.tw,kf. (192,135)
26. (NRTI* or NNRTI*).tw,kf. (6,231)
27. ((nucleoside or non-nucleoside or nonnucleoside) adj2 reverse transcriptase inhibitor*).tw,kf. (7,670)
28. exp HIV Integrase Inhibitors/ (3,304)
29. (integrase adj inhibit*).tw,kf. (2,584)
30. bictegravir.tw,kf. (599)
31. emtricitabine.tw,kf. (3,649)
32. tenofovir.tw,kf. (10,050)
33. efavirenz.tw,kf. (5,255)
34. darunavir*.tw,kf. (2,009)
35. lamivudine.tw,kf. (9,661)
36. abacavir.tw,kf. (2,548)
37. DRV*.tw,kf. (1,526)
38. atazanavir*.tw,kf. (1,992)
39. ATV*.tw,kf. (2,305)
40. raltegravir.tw,kf. (2,155)
41. rilpivirine.tw,kf. (1,271)
42. cobicistat.tw,kf. (772)
43. elvitegravir.tw,kf. (898)
44. dolutegravir.tw,kf. (2,713)
45. (anti-HIV adj2 (therap* or treat* or drug* or medic* or agent* or regime*)).tw,kf. (4,568)
46. or/21-45 (312,133)
47. (vir* adj2 (load* or burden* or titer* or titre* or concentrat*)).ab. /freq=3 (8,935)
48. (vir* adj failure*).ab. /freq=3 (842)
49. *Viral Load/ (7,150)
50. viral load.ti. (5,058)
51. or/47-50 (16,373)
52. 20 and 46 and 50 (5,887)
53. limit 51 to (comment or editorial or letter or news or newspaper article) 341)
54. 51 not 52 (5,546)
55. limit 54 to yr="2015 -Current" (2,838)

Embase <1974 to 4 September 2025>

1. exp Human immunodeficiency virus/ (232,973)
2. exp Human immunodeficiency virus infection/ (788,0430)
3. hiv.tw,kf. (512,357)
4. (hiv-1 or hiv1).tw,kf. (113,260)
5. (hiv-2 or hiv2).tw,kf. (6,461)
6. (hiv adj3 (positiv* or seropositiv* or sero-positiv*)).tw,kf. (72,385)
7. human immunodeficiency virus*.tw,kf. (118,625)

8. human immunodeficiency virus*.tw,kf. (35)
9. human immuno-deficiency virus*.tw,kf. (416)
10. human immune-deficiency virus*.tw,kf. (727)
11. ((people or person* or population*) adj3 (living or live*) adj3 (HIV or AIDS)). tw,kf. (27,824)
12. PLWH.tw,kf. (7,918)
13. PLWHA.tw,kf. (1,762)
14. PLWHIV.tw,kf. (627)
15. (AIDS adj virus*).tw,kf. (1,216)
16. acquired immunodeficiency syndrome*.tw,kf. (21,512)
17. acquired immunodeficiency syndrome*.tw,kf. (25)
18. acquired immuno-deficiency syndrome*.tw,kf. (201)
19. acquired immune-deficiency syndrome*.tw,kf. (7,733)
20. or/1-19 (992,248)
21. exp antiretrovirus agent/ (253,303)
22. exp highly active antiretroviral therapy/ (40,407)
23. (antiretrovir* adj2 (therap* or treat* or drug* or medication* or agent* or regime*)).tw,kf. (100,402)
24. (anti-retrovir* adj2 (therap* or treat* or drug* or medication* or agent* or regime*)).tw,kf. (7,406)
25. ART.tw,kf. (240,210)
26. (NRTI* or NNRTI*).tw,kf. (10,677)
27. ((nucleoside or non-nucleoside or nonnucleoside) adj2 reverse transcriptase inhibitor*).tw,kf. (10,153)
28. exp integrase inhibitor/ (21,682)
29. (integrase adj inhibit*).tw,kf. (4,363)
30. bictegavir.tw,kf. (1,249)
31. emtricitabine.tw,kf. (7,227)
32. tenofovir.tw,kf. (19,800)
33. efavirenz.tw,kf. (8,365)
34. darunavir*.tw,kf. (3,687)
35. lamivudine.tw,kf. (15,946)
36. abacavir.tw,kf. (4,160)
37. DRV*.tw,kf. (3,207)
38. atazanavir*.tw,kf. (3,428)
39. ATV*.tw,kf. (3,695)
40. raltegravir.tw,kf. (4,115)
41. rilpivirine.tw,kf. (2,434)
42. cobicistat.tw,kf. (1,622)
43. elvitegravir.tw,kf. (1,677)
44. dolutegravir.tw,kf. (4,934)
45. (anti-HIV adj2 (therap* or treat* or drug* or medic* or agent* or regime*)).tw,kf. (6,375)
46. or/21-45 (509,597)
47. (vir* adj2 (load* or burden* or titer* or titre* or concentrat*)).ab. /freq=3 (14,036)

48. (vir* adj failure*).ab. /freq=3 (1,284)
49. *virus load/ (8,783)
50. viral load.ti. (6,874)
51. or/47-50 (22,022)
52. 20 and 46 and 51 (7,713)
53. limit 52 to (conference abstract or conference paper or conference review or editorial or letter) (2,047)
54. 52 not 53 (5,666)
55. limit 54 to yr="2015 -Current" (2,648)

Annexe B. BHIVA recommendations for antiretroviral treatment

First-line ART and ART for suppressed switch or maintenance taken from Tables 5.1 and 5.2 of [BHIVA guidelines on antiretroviral treatment for adults living with HIV-1 2022 \(7\)](#)

- Bictegravir/emtricitabine/tenofovir AF
- Dolutegravir plus emtricitabine/tenofovir AF or emtricitabine/tenofovir DX
- Dolutegravir/lamivudine
- Dolutegravir/lamivudine/abacavir
- Darunavir plus cobicistat or ritonavir plus emtricitabine plus tenofovir AF or tenofovir DX
- Doravirine plus emtricitabine or lamivudine plus tenofovir AF or tenofovir DX
- Efavirenz plus emtricitabine or lamivudine plus abacavir or tenofovir AF or tenofovir DX
- Raltegravir plus emtricitabine plus tenofovir AF or tenofovir DX
- Tenofovir DX/emtricitabine or tenofovir AF/ emtricitabine or abacavir/lamivudine plus doravirine
- Tenofovir DX/emtricitabine or tenofovir AF/ emtricitabine or abacavir/lamivudine plus rilpivirine
- Tenofovir DX/emtricitabine or tenofovir AF/ emtricitabine or abacavir/lamivudine plus efavirenz
- Tenofovir DX/emtricitabine or tenofovir AF/ emtricitabine or abacavir/lamivudine plus nevirapine
- Tenofovir DX/emtricitabine or tenofovir AF/ emtricitabine or abacavir/lamivudine with dolutegravir
- Tenofovir AF/emtricitabine/bictegravir
- Tenofovir DX/emtricitabine/elvitegravir/cobicistat or tenofovir AF/emtricitabine/elvitegravir/ cobicistat
- Tenofovir DX/emtricitabine or tenofovir AF/ emtricitabine or abacavir/lamivudine with raltegravir
- Tenofovir DX/emtricitabine or tenofovir AF/ emtricitabine or abacavir/lamivudine with atazanavir/ritonavir or atazanavir/cobicistat
- Tenofovir DX/emtricitabine or tenofovir AF/ emtricitabine or abacavir/lamivudine with darunavir/ritonavir or darunavir/cobicistat
- Tenofovir DX/emtricitabine or tenofovir AF/ emtricitabine or abacavir/lamivudine with lopinavir/ritonavir
- Dolutegravir/lamivudine
- Dolutegravir/rilpivirine
- Cabotegravir plus rilpivirine injectable
- Raltegravir with darunavir/ritonavir or darunavir/cobicistat
- Dolutegravir with darunavir/ritonavir or darunavir/cobicistat

