

Supplemental Information

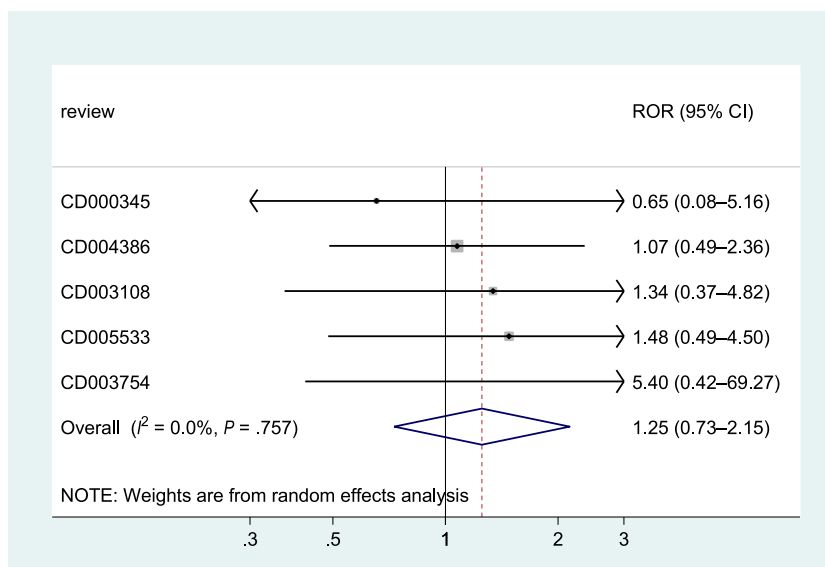
SUPPLEMENTAL APPENDIX 1 SUPPLEMENTAL METHODS

Exclusion criteria

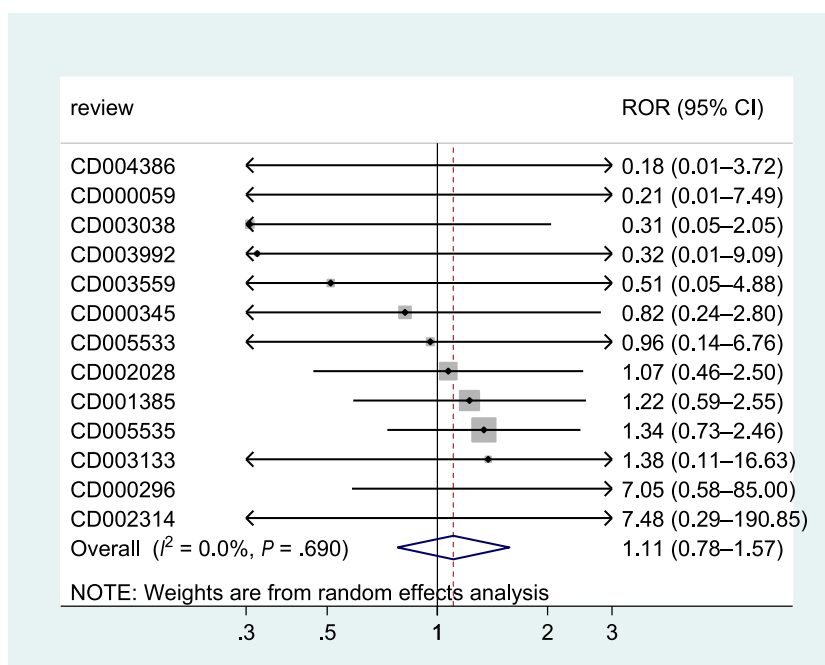
We excluded meta-analyses that did not include ≥ 1 RCT in adults and ≥ 1 RCT in children for any of the study end points and meta-analyses without quantitative synthesis for any of those end points. Furthermore, meta-analyses with no events in the experimental and control intervention arms in all adult or all pediatric trials or all adult and all pediatric trials were excluded only from the quantitative data synthesis because these meta-analyses could not contribute any information (12 such topics were excluded: 3 from the analysis of severe harms, 1 from the analysis for any harm, 1 from the analysis for organ system–level harms, 2 from specific harms, and 5 from mortality).

Characterization of Adult and Pediatric RCTs¹

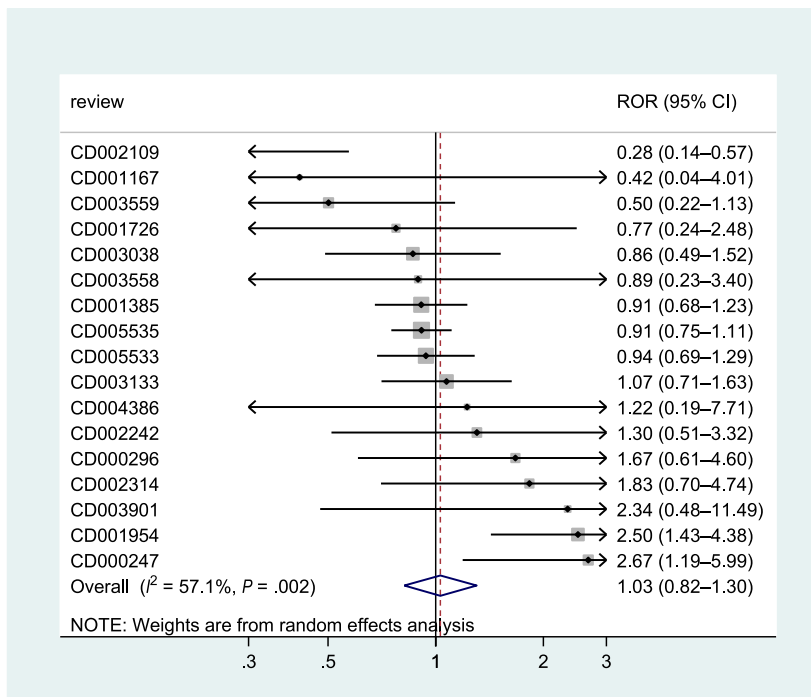
For trials in which the Cochrane review did not specify whether the study included adults or children, we used the following rules to define the age groups. The trial population was considered to be “adult” if all the included patients were >12 years old (more specifically, if the lower age range of the included patients, as reported in the Cochrane review, was >12 years and the upper age range was >12 years and the upper age range was >20 years); “pediatric” if all the included patients were <20 years old (if the lower age range of the included patients was <12 years and the upper age range was <20 years); “mixed” if both patients <12 and >20 years old were included or if patients 12 to 20 years were included; and “unspecified” if the age of the included patients was not reported at all in



