

Switching ARVs for lipodystrophy

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Lipodystrophy: fat redistribution

- Lipoatrophy:
subcutaneous fat loss
- Lipohypertrophy:
fat gain
 - Central (visceral)
 - Focal: dorsocervical or breasts
- Mixed patterns



Clinical implications

- Common
- Visceral fat accumulation is associated with dyslipidaemia and insulin resistance
- Adherence is compromised when patients believe they have lipodystrophy from ARVs



AIDS 2003; 17(Suppl 1) :S141
NEJM 2005; 352: 48
JAIDS 2002; 31 (Suppl 3): S140

Is lipodystrophy an adverse drug reaction?

- Important to avoid unnecessary drug substitutions with risks of
 - treatment failure
 - new toxicities
 - undermining patient confidence

Systematic review

Is fat loss/gain reversed after switching ARVs?

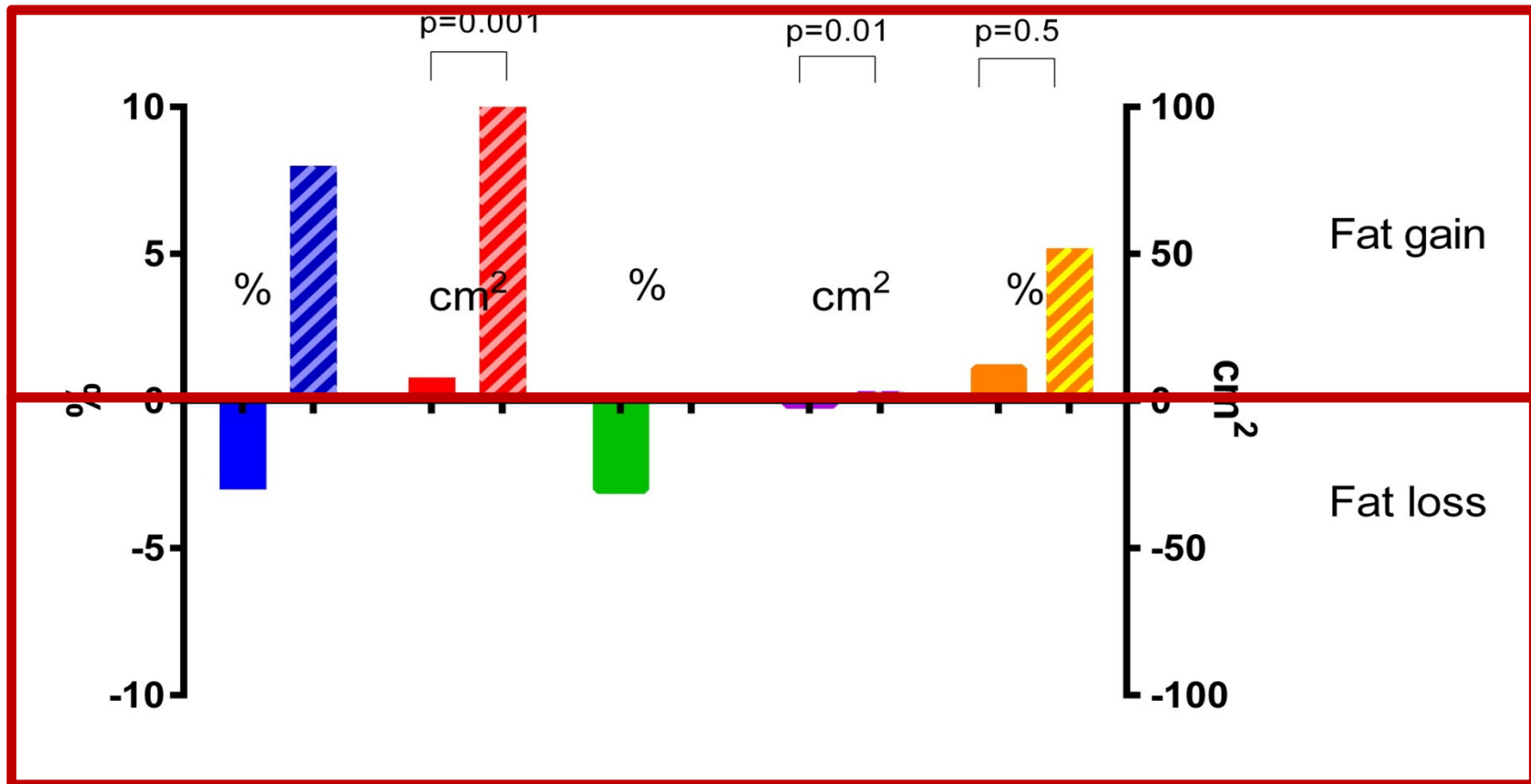
Eligibility criteria:

- Randomised controlled trials
- Patients on ART with and without lipodystrophy at baseline
- Interventions: switch versus continue current ARV regimen
- Objective measure of fat distribution: MRI, CT or DEXA scan