Viral load of people on effective anti-retroviral treatment (ART): a rapid systematic review

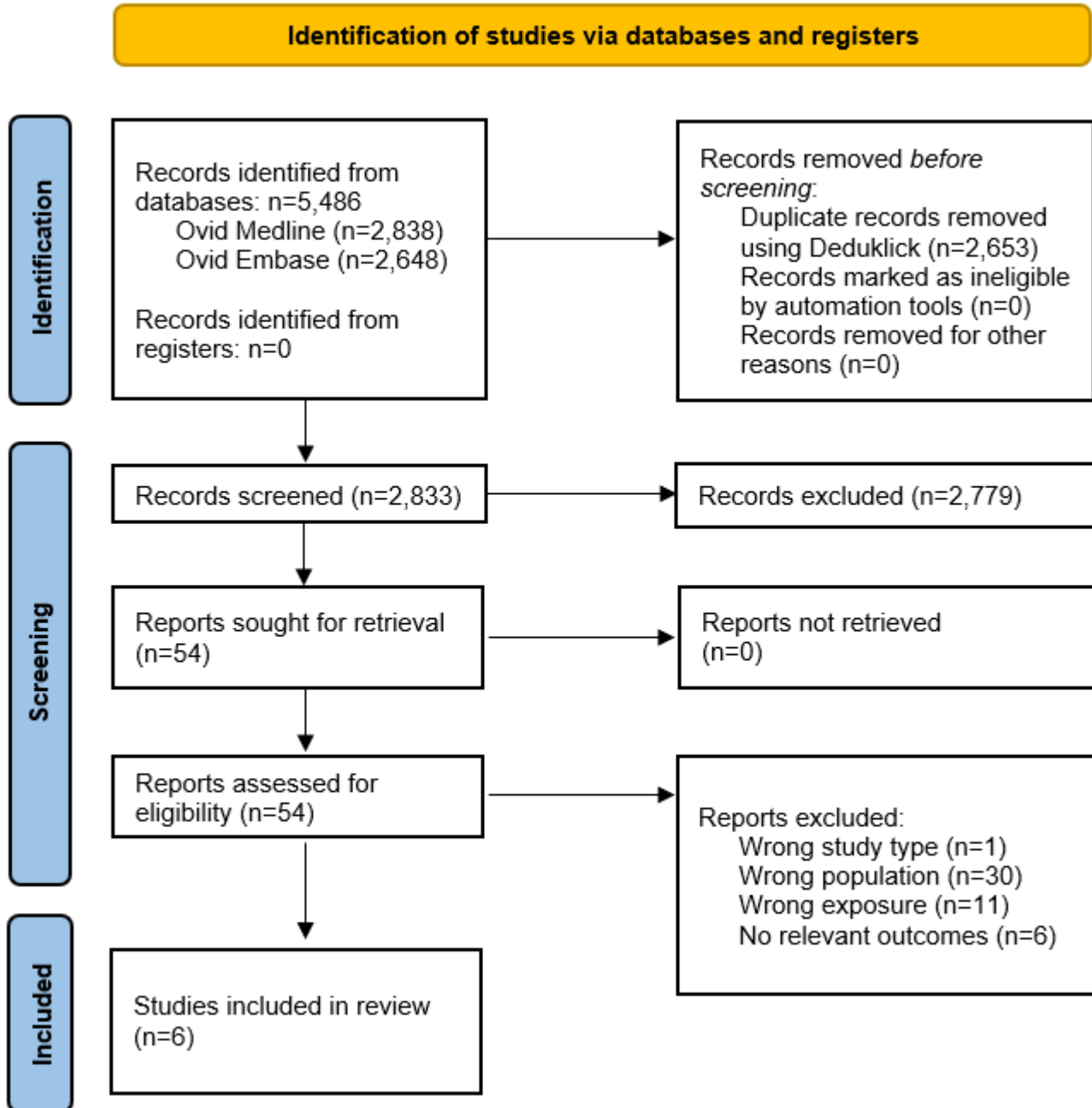
- Lamivudine or emtricitabine with darunavir/ritonavir or darunavir/cobicistat or atazanavir/ritonavir or atazanavir/cobicistat or lopinavir/ritonavir

Though not recommended routinely, there are some agents that may be used based on a need to deliver ART parenterally or an inability to otherwise create a suppressive regimen:

- Zidovudine
- Etravirine
- Maraviroc
- Enfuvirtide
- Fostemsavir
- Ibalizumab

Annexe C. Study selection flowchart

Figure C.1. PRISMA diagram



Text version of Figure C.1. PRISMA diagram

A PRISMA diagram showing the flow of studies through this review, ultimately including 6 studies.

From identification of studies via databases and registers, n=5,486 records identified from databases:

- Ovid Medline (n=2,838)
- Ovid Embase (n=2,648)

From these, records removed before screening:

- duplicate records removed using Deduplicator (n=2,653)
- duplicate records removed manually (n=0)
- records marked as ineligible by automation tools (n=0)
- records removed for other reasons (n=0)

n=2,833 records screened, of which n=2,779 were excluded, leaving n=54 papers sought for retrieval, of which n=0 was not retrieved.

No studies were identified from identification of studies via other methods: n=0 studies were identified from expert consultation.

Of the n=54 papers assessed for eligibility, n=48 reports were excluded:

- wrong study type (n=1)
- wrong population (n=30)
- wrong exposure (n=11)
- no relevant outcomes (n=6)

n=6 papers included in the review.

