Table 1. Classification of levels of evidence and grades of recommendations

Classification of Evidence Levels

1++	High quality meta-analyses, systematic reviews of randomised controlled trials (RCTs) or RCTs with very low risk of bias
1+	Well conducted meta-analyses, systematic reviews of RCTs or RCTs with very low risk of bias
1-	Meta-analyses, systematic reviews of RCTs or RCTs with a high risk of bias
2++	High quality systematic reviews case-control or cohort studies High quality case-control or cohort studies with a very low risk of confounding, bias or chance and a high probability that the relationship is causal
2+	Well conducted case-control or cohort studies with a low risk of confounding, bias or chance and a moderate probability that the relationship is causal
2-	Case-control or cohort studies with a high risk of confounding, bias or chance and a significant risk that the relationship is not causal
3	None analytic studies eg case reports, case series
4	Expert opinion

Classification of Grades of Recommendations

A	At least one meta-analysis, systematic review or randomised controlled trial at 1++ and directly applicable to the target population; **Or** a systematic review of randomised controlled trials or a body of evidence consisting principally of studies rated 1+, directly applicable to the target population and demonstrating overall consistency of results
B	A body of evidence including studies rated as 2++, directly applicable to the target population and demonstrating overall consistency of results; **Or** Extrapolated evidence from studies rated 1+ or 1++
C	A body of evidence including studies rated as 2+, directly applicable to the target population and demonstrating overall consistency of results; **Or** Extrapolated evidence from studies rated 2++
D	Evidence level 3 or 4; **Or** Extrapolated evidence from studies rated 2+

Table 6

FDA Categories of the safety of therapy in pregnancy

A. Adequate and well-controlled studies of pregnant women fail to demonstrate a risk to the fetus during the first trimester of pregnancy (and there is no evidence of risk during later trimesters.

B. Animal reproduction studies fail to demonstrate a risk to the fetus and adequate and well-controlled studies of pregnant women have not been conducted.

C. Safety in human pregnancy has not been determined, animal studies are either positive for fetal risk or have not been conducted. The drug should not be used unless the potential benefit outweighs the potential risk to the fetus.

D. Positive evidence of human risk based on adverse reaction data from investigational or marketing experiences, but the potential benefits from the use of the drug in pregnant women may be acceptable despite its potential risks.

E. Studies in animals or reports of adverse reactions have indicated that the risk associated with the use of the drug in pregnant women clearly outweighs any possible benefit

Table 7

Risk of Congenital abnormalities from the Antiretroviral Pregnancy Register (2000)

	Numbers	%	95% CI
Number of Live Births with at least one defect / Live Births			
Any drug, any combination			
Any trimester of exposure,	22/1027	2.1	1.4 – 3.3
First Trimester Exposure	6/444	1.4	0.6 – 3.1
Second/Third Trimester	16/583	2.7	1.6 – 4.5