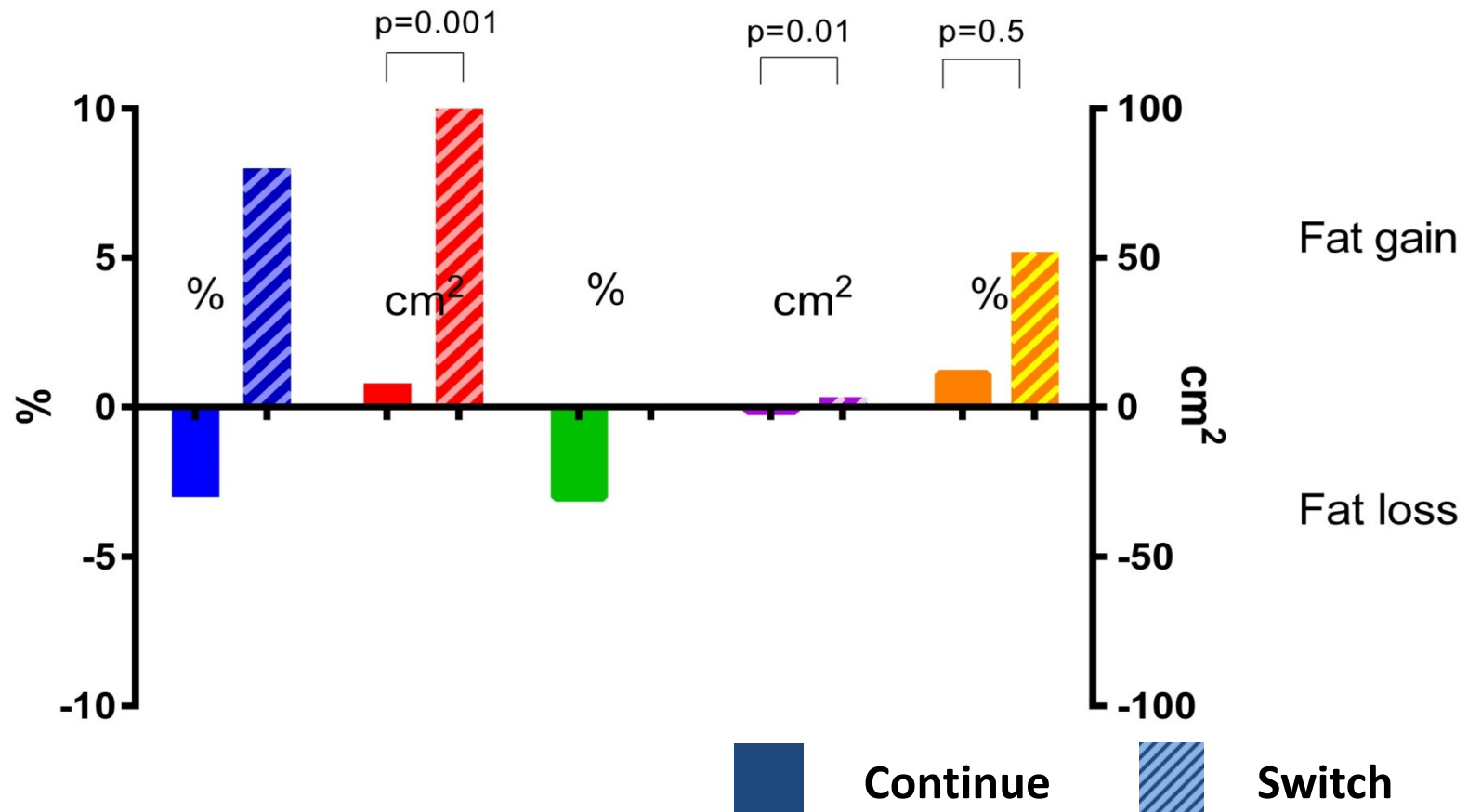
Does fat loss reverse on switching?

Change from baseline: subcutaneous/limb fat



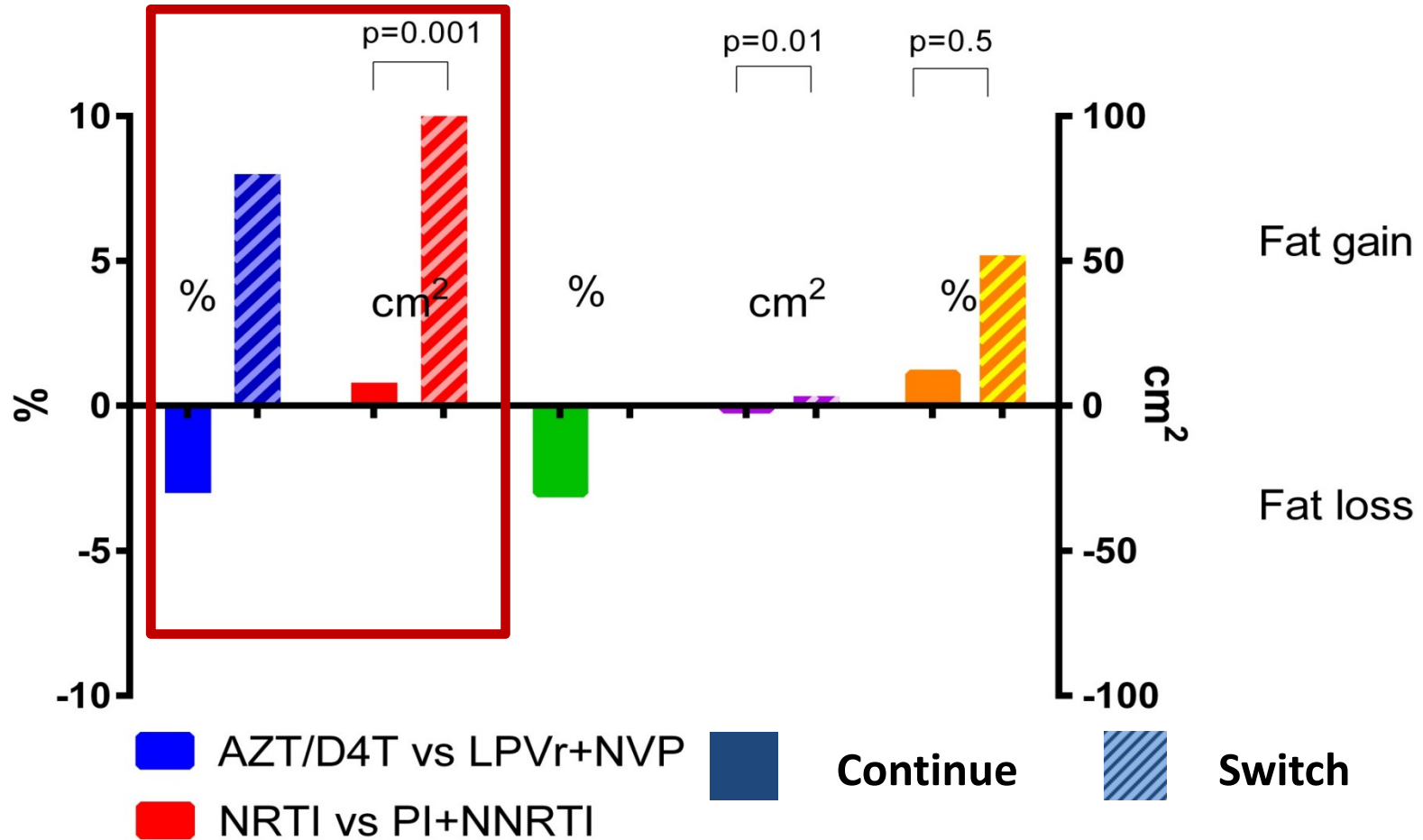
J Antimicrob Chemother 2009; 63:998
 HIV Med 2008; 9:625
 JAMA 2002; 288:207
 CROI 2011