Annexe D. Excluded full texts

Wrong study type (1 study)

Huntington S and others. ['The risk of viral rebound in the year after delivery in women remaining on antiretroviral therapy'](#) AIDS (London, England) 2015: volume 29, issue 17, pages 2,269 to 2,278

Wrong population (30 studies)

Adams JL and others. ['Comparative effectiveness of antiretroviral drug classes for the treatment of HIV infection in patients with high viral loads: a multicentre retrospective cohort study'](#) HIV Medicine 2021: volume 22, issue 1, pages 28 to 36

Benator Debra A and others. ['True durability: HIV virologic suppression in an urban clinic and implications for timing of intensive adherence efforts and viral load monitoring'](#) AIDS and Behavior 2015: volume 19, issue 4, pages 594 to 600

Bogdanic N and others. ['Timeliness of antiretroviral therapy initiation in the era before universal treatment'](#) Scientific Reports 2021: volume 11, issue 1, article number 10508

Caniglia Ellen C and others. ['Comparison of dynamic monitoring strategies based on CD4 cell counts in virally suppressed, HIV-positive individuals on combination antiretroviral therapy in high-income countries: a prospective, observational study'](#) The Lancet. HIV 2017: volume 4, issue 6, pages e251 to e259

Castagna A and others. ['Analytical treatment interruption in chronic HIV-1 infection: time and magnitude of viral rebound in adults with 10 years of undetectable viral load and low HIV-DNA \(APACHE study\)'](#) The Journal of Antimicrobial Chemotherapy 2019: volume 74, issue 7, pages 2,039 to 2,046

Chahine Elias B and others. ['Comparing Safety and Effectiveness of Antiretroviral Therapy in a Diverse Population of Older People With HIV'](#) The Senior Care Pharmacist 2023: volume 38, issue 11, pages 472 to 485

Charuratananon S and others. ['Rate of and predicting factors for virologic failure in HIV-infected patients with persistent low-level viremia under antiretroviral therapy'](#) Journal of the International Association of Providers of AIDS Care 2015: volume 14, issue 1, pages 12 to 16

Chen G-J and others. ['Incidence and impact of low-level viremia among people living with HIV who received protease inhibitor- or dolutegravir-based antiretroviral therapy'](#) International

Journal of Infectious Diseases: IJID: Official Publication of the International Society for Infectious Diseases 2021: volume 105, pages 147 to 151

Davy-Mendez T and others. '[Effectiveness of integrase strand transfer inhibitors among treatment-experienced patients in a clinical setting](#)' AIDS (London, England) 2019: volume 33, issue 7, pages 1,187 to 1,195

De Luca A and others. '[Clinical use, efficacy, and durability of maraviroc for antiretroviral therapy in routine care: A European survey](#)' PLOS One 2019: volume 14, issue 11, e0225381

Dell'Acqua R and others. '[Viro-immunological outcomes after 13-valent pneumococcal vaccination in HIV-1-infected individuals on stable virological suppression](#)' AIDS (London, England) 2019: volume 33, issue 13, pages 1,987 to 1,994

El Bouzidi K and others. '[First-line HIV treatment outcomes following the introduction of integrase inhibitors in UK guidelines](#)' AIDS (London, England) 2020: volume 34, issue 12, pages 1,823 to 1,831

Elvstam O and others. '[Virological failure and all-cause mortality in HIV-positive adults with low-level viremia during antiretroviral treatment](#)' PLOS One 2017: volume 12, issue 7, e0180761

Ferrer E and others. '[Clinical progression of severely immunosuppressed HIV-infected patients depends on virological and immunological improvement irrespective of baseline status](#)' The Journal of Antimicrobial Chemotherapy 2015: volume 70, issue 12, pages 3,332 to 3,338

Girerd-Genessay I and others. '[Higher HIV RNA Viral Load in Recent Patients with Symptomatic Acute HIV Infection in Lyon University Hospitals](#)' PLOS One 2016: volume 11, issue 1, e0146978

Gubavu C and others. '[Dolutegravir-based monotherapy or dual therapy maintains a high proportion of viral suppression even in highly experienced HIV-1-infected patients](#)' The Journal of Antimicrobial Chemotherapy 2016: volume 71, issue 4, pages 1,046 to 1,050

Hickey Matthew D and others. '[Viral Suppression Rates at 48 Weeks in People With HIV Starting Long-Acting Cabotegravir/Rilpivirine With Initial Viremia](#)' Clinical Infectious Diseases: An Official Publication of the Infectious Diseases Society of America 2025: volume 80, issue 4, pages 864 to 870

Lesosky M and others. '[Bias in the estimation of cumulative viremia in cohort studies of HIV-infected individuals](#)' Annals of Epidemiology 2019: volume 38, pages 22 to 27

Lodi S and others. '[Comparative effectiveness of immediate antiretroviral therapy versus CD4-based initiation in HIV-positive individuals in high-income countries: observational cohort study](#)' The Lancet. HIV 2015: volume 2, issue 8, pages e335 to e343

McKellar Mehri S and others. '[Rapid viral suppression using integrase inhibitors during acute HIV-1 infection](#)' The Journal of Antimicrobial Chemotherapy 2025: volume 80, issue 1, pages 169 to 174

Nunez I and others. '[Comparative Effectiveness of Switching to Bictegravir From Dolutegravir-, Efavirenz-, or Raltegravir-Based Antiretroviral Therapy Among Individuals With HIV Who are Virologically Suppressed](#)' Open Forum Infectious Diseases 2024: volume 11, issue 8, ofae446

Orkin C and others. '[Efficacy and safety of switching from boosted protease inhibitors plus emtricitabine and tenofovir disoproxil fumarate regimens to single-tablet darunavir, cobicistat, emtricitabine, and tenofovir alafenamide at 48 weeks in adults with virologically suppressed HIV-1 \(EMERALD\): a phase 3, randomised, non-inferiority trial](#)' The Lancet. HIV 2018: volume 5, issue 1, pages e23 to e34

Orrell C and others. '[Fixed-dose combination dolutegravir, abacavir, and lamivudine versus ritonavir-boosted atazanavir plus tenofovir disoproxil fumarate and emtricitabine in previously untreated women with HIV-1 infection \(ARIA\): week 48 results from a randomised, open-label, non-inferiority, phase 3b study](#)' The Lancet. HIV 2017: volume 4, issue 12, pages e536 to e546

Palella Frank J and others. '[HIV viral exposure and mortality in a multicenter ambulatory HIV adult cohort, United States, 1995-2016](#)' Medicine 2021: volume 100, issue 25, e26285

Palmer A and others. '[Viral suppression and viral rebound among young adults living with HIV in Canada](#)' Medicine 2018: volume 97, issue 22, e10562

Pernas B and others. '[Long-term clinical experience with darunavir \(2007-2015\) in a large cohort of HIV-infected patients in Spain](#)' Journal of Medical Virology 2016: volume 88, issue 12, pages 2,125 to 2,131

Rolle C-P and others. '[Clinical outcomes of once-daily darunavir in treatment-experienced patients with darunavir resistance-associated mutations through 48 weeks of treatment](#)' International Journal of STD and AIDS 2020: volume 31, issue 10, pages 958 to 966