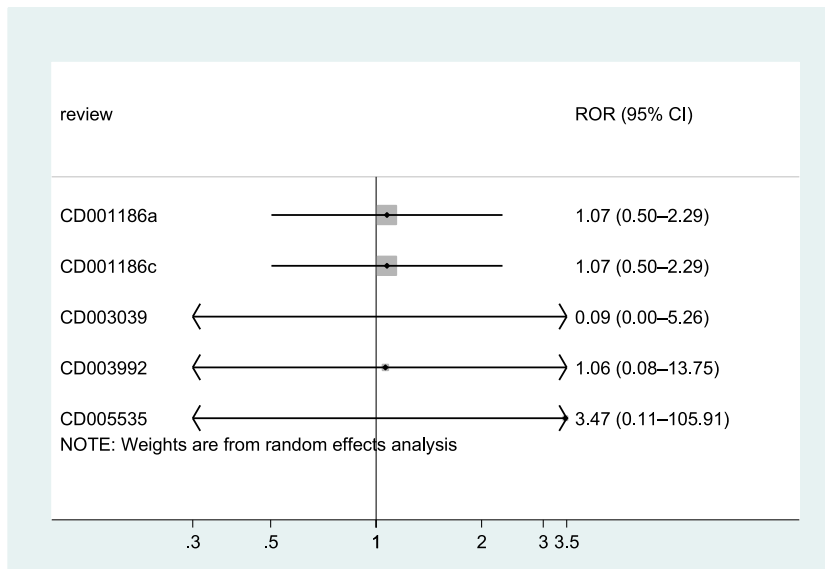
SUPPLEMENTAL FIGURE 2
sROR for severe harms.



SUPPLEMENTAL FIGURE 3
sROR for withdrawals due to harms.



SUPPLEMENTAL FIGURE 4
sROR for any harm.



SUPPLEMENTAL FIGURE 5
Individual RORs for organ system-level harms.

the Cochrane review. We excluded mixed age group ($n = 75$) and unspecified age group studies ($n = 69$).

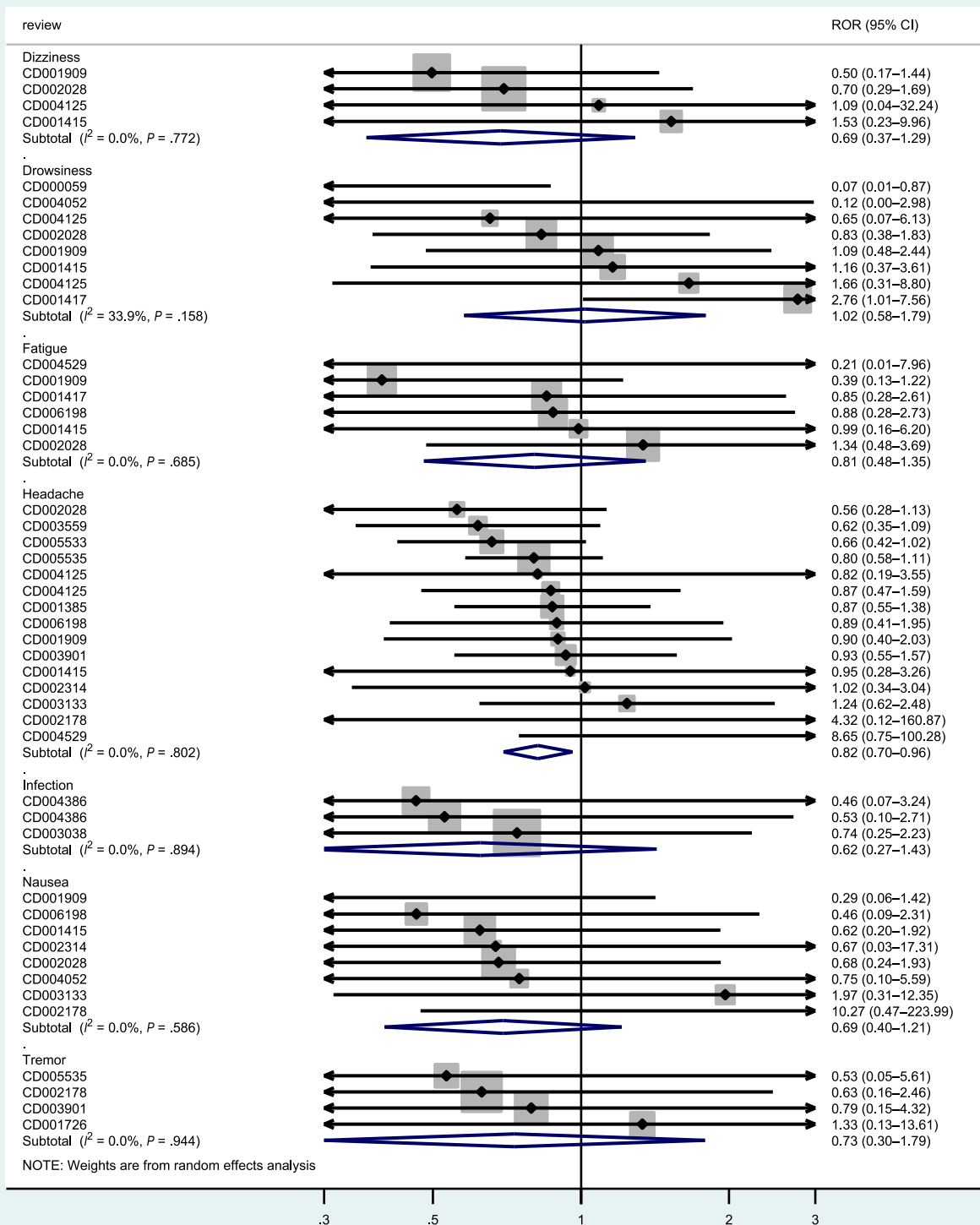
Categorization of Interventions Into Experimental and Control¹

