

**Table E23:** GRADE summary of evidence for mortality with INSTIs

Comparison	Direct Effect	Uncombined Estimates						Combined Estimates				
		Risk Bias	of	Inconsistency	Indirectness	Imprecision	Publication Bias	Quality of direct evidence	NMA Effect	Indirect evidence precision	Network Transitivity	Overall quality of evidence
DTG vs. EFV	0.98 (0.02, 4.92)	0		0	0	-1	0	⊕⊕⊕ Moderate	1.35 (0.41, 5.30)	0	0	⊕⊕⊕ Moderate
RAL vs. EFV	4.06 (0.45, 6.26)	0		0	0	-1	0	⊕⊕⊕ Moderate	1.28 (0.56, 3.00)	0	0	⊕⊕⊕ Moderate
EVG/c vs. EFV	3.05 (0.32, 5.32)	0		0	0	-1	0	⊕⊕⊕ Moderate	0.63 (0.23, 1.79)	0	0	⊕⊕⊕ Moderate
RAL vs. DTG	2.47 (0.33, 4.50)	0		0	0	-1	0	⊕⊕⊕ Moderate	0.95 (0.28, 2.64)	0	0	⊕⊕⊕ Moderate
EVG/c vs. DTG	--	0		0	-1	-1	0	⊕⊕ Low	0.47 (0.10, 1.89)	--	--	⊕⊕ Low
LPV/r vs. DTG	--	0		0	-1	-1	0	⊕⊕ Low	0.70 (0.17, 2.34)	--	--	⊕⊕ Low
ATV/r vs. DTG	--	0		0	-1	-1	0	⊕⊕ Low	0.74 (0.18, 2.42)	--	--	⊕⊕ Low
DRV/r vs. DTG	1.00 (0.02, 4.92)	0		0	0	-1	0	⊕⊕⊕ Moderate	0.85 (0.20, 2.74)	0	0	⊕⊕⊕ Moderate
NVP vs. DTG	--	0		0	-1	-1	0	⊕⊕ Low	0.74 (0.17, 2.67)	--	--	⊕⊕ Low
EVG/c vs. RAL	0.33 (0.09, 1.65)	0		0	0	-1	0	⊕⊕⊕ Moderate	0.49 (0.18, 1.38)	0	0	⊕⊕⊕ Moderate
LPV/r vs. RAL	0.99	0		0	0	-1	0	⊕⊕⊕	0.75	0	0	⊕⊕⊕

	(0.06, 3.77)						Moderate	(0.30, 1.71)			Moderate
ATV/r vs. RAL	1.67 (0.60, 2.69)	0	0	0	-1	0	⊕⊕⊕ Moderate	0.78 (0.33, 1.72)	0	0	⊕⊕⊕ Moderate
DRV/r vs. RAL	2.20 (0.83, 3.17)	0	0	0	-1	0	⊕⊕⊕ Moderate	0.91 (0.34, 2.11)	0	0	⊕⊕⊕ Moderate
NVP vs. RAL	--	0	0	-1	-1	0	⊕⊕ Low	0.78 (0.29, 1.99)	--	--	⊕⊕ Low
LPV/r vs. EVG/c	--	0	0	-1	-1	0	⊕⊕ Low	1.51 (0.48, 4.27)	--	--	⊕⊕ Low
ATV/r vs. EVG/c	7.02 (0.36, 9.99)	0	0	0	-1	0	⊕⊕⊕ Moderate	1.57 (0.55, 4.18)	0	0	⊕⊕⊕ Moderate
DRV/r vs. EVG/c	--	0	0	-1	-1	0	⊕⊕ Low	1.82 (0.53, 5.67)	--	--	⊕⊕ Low
NVP vs. EVG/c	--	0	0	-1	-1	0	⊕⊕ Low	1.59 (0.49, 4.80)	--	--	⊕⊕ Low

**Legend:** Uncombined estimates represent either direct estimates, if available, or indirect NMA estimates otherwise. Combined estimates are NMA estimates for comparisons where direct estimates were available. For uncombined estimates start with high quality evidence. -1 symbolizes a choice to rate down (e.g. high quality to moderate quality evidence); 0 symbolizes choice to not rate down; -- = not applicable because the NMA estimate is the only estimate.

The final quality of evidence updates that of the uncombined evidence. The quality can be moved up if the uncombined score was penalized for precision, which was overcome in network estimates. It can be moved down if the estimates are no longer precise or if there is evidence of inconsistency in loops containing the comparison (i.e. violation of transitivity).

**Precision** – We rated down for precision if the confidence interval crossed the minimally important difference. **Consistency** – We assessed the consistency for direct treatment comparisons using  $I^2$  estimates and visual inspection of point estimates. An  $I^2$  of 75% or higher indicates considerable heterogeneity. This was conducted along the shortest indirect pathway with the largest number of trials for indirect estimates. **Risk of Bias** – For direct estimates we rated down for risk of bias if the majority of studies within a comparison were considered to be at high risk of bias and similarly along the principal indirect pathway for indirect estimates.

#### GRADE confidence in estimates

*High confidence* - Further research is very unlikely to change our confidence in the estimate of effect; *Moderate confidence* - Further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate; *Low confidence* - Further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate; *Very low confidence* - Any estimate of effect is very uncertain.

**Table E40:** GRADE summary of evidence for discontinuations with INSTIs

Comparison	Direct Effect	Uncombined Estimates						Combined Estimates			
		Risk of Bias	Inconsistency	Indirectness	Imprecision	Publication Bias	Quality of direct evidence	NMA Effect	Indirect evidence precision	Network Transitivity	Overall quality of evidence
DTG vs. EFV	0.43 (0.14, 1.59)	0	0	0	-1	0	⊕⊕⊕⊕ Moderate	<b>0.47</b> <b>(0.28, 0.78)</b>	+1	0	⊕⊕⊕⊕ <b>High</b>
RAL vs. EFV	0.70 (0.50, 1.03)	0	0	0	-1	0	⊕⊕⊕⊕ Moderate	<b>0.70</b> <b>(0.49, 0.99)</b>	0	0	⊕⊕⊕⊕ Moderate
EVG/c vs. EFV	0.74 (0.51, 1.10)	0	0	0	-1	0	⊕⊕⊕⊕ Moderate	0.70 (0.44, 1.10)	0	0	⊕⊕⊕⊕ Moderate
RAL vs. DTG	<b>1.41</b> <b>(1.09, 1.68)</b>	0	0	0	0	0	⊕⊕⊕⊕ <b>High</b>	1.49 (0.96, 2.33)	0	0	⊕⊕⊕⊕ <b>High</b>
EVG/c vs. DTG		0	0	-1	-1	0	⊕⊕ Low	1.50 (0.81, 2.78)	0	0	⊕⊕ Low
LPV/r vs. DTG		0	0	-1	-1	0	⊕⊕ Low	1.58 (0.92, 2.67)	0	0	⊕⊕ Low
ATV/r vs. DTG		0	0	-1	-1	0	⊕⊕ Low	1.62 (0.95, 2.75)	0	0	⊕⊕ Low
DRV/r vs. DTG	<b>1.67</b> <b>(1.04, 2.15)</b>	0	0	0	0	0	⊕⊕⊕⊕ <b>High</b>	1.56 (0.92, 2.62)	0	0	⊕⊕⊕⊕ <b>High</b>
NVP vs. DTG		0	0	-1	0	0	⊕⊕⊕⊕ Moderate	<b>3.38</b> <b>(1.91, 6.09)</b>	0	0	⊕⊕⊕⊕ Moderate

EVG/c vs. RAL	1.06 (0.78, 1.36)	0	0	0	-1	0	⊕⊕⊕⊕ Moderate	1.01 (0.62, 1.61)	0	-1	⊕⊕ Low
LPV/r vs. RAL	0.63 (0.36, 1.18)	0	0	0	-1	0	⊕⊕⊕⊕ Moderate	1.06 (0.71, 1.55)	0	-1	⊕⊕ Low
ATV/r vs. RAL	1.27 (0.91, 1.61)	0	0	0	-1	0	⊕⊕⊕⊕ Moderate	1.09 (0.74, 1.59)	0	-1	⊕⊕ Low
DRV/r vs. RAL	<b>1.49</b> <b>(1.08, 1.82)</b>	0	0	0	0	0	⊕⊕⊕⊕ <b>High</b>	1.05 (0.66, 1.63)	0	-1	⊕⊕⊕⊕ Moderate
NVP vs. RAL		0	0	-1	0	0	⊕⊕⊕⊕ Moderate	<b>2.28</b> <b>(1.46, 3.57)</b>	0	0	⊕⊕⊕⊕ Moderate
LPV/r vs. EVG/c		0	0	-1	-1	0	⊕⊕ Low	1.05 (0.63, 1.75)	0	0	⊕⊕ Low
ATV/r vs. EVG/c	1.14 (0.75, 1.55)	0	0	0	-1	0	⊕⊕⊕⊕ Moderate	1.08 (0.68, 1.73)	0	0	⊕⊕⊕⊕ Moderate
DRV/r vs. EVG/c		0	0	-1	-1	0	⊕⊕ Low	1.04 (0.58, 1.86)	0	0	⊕⊕ Low
NVP vs. EVG/c		0	0	-1	0	0	⊕⊕⊕⊕ Moderate	<b>2.26</b> <b>(1.33, 3.92)</b>	0	0	⊕⊕⊕⊕ Moderate

**Legend:** Uncombined estimates represent either direct estimates, if available, or indirect NMA estimates otherwise. Combined estimates are NMA estimates for comparisons where direct estimates were available. For uncombined estimates start with high quality evidence. -1 symbolizes a choice to rate down (e.g. high quality to moderate quality evidence); 0 symbolizes choice to not rate down; -- = not applicable because the NMA estimate is the only estimate.

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**GRADE confidence in estimates**

*High confidence* - Further research is very unlikely to change our confidence in the estimate of effect; *Moderate confidence* - Further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate; *Low confidence* - Further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate; *Very low confidence* - Any estimate of effect is very uncertain.