Sension Michael G and others. '[Cabotegravir + Rilpivirine Long-Acting Injections for HIV Treatment in the US: Real World Data from the OPERA Cohort](#)' Infectious Diseases and Therapy 2023: volume 12, issue 12, pages 2,807 to 2,817

Sterrantino G and others. '[Darunavir-based dual therapy of treatment-experienced HIV-infected patients: analysis from a national multicenter database](#)' Infection 2015: volume 43, issue 3, pages 339 to 343

Vandenhende M-A and others. '[Impact of low-level viremia on clinical and virological outcomes in treated HIV-1-infected patients](#)' AIDS (London, England) 2015: volume 29, issue 3, pages 373 to 383

Wrong exposure (11 studies)

Calcagno A and others. '[HIV-1 Very Low Level Viremia Is Associated with Virological Failure in Highly Active Antiretroviral Treatment-Treated Patients](#)' AIDS Research and Human Retroviruses 2015: volume 31, issue 10, pages 999 to 1,008

De Castro N and others. '[Safety and efficacy of switching to elvitegravir, cobicistat, emtricitabine, tenofovir disoproxil fumarate in treatment-experienced people with HIV: a multicenter cohort study](#)' AIDS Research and Therapy 2023: volume 20, issue 1, page 1

Katlama C and others. '[Dolutegravir as monotherapy in HIV-1-infected individuals with suppressed HIV viraemia](#)' The Journal of Antimicrobial Chemotherapy 2016: volume 71, issue 9, pages 2,646 to 2,650

Morsica G and others. '[Risk of HIV viral rebound in HIV infected patients on direct acting antivirals \(DAAs\) treatment for HCV](#)' PLOS One 2022: volume 17, issue 2, e0262917

Nasreddine R and others. '[Effectiveness of dolutegravir-based antiretroviral therapy in a real-world setting in a Belgian cohort of 4101 HIV patients](#)' AIDS (London, England) 2020: volume 34, issue 8, pages 1,151 to 1,159

Pierone G and others. '[Switching to Dolutegravir/Lamivudine Two-Drug Regimen: Durability and Virologic Outcomes by Age, Sex, and Race in Routine US Clinical Care](#)' HIV/AIDS (Auckland, N.Z.) 2024: volume 16, pages 133 to 140

Serris A and others. '[Real-world data on long-acting intramuscular maintenance therapy with cabotegravir and rilpivirine mirror Phase 3 results](#)' The Journal of Antimicrobial Chemotherapy 2024: volume 79, issue 11, pages 2,932 to 2,938

Spampinato S and others. '[Enhanced metabolic health and immune response with bictegravir/emtricitabine/TAF: Insights from a 96-week retrospective study](#)' Biomedical Reports 2024: volume 21, issue 6, page 179

Swift E and others. '[Impact of omission of routine blood monitoring of stable patients living with HIV during the coronavirus pandemic](#)' HIV Medicine 2024: volume 25, issue 11, pages 1,253 to 1,258

Trottier B and others. '[Removing inactive NRTIs in a salvage regimen is safe, maintains virological suppression and reduces treatment costs: results from the VERITAS study \(TMC114HIV4054\)](#)' HIV Clinical Trials 2015: volume 16, issue 3, pages 111 to 116

Wijting I and others. '[Dolutegravir as maintenance monotherapy for HIV \(DOMONO\): a phase 2, randomised non-inferiority trial](#)' The Lancet. HIV 2017: volume 4, issue 12, pages e547 to e554

No relevant outcomes (6 studies)

Bellagamba R and others. '[Randomized clinical trial on efficacy of fixed-dose efavirenz/tenofovir/emtricitabine on alternate days versus continuous treatment](#)' AIDS (London, England) 2019: volume 33, issue 3, pages 493 to 502

Calza L and others. '[Efficacy and Safety of Switching to Dolutegravir/Lamivudine in Virologically Suppressed People Living with HIV-1 Aged Over 65 Years](#)' AIDS Research and Human Retroviruses 2024: volume 40, issue 2, pages 73 to 79

Jaeger H and others. '[Long-acting cabotegravir and rilpivirine dosed every 2 months in adults with HIV-1 infection \(ATLAS-2M\), 96-week results: a randomised, multicentre, open-label, phase 3b, non-inferiority study](#)' The Lancet. HIV 2021: volume 8, issue 11, pages e679 to e689

Joya C and others. '[Persistent Low-level Viremia While on Antiretroviral Therapy Is an Independent Risk Factor for Virologic Failure](#)' Clinical Infectious Diseases: An Official Publication of the Infectious Diseases Society of America 2019: volume 69, issue 12, pages 2,145 to 2,152

Seang S and others. '[Darunavir/ritonavir monotherapy at a low dose \(600/100 mg/day\) in HIV-1-infected individuals with suppressed HIV viraemia](#)' The Journal of Antimicrobial Chemotherapy 2018: volume 73, issue 2, pages 490 to 493

Teira R and others. '[Very low level viraemia and risk of virological failure in treated HIV-1-infected patients](#)' HIV Medicine 2017: volume 18, issue 3, pages 196 to 203

Annexe E. Data extraction tables

Table D.1 Studies comparing different viral load testing frequencies

Abbreviations: 3TC: lamivudine, AIDS: acquired immunodeficiency syndrome, ART: Antiretroviral therapy, ATV: atazanavir, cART: combination antiretroviral therapy, CNS: Central Nervous System, DB: database, DRM: drug resistance mutation, DRV: darunavir, DRV/c: darunavir/cobicistat, DRV/r: darunavir/ritonavir, DTG: dolutegravir, EFV: efavirenz, ETR: etravirine, FTC: emtricitabine, GSS: genotypic susceptibility score, HBV: hepatitis B virus, HCV: hepatitis C virus, HOPS: HIV Outpatient Study, IDU: injection drug use, INI: integrase inhibitor, INSTI: integrase strand transfer inhibitor, INT: integrase inhibitor, IQR: interquartile range, ITT: intention-to-treat, LPV: lopinavir, LPV/r: lopinavir/ritonavir, MVC: maraviroc, NNRTI: Non-nucleoside reverse transcriptase inhibitors, NRTI: nucleoside reverse transcriptase inhibitors, NVP: nevirapine, PI: protease inhibitor, PP: per-protocol, RAL: raltegravir, SD: standard deviation, SOC: standard of care, STR: single-tablet regimen, TAF: tenofovir alafenamide, TDF: tenofovir disoproxil fumarate, USA: United States of America, VL: Viral Load, ZDV: zidovudine