The identification of the experimental and control intervention when 2 active

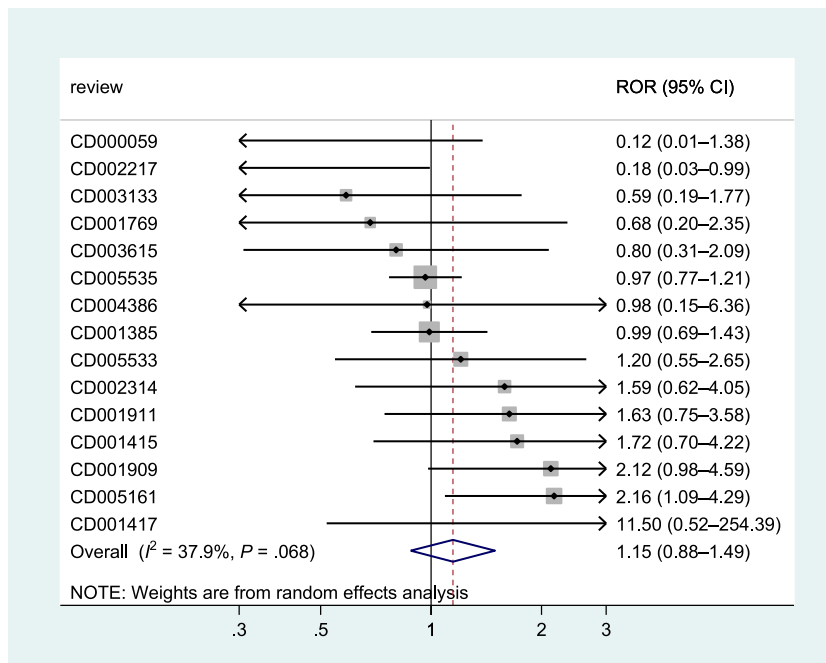
interventions were compared was based on the interpretation of the authors of the Cochrane review. If this was not clear, we identified which intervention had been first discovered according to Merck Index 2006 and/or Wikipedia, and this was considered the control intervention.

Meta-Analyses With Zero Events

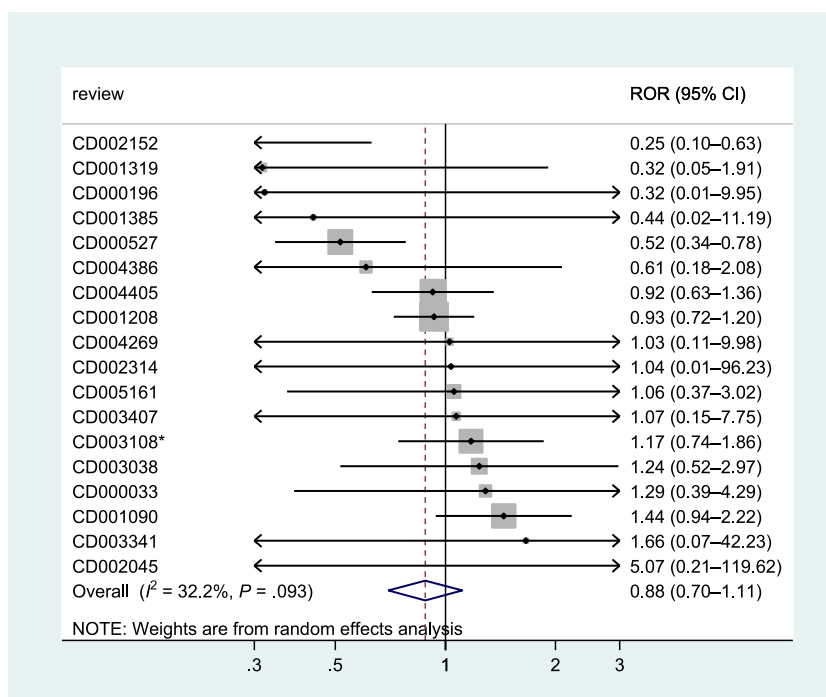
When there were zero events for both the experimental and control arm for all adult or all pediatric or all adult and pediatric trials, RORs were not calculated (11 of 176 meta-analyses; 6%).

**SUPPLEMENTAL FIGURE 6**

sROR for specific harms (shown only those with ≥ 4 meta-analyses per specific harm that were quantitatively synthesized).



SUPPLEMENTAL FIGURE 7
sROR for withdrawals for any reason.



SUPPLEMENTAL FIGURE 8
sROR for mortality.

