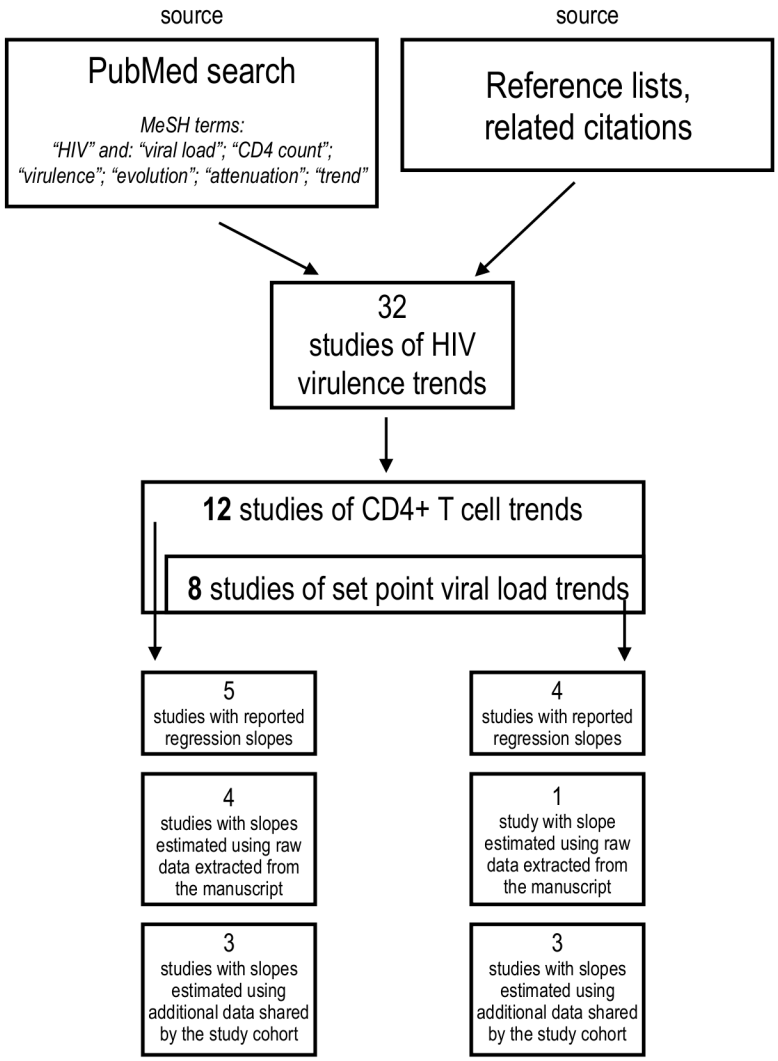
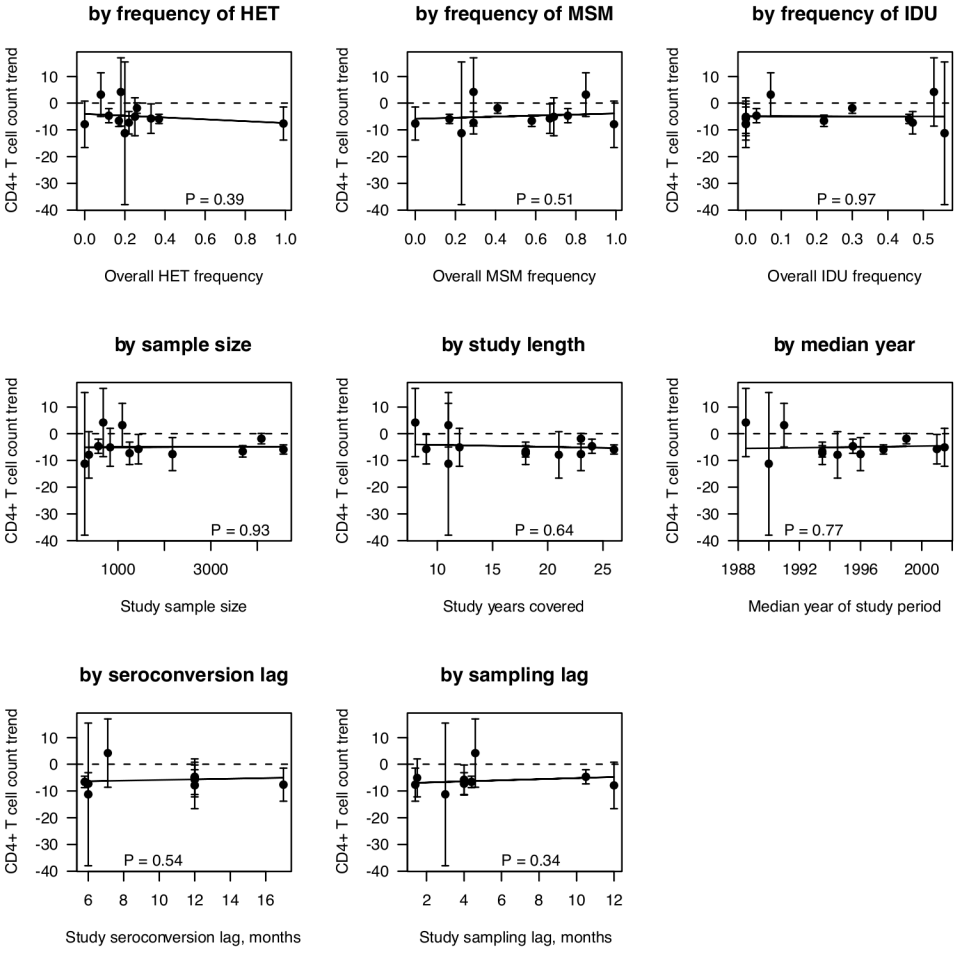
Supplemental Document 1. Publications that have addressed the potential changing virulence of HIV-1.