**Table E41:** GRADE summary of evidence for discontinuations due to adverse events with INSTIs

Comparison	Direct Effect	Uncombined Estimates						Combined Estimates			
		Risk of Bias	Inconsistency	Indirectness	Imprecision	Publication Bias	Quality of direct evidence	NMA Effect	Indirect evidence precision	Network Transitivity	Overall quality of evidence
DTG vs. EFV	0.42 (0.09, 1.97)	0	0	0	-1	0	⊕⊕⊕⊕ Moderate	0.34 (0.11, 1.06)	0	0	⊕⊕⊕⊕ Moderate
RAL vs. EFV	0.61 (0.32, 1.25)	0	0	0	-1	0	⊕⊕⊕⊕ Moderate	0.62 (0.27, 1.42)	0	0	⊕⊕⊕⊕ Moderate
EVG/c vs. EFV	0.77 (0.43, 1.35)	0	0	0	-1	0	⊕⊕⊕⊕ Moderate	0.55 (0.20, 1.48)	0	0	⊕⊕⊕⊕ Moderate
RAL vs. DTG	1.43 (0.73, 2.11)	0	0	0	-1	0	⊕⊕⊕⊕ Moderate	1.82 (0.66, 5.17)	0	0	⊕⊕⊕⊕ Moderate
EVG/c vs. DTG		0	0	-1	-1	0	⊕⊕ Low	1.63 (0.40, 6.44)	0	0	⊕⊕ Low
LPV/r vs. DTG		0	0	-1	-1	0	⊕⊕ Low	2.00 (0.58, 6.87)	0	0	⊕⊕ Low

ATV/r vs. DTG		0	0	-1	-1	0	⊕⊕ Low	2.41 (0.75, 7.95)	0	0	⊕⊕ Low
DRV/r vs. DTG	2.14 (0.83, 3.09)	0	0	0	-1	0	⊕⊕⊕⊕ Moderate	1.53 (0.47, 5.03)	0	0	⊕⊕⊕⊕ Moderate
NVP vs. DTG		0	0	-1	0	0	⊕⊕⊕⊕ Moderate	<b>4.88</b> <b>(1.25, 18.46)</b>	0	0	⊕⊕⊕⊕ Moderate
EVG/c vs. RAL	0.74 (0.34, 1.52)	0	0	0	-1	0	⊕⊕⊕⊕ Moderate	0.90 (0.30, 2.58)	0	0	⊕⊕⊕⊕ Moderate
LPV/r vs. RAL	0.49 (0.14, 1.71)	0	0	0	-1	0	⊕⊕⊕⊕ Moderate	1.10 (0.43, 2.74)	0	-1	⊕⊕ Low
ATV/r vs. RAL	1.94 (0.75, 2.89)	0	0	0	-1	0	⊕⊕⊕⊕ Moderate	1.32 (0.55, 3.19)	0	0	⊕⊕⊕⊕ Moderate
DRV/r vs. RAL	2.27 (0.89, 3.20)	0	0	0	-1	0	⊕⊕⊕⊕ Moderate	0.84 (0.30, 2.35)	0	-1	⊕⊕ Low
NVP vs. RAL		0	0	-1	-1	0	⊕⊕ Low	2.68 (0.90, 7.76)	0	0	⊕⊕ Low
LPV/r vs. EVG/c		0	0	-1	-1	0	⊕⊕ Low	1.23 (0.38, 4.05)	0	0	⊕⊕ Low
ATV/r vs. EVG/c	1.35 (0.75, 1.93)	0	0	0	-1	0	⊕⊕⊕⊕ Moderate	1.48 (0.54, 4.31)	0	0	⊕⊕⊕⊕ Moderate

DRV/r vs. EVG/c		0	0	-1	-1	0	⊕⊕ Low	0.94 (0.26, 3.47)	0	0	⊕⊕ Low
NVP vs. EVG/c		0	0	-1	-1	0	⊕⊕ Low	2.99 (0.86, 10.63)	0	0	⊕⊕ Low

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#### GRADE confidence in estimates

*High confidence* - Further research is very unlikely to change our confidence in the estimate of effect; *Moderate confidence* - Further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate; *Low confidence* - Further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate; *Very low confidence* - Any estimate of effect is very uncertain.

**Table E21:** GRADE summary of evidence for serious adverse events with INSTIs

Comparison	Direct Effect	Uncombined Estimates						Combined Estimates			
		Risk of Bias	Inconsistency	Indirectness	Imprecision	Publication Bias	Quality of direct evidence	NMA Effect	Indirect evidence precision	Network Transitivity	Overall quality of evidence
DTG vs. EFV	0.98 (0.32, 2.11)	0	0	0	-1	0	⊕⊕⊕ Moderate	0.88 (0.54, 1.42)	0	0	⊕⊕⊕ Moderate
RAL vs. EFV	1.06 (0.72, 1.44)	0	0	0	-1	0	⊕⊕⊕ Moderate	0.96 (0.68, 1.37)	0	0	⊕⊕⊕ Moderate
EVG/c vs. EFV	0.46 (0.06, 2.48)	0	0	0	-1	0	⊕⊕⊕ Moderate	0.72 (0.38, 1.30)	0	0	⊕⊕⊕ Moderate
RAL vs. DTG	1.24 (0.89, 1.56)	0	0	0	-1	0	⊕⊕⊕ Moderate	1.09 (0.73, 1.64)	0	0	⊕⊕⊕ Moderate

EVG/c vs. DTG	--	0	0	-1	-1	0	⊕⊕ Low	0.81 (0.39, 1.64)	--	--	⊕⊕ Low
LPV/r vs. DTG	--	0	0	-1	-1	0	⊕⊕ Low	0.99 (0.60, 1.64)	--	--	⊕⊕ Low
ATV/r vs. DTG	--	0	0	-1	-1	0	⊕⊕ Low	1.10 (0.64, 1.92)	--	--	⊕⊕ Low
DRV/r vs. DTG	0.54 (0.31, 1.11)	0	0	0	-1	0	⊕⊕⊕ Moderate	0.73 (0.43, 1.14)	0	0	⊕⊕⊕ Moderate
NVP vs. DTG	--	0	0	-1	-1	0	⊕⊕ Low	1.10 (0.64, 1.92)	--	--	⊕⊕ Low
EVG/c vs. RAL	0.43 (0.11, 1.79)	-1	0	0	-1	0	⊕⊕ Low	0.75 (0.39, 1.37)	0	0	⊕⊕ Low
LPV/r vs. RAL	1.04 (0.35, 2.15)	0	0	0	-1	0	⊕⊕⊕ Moderate	0.91 (0.62, 1.32)	0	0	⊕⊕⊕ Moderate
ATV/r vs. RAL	1.13 (0.86, 1.40)	0	0	0	-1	0	⊕⊕⊕ Moderate	1.02 (0.71, 1.46)	0	0	⊕⊕⊕ Moderate
DRV/r vs. RAL	0.99 (0.75, 1.27)	0	0	0	-1	0	⊕⊕⊕ Moderate	<b>0.67</b> <b>(0.42, 0.96)</b>	0	0	⊕⊕⊕ Moderate
NVP vs. RAL	--	0	0	-1	-1	0	⊕⊕ Low	1.01 (0.66, 1.56)	--	--	⊕⊕ Low
LPV/r vs. EVG/c	--	0	0	-1	-1	0	⊕⊕ Low	0.22 (0.66, 2.36)	--	--	⊕⊕ Low
ATV/r vs. EVG/c	1.18 (0.79, 1.59)	0	0	0	-1	0	⊕⊕⊕ Moderate	1.36 (0.79, 2.48)	0	0	⊕⊕⊕ Moderate
DRV/r vs. EVG/c	--	0	0	-1	-1	0	⊕⊕ Low	0.90	--	--	⊕⊕ Low

							Low	(0.45, 1.70)			Low
NVP vs. EVG/c	--	0	0	-1	-1	0	⊕⊕ Low	1.36 (0.72, 2.68)	--	--	⊕⊕ Low

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#### GRADE confidence in estimates

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**Table E22:** GRADE summary of evidence for treatment-related adverse events with INSTIs

Comparison	Direct Effect	Uncombined Estimates						Combined Estimates			
		Risk of Bias	Inconsistency	Indirectness	Imprecision	Publication Bias	Quality of direct evidence	NMA Effect	Indirect evidence precision	Network Transitivity	Overall quality of evidence
DTG vs. EFV	0.75 (0.34, 1.54)	-1	0	0	-1	0	⊕⊕ Low	0.46 (0.22, 1.07)	0	-1	⊕ Very Low
RAL vs. EFV	<b>0.28</b> <b>(0.20, 0.62)</b>	-1	0	0	0	0	⊕⊕⊕ Moderate	<b>0.39</b> <b>(0.22, 0.72)</b>	0	-1	⊕⊕ Low
EVG/c vs. EFV	0.70 (0.39, 1.28)	-1	0	0	-1	0	⊕⊕⊕ Moderate	<b>0.50</b> <b>(0.26, 0.72)</b>	+1	0	⊕⊕⊕ Moderate
RAL vs. DTG	1.19 (0.79, 1.69)	-1	0	0	-1	0	⊕⊕ Low	0.85 (0.40, 1.69)	0	-1	⊕ Very Low
EVG/c vs. DTG	--	-1	0	-1	-1	0	⊕ Very Low	1.10 (0.42, 2.64)	--	--	⊕ Very Low