Study	Country, Study period	Study type	Participants	ART regimen and dose (study ART only)	ART regimen and dose (pre-switch and rationale for switch)	Monitoring frequency (testing intervals) and follow-up period	Viral load levels	Length of raised VL	Consecutive readings of raised VL readings and interval	Factors coinciding with VL levels
Weissman S and others 2016 (2)	USA, time period not reported	Randomised Controlled Trial	Participants aged at least 18 years at enrolment in an HIV clinic in South Carolina on ART, and an undetectable HIV viral load <50 copies/mL (as confirmed by study author) by an ultrasensitive assay for at least 1 year Sample size: Total: 142 4-months group: 66 6-months group: 76 Median Age: 4-months group: 45.8 years (SD 10.1) 6-months group: 46.0 years (SD	ART regimen: NNRTI: 4-months group: 12 out of 66 (18.2%) 6-months group: 10 out of 76 (13.2%) PI: 4-months group: 32 out of 66 (48.5%) 6-months group: 34 out of 76 (44.7%) Other: 4-months group: 22 out of 66 (33.3%) 6-months group: 32 out of 76 (42.1%) Note: names of exact regimens not mentioned rather only drug classes mentioned but protease inhibitors	Other NNRTI, PI and other regimens NNRTI: 4-months group: 12 out of 66 (18.2%) 6-months group: 10 out of 76 (13.2%) PI: 4-months group: 32 out of 66 (48.5%) 6-months group: 34 out of 76 (44.7%) Other: 4-months group: 22 out of 66 (33.3%) 6-months group: 32 out of 76 (42.1%) Rationale for switching ART: Detectable viral load: 4-month group: 1 out of 66 (1.5%)	4 months versus 6 months intervals for standard HIV care and laboratory monitoring Follow-up period: 4-months group: 766 days 6-months group: 696 days	Single detectable VL >200 copies/mL: 4-months group: 7 out of 66 (10.6 %) 6-months group: 5 out of 76 (6.6 %) p value 0.39 Two successive VL >200 copies/mL (in this case, VL>1000 copies/mL): 4-months group: 0 out of 76 (0.0%)	Not reported	VL>200copies/mL in the 6-months group: Person 1: 2,207 copies/mL at 21 months post enrolment with a subsequent VL 6 months later at 204 copies/mL Person 2: Viral load of 19,307 copies/mL at 7 months with a subsequent VL of 17,198 copies/mL after 7 months	Not reported

Study	Country, Study period	Study type	Participants	ART regimen and dose (study ART only)	ART regimen and dose (pre-switch and rationale for switch)	Monitoring frequency (testing intervals) and follow-up period	Viral load levels	Length of raised VL	Consecutive readings of raised VL readings and interval	Factors coinciding with VL levels
			<p>11.2)</p> <p>Sex: Total: Male: 102 out of 142 (71.8%), Female/other: 40 out of 142 (28.2%)</p> <p>4-months group: Males: 44 out of 66 (66.7%), Female/other: 22 out of 66 (33.3%)</p> <p>6-months group: Males: 58 out of 76 (76.3%), Female/other: 18 out of 76 (23.7%)</p> <p>Medical history:</p> <p>4-months group: Any comorbid conditions: 55 out of 66 (83.3%)</p> <p>Transfusion: 2 out of 66 (3.0%)</p> <p>IDU: 1 out of 66 (1.5%)</p> <p>6-months group: Any comorbid conditions: 65 out of 76 (85.5%)</p>	(PIs) were most frequent regimen	<p>6-months group: 3 out of 76 (3.9%)</p> <p>Adverse drug reaction: 4-months group: 2 out of 66 (3%) 6-months group: 12 out of 76 (1.3%)</p> <p>Non-adherence: 4-months group: 1 out of 66 (1.5%) 6-months group: 1 out of 76 (1.3%)</p> <p>Other: 4-months group: 22 out of 66 (33.3%) 6-months group: 9 out of 76 (11.8%)</p>		<p>6-months group: 2 out of 76 (2.6%) p value 0.50</p>			

Study	Country, Study period	Study type	Participants	ART regimen and dose (study ART only)	ART regimen and dose (pre-switch and rationale for switch)	Monitoring frequency (testing intervals) and follow-up period	Viral load levels	Length of raised VL	Consecutive readings of raised VL readings and interval	Factors coinciding with VL levels
			transfusion: 1 out of 76 (1.3%) IDU: 3 out of 76 (3.9%)							
Young B and others 2015 (6)	USA, 1999 to 2013	Prospective cohort study	<p>People enrolled in HOPS who had suppressed plasma HIV VLs (<50 copies/mL) for at least 2 years and were prescribed a stable, non-salvage cART regimen outside a research clinical trial for the same 2-year period</p> <p>Sample size: 573</p> <p>Median age: 46.1 years (IQR 39.9 to 53.5 years)</p> <p>Sex: Male: 462 out of 573 (80.6%) Female/other: 111 out of 573 (20.4%)</p> <p>Medical history: Diagnosis of hepatitis C co-infection: 107 out of 573 (18.6%)</p> <p>Smoking tobacco: 265 out of 573 (46.2%)</p>	<p>Stable, non-salvage cART for ≥ 2 years:</p> <p>≥3 NRTIs: 22 out of 573 (3.8%)</p> <p>INT + NRTIs: 18 out of 573 (3.1%)</p> <p>NNRTI + NRTIs: 304 out of 573 (53.1%)</p> <p>NNRTI + PI + NRTIs: 11 out of 753 (1.9%)</p> <p>PI + enhancers + NRTIs: 104 out of 573 (18.2%)</p> <p>PI + NRTIs: 114 out of 573 (19.9%)</p> <p>Note: Specific drug doses not reported</p>	Not reported	<p>Every 3 to 4 months</p> <p>[Required ≥3VL with first and last ≥6 months apart (specifically, every 3 to 4 months)]</p> <p>Follow-up period: 2 years</p>	<p>≥200copies/mL : 116 (20%)</p> <p>Patients over 2 years frequent VL testers: 53 (21%)</p> <p>Less frequent VL testers: 63 (19.6%)</p> <p>chi-square p value 0.71</p>	Not reported	Not reported	Not reported

Table D.2 Studies reporting natural history of viral load over time

Abbreviations: 3TC: lamivudine, AIDS: acquired immunodeficiency syndrome, ART: antiretroviral therapy, ATV: atazanavir, cART: combination antiretroviral therapy, CNS: Central Nervous System, DRM: drug resistance mutation, DRV: darunavir, DRV/c: darunavir/cobicistat, DRV/r: darunavir/ritonavir, DTG: dolutegravir, EFV: efavirenz, ETR: etravirine, FTC: emtricitabine, GSS: genotypic susceptibility score, HBV: hepatitis B virus, HCV: hepatitis C virus, IDU: injection drug use, INI: integrase inhibitor, INSTI: integrase strand transfer inhibitor, INT: integrase inhibitor, IQR: interquartile range, ITT: intention-to-treat, LPV: lopinavir, LPV/r: lopinavir/ritonavir, MVC: maraviroc, NNRTI: Non-nucleoside reverse transcriptase inhibitors, NRTI: nucleoside reverse transcriptase inhibitors, NVP: nevirapine, PI: protease inhibitor, PP: per-protocol, RAL: raltegravir, RNA: ribonucleic acid, SD: standard deviation, SOC: standard of care, TAF: tenofovir alafenamide, TDF: tenofovir disoproxil fumarate, TLOVR: Time to Loss of Virologic Response, VL: viral load, ZDV: zidovudine