SUPPLEMENTAL TABLE 3 Characteristics of Included Systematic Reviews

Topics	<i>n</i>
Infectious diseases	17 reviews (52 meta-analyses)
Neurologic/psychiatric diseases	15 reviews (46 meta-analyses)
Allergic/respiratory diseases	13 reviews (58 meta-analyses)
Hematologic/oncologic/transplant	4 reviews (9 meta-analyses)
Intensive care	3 reviews (3 meta-analyses)
Other	8 reviews (8 meta-analyses)
Types of interventions	
Drugs	47 reviews (162 meta-analyses)
Vaccines	1 review (7 meta-analyses)
Biologic agents/immunotherapy	3 reviews (5 meta-analyses)
Rehydration solutions	2 reviews (2 meta-analyses)
Types of controls	
Placebo or no treatment	32 reviews (114 meta-analyses)
Another active control agent	22 reviews (62 meta-analyses)

SUPPLEMENTAL TABLE 4 Summary ROR for each individual Harm/Harm related endpoint; ROR adults vs children in each individual meta-analysis and OR (95% confidence intervals) for the experimental vs control intervention in adults (OR adults; LCI, UCI) and children respectively (OR peds, LCI, UCI)

Review	Title	Comparison	Severe adverse events	sROR		UCI_sROR		i2		OR		LCI OR		UCI OR	
				ROR	LCI ROR	ROR	LCI ROR	OR adults	OR peds	LCI OR adults	LCI OR peds	UCI OR adults	UCI OR peds		
CD000345	Sequential combination of glucocorticosteroids and alfa interferon versus alfa interferon alone for HBeAg-positive chronic hepatitis B	Glucoc + IFN vs control + IFN	Severe adverse events	.6542	.083	5.158	2.15	.8863	0%	2.17	1.355	.2107	2.107	8.71	
CD004386	Antibiotic prophylaxis for bacterial infections in atebriile neutropenic patients following chemotherapy	Drug vs placebo/no intervention	Serious adverse events	1.073	.4886	2.357	1.759	1.345	2.301	1.639	.7824	3.453			
CD003108*	Cotrimoxazole prophylaxis for opportunistic infections in adults with HIV (combined with pediatric CD0003508)	Cotrimoxazole vs control	Adverse events (causing discontinuation of therapy or hospitalization)	1.338	.3714	4.824	1.199	.4086	3.52	.896	.4468	1.797			
CD005533	Combination of inhaled long-acting beta2-agonists and inhaled steroids versus higher dose of inhaled steroids in children and adults with persistent asthma	LABA + ICS vs higher dose ICS	Serious adverse events	1.478	.4859	4.496	1.126	.8998	1.41	.7621	.2563	2.266			
CD003754	Reduced osmolarity oral rehydration solution for treating cholera	Reduced osmolarity (glucose-based) oral rehydration solution vs standard oral rehydration solution	Severe biochemical hyponatremia (serum sodium < 125 mmol/L)	5.402	.4212	69.27	1.801	.6049	5.36	.3333	.0332	3.346			
CD003038	Beta-lactam versus beta-lactam-aminoglycoside combination therapy in cancer patients with neutropenia	Beta-lactam vs beta-lactam-aminoglycoside combination therapy	Severe nephrotoxicity			.1839		.0308	1.096						
CD001385	Long-acting beta2-agonists for chronic asthma in adults and children where background therapy contains varied or no inhaled corticosteroid	LAB2A vs placebo	Serious adverse event related to study drug							1.89	.8973	3.98			
CD001490	Magnesium sulfate for treating exacerbations of acute asthma in the emergency de	Intravenous MgSO4 vs placebo	Major Side Effects												
Review	Title	Comparison	Discontinuations due to adverse events	sROR	LCI_sROR	UCI_sROR	i2	ROR	LCI ROR	UCI ROR	OR adults	LCI OR adults	OR peds	UCI OR peds	
				1.11	.78	1.57	0%								

SUPPLEMENTAL TABLE 4 Continued

Review	Title	Comparison	Severe adverse events	sROR		LCI_sROR		UCI_sROR		i2		OR		pedts	
				ROR	LCI ROR	UCI ROR	OR	LCI OR	UCI OR	adults	adults	OR	LCI OR	UCI OR	pedts
CD004386	Antibiotic prophylaxis for bacterial infections in febrile neutropenic patients following chemotherapy	Drug vs placebo/no intervention	Side effects requiring discontinuation	.183	8.9e-03	3.72	2.02	0%	1.25	0.73	2.15	3.74	11.1	.577	212
CD000059	Clozapine versus typical neuroleptic medication for schizophrenia	Clozapine vs typical antipsychotics	Blood problems requiring withdrawals or leucopenia or neutropenia	.207	5.7e-03	7.49	3.3		.207	5.7e-03	7.49	20.9	15.9	.735	345
CD003038	Beta-lactam versus beta-lactam-aminoglycoside combination therapy in cancer patients with neutropenia	Beta-lactam vs beta-lactam-aminoglycoside combination therapy	Discontinuation due to adverse events	.307	.046	2.05	.559		.307	.046	2.05	.926	1.82	.293	11.3
CD003992	Oral versus intravenous antibiotic treatment for febrile neutropenia in cancer patients	Oral vs intravenous antibiotic therapy	Adverse events requiring discontinuation of antibiotics	.322	.011	9.09	.82		.322	.011	9.09	1.89	2.54	.1	64.6
CD003559	Anti-IgE for chronic asthma in adults and children (inhaled or oral steroid users)	Subcutaneous Omalizumab + steroid vs placebo + steroid	Withdrawal due to adverse events	.511	.054	4.88	.411		.511	.054	4.88	2.31	.803	.188	3.42
CD000345	Sequential combination of glucocorticosteroids and alfa interferon versus alfa interferon alone for HBeAg-positive chronic hepatitis B	Glucoc + IFN vs control + IFN	Dose reduction or discontinuation of treatment due to adverse events	.816	.238	2.8	.658		.816	.238	2.8	1.13	.806	.266	2.44
CD005533	Combination of inhaled long-acting beta2-agonists and inhaled steroids versus higher dose of inhaled steroids in children and adults with persistent asthma	LABA + ICS vs higher dose ICS	Withdrawals due to adverse events	.957	.136	6.76	1.01		.957	.136	6.76	1.33	1.06	.153	7.33
CD002028	Oxcarbazepine add-on for drug-resistant partial epilepsy	Oxcarbazepine in add-on vs placebo	Withdrawals (due to side effects)	1.07	.458	2.5	2.3		1.07	.458	2.5	3.34	2.15	1.000	4.6
CD001385	Long-acting beta2-agonists for chronic asthma in adults and children where background therapy contains varied or no inhaled corticosteroid	LAB2A vs placebo	Withdrawals due to adverse events	1.22	.589	2.55	1.14		1.22	.589	2.55	1.37	.93	.458	1.89
CD005535	Long-acting beta2-agonists versus placebo in addition to inhaled corticosteroids	Long-acting beta2 vs placebo (both groups receiving similar dose ICS)	Withdrawals due to adverse events	1.34	.73	2.46	1.08		1.34	.73	2.46	1.36	.804	.459	1.41
CD003133	Addition of anti-leukotriene agents to inhaled corticosteroids for chronic asthma	Leukotriene receptor antagonists + ICS vs same dose of ICS in symptomatic patients	Withdrawals due to adverse events	1.38	.114	16.6	.673		1.38	.114	16.6	1.28	.489	.044	5.43