Study	Cohort location	Result	Virulence measurement						
Anonymous (1988)	US	less virulent	AIDS cases						
Gail (1990)	US	less virulent	AIDS cases						
Biggar (1990)	CA, UA, Eur, AU	stable		Time to AIDS					
Taylor (1991)	US	less virulent		Time to AIDS					
van Griensven (1992)	NL, US	more virulent		Time to AIDS					
Veugelers (1994)	CA, NL, US	more virulent		Time to AIDS					
Holmberg (1995)	US	stable				CD4 slope			
O'Brien (1995)	US	less virulent		Time to AIDS					p24 antigenemia
Galai (1996)	IT	stable			CD4 count				
Hessol (1996)	NL, US	less virulent		Time to AIDS					
Keet (1996)	NL	less virulent		Time to AIDS		CD4 slope			p24 antigenemia
Munoz (1996)	US	less virulent		Time to AIDS					
Carre (1997)	FR	stable		Time to AIDS					
Sinicco (1997)	IT	more virulent				CD4 slope			
Webber (1998)	US	less virulent		Time to AIDS					
Vanhems (1999)	CH	stable			CD4 count	CD4 slope			
Easterbrook (2000)	GB	stable			CD4 count				
CASCADE (2000)	Eur, AU, CA	stable		Time to AIDS					
Hendriks (2000)	CA, NL	stable				CD4 slope			
CASCADE (2003)	Eur, AU, CA	stable				CD4 slope			
Arien (2005)	BE	less virulent							Fitness assay
Dorrucci (2005)	IT	more virulent			CD4 count				
Müller (2006)	CH	stable				CD4 slope	CD4:CD8 slope	Viral load	
Gali (2007)	NL	more virulent							Fitness assay
Dorrucci (2007)	Eur, AU, CA	more virulent			CD4 count			Viral load	
Herbeck (2008)	US	stable			CD4 count	CD4 slope		Viral load	
Crum-Cianflone (2009)	US	more virulent			CD4 count				
Gras (2009)	NL	more virulent			CD4 count			Viral load	
Müller (2009)	IT	more virulent				CD4 slope		Viral load	
Potard (2009)	FR	more virulent			CD4 count			Viral load	
Troude (2009)	FR	stable			CD4 count			Viral load	
Crum-Cianflone (2010)	US	more virulent				CD4 slope			

Supplemental Document 2. Schematic of the study selection for inclusion in meta-analysis.



Supplemental Document 3. Meta-regression analyses of study level covariates for studies of trends in baseline CD4+ T cell counts. Mixed-effect model analysis of the relationships between study characteristics and the magnitude of trends in baseline CD4+ T cell counts. No covariate had a significant effect on the trend.



Supplemental Document 4. Meta-regression analyses of study level covariates for studies of trends in viral loads. Mixed-effect model analysis of the relationships between study characteristics and the magnitude of trends in set point viral loads. Seroconversion lag was the only covariate associated with a significant effect on the trend.