**Table 1 Individual studies characteristics and quality of evidence assessment**

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| **Study Characteristics** | | | | | | **Key Findings** | | **Quality of Evidence for**  **Individual Studies** | | | **Evidence from Economic Evaluation** | **Comments** |
| **External**  **and**  **Internal Validity** | | **Overall Quality of Evidence Rating** |
| **Citation** | **Study design** | | **Study period** | | **Number**  **patients** | **Internal Validity (Bias)** | **External**  **Validity** |
| **MORBIDITY** | | | | | | | | | | | | |
| **Anglaret *et al*. 1999 1** | RCT | 1996- 1998  **Cote d' Ivoire** | | 545 | | | CG: CTX: 271)  Placebo: 270 “Incidence Severe malaria events”: 2 in the CTX group; 12 in the placebo group (Log rank test, P= 0·007) | Fair | Fair | Strong | No | SP: general population GP ART: No WHO stage: CTX: stage 2 = 34%; stage 3 = 59%; stage 4 = 7% Placebo: stage 2 = 36%; stage 3 = 59%; stage 4 = 5%  CD4 count: CTX (mean: 322)–placebo (mean: 331) |
| **Bulabula *et al*. 2009 2** | OS | 2009 **DRC** | | 345 | | | CG: HIV positive on CTX to and HIV negative off CTX Use of CTX: Malaria (parasitemia prevalence) OR = 1.5 (95% CI, P <0.05.) OR = 1.5 (95% CI 0.58 - 3.81) | Poor | Fair | Weak | No | SP: GP (HIV-infected and non-infected individuals) ART: Unknown status  WHO stage: not reported  CD4: not reported |
| **Campbell *et al*. 2012 3** | RCT | 2007-2008 **Uganda** | | 836 | | | CG “continuing CTX”: 452 vs. “discontinuing CTX”384 continuing vs. discontinuing CTX: 0.4 and 12.2%, respectively, had at least 1 episode of malaria (fever and positive smear test) (P<0.001) | Fair | Fair | Strong | No | SP: GP ART: Yes WHO stage: not reported  CD4 Mean: Discontinuation group: 505 cells/ µL; Continuation group: 476 (P= 0.05) |
| **Denoeud-Ndam *et al*. 2013 4** | RCT | 2009- 2011 **Benin** | | 432 | | | CG: In “CNM trial” CTX: 72. MQ-IPTp: 68 allocated; 67 received; In the “CM trial”: 292 CTX: 146, CTX+IPTp-MQ: 146 In “CM trial”, efficacy for the prevention of placental parasitemia not more than CTX <5% inferior, in  preventing placental malaria,  to the CTX + IPTp-MQ)  In CM trial, CTX + MQ group compared with CTX alone (0/105 vs. 5/103, P = 0.03) | Good | Good | Strong | No | SP: HIV-infected pregnant women ART: Yes WHO stage: not reported CD4: In the CTX-mandatory trial, CD4 <350 uL; in the CTX not- mandatory trial they had CD4 >\_ 350/uL |
| **Dow *et al*. 2013 5** | OS | 2004- 2009 **Malawi** | | 1236 | | | CG: “CTX-exposed”: 468  “CTX-unexposed”: 768 CTX vs IPTp Malaria (positive smear and malaria symptoms) HR = 0.35, 95% (CI): 0.20, 0.60) | Poor | Fair | Medium | No | SP: Pregnant women ART: Yes  WHO stage: not reported CD4: Yes  CTX-unexposed median CD4 count= 350 (IQR: 276−421)  CTX-exposed median CD4 count= 362 (IQR: 303−429)] |
| **Hamel *et al*. 2008 6** | OS | 2002- 2003 **Kenya** | | 1160 | | | CG: HIV-positive subjects with CTX: CD4 cell count < 350 cells/ µL (lower- CTX; CD4 cell count >350 cells/µL and HIV-negative : multivitamins *P.f* parasitemia density (prevalence) ARR lower-CD4 vs. higher-CD4 = 0.11; 95% [CI] = 0.06–0.15; P < 0.001) | Good | Fair | Medium | No | SP: GP (HIV-infected enrollees; HIV uninfected) ART: no  WHO stage: not reported  CD4: yes [Median CD4 cell count in cells/uL (range): <350 cells/uL = 168 (0–349); >\_350 cells/uL = 561 (350–1739)] |