Review	Title	Comparison	Severe adverse events	sROR		LCI_sROR		UCI_sROR		i2		OR		UCI OR		LCI OR		UCI OR	
				ROR	LCI ROR	UCI ROR	UCI ROR	adults	OR	adults	adults	adults	adults	adults	adults	adults	adults	adults	adults
CD000296	Budesonide for induction of remission in Crohn's disease	Budesonide vs conventional steroids	Withdrawals due to adverse events	1.25	0.73	2.15	0%	85	.911	.276	3.000	.129	.015	1.15					
CD002314	Anti-Heukotriene agents compared to inhaled corticosteroids in the management of recurrent and/or chronic asthma in adults and children	Anti-Heukotriene vs inhaled glucocorticoids	Withdrawals due to adverse events	7.05	.585	85		191	1.21	.875	1.67	.162	6.4e-03	4.06					
Review	Title	Comparison	Any adverse event	sROR	LCI_sROR	UCI_sROR	i2	sROR	LCI ROR	UCI ROR	UCI OR	OR	LCI OR	UCI OR					
				1.03	.82	1.3	0.006												
CD002109*	Antibiotics for community acquired pneumonia in adult outpatients (combined with pediatric CD004874)	Clarithromycin vs erythromycin	Drug-related adverse events	.2825	.1394	.5723	.3024	.5723	.2005	.2005	.4562	1.071	.6029	1.901					
CD001167	Antibiotics for treating salmonella gut infections	Any antibiotics vs placebo	Adverse events	.4165	.0433	4.006	1.274	4.006	.7694	.7694	2.111	3.06	.3367	27.81					
CD003559	Anti-IgE for chronic asthma in adults and children (inhaled or oral steroid users)	Subcutaneous Omalizumab + steroid vs placebo + steroid	Number of participants with adverse events	.5018	.2223	1.133	1.035	1.133	.7893	.7893	1.358	2.063	.9575	4.445					
CD001726	Beta2-agonists for acute bronchitis	B2 agonists vs Control	Other Side effects	.7743	.2422	2.475	.7883	2.475	.3373	.3373	1.842	1.018	.4603	2.252					
CD003038	Beta-lactam versus beta-lactam-aminoglycoside combination therapy in cancer patients with neutropenia	Beta-lactam vs beta-lactam-aminoglycoside combination therapy	Any adverse event	.8635	.4907	1.52	.7305	1.52	.6334	.6334	.8424	.846	.4896	1.462					
CD003558	Inhaled corticosteroids versus sodium cromoglycate in children and adults with asthma	Inhaled corticosteroids vs cromolyn	Total adverse effects	.8928	.2342	3.404	1.044	3.404	.3025	.3025	3.604	1.169	.7049	1.94					
CD001385	Long-acting beta2-agonists for chronic asthma in adults and children where background therapy contains varied or no inhaled corticosteroid	LAB2A vs placebo	Total adverse events	.9107	.6767	1.226	1.136	1.226	.9526	.9526	1.354	1.247	.9815	1.584					
CD005535	Long-acting beta2-agonists versus placebo in addition to inhaled corticosteroids	Long-acting beta2 vs placebo (both groups receiving similar dose ICS)	Total adverse events	.9124	.7512	1.108	.9944	1.108	.8955	.8955	1.104	1.09	.9251	1.284					
CD005533	Combination of inhaled long-acting beta2-agonists and inhaled steroids versus higher dose of inhaled steroids in children and adults with persistent asthma	LABA + ICS vs higher dose ICS	Total adverse events	.9388	.6855	1.286	.9305	1.286	.8453	.8453	1.027	.9911	.7352	1.356					