LPV/r vs. DTG	--	-1	0	-1	-1	0	⊕ Very Low	0.94 (0.32, 2.20)	--	--	⊕ Very Low
ATV/r vs. DTG	--	-1	0	-1	-1	0	⊕ Very Low	1.05 (0.33, 2.76)	--	--	⊕ Very Low
DRV/r vs. DTG	0.14 (0.01, 3.11)	-1	0	0	-1	0	⊕⊕ Low	0.49 (0.12, 1.32)	0	0	⊕⊕ Low
NVP vs. DTG	--	-1	0	-1	-1	0	⊕ Very Low	0.49 (0.10, 2.08)	--	--	⊕ Very Low
EVG/c vs. RAL	1.21 (0.54, 1.87)	-1	0	0	-1	0	⊕⊕ Low	1.29 (0.65, 2.51)	0	0	⊕⊕ Low
LPV/r vs. RAL	--	-1	0	-1	-1	0	⊕ Very Low	1.10 (0.51, 2.03)	--	--	⊕ Very Low
ATV/r vs. RAL	1.40 (0.67, 2.13)	-1	0	0	-1	0	⊕⊕ Low	1.24 (0.50, 2.71)	0	0	⊕⊕ Low
DRV/r vs. RAL	--	-1	0	-1	-1	0	⊕ Very Low	0.58 (0.17, 1.33)	--	--	⊕ Very Low
NVP vs. RAL	--	-1	0	-1	-1	0	⊕ Very Low	0.58 (0.13, 2.21)	--	--	⊕ Very Low
LPV/r vs. EVG/c	--	-1	0	-1	-1	0	⊕ Very Low	0.86 (0.34, 1.86)	--	--	⊕ Very Low
ATV/r vs. EVG/c	1.40 (0.67, 2.13)	-1	0	0	-1	0	⊕⊕ Low	0.96 (0.38, 2.16)	0	0	⊕⊕ Low
DRV/r vs. EVG/c	--	-1	0	-1	-1	0	⊕ Very Low	0.45 (0.12, 1.12)	--	--	⊕ Very Low

NVP vs. EVG/c	--	-1	0	-1	-1	0	⊕ Very Low	0.44 (0.10, 1.75)	--	--	⊕ Very Low
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**Legend:** Uncombined estimates represent either direct estimates, if available, or indirect NMA estimates otherwise. Combined estimates are NMA estimates for comparisons where direct estimates were available. For uncombined estimates start with high quality evidence. -1 symbolizes a choice to rate down (e.g. high quality to moderate quality evidence); 0 symbolizes choice to not rate down; -- = not applicable because the NMA estimate is the only estimate.

The final quality of evidence updates that of the uncombined evidence. The quality can be moved up if the uncombined score was penalized for precision, which was overcome in network estimates. It can be moved down if the estimates are no longer precise or if there is evidence of inconsistency in loops containing the comparison (i.e. violation of transitivity).

**Precision** – We rated down for precision if the confidence interval crossed the minimally important difference. **Consistency** – We assessed the consistency for direct treatment comparisons using I<sup>2</sup> estimates and visual inspection of point estimates. An I<sup>2</sup> of 75% or higher indicates considerable heterogeneity. This was conducted along the shortest indirect pathway with the largest number of trials for indirect estimates. **Risk of Bias** – For direct estimates we rated down for risk of bias if the majority of studies within a comparison were considered to be at high risk of bias and similarly along the principal indirect pathway for indirect estimates.

#### GRADE confidence in estimates

*High confidence* - Further research is very unlikely to change our confidence in the estimate of effect; *Moderate confidence* - Further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate; *Low confidence* - Further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate; *Very low confidence* - Any estimate of effect is very uncertain.

**Table E24:** GRADE summary of evidence for hepatotoxicity with INSTIs

Comparison	Direct Effect	Uncombined Estimates						Combined Estimates			
		Risk of Bias	Inconsistency	Indirectness	Imprecision	Publication Bias	Quality of direct evidence	NMA Effect	Indirect evidence precision	Network Transitivity	Overall quality of evidence
DTG vs. EFV	0.32 (0.01, 3.54)	0	0	0	-1	0	⊕⊕⊕ Moderate	1.21 (0.45, 3.34)	0	0	⊕⊕⊕ Moderate
RAL vs. EFV	0.64 (0.37, 1.20)	0	0	0	-1	0	⊕⊕ Low	1.07 (0.53, 2.36)	0	-1	⊕ Very Low
EVG/c vs. EFV	3.04 (0.12, 6.25)	0	0	0	-1	0	⊕⊕⊕ Moderate	0.60 (0.20, 1.97)	0	0	⊕⊕⊕ Moderate
RAL vs. DTG	0.79 (0.41, 1.46)	0	0	0	-1	0	⊕⊕⊕ Moderate	0.89 (0.39, 2.11)	0	0	⊕⊕⊕ Moderate
EVG/c vs. DTG	--	0	0	-1	-1	0	⊕⊕ Low	0.50 (0.14, 1.93)	--	--	⊕⊕ Low
LPV/r vs. DTG	--	0	0	-1	-1	0	⊕⊕	0.65	--	--	⊕⊕

							Low	(0.22, 1.75)			Low
ATV/r vs. DTG	--	0	0	-1	-1	0	⊕⊕ Low	0.64 (0.19, 1.89)	--	--	⊕⊕ Low
DRV/r vs. DTG	0.62 (0.26, 1.49)	0	0	0	-1	0	⊕⊕⊕ Moderate	0.62 (0.22, 1.75)	0	0	⊕⊕⊕ Moderate
NVP vs. DTG	--	0	0	-1	-1	0	⊕⊕ Low	1.75 (0.55, 5.09)	--	--	⊕⊕ Low
EVG/c vs. RAL	0.32 (0.13, 1.22)	0	0	0	-1	0	⊕⊕⊕ Moderate	0.56 (0.20, 1.66)	0	0	⊕⊕⊕ Moderate
LPV/r vs. RAL	0.38 (0.11, 1.65)	0	0	0	-1	0	⊕⊕⊕ Moderate	0.73 (0.29, 1.57)	0	-1	⊕⊕ Low
ATV/r vs. RAL	--	0	0	-1	-1	0	⊕⊕ Low	0.72 (0.25, 1.76)	--	--	⊕⊕ Low
DRV/r vs. RAL	--	0	0	-1	-1	0	⊕⊕ Low	0.69 (0.24, 1.95)	--	--	⊕⊕ Low
NVP vs. RAL	--	0	0	-1	-1	0	⊕⊕ Low	1.96 (0.74, 4.57)	--	--	⊕⊕ Low
LPV/r vs. EVG/c	--	0	0	-1	-1	0	⊕⊕ Low	1.31 (0.34, 4.09)	--	--	⊕⊕ Low
ATV/r vs. EVG/c	--	0	0	-1	-1	0	⊕⊕ Low	1.29 (0.34, 3.90)	--	--	⊕⊕ Low
DRV/r vs. EVG/c	--	0	0	-1	-1	0	⊕⊕ Low	1.25 (0.29, 4.71)	--	--	⊕⊕ Low
NVP vs. EVG/c	0.33 (0.01, 3.53)	0	0	0	-1	0	⊕⊕⊕ Moderate	3.51 (0.93, 11.14)	0	0	⊕⊕⊕ Moderate

**Legend:** Uncombined estimates represent either direct estimates, if available, or indirect NMA estimates otherwise. Combined estimates are NMA estimates for comparisons where direct estimates were available. For uncombined estimates start with high quality evidence. -1 symbolizes a choice to rate down (e.g. high quality to moderate quality evidence); 0 symbolizes choice to not rate down; -- = not applicable because the NMA estimate is the only estimate.

The final quality of evidence updates that of the uncombined evidence. The quality can be moved up if the uncombined score was penalized for precision, which was overcome in network estimates. It can be moved down if the estimates are no longer precise or if there is evidence of inconsistency in loops containing the comparison (i.e. violation of transitivity).

**Precision** – We rated down for precision if the confidence interval crossed the minimally important difference. **Consistency** – We assessed the consistency for direct treatment comparisons using I<sup>2</sup> estimates and visual inspection of point estimates. An I<sup>2</sup> of 75% or higher indicates considerable heterogeneity. This was conducted along the shortest indirect pathway with the largest number of trials for indirect estimates. **Risk of Bias** – For direct estimates we rated down for risk of bias if the majority of studies within a comparison were considered to be at high risk of bias and similarly along the principal indirect pathway for indirect estimates.

**GRADE confidence in estimates**

*High confidence* - Further research is very unlikely to change our confidence in the estimate of effect; *Moderate confidence* - Further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate; *Low confidence* - Further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate; *Very low confidence* - Any estimate of effect is very uncertain.

**Table E26:** GRADE summary of evidence for hypersensitivity with INSTIs

Comparison	Direct Effect	Uncombined Estimates						Combined Estimates			
		Risk of Bias	Inconsistency	Indirectness	Imprecision	Publication Bias	Quality of direct evidence	NMA Effect	Indirect evidence precision	Network Transitivity	Overall quality of evidence
DTG vs. EFV	--	0	0	-1	-2	0	⊕ Very Low	8.30 (0.05, 293.60)	--	--	⊕ Very Low
RAL vs. EFV	1.00 (0.14, 2.97)	0	0	0	-1	0	⊕⊕⊕ Moderate	1.92 (0.05, 71.25)	-1	0	⊕⊕ Low
EVG/c vs. EFV	0.34 (0.01, 3.54)	0	0	0	-1	0	⊕⊕⊕ Moderate	0.60 (0.01, 43.95)	-1	0	⊕⊕ Low
RAL vs. DTG	0.14 (0.01, 3.11)	0	0	0	-1	0	⊕⊕⊕ Moderate	0.27 (0.00, 21.89)	0	0	⊕⊕⊕ Moderate
EVG/c vs. DTG	--	0	0	-1	-2	0	⊕ Very Low	0.08 (0.00, 47.01)	--	--	⊕ Very Low
LPV/r vs. DTG	--	0	0	-1	-1	0	⊕⊕ Low	0.06 (0.00, 19.53)	--	--	⊕⊕ Low
ATV/r vs. DTG	--	0	0	-1	-1	0	⊕	0.04	--	--	⊕