Change from baseline: subcutaneous/limb fat



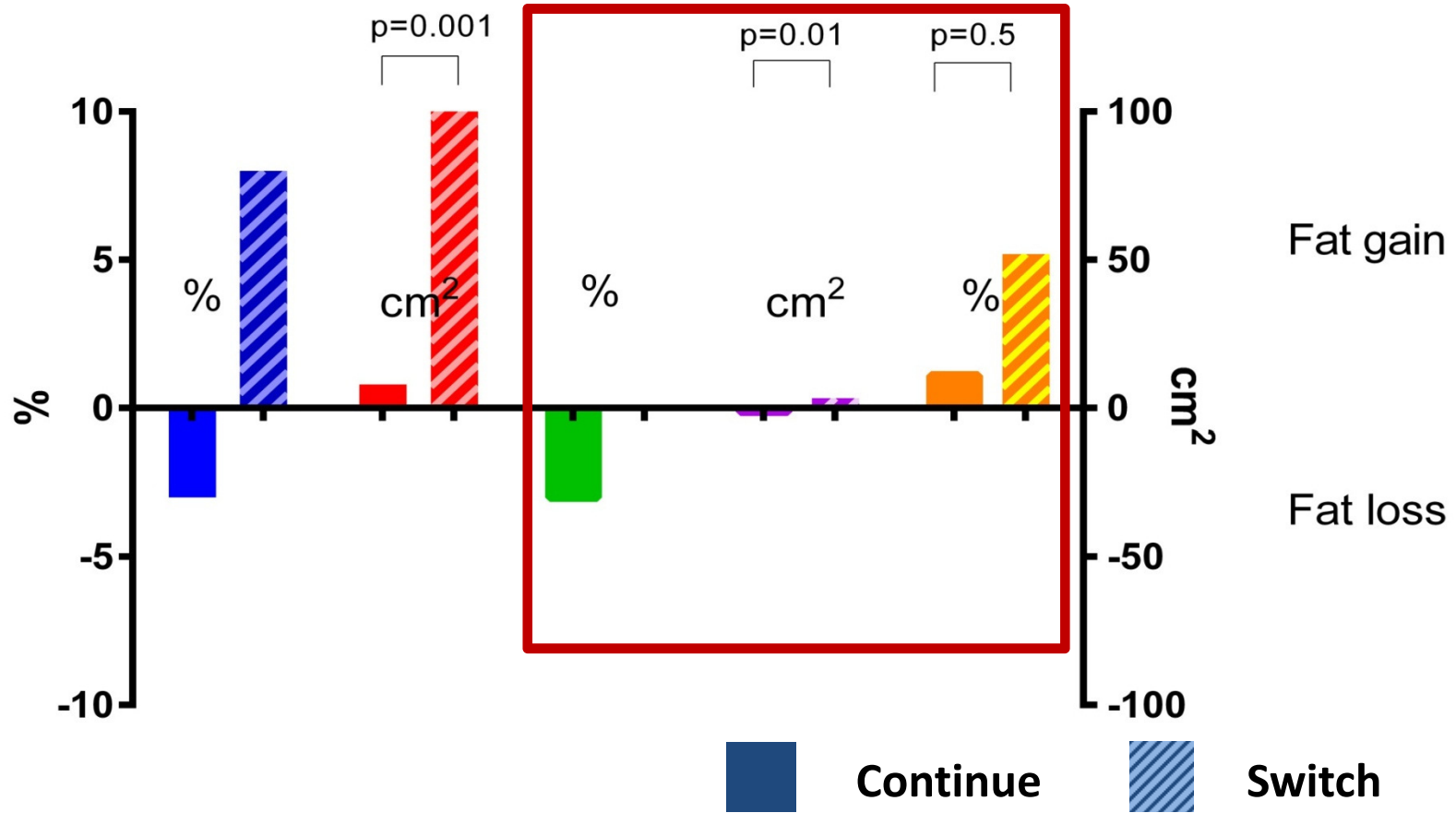
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Change from baseline: subcutaneous/limb fat



- AZT/D4T vs ABC
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- AZT vs TDF

J Antimicrob Chemother 2009; 63:998
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 CROI 2011

Does fat loss reverse on switching?

- Switching away from NRTIs, especially thymidine analogues, led to significantly more fat gain, or less fat loss, over time compared with controls.

Switching is a treatment option



Does fat loss reverse on switching?

- Switching from
 - PI to NNRTI
 - Ritonavir-boosted PI to ritonavir-boosted atazanavir
 - PI to raltegravirled to no significant between-group differences in limb fat over time.