SUPPLEMENTAL TABLE 4 Continued

Review	Title	Comparison	Severe adverse events	sROR		LCI_sROR		UCI_sROR		i2		LCI OR peds	UCI OR peds
				ROR	LCI ROR	LCI ROR	UCI ROR	OR adults	OR adults	OR peds	OR peds		
CD000133	Addition of anti-leukotriene agents to inhaled corticosteroids for chronic asthma	Leukotriene receptor antagonists + ICS vs same dose of ICS in symptomatic patients	Overall adverse events	1.072	.7054	1.63	2.15	.9373	.7326	1.199	.8741	.6231	1.226
CD0004386	Antibiotic prophylaxis for bacterial infections in afebrile neutropenic patients following chemotherapy	Quinolone vs TMP-SMZ	Side effects (Quinolones vs TMP-SMZ)	1.224	.1943	7.713	.6122	.8427	.5	.8427	.0816	3.063	
CD0002242	Antibiotic treatment for travellers' diarrhoea	Antibiotic vs placebo	Side effects (any)	1.304	.5115	3.323	2.535	1.367	1.944	4.701	1.944	9628	3.927
CD000296	Budesonide for induction of remission in Crohn's disease	Budesonide vs conventional steroids	Corticosteroid related adverse events	1.669	.6064	4.596	.4121	.2959	.5738	.2468	.0948	.6428	
CD0002314	Anti-leukotriene agents compared to inhaled corticosteroids in the management of recurrent and/or chronic asthma in adults and children	Anti-leukotriene vs inhaled glucocorticoids	Overall adverse events	1.826	.704	4.736	.9807	.8663	1.11	.5371	.2088	1.382	
CD0003901	Regular treatment with long acting beta agonists versus daily regular treatment with short acting beta agonists in adults and children with stable asthma	Regular treatment with LAB2A vs daily regular treatment with SAB2A	Adverse events (palpitations, headache, tremor and cramps)	2.338	.4757	11.49	1.214	.3571	4.127	.5192	.1874	1.438	
CD001954	Azithromycin for acute lower respiratory tract infections	Azithromycin vs amoxicillin or amoxicillin-clavulanate	Adverse events	2.499	1.425	4.382	.7474	.5892	.948	.2991	.1798	.4974	
CD000247	Antibiotics for the common cold and acute purulent rhinitis	Antibiotic vs placebo	Adverse events	2.67	1.19	5.991	2.417	1.676	3.485	.9052	.4403	1.861	
CD0003723	Anticonvulsant therapy for status epilepticus	Lorazepam IV vs diazepam IV	Adverse events			.7606	.2696	2.145					
Review	Title	Comparison	Organ-System specific adverse events	ROR	LCI ROR	UCI ROR	OR adults	LCI OR adults	UCI OR adults	OR peds	LCI OR peds	UCI OR peds	
CD001186	Allergen immunotherapy for asthma	Allergen immunotherapy vs placebo	Systemic reactions (anaphylaxis, asthma, rhinitis or urticaria)	.7143	.2599	1.963	1.735	1.109	2.714	2.429	.981	6.016	
CD001186	Allergen immunotherapy for asthma	Allergen immunotherapy vs Untreated control	Systemic reactions (anaphylaxis, asthma, rhinitis or urticaria, or any combination of these)			15.63	.7692	317.7					
CD001186	Allergen immunotherapy for asthma	Allergen immunotherapy vs placebo	Local reactions (large or delayed wheals at injection site)	1.69	.4749	6.013	1.836	.7671	4.395	1.087	.4324	2.731	

Review	Title	Comparison	Severe adverse events	sROR		LCI_sROR		UCI_sROR		i2	OR		LCI OR		UCI OR					
				ROR	LCI ROR	LCI ROR	UCI ROR	UCI ROR	OR		LCI OR	LCI OR	UCI OR	UCI OR	OR	LCI OR	LCI OR	UCI OR		
CD003039	Colony stimulating factors for chemotherapy induced febrile neutropenia	Colony stimulating factor + antibiotics vs antibiotics alone	Bone and joint pain OR flu like symptoms	.0893	.0015	.0015	5.264	5.264	1.000	0%	1.25	0.73	2.15	0%	16.34	11.2	.5749	218.3		
CD003992	Oral versus intravenous antibiotic treatment for febrile neutropenia in cancer patients	Oral vs intravenous antibiotic therapy	GI adverse events	1.063	.0822	.0822	13.76	13.76	3.07	3.07	1.063	.0822	13.76	3.07	29.91	2.888	.8947	9.32		
CD005535	Long-acting beta2-agonists versus placebo in addition to inhaled corticosteroids	Long-acting beta2 vs placebo (both groups receiving similar dose ICS)	Adverse cardiovascular events	3.47	.1137	.1137	105.9	105.9	1.061	1.061	3.47	.1137	105.9	1.061	3.331	.3058	.0122	7.663		
Review	Title	Comparison	Specific adverse signs or symptoms	sROR	LCI_sROR	UCI_sROR	i2	i2	OR	OR	OR	LCI OR	LCI OR	UCI OR	UCI OR	OR	LCI OR	LCI OR	UCI OR	
CD002028	Oxcarbazepine add-on for drug-resistant partial epilepsy	Oxcarbazepine in add-on vs placebo	Headache	.82	.70	.96	0%	0%	.82	.70	.96	0%	0%	1.799	2.157	1.213	.7928	3.836	2.117	
CD003559	Anti-IgE for chronic asthma in adults and children (inhaled or oral steroid users)	Subcutaneous Omalizumab + steroid vs placebo + steroid	Headache	.5592	.2774	1.127	1.206	1.206	1.206	1.206	.5592	.2774	1.127	1.206	1.799	2.157	1.213	.7928	3.836	2.117
CD005533	Combination of inhaled long-acting beta2-agonists and inhaled steroids versus higher dose of inhaled steroids in children and adults with persistent asthma	LABA + ICS vs higher dose ICS	Headache	.658	.4229	1.024	.9736	.9736	.9736	.9736	.658	.4229	1.024	.9736	1.135	1.48	.9774	2.24	2.24	2.24
CD005535	Long-acting beta2-agonists versus placebo in addition to inhaled corticosteroids	Long-acting beta2 vs placebo (both groups receiving similar dose ICS)	Headache	.8021	.5806	1.108	.8877	.8877	.8877	.8877	.8021	.5806	1.108	.8877	1.104	1.107	.8716	1.405	1.405	1.405
CD004125	Drugs for preventing postoperative nausea and vomiting	Droperidol vs placebo	Headache	.8159	.1876	3.549	.8159	.8159	.8159	.8159	.8159	.1876	3.549	.8159	1.055	1.000	.2551	4.253	4.253	4.253
CD004125	Drugs for preventing postoperative nausea and vomiting	Ondansetron vs placebo	Headache	.8686	.4731	1.594	1.294	1.294	1.294	1.294	.8686	.4731	1.594	1.294	1.553	1.489	.8345	2.658	2.658	2.658
CD001385	Long-acting beta2-agonists for chronic asthma in adults and children where background therapy contains varied or no inhaled corticosteroid	LAB2A vs placebo	Adverse events - headache	.8747	.5526	1.385	1.221	1.221	1.221	1.221	.8747	.5526	1.385	1.221	1.559	1.396	.946	2.059	2.059	2.059
CD006198	Vaccines for preventing malaria (pre-erythrocytic)	RTS,S vaccine vs control	Headache	.892	.408	1.95	1.669	1.669	1.669	1.669	.892	.408	1.95	1.669	2.227	1.871	.9044	3.872	3.872	3.872
CD001909	Lamotrigine add-on for drug-resistant partial epilepsy	Add-on lamotrigine vs placebo	Headache	.8988	.3965	2.028	1.157	1.157	1.157	1.157	.8988	.3965	2.028	1.157	1.596	1.29	.6095	2.73	2.73	2.73