							Very Low	(0.00, 6.09)			Very Low
DRV/r vs. DTG	3.01 (0.12, 6.22)	0	0	0	-1	0	⊕⊕⊕ Moderate	0.08 (0.00, 5.11)	0	0	⊕⊕⊕ Moderate
NVP vs. DTG	--	0	0	-1	-1	0	⊕⊕ Low	0.02 (0.00, 5.20)	--	--	⊕⊕ Low
EVG/c vs. RAL	--	0	0	-1	-2	0	⊕ Very Low	0.31 (0.00, 74.19)	--	--	⊕ Very Low
LPV/r vs. RAL	--	0	0	-1	-1	0	⊕⊕ Low	0.25 (0.00, 27.20)	--	--	⊕⊕ Low
ATV/r vs. RAL	0.33 (0.01, 3.53)	0	0	0	-1	0	⊕⊕⊕ Moderate	0.17 (0.00, 6.20)	0	0	⊕⊕⊕ Moderate
DRV/r vs. RAL	0.33 (0.01, 3.54)	0	0	0	-1	0	⊕⊕⊕ Moderate	0.30 (0.00, 23.72)	0	0	⊕⊕⊕ Moderate
NVP vs. RAL	--	0	0	-1	-1	0	⊕⊕ Low	0.10 (0.00, 6.00)	--	--	⊕⊕ Low
LPV/r vs. EVG/c	--	0	0	-1	-2	0	⊕ Very Low	0.78 (0.00, 124.30)	--	--	⊕ Very Low
ATV/r vs. EVG/c	0.33 (0.01, 3.53)	0	0	0	-1	0	⊕⊕⊕ Moderate	0.56 (0.00, 27.89)	0	0	⊕⊕⊕ Moderate
DRV/r vs. EVG/c	--	0	0	-1	-2	0	⊕ Very Low	0.92 (0.00, 465.10)	--	--	⊕ Very Low
NVP vs. EVG/c	--	0	0	-1	-1	0	⊕⊕ Low	0.31 (0.00, 30.35)	--	--	⊕⊕ Low

**Legend:** Uncombined estimates represent either direct estimates, if available, or indirect NMA estimates otherwise. Combined estimates are NMA estimates for comparisons where direct estimates were available. For uncombined estimates start with high quality evidence. -1 symbolizes a choice to rate down (e.g. high quality to moderate quality evidence); 0 symbolizes choice to not rate down; -- = not applicable because the NMA estimate is the only estimate.

The final quality of evidence updates that of the uncombined evidence. The quality can be moved up if the uncombined score was penalized for precision, which was overcome in network estimates. It can be moved down if the estimates are no longer precise or if there is evidence of inconsistency in loops containing the comparison (i.e. violation of transitivity).

**Precision** – We rated down for precision if the confidence interval crossed the minimally important difference. **Consistency** – We assessed the consistency for direct treatment comparisons using I<sup>2</sup> estimates and visual inspection of point estimates. An I<sup>2</sup> of 75% or higher indicates considerable heterogeneity. This was conducted along the shortest indirect pathway with the largest number of trials for indirect estimates. **Risk of Bias** – For direct estimates we rated down for risk of bias if the majority of studies within a comparison were considered to be at high risk of bias and similarly along the principal indirect pathway for indirect estimates.

**GRADE confidence in estimates**

*High confidence* - Further research is very unlikely to change our confidence in the estimate of effect; *Moderate confidence* - Further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate; *Low confidence* - Further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate; *Very low confidence* - Any estimate of effect is very uncertain.

**Table E28:** GRADE summary of evidence for dyslipemia with INSTIs

Comparison	Direct Effect	Uncombined Estimates						Combined Estimates			
		Risk of Bias	Inconsistency	Indirectness	Imprecision	Publication Bias	Quality of direct evidence	NMA Effect	Indirect evidence precision	Network Transitivity	Overall quality of evidence
DTG vs. EFV	--	0	0	-1	-1	0	⊕⊕ Low	0.22 (0.04, 1.03)	--	--	⊕⊕ Low
RAL vs. EFV	0.75 (0.17, 2.26)	0	0	0	-1	0	⊕⊕⊕ Moderate	0.54 (0.16, 1.78)	0	0	⊕⊕⊕ Moderate
EVG/c vs. EFV	--	0	0	-1	-1	0	⊕⊕ Low	0.35 (0.08, 1.45)	--	--	⊕⊕ Low
RAL vs. DTG	2.35 (0.89, 3.32)	0	0	0	-1	0	⊕⊕⊕ Moderate	2.43 (0.95, 7.05)	0	0	⊕⊕⊕ Moderate
EVG/c vs. DTG	--	0	0	-1	-1	0	⊕⊕ Low	1.59 (0.47, 5.83)	--	--	⊕⊕ Low
LPV/r vs. DTG	--	0	0	-1	0	0	⊕⊕⊕ Moderate	<b>9.11</b> <b>(1.96, 43.52)</b>	--	--	⊕⊕⊕ Moderate
ATV/r vs. DTG	--	0	0	-1	-1	0	⊕⊕ Low	3.73 (0.74, 18.91)	--	--	⊕⊕ Low
DRV/r vs. DTG	--	0	0	-1	-1	0	⊕⊕	<b>5.22</b>	--	--	⊕⊕

							Low	<b>(1.08, 25.79)</b>			Low
NVP vs. DTG	--	0	0	-1	0	0	⊕⊕⊕ Moderate	<b>7.13</b> <b>(1.44, 36.51)</b>	--	--	⊕⊕⊕ Moderate
EVG/c vs. RAL	0.66 (0.31, 1.41)	0	0	0	-1	0	⊕⊕⊕ Moderate	0.66 (0.30, 1.38)	0	0	⊕⊕⊕ Moderate
LPV/r vs. RAL	6.10 (0.73, 8.23)	0	0	0	-1	0	⊕⊕⊕ Moderate	<b>3.71</b> <b>(1.11, 11.94)</b>	0	0	⊕⊕⊕ Moderate
ATV/r vs. RAL	--	0	0	-1	-1	0	⊕⊕ Low	1.52 (0.42, 5.39)	--	--	⊕⊕ Low
DRV/r vs. RAL	--	0	0	-1	-1	0	⊕⊕ Low	2.13 (0.61, 7.23)	--	--	⊕⊕ Low
NVP vs. RAL	--	0	0	-1	-1	0	⊕⊕ Low	2.91 (0.81, 10.34)	--	--	⊕⊕ Low
LPV/r vs. EVG/c	--	0	0	-1	0	0	⊕⊕⊕ Moderate	<b>5.68</b> <b>(1.37, 23.06)</b>	--	--	⊕⊕⊕ Moderate
ATV/r vs. EVG/c	--	0	0	-1	-1	0	⊕⊕ Low	2.32 (0.52, 10.14)	--	--	⊕⊕ Low
DRV/r vs. EVG/c	--	0	0	-1	-1	0	⊕⊕ Low	3.25 (0.76, 13.72)	--	--	⊕⊕ Low
NVP vs. EVG/c	--	0	0	-1	-1	0	⊕⊕ Low	4.45 (1.00, 19.64)	--	--	⊕⊕ Low

**Legend:** Uncombined estimates represent either direct estimates, if available, or indirect NMA estimates otherwise. Combined estimates are NMA estimates for comparisons where direct estimates were available. For uncombined estimates start with high quality evidence. -1 symbolizes a choice to rate down (e.g. high quality to moderate quality evidence); 0 symbolizes choice to not rate down; -- = not applicable because the NMA estimate is the only estimate.

The final quality of evidence updates that of the uncombined evidence. The quality can be moved up if the uncombined score was penalized for precision, which was overcome in network estimates. It can be moved down if the estimates are no longer precise or if there is evidence of inconsistency in loops containing the comparison (i.e. violation of transitivity).

**Precision** – We rated down for precision if the confidence interval crossed the minimally important difference. **Consistency** – We assessed the consistency for direct treatment comparisons using I<sup>2</sup> estimates and visual inspection of point estimates. An I<sup>2</sup> of 75% or higher indicates considerable heterogeneity. This was conducted along the shortest indirect pathway with the largest number of trials for indirect estimates. **Risk of Bias** – For direct estimates we rated down for risk of bias if the majority of studies within a comparison were considered to be at high risk of bias and similarly along the principal indirect pathway for indirect estimates.

**GRADE confidence in estimates**

*High confidence* - Further research is very unlikely to change our confidence in the estimate of effect; *Moderate confidence* - Further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate; *Low confidence* - Further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate; *Very low confidence* - Any estimate of effect is very uncertain.