Study	Country, Study period	Study type	Participants	ART regimen and dose (study ART only)	ART regimen and dose (pre-switch and rationale for switch)	Monitoring frequency (testing intervals) and follow-up period	Viral load levels	Length of raised VL	Consecutive readings of raised VL readings and interval	Factors coinciding with VL levels
Santos Jose R and others 2023 (1)	Spain, December 2018 to January 2021	Randomised Controlled Trial	<p>Adults on ART with at least 3 antiretroviral drugs with HIV-1 RNA <50 copies/mL for ≥6 months preceding the study randomisation</p> <p>Sample size: Total: 89 (participants randomised from 12 HIV care centres across Spain)</p> <p>Study participants randomised 1:1 to control group and intervention group: 44</p> <p>Median age: Total: 55 years (range 50 to 60 years) Control group: 55 (IQR 50 to 60 years) Intervention (DRV/c + DTG) group: 55 years (IQR 50 to 61 years)</p> <p>Sex: Total: Males: 68 out of 89 (76.4%) Females/Other: 21 out of 89</p>	DTG 50 mg + DRV/c 800/150 mg once daily (intervention group) or a continuation of their current stable and SOC ART (control group).	<p>PIs (84.2%), NRTIs (97.8%), NNRTIs (49.4 to 53.9%), fusion inhibitors (13.5%), CCR5 antagonists (17.9%), integrase inhibitors (62.9%)</p> <p>Optimised ARTs at baseline for control group: 1. DRV/c + RAL 400 mg twice daily + ETR twice daily 2. DRV/c + FTC/TAF</p> <p>Rationale for switch: simplification of ART in virologically suppressed treatment-experienced people with ≥ 2-class resistance and pill fatigue concerns</p>	<p>Week 12, 24, 36, 48</p> <p>Follow-up period: 48 weeks</p>	<p><50 copies/mL</p> <p>In week 12: Intervention [DRV/c plus DTG]: 43/45 participants (95.6%) Control : 42/44 participants (95.5%)</p> <p>In week 24: Intervention [DRV/c plus DTG]: 42/45 participants (93.3%) Control: 42/44 participants (95.5%)</p> <p>In week 36: Intervention [DRV/c plus DTG]: 39/45 participants (86.7%) Control : 42/44 participants (95.5%)</p>	Not reported	<p>2 participants had HIV-1 RNA ≥50 copies/mL at 2 consecutive visits measured within 2 to 4 weeks (both in the control group)</p> <p>Person 1: Week 12: 83 copies/mL HIV-1 RNA At confirmation: 89 copies/mL (Changes in ART were not performed. Loss of follow-up)</p> <p>Person 2: Week 24: 74copies/mL HIV-1 RNA At confirmation: 2,115 copies/mL (Changes in ART were not</p>	<p>Observed blips: Control group: 5 participants (11.4%) Intervention group: 3 participants (6.7%)</p> <p>p value 0.480</p> <p>Of 2 participants had HIV-1 RNA ≥50 copies/mL at 2 consecutive visits measured within 2 to 4 weeks Person 1: no adherence issues, lost to follow-up Person 2: poor adherence (43%) and voluntary ART interruption (week 24), resuppressed</p>

Study	Country, Study period	Study type	Participants	ART regimen and dose (study ART only)	ART regimen and dose (pre-switch and rationale for switch)	Monitoring frequency (testing intervals) and follow-up period	Viral load levels	Length of raised VL	Consecutive readings of raised VL readings and interval	Factors coinciding with VL levels
			<p>(23.6%)</p> <p>Control group: Males: 32 out of 44 (72.7%) Females/other: 12 out of 44 (27.2%)</p> <p>Intervention (DRV/c + DTG) group: Males: 36 out of 45 (80%) Females/Other: 9 out of 45 (20%)</p> <p>Medical history: HCV coinfection: Control group: 5 out of 44 (11.4%) Intervention group: 6 out of 45 (13.3%)</p> <p>People had to have historical genotypic evidence of DRM against ≥ 2 antiretroviral classes according to the Stanford DB such as participants had a median 3 (2 to 8) and 5 (4 to 7) associated DRMs in the genes of protease and reverse transcriptase, respectively. Before randomisation, 61 (68%) and 59 (66%) participants were taking boosted DRV or INSTIs. In addition, 33 (37.1%) were following twice-daily regimens and had previously taken a</p>				<p>In week 48: Intervention [DRV/c plus DTG]: 39/45 participants (86.7%) Control: 42/44 participants (95.5%)</p> <p>≥ 50 copies/mL:</p> <p>In week 12: Intervention [DRV/c plus DTG]: 2/45 participants (4.4%) Control : 2/44 participants (4.5%)</p> <p>In week 24: Intervention [DRV/c plus DTG]: 3/45 participants (6.7%) Control : 2/44 participants (4.5%)</p> <p>In week 36: Intervention [DRV/c plus DTG]: 6/45 participants (13.3%)</p>		<p>performed. Re-suppression of HIV-1 was achieved at week 36 (VL <50 copies/mL)</p>	<p>after ART counselling</p>

Study	Country, Study period	Study type	Participants	ART regimen and dose (study ART only)	ART regimen and dose (pre-switch and rationale for switch)	Monitoring frequency (testing intervals) and follow-up period	Viral load levels	Length of raised VL	Consecutive readings of raised VL readings and interval	Factors coinciding with VL levels
			median 13 (10 to 17) antiretroviral drugs				Control: 2/44 participants (4.5%) In week 48: Intervention [DRV/c plus DTG]: 6 out of 45 participants (13.3%) Control : 2 out of 44 participants (4.5%)			
Charpentier C and others 2015 (3)	France, September 2012 to February 2013	Single-centre cohort study	<p>People on ART , with a VL <50 copies/mL for 17 months (IQR 7 to 43 months) and thereafter switching to tenofovir/emtricitabine/rilpivirine single-tablet regimen)</p> <p>Sample size: 116</p> <p>Median age: 43 years (IQR 39 to 50 years)</p> <p>Sex: Male:78 out of 116 (67%) Female/others: 38 out of 116 (33%)</p> <p>Medical history: Active hepatitis co-infection: HBV: 14 out of 115 (12%) HCV: 1 out of 116 (1%)</p>	Single-tablet regimen (STR) once daily: tenofovir disoproxil fumarate emtricitabine rilpivirine	<p>Two NRTIs + one NNRTI: 54 out of 116 (47%) EFV: 41 ETR: 11 NVP: 2</p> <p>Two NRTIs + one PI (boosted): 51 out of 116 (44%) DRV: 24 ATV: 15 LPV: 12</p> <p>Two NRTIs + RAL: 5 out of 116 (4%)</p> <p>Other ART Regimens: 6 out of 116 (5%) LPV/r monotherapy: 2 TDF + RAL + MVC: 1 RAL + DRV/r: 1 TDF/FTC/EFV + LPV/r: 1 ATV/r + ETR: 1</p>	Weeks 4, 12, 24, 36 and 48 Follow-up period: 96 weeks	<50 copies/mL: week 12: 105 (98%) week 24: 85 (99%) week 36: 66 (100%) week 48: 81 (100%) week 72: 88 (100%) week 96: 77 (100%)	At least 12 weeks (3 people) in Week 12 or Week 24	>50 copies/mL at weeks 12 or 24: Person 1: 60 copies/mL Person 2: 70 copies/mL Person 3: 75 copies/mL reverted to <50 copies/mL at next test (interval ≤12 weeks)	Not reported