SUPPLEMENTAL TABLE 4 Continued

Review	Title	Comparison	Severe adverse events	sROR		UCI_sROR		i2		OR		UCI OR		pedis	
				ROR	LCI	ROR	LCI	OR	adults	OR	adults	OR	pedis	OR	pedis
CD0003901	Regular treatment with long acting beta agonists versus daily regular treatment with short acting beta agonists in adults and children with stable asthma	Regular treatment with LAB2A vs daily regular treatment with SAB2A	Headache	.9306	.5525	1.567		1.224	0%	1.315	1.618	.9259	1.618	.8466	2.043
CD001415	Gabapentin add-on for drug-resistant partial epilepsy	Gabapentin vs placebo	Headache	.9505	.2769	3.263		.7571		.7965	1.35	.4245	1.35	.268	2.367
CD002314	Anti-leukotriene agents compared to inhaled corticosteroids in the management of recurrent and/or chronic asthma in adults and children	Anti-leukotriene vs inhaled glucocorticoids	Headache	1.019	.3418	3.036		.9078		.8912	1.109	.7434	1.109	.3046	2.608
CD0003133	Addition of anti-leukotriene agents to inhaled corticosteroids for chronic asthma	Leukotriene receptor antagonists + ICS vs same dose of ICS in symptomatic patients	Headache	1.241	.6213	2.48		1.267		1.021	1.757	.9138	1.757	.5546	1.879
CD002178	Early emergency department treatment of acute asthma with systemic corticosteroids	Any steroid (po, IM, IV, inhaled) vs placebo	Headache	4.323	.1161	160.9		1.363		.3153	6.437	.2886	6.437	.012	8.269
CD004529	Atovaquone-proguanil for treating uncomplicated malaria	Atovaquone-proguanil vs amodiaquine	Headache	8.654	.7469	100.3		4.19		.4842	40.62	.4323	40.62	.1934	1.212
	Review Title	Comparison	Specific adverse signs or symptoms	sROR	LCI_sROR	UCI_sROR	i2								
			Drowsiness	1.02	.58	1.79	33.9%								
CD000059	Clozapine versus typical neuroleptic medication for schizophrenia	Clozapine vs typical antipsychotics	Drowsiness	.0734	.0062	.8683		1.761		24.000	2.317	1.339	2.317	2.06	279.6
CD004052	Valproate for acute mood episodes in bipolar disorder	Valproate vs lithium	Sedation	.1184	.0047	2.978		.9617		8.12	2.674	.346	2.674	.3814	172.9
CD004125	Drugs for preventing postoperative nausea and vomiting	Droperidol vs no treatment	Drowsiness or sedation	.6523	.0694	6.13		3.131		4.8	9.406	1.042	9.406	.6817	33.8
CD002028	Oxcarbazepine add-on for drug-resistant partial epilepsy	Oxcarbazepine in add-on vs placebo	Somnolence	.8299	.3762	1.831		2.729		3.289	4.523	1.647	4.523	1.789	6.046
CD001909	Lamotrigine add-on for drug-resistant partial epilepsy	Add-on lamotrigine vs placebo	Somnolence	1.086	.4829	2.443		1.624		1.495	2.498	1.056	2.498	.7525	2.971
CD001415	Gabapentin add-on for drug-resistant partial epilepsy	Gabapentin vs placebo	Somnolence	1.161	.3732	3.612		2.166		1.865	3.375	1.389	3.375	.6563	5.302
CD004125	Drugs for preventing postoperative nausea and vomiting	Droperidol vs placebo	Drowsiness or sedation	1.657	.312	8.804		1.657		1.000	2.123	1.294	2.123	.1917	5.215