**Table E30: GRADE summary of evidence for tubular toxicity with INSTIs**

Comparison	Direct Effect	Uncombined Estimates						Combined Estimates			
		Risk of Bias	Inconsistency	Indirectness	Imprecision	Publication Bias	Quality of direct evidence	NMA Effect	Indirect evidence precision	Network Transitivity	Overall quality of evidence
DTG vs. EFV	--	--	--	--	--	--	--	--	--	--	--
RAL vs. EFV	--	-1	0	-1	0	0	⊕⊕ Low	<b>21.58</b> <b>(1.85, 272.50)</b>	--	--	⊕⊕ Low
EVG/c vs. EFV	9.21 (0.49, 12.13)	-1	0	0	-1	0	⊕⊕ Low	2.77 (0.66, 7.89)	0	0	⊕⊕ Low
RAL vs. DTG	--	--	--	--	--	--	--	--	--	--	--
EVG/c vs. DTG	--	--	--	--	--	--	--	--	--	--	--
LPV/r vs. DTG	--	--	--	--	--	--	--	--	--	--	--
ATV/r vs. DTG	--	--	--	--	--	--	--	--	--	--	--
DRV/r vs. DTG	--	--	--	--	--	--	--	--	--	--	--
NVP vs. DTG	--	--	--	--	--	--	--	--	--	--	--
EVG/c vs. RAL	3.04 (0.12, 6.25)	-1	0	0	-1	0	⊕⊕ Low	<b>0.13</b> <b>(0.01, 0.98)</b>	0	0	⊕⊕ Low

LPV/r vs. RAL	--	--	--	--	--	--	--	--	--	--	--
ATV/r vs. RAL	0.33 (0.01, 3.53)	-1	0	0	-1	0	⊕⊕ Low	0.17 (0.01, 1.12)	0	0	⊕⊕ Low
DRV/r vs. RAL	0.33 (0.01, 3.54)	-1	0	0	-1	0	⊕⊕⊕ Moderate	<b>0.01</b> <b>(0.00, 0.52)</b>	+1	0	⊕⊕⊕ Moderate
NVP vs. RAL	--	--	--	--	--	--	--	--	--	--	--
LPV/r vs. EVG/c	--	--	--	--	--	--	--	--	--	--	--
ATV/r vs. EVG/c	7.02 (0.36, 9.99)	-1	0	0	-1	0	⊕⊕ Low	1.36 (0.25, 4.88)	0	0	⊕⊕ Low
DRV/r vs. EVG/c	--	-1	0	-1	-1	0	⊕ Very Low	0.04 (0.00, 7.27)	--	--	⊕ Very Low
NVP vs. EVG/c	--	--	--	--	--	--	--	--	--	--	--

**Legend:** Uncombined estimates represent either direct estimates, if available, or indirect NMA estimates otherwise. Combined estimates are NMA estimates for comparisons where direct estimates were available. For uncombined estimates start with high quality evidence. -1 symbolizes a choice to rate down (e.g. high quality to moderate quality evidence); 0 symbolizes choice to not rate down; -- = not applicable because the NMA estimate is the only estimate.

The final quality of evidence updates that of the uncombined evidence. The quality can be moved up if the uncombined score was penalized for precision, which was overcome in network estimates. It can be moved down if the estimates are no longer precise or if there is evidence of inconsistency in loops containing the comparison (i.e. violation of transitivity).

**Precision** – We rated down for precision if the confidence interval crossed the minimally important difference. **Consistency** – We assessed the consistency for direct treatment comparisons using  $I^2$  estimates and visual inspection of point estimates. An  $I^2$  of 75% or higher indicates considerable heterogeneity. This was conducted along the shortest indirect pathway with the largest number of trials for indirect estimates. **Risk of Bias** – For direct estimates we rated down for risk of bias if the majority of studies within a comparison were considered to be at high risk of bias and similarly along the principal indirect pathway for indirect estimates.

#### GRADE confidence in estimates

*High confidence* - Further research is very unlikely to change our confidence in the estimate of effect; *Moderate confidence* - Further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate; *Low confidence* - Further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate; *Very low confidence* - Any estimate of effect is very uncertain.

**Table E31:** GRADE summary of evidence for eGFR at 48 weeks with INSTIs

Comparison	Direct Effect	Uncombined Estimates						Combined Estimates			
		Risk of Bias	Inconsistency	Indirectness	Imprecision	Publication Bias	Quality of direct evidence	NMA Effect	Indirect evidence precision	Network Transitivity	Overall quality of evidence
DTG vs. EFV	--	--	--	--	--	--	--	--	--	--	--
RAL vs. EFV	--	--	--	--	--	--	--	--	--	--	--
EVG/c vs. EFV	<b>-11.38</b> <b>(-13.52, -9.23)</b>	-1	0	0	0	0	⊕⊕⊕ Moderate	<b>-11.37</b> <b>(-13.52, -9.25)</b>	0	0	⊕⊕⊕ Moderate
RAL vs. DTG	--	--	--	--	--	--	--	--	--	--	--
EVG/c vs. DTG	--	--	--	--	--	--	--	--	--	--	--
LPV/r vs. DTG	--	--	--	--	--	--	--	--	--	--	--
ATV/r vs. DTG	--	--	--	--	--	--	--	--	--	--	--
DRV/r vs. DTG	--	--	--	--	--	--	--	--	--	--	--
NVP vs. DTG	--	--	--	--	--	--	--	--	--	--	--
EVG/c vs. RAL	--	--	--	--	--	--	--	--	--	--	--
LPV/r vs. RAL	--	--	--	--	--	--	--	--	--	--	--
ATV/r vs. RAL	--	--	--	--	--	--	--	--	--	--	--
DRV/r vs. RAL	--	--	--	--	--	--	--	--	--	--	--
NVP vs. RAL	--	--	--	--	--	--	--	--	--	--	--
LPV/r vs. EVG/c	--	--	--	--	--	--	--	--	--	--	--
ATV/r vs. EVG/c	<b>3.20</b>	-1	0	0	-1	0	⊕⊕	<b>3.19</b>	0	0	⊕⊕

	(1.26, 5.14)						Low	(1.26, 5.14)			Low
DRV/r vs. EVG/c	--	--	--	--	--	--	--	--	--	--	--
NVP vs. EVG/c	--	-1	0	-1	-1	0	⊕ Very Low	<b>6.10</b> (2.71, 9.51)	--	--	⊕ Very Low

**Legend:** Uncombined estimates represent either direct estimates, if available, or indirect NMA estimates otherwise. Combined estimates are NMA estimates for comparisons where direct estimates were available. For uncombined estimates start with high quality evidence. -1 symbolizes a choice to rate down (e.g. high quality to moderate quality evidence); 0 symbolizes choice to not rate down; -- = not applicable because the NMA estimate is the only estimate.

The final quality of evidence updates that of the uncombined evidence. The quality can be moved up if the uncombined score was penalized for precision, which was overcome in network estimates. It can be moved down if the estimates are no longer precise or if there is evidence of inconsistency in loops containing the comparison (i.e. violation of transitivity).

**Precision** – We rated down for precision if the confidence interval crossed the minimally important difference. **Consistency** – We assessed the consistency for direct treatment comparisons using I<sup>2</sup> estimates and visual inspection of point estimates. An I<sup>2</sup> of 75% or higher indicates considerable heterogeneity. This was conducted along the shortest indirect pathway with the largest number of trials for indirect estimates. **Risk of Bias** – For direct estimates we rated down for risk of bias if the majority of studies within a comparison were considered to be at high risk of bias and similarly along the principal indirect pathway for indirect estimates.

**GRADE confidence in estimates**

*High confidence* - Further research is very unlikely to change our confidence in the estimate of effect; *Moderate confidence* - Further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate; *Low confidence* - Further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate; *Very low confidence* - Any estimate of effect is very uncertain.

**Table E32:** GRADE summary of evidence for creatinine clearance with INSTIs

Comparison	Direct Effect	Uncombined Estimates						Combined Estimates			
		Risk of Bias	Inconsistency	Indirectness	Imprecision	Publication Bias	Quality of direct evidence	NMA Effect	Indirect evidence precision	Network Transitivity	Overall quality of evidence
DTG vs. EFV	--	0	0	-1	0	0	⊕⊕⊕ Moderate	<b>-33.84</b> (-48.85, -19.25)	--	--	⊕⊕⊕ Moderate
RAL vs. EFV	<b>-23.94</b> (-37.36, -10.52)	-1	0	0	0	0	⊕⊕⊕ Moderate	<b>-23.60</b> (-37.19, -10.34)	0	0	⊕⊕⊕ Moderate
EVG/c vs. EFV		--	--	--	--	--	--	--	--	--	--
RAL vs. DTG	<b>10.30</b>	0	0	0	0	0	⊕⊕⊕⊕	<b>10.25</b>	0	0	⊕⊕⊕⊕

	(4.12, 16.48)						High	(4.02, 16.43)			High
EVG/c vs. DTG		--	--	--	--	--	--	--	--	--	--
LPV/r vs. DTG	--	-1	0	-1	0	0	⊕⊕ Low	26.98 (11.00, 43.20)	--	--	⊕⊕ Low
ATV/r vs. DTG	--	-1	0	-1	0	0	⊕⊕ Low	27.62 (12.89, 42.83)	--	--	⊕⊕ Low
DRV/r vs. DTG	--	-1	0	-1	0	0	⊕⊕ Low	27.66 (12.94, 42.85)	--	--	⊕⊕ Low
NVP vs. DTG		--	--	--	--	--	--	--	--	--	--
EVG/c vs. RAL		--	--	--	--	--	--	--	--	--	--
LPV/r vs. RAL	--	-1	0	-1	0	0	⊕⊕ Low	16.71 (2.00, 31.78)	--	--	⊕⊕ Low
ATV/r vs. RAL	--	-1	0	-1	0	0	⊕⊕ Low	17.38 (4.01, 31.15)	--	--	⊕⊕ Low
DRV/r vs. RAL	--	-1	0	-1	0	0	⊕⊕ Low	17.41 (4.05, 31.19)	--	--	⊕⊕ Low
NVP vs. RAL		--	--	--	--	--	--	--	--	--	--

LPV/r vs. EVG/c		--	--	--	--	--	--	--	--	--	--
ATV/r vs. EVG/c		--	--	--	--	--	--	--	--	--	--
DRV/r vs. EVG/c	--	--	--	--	--	--	--	--	--	--	--
NVP vs. EVG/c		--	--	--	--	--	--	--	--	--	--

**Legend:** Uncombined estimates represent either direct estimates, if available, or indirect NMA estimates otherwise. Combined estimates are NMA estimates for comparisons where direct estimates were available. For uncombined estimates start with high quality evidence. -1 symbolizes a choice to rate down (e.g. high quality to moderate quality evidence); 0 symbolizes choice to not rate down; -- = not applicable because the NMA estimate is the only estimate.

The final quality of evidence updates that of the uncombined evidence. The quality can be moved up if the uncombined score was penalized for precision, which was overcome in network estimates. It can be moved down if the estimates are no longer precise or if there is evidence of inconsistency in loops containing the comparison (i.e. violation of transitivity).