Study	Country, Study period	Study type	Participants	ART regimen and dose (study ART only)	ART regimen and dose (pre-switch and rationale for switch)	Monitoring frequency (testing intervals) and follow-up period	Viral load levels	Length of raised VL	Consecutive readings of raised VL readings and interval	Factors coinciding with VL levels
					Rationale for switching: simplification: 70 (60%) treatment-related adverse events: neuropsychiatric side effects: 22 (19%) cardio-vascular comorbidities: 11 (10%) dyslipidemia: 8 (7%) others: 5 (4%)					
Charpentier C and others 2018 (4)	France, September 2014 to March 2016	Prospective cohort study	People with HIV treated with cART (VL <50 copies/mL) for ≥ 6 months switching to dolutegravir-based regimen were included Sample size: 239 people were grouped according to GSS Group 1 (GSS 1 or 1.5) sample size: 28 (12%) Group 2 (GSS 2 or 2.5) sample size: 70 (29%) Group 3 (GSS 3) sample size: 141 (59%) Median age: Group 1: 51 years (IQR 47 to 57 years) Group 2: 52 years (IQR 46 to 58 years) Group 3: 51 years (IQR 42 to 58 years) Sex: Group 1:	Dolutegravir 50 mg once daily in 229 out of 239 (96%) people Associated drugs varied by GSS: Group 1: Dolutegravir + (abacavir + lamivudine) (n= 20/28, 71%) Group 2: Dolutegravir + rilpivirine (n= 24/70, 34%) or Dolutegravir + abacavir + lamivudine (n= 8/70, 11%) Group 3: Dolutegravir + abacavir + lamivudine (n= 96/141, 68%) or Dolutegravir + tenofovir DF +	Pre-switch regimens: 2 NRTI + 1 NNRTI: Group 1: 4 out of 28 (14%) Group 2: 8 out of 70 (11%) Group 3: 40 out of 141 (28%) 2 NRTI + 1 PI/r: Group 1: 15 out of 28 (54%) Group 2: 31 out of 70 (44%) Group 3: 63 out of 141 (45%) INI-based treatment: Group 1: 5 out of 28 (18%) Group 2: 25 out of 70 (36%) Group 3: 31 out of 141 (22%) 2 NRTI + raltegravir:	VL measured at W4, W12, W24, W36, W48 (±1 month except W4). At least 2 measurements per person in follow-up year Follow-up period: 48 weeks	Plasma specimens available at week 4: 119 people week 12: 140 people week 24: 129 people week 36: 151 people week 48: 147 people VL <50 copies/mL: 661 out of 686 measurements (96.4%) during first year VL 91 to 200 copies/mL: 4 out of 235 people (1.7%) (VF as per study)	Not reported	Person 1: (on (DTG) + DRV/r) week 48: 200 copies/mL VL control (week 60): 89 copies/mL Person 2: (on (DTG) + ABC/3TC + DRV/r) week 48: 91 copies/mL VL control (week 52): 84 copies/mL Person 3: (on (DTG) + TDF/FTC) week 4: 91 copies/mL VL control (week 8): 64 copies/mL Person 4: (on (DTG) + ABC/3TC) week 24: 101	Suboptimal dolutegravir or darunavir plasma levels in 2 people Two out of 4 people with VF had prior raltegravir exposure GSS at VF ranged 2 to 3 No emergent integrase resistance in sequenced people Drug to drug interactions with darunavir/ritonavir noted in VF cases

Study	Country, Study period	Study type	Participants	ART regimen and dose (study ART only)	ART regimen and dose (pre-switch and rationale for switch)	Monitoring frequency (testing intervals) and follow-up period	Viral load levels	Length of raised VL	Consecutive readings of raised VL readings and interval	Factors coinciding with VL levels
			<p>males: 22 out of 28 (78.6%) females: 6 out of 28 (21.4%)</p> <p>Group 2: males: 37 out of 70 (53%) females: 33 out of 70 (47%)</p> <p>Group 3: males: 99 out of 141 (70%) females: 42 out of 141 (30%)</p> <p>Comorbidities: HBV coinfection: Group 1: 3 out of 28 (11%) Group 2: 5 out of 70 (7%) Group 3: 8 out of 141 (6%)</p> <p>HCV coinfection: Group 1: 0 out of 28 (0%) Group 2: 4 out of 70 (6%) Group 3: 13 out of 141 (9%)</p>	emtricitabine (n= 27/141, 19%)	<p>Group 1: 0 Group 2: 5 Group 3: 15</p> <p>tenofovir disoproxil fumarate/emtricitabine/elvitegravir/boosted with cobicistat: Group 1: 0 Group 2: 0 Group 3: 4</p> <p>other raltegravir based treatment: Group 1: 5 Group 2: 20 Group 3: 12</p> <p>other ART: Group 1: 4 out of 28 (14%) Group 2: 6 out of 70 (9%) Group 3: 7 out of 141 (5%)</p> <p>Rationale for switch: physician decision for maintenance in suppressed people, some had prior INI exposure (raltegravir 8.4%, elvitegravir/cobicistat 1.7%)</p> <p>Previous antiretroviral regimens used by</p>		<p>VL >50 but <1000 copies/mL: 16 out of 239 people (6.7%) (viral blip as per study)</p>		copies/mL VL control (week 30): 73 copies/mL	<p>Underlying resistance patterns:</p> <p>Among the 4 people who experienced VF, 3 were infected with a B subtype and one with a CRF12_BF recombinant. One person with VF had a GSS of 2.5 due to an historical M184V mutation, 2 people had a thymidine-associated mutation (T215F/I/L/Y) in an historical plasma resistance genotype.</p>