| **Kapito-Tembo *et al*. 2011 7** | OS | 2005- 2009 **Malawi** | | 1142 | | | CG: Comparison of 3 groups:  “IPTp-SP only”, “CTX only” ; “SP-IPTp plus CTX” “IPTp-SP plus CTX” vs. IPTp-SP” and vs. “CTX” : malaria parasitemia (prevalence) OR, [95%CI]: 0.09, [0.01-0.66] and 0.43, [0.19-0.97], respectively | Good | Good | Medium | No | SP: HIV-infected pregnant women aged 15 or more and with gestation Over 34 weeks ART: Yes  WHO stage: yes  SP & CTX (n=173):1 or 2 (83.0%); 3 or 4 (17%)  CTX only (n=334): 1 or 2 (89.8%); 3 or 4 (10.2%)  SP only (n=557): 1 or 2 (87.4%); 3 or 4 (12.6%)  None (n=57): 1 or 2 (92.9%); 3 or 4 (7.1%)  CD4: yes  SP & CTX (n=173):  <200 (11%); 200–499 (57.8%); >\_ 500 (31.2%)  CTX only (n= 334):  <200 (7.5%); 200–499 (50.9%); >\_ 500 (41.6%)  CTX only (n= 557):  <200 (11.7%); 200–499 (53.1%); >\_ 500 (35.2%)  None (n= 57):  <200 (8.8%); 200–499 (42.1%); >\_ 500 (49.1%) |
| **Klement *et al*. 2013 8** | RCT | 2009- 2011 **Togo** | | 264 | | | CG: CTX (126 of 132) or IPTp-SP (124 of 132)  Proportions of women malaria-free during pregnancy : 75.4% women on CTX and 84.7% on IPTp-SP: (malaria: symptomatic parasitemia) (difference of 9.3%; 95% [CI], –.53 to 19.1, not meeting the predefined non-inferiority criterion) | Good | Good | Strong | No | SP: HIV-infected pregnant women ART: Yes WHO stage: CTX (n= 126): Stage 1 (91.3 %); Stage 2 (4.8%); Stage 3 (4%); Stage 4 (0%) SP-IPTp (n= 124): Stage 1 (92.7%); Stage 2 (4.0%); Stage 3 (3.2%); Stage 4 (0%)  CD4: CTX (n= 126):200-349 (42.1%); 350-499 (23.0%); >\_500 (34.9%) SP-IPTp (n= 124): 200-349 (23.4%); 350-499 (33.9%); >\_500 (42.7%)" |
| **Manyando *et al*. 2013 9** | SR | SR | | SR | | | CTX reduces incidence of clinical malaria by 46%–97% (see individual studies elsewhere in this table) | Fair | Fair | Strong | No | See individual studies |
| **Mermin *et al*. 2004 10** | OS | 2001- 2003**. Uganda** | | 509 individuals with HIV-1 infection and their 1522 HIV-negative household members | | | CG: Comparison “before/after” CTX implementation 72% (IRR) reduction of malaria (fever and positive thick smear) irrespective of age and CD4 count-cell count | Fair | Fair | Medium | No | SP: GP HIV-1 infected individuals and their HIV-negative household members ART: No WHO stage: distribution not reported for the morbidity outcome  CD4: yes (proportions reported by morbidity outcome and by person-years of follow-up) |
| **Newman *et al*. 2009 11** | OS | 2008-2009**. Uganda.** | | 517 | | | CG: HIV-infected mothers 89% on CTX HIV-uninfected mothers 94% on IPTp-SP  No increased risk of placental malaria in HIV-infected (prevalence) women on CTX vs. HIV uninfected on IPTp-SP | Fair | Fair | Medium | No | SP: HIV-infected and uninfected pregnant women ART: Yes WHO stage: Not reported CD4: Not reported |