Switching drugs other than NRTIs does not work

JAIDS 2001; 27:229

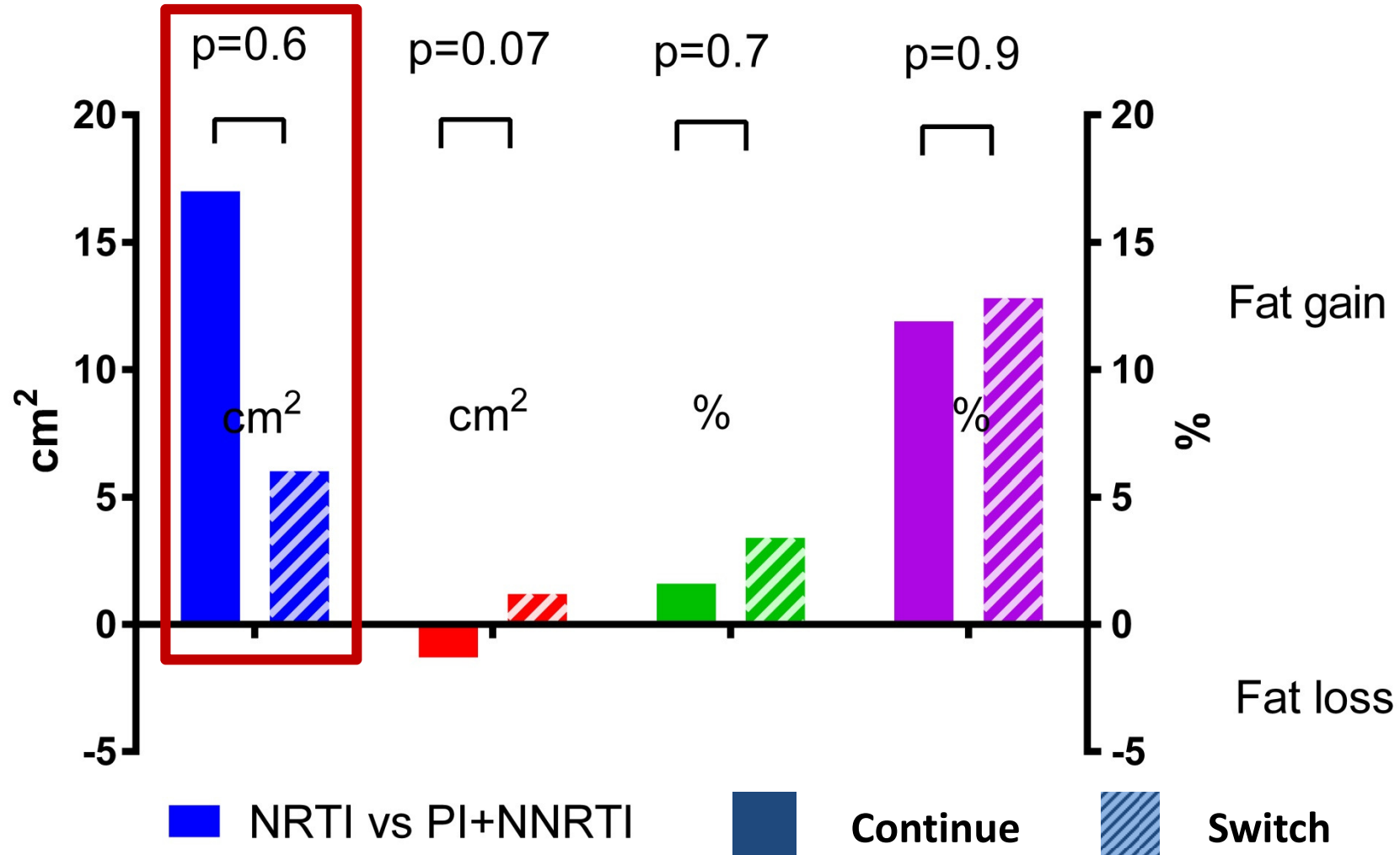
Antivir ther 2012; 17:689

AIDS 2012; 26:475



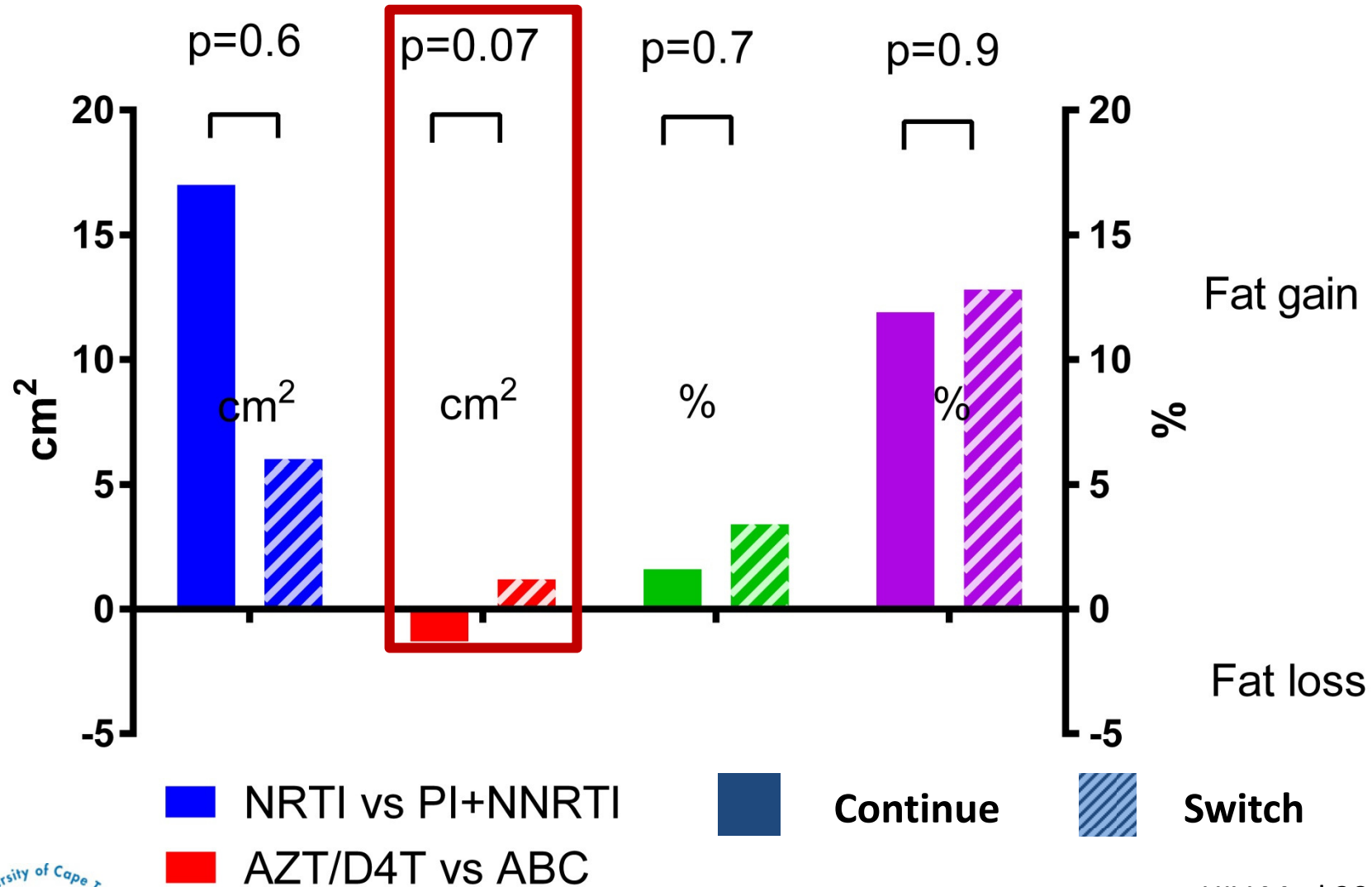
Does fat gain reverse on switching?