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**Precision** – We rated down for precision if the confidence interval crossed the minimally important difference. **Consistency** – We assessed the consistency for direct treatment comparisons using  $I^2$  estimates and visual inspection of point estimates. An  $I^2$  of 75% or higher indicates considerable heterogeneity. This was conducted along the shortest indirect pathway with the largest number of trials for indirect estimates. **Risk of Bias** – For direct estimates we rated down for risk of bias if the majority of studies within a comparison were considered to be at high risk of bias and similarly along the principal indirect pathway for indirect estimates.

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**GRADE confidence in estimates**

*High confidence* - Further research is very unlikely to change our confidence in the estimate of effect; *Moderate confidence* - Further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate; *Low confidence* - Further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate; *Very low confidence* - Any estimate of effect is very uncertain.

**Table E33:** GRADE summary of evidence for change in serum creatinine at 24 weeks with INSTIs

Comparison	Direct Effect	Uncombined Estimates						Combined Estimates			
		Risk of Bias	Inconsistency	Indirectness	Imprecision	Publication Bias	Quality of direct evidence	NMA Effect	Indirect evidence precision	Network Transitivity	Overall quality of evidence
DTG vs. EFV	<b>0.14</b> <b>(0.10, 0.18)</b>	0	0	0	-1	0	⊕⊕⊕ Moderate	<b>0.15</b> <b>(0.12, 0.18)</b>	0	0	⊕⊕⊕ Moderate
RAL vs. EFV	--	0	0	-1	0	0	⊕⊕⊕ Moderate	<b>0.07</b> <b>(0.04, 0.11)</b>	0	0	⊕⊕⊕ Moderate
EVG/c vs. EFV	<b>0.12</b> <b>(0.11, 0.13)</b>	0	0	0	0	0	⊕⊕⊕⊕ High	<b>0.12</b> <b>(0.11, 0.13)</b>	0	0	⊕⊕⊕⊕ High
RAL vs. DTG	-0.08 (-0.09, -0.07)	0	0	0	0	0	⊕⊕⊕⊕ High	<b>-0.08</b> <b>(-0.09, -0.07)</b>	0	0	⊕⊕⊕⊕ High
EVG/c vs. DTG		0	0	-1	0	0	⊕⊕⊕ Moderate	-0.03 (-0.07, 0.01)	--	--	⊕⊕⊕ Moderate
LPV/r vs. DTG		--	--	--	--	--	--	--	--	--	--
ATV/r vs. DTG		--	--	--	--	--	--	--	--	--	--
DRV/r vs. DTG	-0.12 (-0.15, -0.09)	0	0	0	0	0	⊕⊕⊕⊕ High	<b>-0.12</b> <b>(-0.15, -0.09)</b>	0	0	⊕⊕⊕⊕ High
NVP vs. DTG		--	--	--	--	--	--	--	--	--	--

EVG/c vs. RAL		0	0	-1	0	0	⊕⊕⊕ Moderate	<b>0.05</b> <b>(0.01, 0.08)</b>	--	--	⊕⊕⊕ Moderate
LPV/r vs. RAL		--	--	--	--	--	--	--	--	--	--
ATV/r vs. RAL		--	--	--	--	--	--	--	--	--	--
DRV/r vs. RAL		0	0	-1	0	0	⊕⊕⊕ Moderate	<b>-0.04</b> <b>(-0.08, -0.01)</b>	--	--	⊕⊕⊕ Moderate
NVP vs. RAL		--	--	--	--	--	--	--	--	--	--
LPV/r vs. EVG/c		--	--	--	--	--	--	--	--	--	--
ATV/r vs. EVG/c		--	--	--	--	--	--	--	--	--	--
DRV/r vs. EVG/c		0	0	-1	0	0	⊕⊕⊕ Moderate	<b>-0.09</b> <b>(-0.14, -0.04)</b>	--	--	⊕⊕⊕ Moderate
NVP vs. EVG/c		--	--	--	--	--	--	--	--	--	--

**Legend:** Uncombined estimates represent either direct estimates, if available, or indirect NMA estimates otherwise. Combined estimates are NMA estimates for comparisons where direct estimates were available. For uncombined estimates start with high quality evidence. -1 symbolizes a choice to rate down (e.g. high quality to moderate quality evidence); 0 symbolizes choice to not rate down; -- = not applicable because the NMA estimate is the only estimate.

The final quality of evidence updates that of the uncombined evidence. The quality can be moved up if the uncombined score was penalized for precision, which was overcome in network estimates. It can be moved down if the estimates are no longer precise or if there is evidence of inconsistency in loops containing the comparison (i.e. violation of transitivity).

**Precision** – We rated down for precision if the confidence interval crossed the minimally important difference. **Consistency** – We assessed the consistency for direct treatment comparisons using I<sup>2</sup> estimates and visual inspection of point estimates. An I<sup>2</sup> of 75% or higher indicates considerable heterogeneity. This was conducted along the shortest indirect pathway with the largest number of trials for indirect estimates. **Risk of Bias** – For direct estimates we rated down for risk of bias if the majority of studies within a comparison were considered to be at high risk of bias and similarly along the principal indirect pathway for indirect estimates.

**GRADE confidence in estimates**

*High confidence* - Further research is very unlikely to change our confidence in the estimate of effect; *Moderate confidence* - Further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate; *Low confidence* - Further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate; *Very low confidence* - Any estimate of effect is very uncertain.

**E34: GRADE summary of evidence for change in serum creatinine at 48 weeks with INSTIs**

Comparison	Direct Effect	Uncombined Estimates						Combined Estimates			
		Risk of Bias	Inconsistency	Indirectness	Imprecision	Publication Bias	Quality of direct evidence	NMA Effect	Indirect evidence precision	Network Transitivity	Overall quality of evidence
DTG vs. EFV	<b>0.14</b> <b>(0.10, 0.18)</b>	0	0	0	0	0	⊕⊕⊕⊕ High	<b>0.14</b> <b>(0.10, 0.18)</b>	0	0	⊕⊕⊕⊕ High
RAL vs. EFV		0	0	-1	0	0	⊕⊕⊕ Moderate	<b>0.06</b> <b>(0.02, 0.10)</b>	--	--	⊕⊕⊕ Moderate
EVG/c vs. EFV	<b>0.14</b> <b>(0.12, 0.16)</b>	0	0	0	0	0	⊕⊕⊕⊕ High	<b>0.14</b> <b>(0.12, 0.16)</b>	0	0	⊕⊕⊕⊕ High
RAL vs. DTG	<b>-0.08</b> <b>(-0.09, -0.07)</b>	0	0	0	0	0	⊕⊕⊕⊕ High	<b>-0.08</b> <b>(-0.09, -0.07)</b>	0	0	⊕⊕⊕⊕ High
EVG/c vs. DTG		0	0	-1	-1	0	⊕⊕ Low	-0.00 <b>(-0.05, 0.04)</b>	--	--	⊕⊕ Low
LPV/r vs. DTG		--	--	--	--	--	--		--	--	--
ATV/r vs. DTG		0	0	-1	-1	0	⊕⊕ Low	-0.04 <b>(-0.09, 0.01)</b>	--	--	⊕⊕ Low

DRV/r vs. DTG	<b>-0.12</b> <b>(-0.15, -0.09)</b>	0	0	0	0	0	⊕⊕⊕⊕ High	<b>-0.12</b> <b>(-0.15, -0.09)</b>	0	0	⊕⊕⊕⊕ High
NVP vs. DTG		--	--	--	--	--	--	--	--	--	--
EVG/c vs. RAL		0	0	-1	0	0	⊕⊕⊕ Moderate	<b>0.08</b> <b>(0.03, 0.13)</b>	--	--	⊕⊕⊕ Moderate
LPV/r vs. RAL		--	--	--	--	--	--	--	--	--	--
ATV/r vs. RAL		0	0	-1	-1	0	⊕⊕ Low	0.04 <b>(-0.01, 0.09)</b>	--	--	⊕⊕ Low
DRV/r vs. RAL		0	0	-1	0	0	⊕⊕⊕ Moderate	<b>-0.04</b> <b>(-0.07, -0.00)</b>	--	--	⊕⊕⊕ Moderate
NVP vs. RAL		--	--	--	--	--	--	--	--	--	--
LPV/r vs. EVG/c		--	--	--	--	--	--	--	--	--	--
ATV/r vs. EVG/c	<b>-0.04</b> <b>(-0.06, -0.02)</b>	0	0	0	0	0	⊕⊕⊕⊕ High	<b>-0.04</b> <b>(-0.06, -0.02)</b>	0	0	⊕⊕⊕⊕ High
DRV/r vs. EVG/c		0	0	-1	0	0	⊕⊕⊕ Moderate	<b>-0.12</b> <b>(-0.18, -0.06)</b>	--	--	⊕⊕⊕ Moderate
NVP vs. EVG/c		--	--	--	--	--	--	--	--	--	--

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**Legend:** Uncombined estimates represent either direct estimates, if available, or indirect NMA estimates otherwise. Combined estimates are NMA estimates for comparisons where direct estimates were available. For uncombined estimates start with high quality evidence. -1 symbolizes a choice to rate down (e.g. high quality to moderate quality evidence); 0 symbolizes choice to not rate down; -- = not applicable because the NMA estimate is the only estimate.

The final quality of evidence updates that of the uncombined evidence. The quality can be moved up if the uncombined score was penalized for precision, which was overcome in network estimates. It can be moved down if the estimates are no longer precise or if there is evidence of inconsistency in loops containing the comparison (i.e. violation of transitivity).

**Precision** – We rated down for precision if the confidence interval crossed the minimally important difference. **Consistency** – We assessed the consistency for direct treatment comparisons using I<sup>2</sup> estimates and visual inspection of point estimates. An I<sup>2</sup> of 75% or higher indicates considerable heterogeneity. This was conducted along the shortest indirect pathway with the largest number of trials for indirect estimates. **Risk of Bias** – For direct estimates we rated down for risk of bias if the majority of studies within a comparison were considered to be at high risk of bias and similarly along the principal indirect pathway for indirect estimates.