| **Polyak *et al*. 2014 12** | RCT | 2012- 2013 **Kenya.** | | 500 | | | CG: 250 enrolled in each of the two arms (CTX and No-CTX) CTX discontinuation: morbidity/mortality end-point (including symptomatic parasitemia) IRR= 2.27, 95% CI: 1.52-3.38; p < 0.001) | Good | Good | Strong | No | SP: GP  ART: yes  WHO stage: not reported  CD4: median enrollment CD4 count 595 cells/uL |
| **Saracino et al. 2012 13** | OS | 2010 **Mozambique** | | 342 | | | CG: CTX: 78 HIV-positive individuals Off-CTX= 252 (142 HIV positive and 110 HIV negative) Diagnosis of malaria (symptomatic parasitemia) significantly less likely to be made among “CTX group” vs. “Off-CTX” (prevalence): 12.8% vs. 32.9%, p<0.001) | Fair | Fair | Medium | No | SP: GP (hospitalized HIV-infected and uninfected enrollees) ART: Yes (31.4% of 220 HIV-infected enrollees).  WHO stage: yes (WHO stage 3 and 4 accounted for 77% of the 182 patients with available information)  CD4: median enrollment CD4 count 595 cells/uL CD4: available in a minority of enrollees (not considered in the analysis) |
| **Walker *et al*. 2010 14** | OS | 2003- 2004 **Uganda and Zimbabwe** | | 3179 | | | CG: Total enrollees: 3179  “On CTX at ART initiation” 61% “Off CTX at ART initiation” 39% CTX associated with reduction of frequency of malaria (symptoms and positive smear) (0·74, 0·63–0·88; p = 0·0005) | Fair | Fair | Medium | No | SP: GP ART: Yes WHO stage: stages 2 and 4  CD4: Yes[CD4 cell count ≤ 200  cells/μL] |
| **Watera *et al*. 2006 15** | OS | 2000- 2001 **Uganda** | | 353 | | | CG: comparison of outcomes between “Pre” and “Post” CTX prophylaxis implementation No difference in primary outcomes (febrile events incidence rates )  69% reduction in the incidence of malaria illness | Fair | Fair | Medium | No | SP: GP  ART: no  WHO stage: not reported for morbidity analysis  CD4: yes for morbidity analysis. In the first period: 115 participants with CD4 > 500 cells/uL, 160 between 200 and 499 cells/uL, and 78 with < 200 cells/uL. By the second period, 101, 161, and 91 for each of the 3 categories |
| **Mermin *et al*. 2006 16**  **(LLINs and CTX)** | OS | 2001-2004 **Uganda.** | | 1363 | | | CG: comparison CTX vs. no CTX during the FU period= phase 1 no CTX: 466; phase 2 CTX: 399; phase 3 CTX and ART:1035; phase 4 CTX, ART and ITNs: 989  Malaria (fever and parasitemia) incidence ART and CTX vs. CTX alone: IRR= 0·36 [95% CI 0·18–0·74], p=0·0056) | Fair | Fair | Medium | No | SG: GP  ART: yes  WHO stage: data collected and used for analysis, but specific proportions not reported  CD4: yes (median cells count 124 cells/uL) |
| **Iliyasu *et al*. 2013 17**  **(LLINs and CTX)** | OS | 2012 **Nigeria** | | 363 | | | CG:  ITNs use vs. non-use; and on CTX vs. off- CTX  53.5% reported use of ITN; 35.8% were on CTX at the time of the survey  Non-use of ITN (aOR = 1.97, 95% CI 1.17–2.85; P value = 0.017) (predictor of clinical malaria, defined as symptomatic positive parasitemia)  No association between not being on CTX and clinical malaria: Adjusted OR (95% CI)1.27 (0.98–1.64) | Fair | Fair | Medium | No | SP: HIV-infected women in post-partum ART: Yes WHO stage: Yes  Total 363 (100.0%)  Stage 1: 26.7%); stage 2: 24.2%; stage 3: 17.3%; stage 4: 31.7%; CD4: Yes; Baseline CD4 count (cells/ µL): Total enrollees: 363 (100.0%): <350 CD4 : 57.3% 350–599 CD4: 24.5% ≥600 CD4: 18.2% |