Change from baseline: visceral adipose tissue



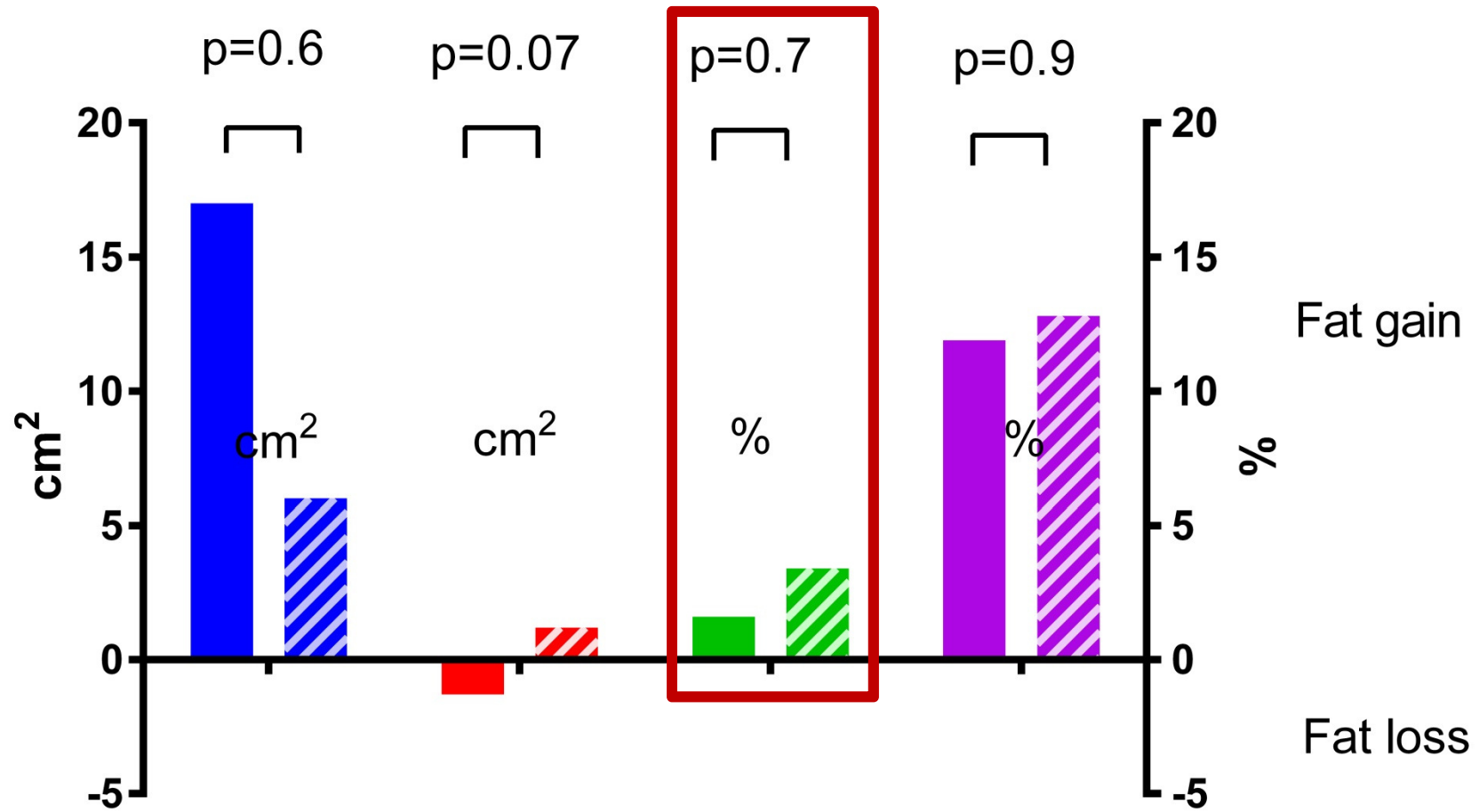
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Change from baseline: visceral adipose tissue



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Change from baseline: visceral adipose tissue