**GRADE confidence in estimates**

*High confidence* - Further research is very unlikely to change our confidence in the estimate of effect; *Moderate confidence* - Further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate; *Low confidence* - Further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate; *Very low confidence* - Any estimate of effect is very uncertain.

**Table E35: GRADE summary of evidence for change in serum creatinine at 96 weeks with INSTIs**

Comparison	Direct Effect	Uncombined Estimates						Combined Estimates			
		Risk of Bias	Inconsistency	Indirectness	Imprecision	Publication Bias	Quality of direct evidence	NMA Effect	Indirect evidence precision	Network Transitivity	Overall quality of evidence
DTG vs. EFV	<b>0.14</b> <b>(0.09, 0.19)</b>	0	0	0	0	0	⊕⊕⊕⊕ High	<b>0.14</b> <b>(0.10, 0.18)</b>			
RAL vs. EFV	--	0	0	-1	0	0	⊕⊕⊕ Moderate	<b>0.06</b> <b>(0.00, 0.12)</b>			
EVG/c vs. EFV	--	0	0	-1	0	0	⊕⊕⊕ Moderate	<b>0.12</b> <b>(0.10, 0.14)</b>			
RAL vs. DTG	<b>-0.08</b> <b>(-0.12, -0.04)</b>	0	0	0	0	0	⊕⊕⊕⊕ High	<b>-0.08</b> <b>(-0.12, -0.04)</b>			
EVG/c vs. DTG	--	0	0	-1	-1	0	⊕⊕ Low	-0.02 <b>(-0.07, 0.03)</b>			

LPV/r vs. DTG		--	--	--	--	--	--	--	--	--	--
ATV/r vs. DTG	--	0	0	-1	0	0	⊕⊕⊕ Moderate	<b>-0.06</b> <b>(-0.11, -0.01)</b>			
DRV/r vs. DTG	<b>-0.13</b> <b>(-0.16, -0.10)</b>	0	0	0	0	0	⊕⊕⊕⊕ High	<b>-0.13</b> <b>(-0.16, -0.10)</b>			
NVP vs. DTG		--	--	--	--	--	--	--	--	--	--
EVG/c vs. RAL	--	0	0	-1	-1	0	⊕⊕ Low	0.06 (-0.00, 0.12)			
LPV/r vs. RAL		--	--	--	--	--	--	--	--	--	--
ATV/r vs. RAL	--	0	0	-1	-1	0	⊕⊕ Low	0.02 (-0.04, 0.08)			
DRV/r vs. RAL	--	0	0	-1	-1	0	⊕⊕ Low	-0.05 (-0.10, -0.00)			
NVP vs. RAL		--	--	--	--	--	--	--	--	--	--
LPV/r vs. EVG/c		--	--	--	--	--	--	--	--	--	--
ATV/r vs. EVG/c	<b>-0.04</b>	0	0	0	0	0	⊕⊕⊕⊕	<b>-0.04</b> <b>(-0.06, -0.02)</b>			

	<b>(-0.06, -0.02)</b>						<b>High</b>				
DRV/r vs. EVG/c	--	0	0	-1	0	0	⊕⊕⊕ Moderate	<b>-0.11</b> <b>(-0.17, -0.05)</b>			
NVP vs. EVG/c		--	--	--	--	--	--	--	--	--	--

**Legend:** Uncombined estimates represent either direct estimates, if available, or indirect NMA estimates otherwise. Combined estimates are NMA estimates for comparisons where direct estimates were available. For uncombined estimates start with high quality evidence. -1 symbolizes a choice to rate down (e.g. high quality to moderate quality evidence); 0 symbolizes choice to not rate down; -- = not applicable because the NMA estimate is the only estimate.

The final quality of evidence updates that of the uncombined evidence. The quality can be moved up if the uncombined score was penalized for precision, which was overcome in network estimates. It can be moved down if the estimates are no longer precise or if there is evidence of inconsistency in loops containing the comparison (i.e. violation of transitivity).

**Precision** – We rated down for precision if the confidence interval crossed the minimally important difference. **Consistency** – We assessed the consistency for direct treatment comparisons using  $I^2$  estimates and visual inspection of point estimates. An  $I^2$  of 75% or higher indicates considerable heterogeneity. This was conducted along the shortest indirect pathway with the largest number of trials for indirect estimates. **Risk of Bias** – For direct estimates we rated down for risk of bias if the majority of studies within a comparison were considered to be at high risk of bias and similarly along the principal indirect pathway for indirect estimates.

**GRADE confidence in estimates**

*High confidence* - Further research is very unlikely to change our confidence in the estimate of effect; *Moderate confidence* - Further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate; *Low confidence* - Further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate; *Very low confidence* - Any estimate of effect is very uncertain.

**Table E36:** GRADE summary of evidence for change in hip bone mineral density at 48 weeks with INSTIs

Comparison	Direct Effect	Uncombined Estimates						Combined Estimates			
		Risk of Bias	Inconsistency	Indirectness	Imprecision	Publication Bias	Quality of direct evidence	NMA Effect	Indirect evidence precision	Network Transitivity	Overall quality of evidence
DTG vs. EFV		--	--	--	--	--	--	--	--	--	--
RAL vs. EFV		--	--	--	--	--	--	--	--	--	--
EVG/c vs. EFV		0	0	-1	-1	0	⊕⊕ Low	0.47 (-3.52, 4.35)	--	--	⊕⊕ Low

RAL vs. DTG		--	--	--	--	--	--	--	--	--	--
EVG/c vs. DTG		--	--	--	--	--	--	--	--	--	--
LPV/r vs. DTG		--	--	--	--	--	--	--	--	--	--
ATV/r vs. DTG		--	--	--	--	--	--	--	--	--	--
DRV/r vs. DTG		--	--	--	--	--	--	--	--	--	--
NVP vs. DTG		--	--	--	--	--	--	--	--	--	--
EVG/c vs. RAL		--	--	--	--	--	--	--	--	--	--
LPV/r vs. RAL		--	--	--	--	--	--	--	--	--	--
ATV/r vs. RAL		--	--	--	--	--	--	--	--	--	--
DRV/r vs. RAL		--	--	--	--	--	--	--	--	--	--

NVP vs. RAL		--	--	--	--	--	--	--	--	--	--
LPV/r vs. EVG/c		--	--	--	--	--	--	--	--	--	--
ATV/r vs. EVG/c	<b>-0.82</b> <b>(-1.35, -0.29)</b>	0	0	0	0	0	⊕⊕⊕⊕ <b>High</b>	<b>-0.82</b> <b>(-1.36, -0.29)</b>	0	0	⊕⊕⊕⊕ <b>High</b>
DRV/r vs. EVG/c		--	--	--	--	--	--	--	--	--	--
NVP vs. EVG/c		--	--	--	--	--	--	--	--	--	--

**Legend:** Uncombined estimates represent either direct estimates, if available, or indirect NMA estimates otherwise. Combined estimates are NMA estimates for comparisons where direct estimates were available. For uncombined estimates start with high quality evidence. -1 symbolizes a choice to rate down (e.g. high quality to moderate quality evidence); 0 symbolizes choice to not rate down; -- = not applicable because the NMA estimate is the only estimate.

The final quality of evidence updates that of the uncombined evidence. The quality can be moved up if the uncombined score was penalized for precision, which was overcome in network estimates. It can be moved down if the estimates are no longer precise or if there is evidence of inconsistency in loops containing the comparison (i.e. violation of transitivity).

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**Precision** – We rated down for precision if the confidence interval crossed the minimally important difference. **Consistency** – We assessed the consistency for direct treatment comparisons using I<sup>2</sup> estimates and visual inspection of point estimates. An I<sup>2</sup> of 75% or higher indicates considerable heterogeneity. This was conducted along the shortest indirect pathway with the largest number of trials for indirect estimates. **Risk of Bias** – For direct estimates we rated down for risk of bias if the majority of studies within a comparison were considered to be at high risk of bias and similarly along the principal indirect pathway for indirect estimates.

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**GRADE confidence in estimates**

*High confidence* - Further research is very unlikely to change our confidence in the estimate of effect; *Moderate confidence* - Further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate; *Low confidence* - Further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate; *Very low confidence* - Any estimate of effect is very uncertain.

**Table E37:** GRADE summary of evidence for change in hip bone mineral density at 96 weeks with INSTIs

Comparison	Direct Effect	Uncombined Estimates						Combined Estimates			
		Risk of Bias	Inconsistency	Indirectness	Imprecision	Publication Bias	Quality of direct evidence	NMA Effect	Indirect evidence precision	Network Transitivity	Overall quality of evidence
DTG vs. EFV		--	--	--	--	--	--	--	--	--	--
RAL vs. EFV		0	0	-1	0	0	⊕⊕⊕⊕ Moderate	<b>1.62</b> <b>(0.33, 2.99)</b>	0	0	⊕⊕⊕⊕ <b>High</b>
EVG/c vs. EFV		0	0	-1	-1	0	⊕⊕ Low	1.17 (-0.75, 3.09)	0	0	⊕⊕ Low
RAL vs. DTG		--	--	--	--	--	--	--	--	--	--
EVG/c vs. DTG		--	--	--	--	--	--	--	--	--	--
LPV/r vs. DTG		--	--	--	--	--	--	--	--	--	--
ATV/r vs. DTG		--	--	--	--	--	--	--	--	--	--
DRV/r vs. DTG		--	--	--	--	--	--	--	--	--	--

NVP vs. DTG		--	--	--	--	--	--	--	--	--	--
EVG/c vs. RAL		0	0	-1	-1	0	⊕⊕ Low	-0.46 (-2.18, 1.27)	0	0	⊕⊕ Low
LPV/r vs. RAL		--	--	--	--	--	--	--	--	--	--
ATV/r vs. RAL	<b>-1.50</b> <b>(-2.21, -0.79)</b>	0	0	0	0	0	⊕⊕⊕⊕ High	<b>-1.50</b> <b>(-2.22, -0.79)</b>	0	0	⊕⊕⊕⊕ High
DRV/r vs. RAL	<b>-1.00</b> <b>(-1.72, -0.28)</b>	0	0	0	0	0	⊕⊕⊕⊕ High	<b>-1.00</b> <b>(-1.71, -0.29)</b>	0	0	⊕⊕⊕⊕ High
NVP vs. RAL		--	--	--	--	--	--	--	--	--	--
LPV/r vs. EVG/c		--	--	--	--	--	--	--	--	--	--
ATV/r vs. EVG/c	-1.03 (-2.60, 0.54)	0	0	0	-1	0	⊕⊕⊕ Moderate	-1.04 (-2.60, 0.53)	0	0	⊕⊕⊕ Moderate
DRV/r vs. EVG/c		0	0	-1	-1	0	⊕⊕ Low	-0.54 (-2.27, 1.19)	0	0	⊕⊕ Low
NVP vs. EVG/c		--	--	--	--	--	--	--	--	--	--

**Legend:** Uncombined estimates represent either direct estimates, if available, or indirect NMA estimates otherwise. Combined estimates are NMA estimates for comparisons where direct estimates were available. For uncombined estimates start with high quality evidence. -1 symbolizes a choice to rate down (e.g. high quality to moderate quality evidence); 0 symbolizes choice to not rate down; -- = not applicable because the NMA estimate is the only estimate.