| **Olowookere *et al*. 2013 18**  **(LLINs)** | OS | 2010 **Nigeria** | | 425 | | | CG: *p.f* parasitemia prevalence measured at baseline and at end of F.U duration, among Reduction from 60%  baseline of malaria p.f parasitemia to 5% at three months with ITN use and malaria prevention education | Fair | Fair | Medium | No | SP: GP ART: Yes (No information on proportions) WHO stage: Not reported CD4 distribution: Not reported |
| **Walson *et al*. 2013 19**  **(LLINs)** | OS | 2008-2010 | | 589 | | | CG: “Standard of care”: 228; Intervention: “LLINs and water filters provision”: 361  Incidence of “Self-report malaria (fever and positive parasitemia)within the previous 3 months” (RR= 0.75; 95% CI 0.60–0.93)  Incidence of “clinically diagnosed malaria illness within the  Previous 3 months” (RR 0.66; 95% CI 0.49–0.88) | Fair | Fair | Medium | Yes (separate paper) Kern et al. 2013) | SP: GP (HIV-1-infected adults not yet meeting criteria for ART)  ART: no (all participants were provided CTX. Intervention cohort: 99.7%, control cohort: 99.8%, P = 0.8)  WHO clinical: yes stage 1 or 2  CD4: yes (> 350 cells/uL within the previous 3 mo) |
| **Kahn *et al*. 2011 20,** | Costing study  Kenya | NA | | NA | | | NA | NA | NA | NA | Cost per person served was:$41.66 for the initial campaign and was projected at $31.98 for the scaled-up replication | CE study (ART: No; CD4: Yes) |
| **Kahn et al. 2012 21,** | CE study  Kenya | NA | | NA | | | NA | NA | NA | NA | Per 1000 campaign beneficiaries , provision of LLINs led to:  The aversion of:  . 4.31 deaths  . 1304 malaria episodes  . 125 DALYS  . And $10.420 of costs | CE study (ART and CD4 costs included in model) |
| **Kern *et al*. 2013 22**  **CE** | CE study  **Kenya** | NA | | NA | | | NA | NA | NA | NA | Intervention 86 DALYs. LLINs and water filters accounted for 54% and 36% of the reduction in the burden of disease, respectively Net cost savings of about  US$ 26 000 for the intervention, over 1.7 years | CE study (ART: Yes; CD4: Yes) |

***Abbreviations:*** *aOR: adjusted odds ratio; ART: antiretroviral therapy; CDC: Centers for Disease Control; CE: cost-effectiveness; CG: comparison group; CI: confidence interval; CM trial: co-trimoxazole mandatory trial; CNM trial: co-trimoxazole non-mandatory trial; CTX: co-trimoxazole; DALY: disability adjusted life years; F.U: Follow-up; SP: study population; GP: general population; HR: hazard ratio; IPT-SP: intermittent preventive treatment with sulfadoxine-pyrimethamine; IRR: incidence rate ratio; mITT and PP analyses: modified intention-to-treat and per-protocol analyses; MQ-IPTp: mefloquine-intermittent preventive therapy for pregnant women; MQ: mefloquine; OI: opportunistic infection; OR: odds ratio; OS: observational study; P.F: plasmodium falciparum; RCT: randomized controlled trial; SR: systematic review; RR: relative risk; WHO: World Health Organization.*

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