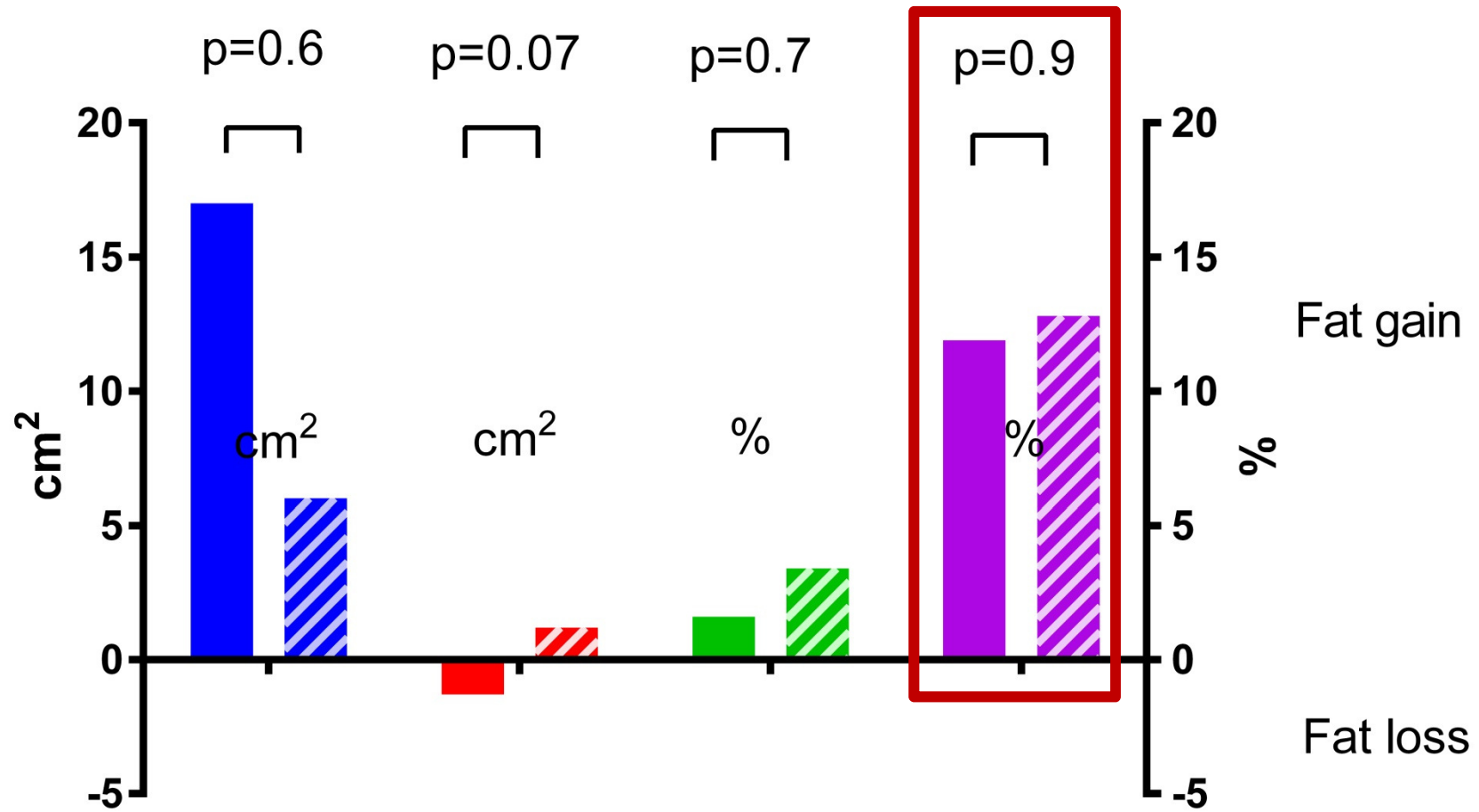


- NRTI vs PI+NNRTI
- AZT/D4T vs ABC
- Plr vs ATVr
- Continue
- ▨ Switch



HIV Med 2008; 9:625
 JAMA 2002; 288:207
 Antivir ther 2012; 17:689
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Change from baseline: visceral adipose tissue

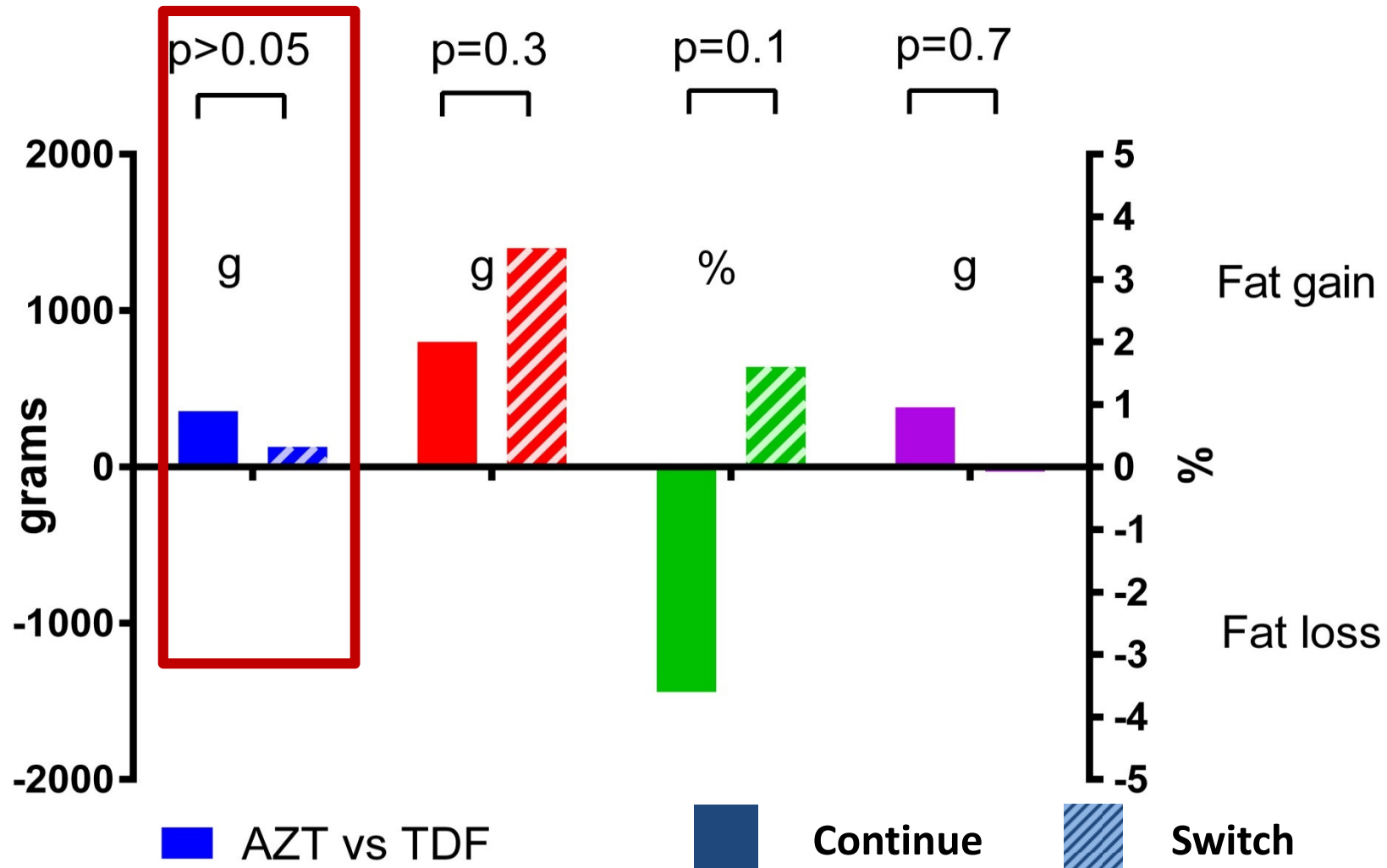


- NRTI vs PI+NNRTI
- AZT/D4T vs ABC
- Plr vs ATVr
- PI vs RAL
- Continue
- ▨ Switch