Study	Country, Study period	Study type	Participants	ART regimen and dose (study ART only)	ART regimen and dose (pre-switch and rationale for switch)	Monitoring frequency (testing intervals) and follow-up period	Viral load levels	Length of raised VL	Consecutive readings of raised VL readings and interval	Factors coinciding with VL levels
					people experiencing VF: Case 1: RAL + DRV/r Case 2: ABC/3TC + DRV/r Case 3: TDF/FTC + ETR + RAL Case 4: ZDV/3TC + LPV/r					
Maggiolo F and others 2017 (5)	Italy, not reported	Prospective cohort study	<p>People previously switched to 3TC + DTG who were 18 years or older, with no previous resistance mutations to the used drugs, having a HIV-RNA <50 copies/mL for 6 months or longer and on stable cART for >6 months</p> <p>Sample size: 94</p> <p>Median age: 52 years</p> <p>Gender: Males: 73 out of 94 (77.7%) Females/Others: 21 out of 94 (22.3%)</p> <p>Medical history: IV drug users: 20.2% 159 co-morbidities among 94 people, including cardiovascular, bone, hepatic, kidney, and CNS diseases</p>	Lamivudine (50mg once daily) + dolutegravir (300mg once daily) dual therapy	At baseline, nearly all (93.6%) were on standard triple-drug regimens. The most common NRTI backbones included tenofovir disoproxil fumarate with emtricitabine, and abacavir with lamivudine. These were typically combined with NNRTIs like efavirenz or nevirapine, or with ritonavir-boosted protease inhibitors such as atazanavir or darunavir. Some people had prior exposure to integrase inhibitors, including raltegravir, dolutegravir, or elvitegravir. A small subset (6 people) was on dual therapy regimens involving combinations like maraviroc plus darunavir/r or etravirine	2, 4, 6 month and thereafter every 3 to 4 months Follow-up period: Median: 17.4 months (IQR 6.6)	All people had VL <50 copies/mL at baseline, 2 months, and 6 months Viral load above 50 copies/mL was not detected At the end of follow-up (17.4 months), all people receiving the same anti-retroviral therapy (91 out of 94 participants) had VL <50 copies/mL	Not reported	Not reported (no raised VL observed)	Not reported

Study	Country, Study period	Study type	Participants	ART regimen and dose (study ART only)	ART regimen and dose (pre-switch and rationale for switch)	Monitoring frequency (testing intervals) and follow-up period	Viral load levels	Length of raised VL	Consecutive readings of raised VL readings and interval	Factors coinciding with VL levels
					plus raltegravir. Rationale for switching: Presence of comorbidities, abnormal laboratory findings, adverse drug events, and potential drug–drug interactions					

Annexe F. Risk of bias assessment

Table F.1. Risk of bias assessment for RCTs

Study	Q1	Q2	Q3	Q4	Q5	Q6	Q7	Q8	Q9	Q10	Q11	Q12	Q13	Comments (including reason for no)
Santos Jose R and others, 2023 (1)	Yes	Unclear	Yes	No	No	Unclear	Yes	Yes	Yes	Yes	Unclear	Yes	Yes	Q2: Open label trial Q4: Participants were not blinded Q5: Not reported to be blinded Q6: Not reported if staff analysing data were blinded or not Q11: Outcome measurement not explicitly stated
Weissman S and others, 2016 (2)	Yes	Unclear	Yes	No	No	Unclear	No	Yes	Yes	Yes	Unclear	Yes	Yes	Q2: Study does not describe whether allocation was concealed from staff or participants prior to assignment Q4: Participants were informed whether they were assigned to 4-month or 6-month visits Q5: Not reported if blinded or not Q6: Not explicitly reported if staff/laboratory personnel analysing data were blinded Q7: Post randomisation differences in how participants were treated Q11: No outcome measurement stated

Q: question

Critical appraisal was done using the JBI checklist for RCTs (9).

List of questions:

Q1: Was true randomisation used for assignment of participants to treatment groups?

Q2: Was allocation to treatment groups concealed?

Q3: Were treatment groups similar at the baseline?

Q4: Were participants blind to treatment assignment?

Q5: Were those delivering treatment blind to treatment assignment?

Q6: Were outcome assessors blind to treatment assignment?

Q7: Were treatment groups treated identically other than the intervention of interest?

Q8: Was follow-up complete and, if not, were differences between groups in terms of their follow-up adequately described and analysed?

Q9: Were participants analysed in the groups to which they were randomised?

Q10: Were outcomes measured in the same way for treatment groups?

Q11: Were outcomes measured in a reliable way?

Table E.2 Risk of bias assessment for cohort studies

Study	Q1	Q2	Q3	Q4	Q5	Q6	Q7	Q8	Q9	Q10	Q11	Comments (including reason for no)
Charpentier C and others, 2015 (3)	N/A	N/A	Yes	Yes	No	Yes	Yes	Yes	Yes	No	No	Q1 & Q2: Not applicable as only one study group Q5: Only descriptive analysis provided Q10: No sensitivity analyses for missing data reported Q11: Descriptive statistics reported but no analysis to adjust for confounders
Charpentier C and others, 2018 (4)	Yes	N/A	Yes	Yes	No	Yes	Yes	Yes	Yes	No	Yes	Q5: No statistical adjustments done Q10: No statistical methods used to handle missing data/loss to follow-up
Maggiolo F and others, 2017 (5)	N/A	N/A	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Q1 & Q2: Not applicable as only one study group
Young B and others, 2015 (6)	Yes	Yes	Yes	Yes	Yes	Yes	Unclear	Yes	Unclear	No	Yes	Q7: Values were taken from laboratory records Q9: Reasons not described clearly Q10: Censoring was applied, but no explicit sensitivity analyses or additional strategies for incomplete follow-up reported

N/A: Not Applicable; Q: question

Critical appraisal was done using the JBI checklist for Cohort Studies (9).

List of questions:

Q1: Were the 2 groups similar and recruited from the same population?

Q2: Were the exposures measured similarly to assign people to both exposed and unexposed groups?

Q3: Was the exposure measured in a valid and reliable way?

Q4: Were confounding factors identified?

Q5: Were strategies to deal with confounding factors stated?

Q6: Were the groups/participants free of the outcome at the start of the study (or at the moment of exposure)?

Q7: Were the outcomes measured in a valid and reliable way?

Q8: Was the follow-up time reported and sufficient to be long enough for outcomes to occur?

Q9: Was follow-up complete, and if not, were the reasons for loss to follow-up described and explored?

Q10: Were strategies to address incomplete follow-up utilised?

Q11: Was appropriate statistical analysis used?

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Completed: 4 November 2025

Published: March 2026

Publication reference: GOV-19962 (PHR038)

Suggested citation: Bhatia A, Shaju AM, Walker J, Brown S, Carville S. 'Viral load of people on effective anti-retroviral treatment: a rapid systematic review' UKHSA 2026



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