The final quality of evidence updates that of the uncombined evidence. The quality can be moved up if the uncombined score was penalized for precision, which was overcome in network estimates. It can be moved down if the estimates are no longer precise or if there is evidence of inconsistency in loops containing the comparison (i.e. violation of transitivity).

**Precision** – We rated down for precision if the confidence interval crossed the minimally important difference. **Consistency** – We assessed the consistency for direct treatment comparisons using  $I^2$  estimates and visual inspection of point estimates. An  $I^2$  of 75% or higher indicates considerable heterogeneity. This was conducted along the shortest indirect pathway with the largest number of trials for indirect estimates. **Risk of Bias** – For direct estimates we rated down for risk of bias if the majority of studies within a comparison were considered to be at high risk of bias and similarly along the principal indirect pathway for indirect estimates.

**GRADE confidence in estimates**

*High confidence* - Further research is very unlikely to change our confidence in the estimate of effect; *Moderate confidence* - Further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate; *Low confidence* - Further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate; *Very low confidence* - Any estimate of effect is very uncertain.

**Table E38:** GRADE summary of evidence for change in spine bone mineral density at 48 weeks with INSTIs

Comparison	Direct Effect	Uncombined Estimates						Combined Estimates			
		Risk of Bias	Inconsistency	Indirectness	Imprecision	Publication Bias	Quality of direct evidence	NMA Effect	Indirect evidence precision	Network Transitivity	Overall quality of evidence
DTG vs. EFV		--	--	--	--	--	--	--	--	--	--
RAL vs. EFV		--	--	--	--	--	--	--	--	--	--
EVG/c vs. EFV	--	0	0	-1	-1	0	⊕⊕ Low	-0.19 (-1.48, 1.12)	--	--	⊕⊕ Low
RAL vs. DTG		--	--	--	--	--	--	--	--	--	--
EVG/c vs. DTG		--	--	--	--	--	--	--	--	--	--
LPV/r vs. DTG		--	--	--	--	--	--	--	--	--	--

ATV/r vs. DTG		--	--	--	--	--	--	--	--	--	--
DRV/r vs. DTG		--	--	--	--	--	--	--	--	--	--
NVP vs. DTG		--	--	--	--	--	--	--	--	--	--
EVG/c vs. RAL		--	--	--	--	--	--	--	--	--	--
LPV/r vs. RAL		--	--	--	--	--	--	--	--	--	--
ATV/r vs. RAL		--	--	--	--	--	--	--	--	--	--
DRV/r vs. RAL		--	--	--	--	--	--	--	--	--	--
NVP vs. RAL		--	--	--	--	--	--	--	--	--	--
LPV/r vs. EVG/c		--	--	--	--	--	--	--	--	--	--
ATV/r vs. EVG/c	<b>-0.70</b> <b>(-1.32, -0.08)</b>	0	0	0	0	0	⊕⊕⊕⊕ <b>High</b>	<b>-0.70</b> <b>(-1.33, -0.09)</b>	0	0	⊕⊕⊕⊕ <b>High</b>

DRV/r vs. EVG/c		--	--	--	--	--	--	--	--	--	--
NVP vs. EVG/c		--	--	--	--	--	--	--	--	--	--

**Legend:** Uncombined estimates represent either direct estimates, if available, or indirect NMA estimates otherwise. Combined estimates are NMA estimates for comparisons where direct estimates were available. For uncombined estimates start with high quality evidence. -1 symbolizes a choice to rate down (e.g. high quality to moderate quality evidence); 0 symbolizes choice to not rate down; -- = not applicable because the NMA estimate is the only estimate.

The final quality of evidence updates that of the uncombined evidence. The quality can be moved up if the uncombined score was penalized for precision, which was overcome in network estimates. It can be moved down if the estimates are no longer precise or if there is evidence of inconsistency in loops containing the comparison (i.e. violation of transitivity).

**Precision** – We rated down for precision if the confidence interval crossed the minimally important difference. **Consistency** – We assessed the consistency for direct treatment comparisons using  $I^2$  estimates and visual inspection of point estimates. An  $I^2$  of 75% or higher indicates considerable heterogeneity. This was conducted along the shortest indirect pathway with the largest number of trials for indirect estimates. **Risk of Bias** – For direct estimates we rated down for risk of bias if the majority of studies within a comparison were considered to be at high risk of bias and similarly along the principal indirect pathway for indirect estimates.

**GRADE confidence in estimates**

*High confidence* - Further research is very unlikely to change our confidence in the estimate of effect; *Moderate confidence* - Further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate; *Low confidence* - Further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate; *Very low confidence* - Any estimate of effect is very uncertain.

**Table E39:** GRADE summary of evidence for change in spine bone mineral density at 96 weeks with INSTIs

Comparison	Direct Effect	Uncombined Estimates						Combined Estimates			
		Risk of Bias	Inconsistency	Indirectness	Imprecision	Publication Bias	Quality of direct evidence	NMA Effect	Indirect evidence precision	Network Transitivity	Overall quality of evidence
DTG vs. EFV		--	--	--	--	--	--	--	--	--	--
RAL vs. EFV		0	0	-1	0	0	⊕⊕⊕⊕ Moderate	1.02 (-0.55, 2.67)	0	0	⊕⊕⊕⊕ High
EVG/c vs. EFV		0	0	-1	-1	0	⊕⊕ Low	0.43 (-2.14, 3.00)	0	0	⊕⊕ Low
RAL vs. DTG		--	--	--	--	--	--	--	--	--	--

EVG/c vs. DTG		--	--	--	--	--	--	--	--	--	--
LPV/r vs. DTG		--	--	--	--	--	--	--	--	--	--
ATV/r vs. DTG		--	--	--	--	--	--	--	--	--	--
DRV/r vs. DTG		--	--	--	--	--	--	--	--	--	--
NVP vs. DTG		--	--	--	--	--	--	--	--	--	--
EVG/c vs. RAL		0	0	-1	-1	0	⊕⊕ Low	-0.60 (-3.01, 1.82)	0	0	⊕⊕ Low
LPV/r vs. RAL		--	--	--	--	--	--	--	--	--	--
ATV/r vs. RAL	<b>-2.20</b> <b>(-3.12, -1.28)</b>	0	0	0	0	0	⊕⊕⊕⊕ High	<b>-2.20</b> <b>(-3.13, -1.28)</b>	0	0	⊕⊕⊕⊕ High
DRV/r vs. RAL	<b>-1.80</b> <b>(-2.72, -0.88)</b>	0	0	0	0	0	⊕⊕⊕⊕ High	<b>-1.80</b> <b>(-2.72, -0.89)</b>	0	0	⊕⊕⊕⊕ High
NVP vs. RAL		--	--	--	--	--	--	--	--	--	--

LPV/r vs. EVG/c		--	--	--	--	--	--	--	--	--	--
ATV/r vs. EVG/c	-1.58 (-3.80, 0.64)	0	0	0	-1	0	⊕⊕⊕ Moderate	-1.60 (-3.80, 0.63)	0	0	⊕⊕⊕ Moderate
DRV/r vs. EVG/c		0	0	-1	-1	0	⊕⊕ Low	-1.20 (-3.60, 1.22)	0	0	⊕⊕ Low
NVP vs. EVG/c		--	--	--	--	--	--	--	--	--	--

**Legend:** Uncombined estimates represent either direct estimates, if available, or indirect NMA estimates otherwise. Combined estimates are NMA estimates for comparisons where direct estimates were available. For uncombined estimates start with high quality evidence. -1 symbolizes a choice to rate down (e.g. high quality to moderate quality evidence); 0 symbolizes choice to not rate down; -- = not applicable because the NMA estimate is the only estimate.

The final quality of evidence updates that of the uncombined evidence. The quality can be moved up if the uncombined score was penalized for precision, which was overcome in network estimates. It can be moved down if the estimates are no longer precise or if there is evidence of inconsistency in loops containing the comparison (i.e. violation of transitivity).

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**Precision** – We rated down for precision if the confidence interval crossed the minimally important difference. **Consistency** – We assessed the consistency for direct treatment comparisons using  $I^2$  estimates and visual inspection of point estimates. An  $I^2$  of 75% or higher indicates considerable heterogeneity. This was conducted along the shortest indirect pathway with the largest number of trials for indirect estimates. **Risk of Bias** – For direct estimates we rated down for risk of bias if the majority of studies within a comparison were considered to be at high risk of bias and similarly along the principal indirect pathway for indirect estimates.

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#### GRADE confidence in estimates

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