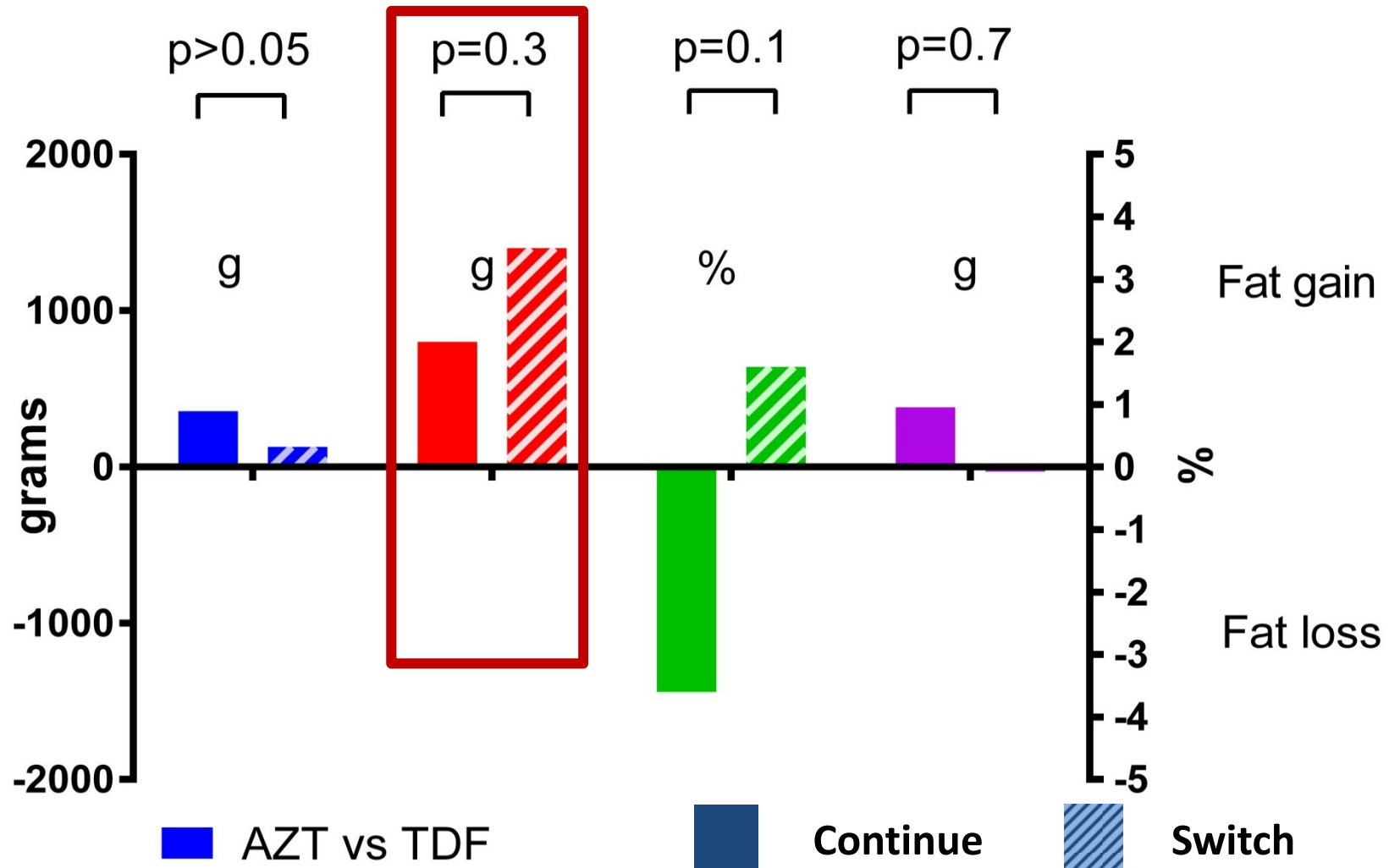
HIV Med 2008; 9:625
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Change from baseline: trunk fat



JAIDS 2009; 51:562
 JAMA 2002; 288:207
 Antivir ther 2012; 17:689
 AIDS 2012; 26:475

Change from baseline: trunk fat



■ AZT vs TDF

■ AZT/D4T vs ABC

■ Continue

■ Switch

JAIDS 2009; 51:562

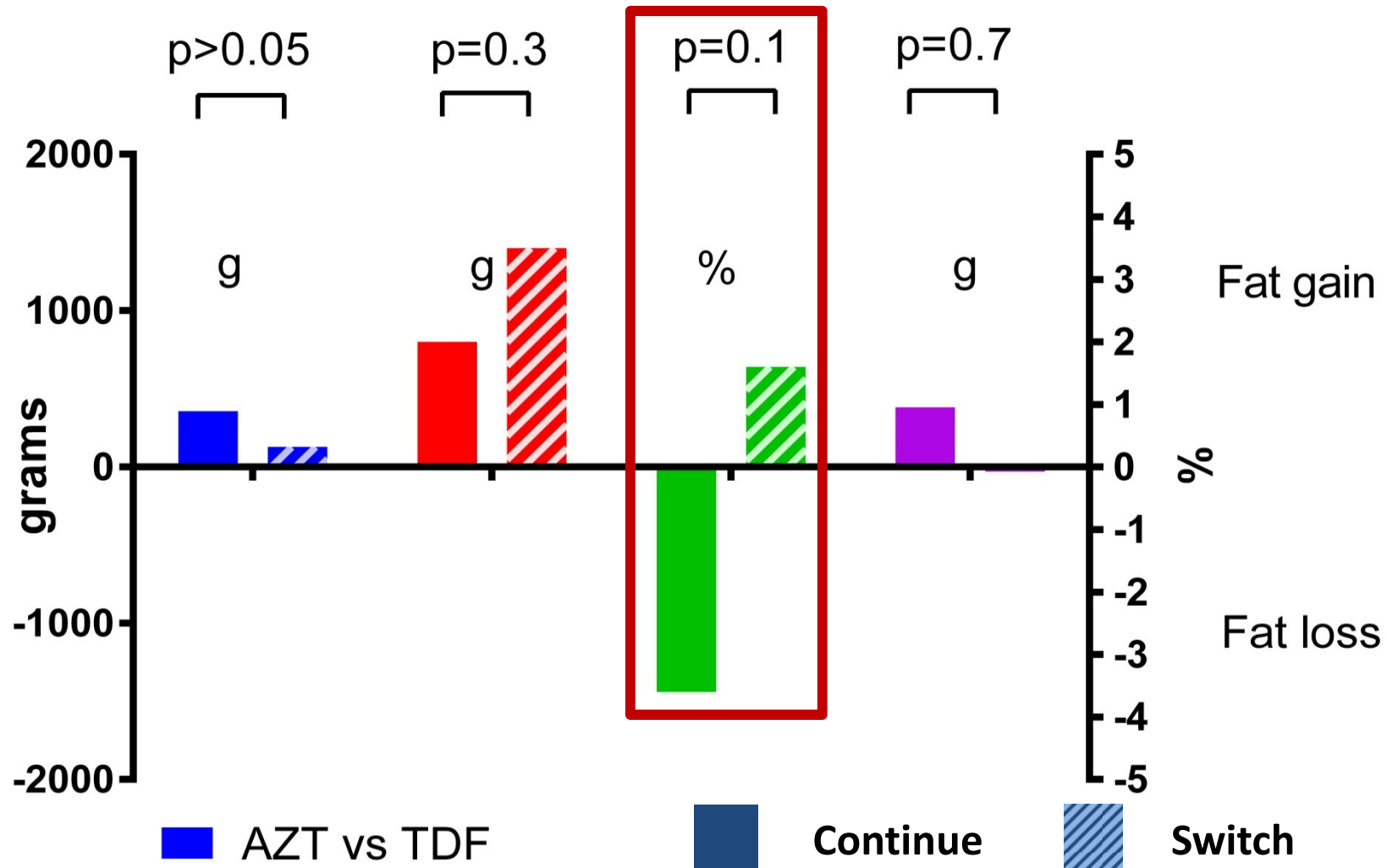
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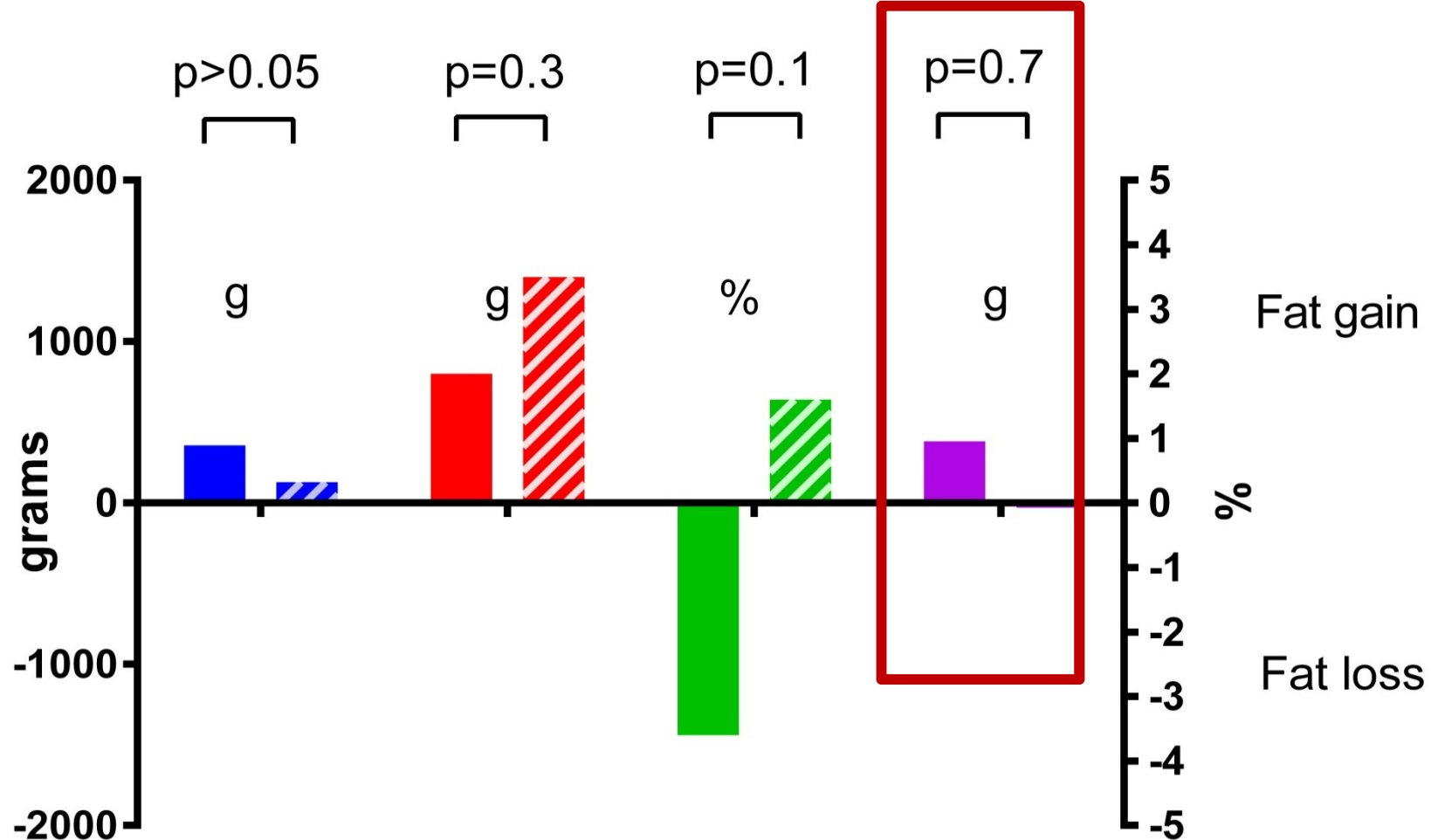
JAMA 2002; 288:207

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Change from baseline: trunk fat



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 AIDS 2012; 26:475



Does fat gain reverse on switching?

- Similar increases over time in all ARV regimens

Switching to reverse fat gain does not work



Treatment options for central fat gain

- Diet and exercise
 - VAT: modest effect; lipid profile: inconsistent results
- Metformin
 - Trend toward decreased VAT; but decreases LF too
- Growth hormone releasing hormone (tesamorelin)
 - Decreases VAT and improves lipid profile
 - Expensive



AIDS Patient Care STDS 2009; 23: 5
Curr HIV/AIDS Rep 2011; 8: 200
HIV/AIDS (Auckl) 2011; 3: 69

Conclusions

- Lipoatrophy is an adverse drug reaction
- Switching away from NRTIs with mitochondrial toxicity
 - Halts progression
 - Slow, modest improvements over time



Conclusions

- Central fat gain is not an adverse drug reaction, but probably a consequence of treating HIV.
- Treatment options for fat gain are limited, but important to avoid unnecessary ARV switches.