Review	Title	Comparison	Severe adverse events																
			sROR	LCI_sROR	UCI_sROR	i2	OR	UCI OR											
CD001417	Topiramate add-on for drug-resistant partial epilepsy	Topiramate vs placebo	1.25	0.73	2.15	0%													
			ROR	LCI ROR	UCI ROR	OR adults	OR adults	LCI OR adults	UCI OR adults	OR peds	LCI OR peds	UCI OR peds	OR peds	LCI OR peds	UCI OR peds	OR peds	LCI OR peds	UCI OR peds	OR peds
			2.761	1.01	7.556	2.812	0.000	1.921	4.117	1.019	.4012	2.586							
			sROR	LCI_sROR	UCI_sROR	i2													
			.69	.40	1.21	0.000													
			ROR	LCI ROR	UCI ROR	OR adults	OR adults	LCI OR adults	UCI OR adults	OR peds	LCI OR peds	UCI OR peds	OR peds	LCI OR peds	UCI OR peds	OR peds	LCI OR peds	UCI OR peds	OR peds
			.2928	.0605	1.417	1.832	1.832	1.271	2.642	6.259	1.35	29.02							
			.4623	.0926	2.309	1.462	.8615	2.48	3.162	.6921	14.44								
			.623	.202	1.921	.7557	.4047	1.411	1.213	.4751	3.097								
			.6699	.0259	17.31	1.011	.6513	1.569	1.509	.0602	37.86								
			sROR	LCI_sROR	UCI_sROR	i2													
			.6794	.2398	1.925	3.289	1.834	5.897	4.841	2.044	11.47								
			.7485	.1001	5.594	.6861	.2781	1.693	9.167	.1519	5.531								
			1.968	.3135	12.35	.7585	.3374	1.705	.3855	.0741	2.004								
			10.27	.4713	224	2.043	.1791	23.29	.1988	.03	1.317								
			sROR	LCI_sROR	UCI_sROR	i2													
			.81	.48	1.35	0.000													
			ROR	LCI ROR	UCI ROR	OR adults	OR adults	LCI OR adults	UCI OR adults	OR peds	LCI OR peds	UCI OR peds	OR peds	LCI OR peds	UCI OR peds	OR peds	LCI OR peds	UCI OR peds	OR peds
			.2121	.0056	7.964	.0514	.0029	.9112	.2424	.0266	2.208								
			.393	.1268	1.218	.7867	.4998	1.238	2.002	.7101	5.643								
			.8507	.2769	2.613	2.664	1.693	4.194	3.132	1.122	8.742								
			sROR	LCI_sROR	UCI_sROR	i2													
			.81	.48	1.35	0.000													
			ROR	LCI ROR	UCI ROR	OR adults	OR adults	LCI OR adults	UCI OR adults	OR peds	LCI OR peds	UCI OR peds	OR peds	LCI OR peds	UCI OR peds	OR peds	LCI OR peds	UCI OR peds	OR peds
			.2121	.0056	7.964	.0514	.0029	.9112	.2424	.0266	2.208								
			.393	.1268	1.218	.7867	.4998	1.238	2.002	.7101	5.643								
			.8507	.2769	2.613	2.664	1.693	4.194	3.132	1.122	8.742								
			sROR	LCI_sROR	UCI_sROR	i2													
			.81	.48	1.35	0.000													
			ROR	LCI ROR	UCI ROR	OR adults	OR adults	LCI OR adults	UCI OR adults	OR peds	LCI OR peds	UCI OR peds	OR peds	LCI OR peds	UCI OR peds	OR peds	LCI OR peds	UCI OR peds	OR peds
			.2121	.0056	7.964	.0514	.0029	.9112	.2424	.0266	2.208								
			.393	.1268	1.218	.7867	.4998	1.238	2.002	.7101	5.643								
			.8507	.2769	2.613	2.664	1.693	4.194	3.132	1.122	8.742								
			sROR	LCI_sROR	UCI_sROR	i2													
			.81	.48	1.35	0.000													
			ROR	LCI ROR	UCI ROR	OR adults	OR adults	LCI OR adults	UCI OR adults	OR peds	LCI OR peds	UCI OR peds	OR peds	LCI OR peds	UCI OR peds	OR peds	LCI OR peds	UCI OR peds	OR peds
			.2121	.0056	7.964	.0514	.0029	.9112	.2424	.0266	2.208								
			.393	.1268	1.218	.7867	.4998	1.238	2.002	.7101	5.643								
			.8507	.2769	2.613	2.664	1.693	4.194	3.132	1.122	8.742								
			sROR	LCI_sROR	UCI_sROR	i2													
			.81	.48	1.35	0.000													
			ROR	LCI ROR	UCI ROR	OR adults	OR adults	LCI OR adults	UCI OR adults	OR peds	LCI OR peds	UCI OR peds	OR peds	LCI OR peds	UCI OR peds	OR peds	LCI OR peds	UCI OR peds	OR peds
			.2121	.0056	7.964	.0514	.0029	.9112	.2424	.0266	2.208								
			.393	.1268	1.218	.7867	.4998	1.238	2.002	.7101	5.643								
			.8507	.2769	2.613	2.664	1.693	4.194	3.132	1.122	8.742								
			sROR	LCI_sROR	UCI_sROR	i2													
			.81	.48	1.35	0.000													
			ROR	LCI ROR	UCI ROR	OR adults	OR adults	LCI OR adults	UCI OR adults	OR peds	LCI OR peds	UCI OR peds	OR peds	LCI OR peds	UCI OR peds	OR peds	LCI OR peds	UCI OR peds	OR peds
			.2121	.0056	7.964	.0514	.0029	.9112	.2424	.0266	2.208								
			.393	.1268	1.218	.7867	.4998	1.238	2.002	.7101	5.643								
			.8507	.2769	2.613	2.664	1.693	4.194	3.132	1.122	8.742								
			sROR	LCI_sROR	UCI_sROR	i2													
			.81	.48	1.35	0.000													
			ROR	LCI ROR	UCI ROR	OR adults	OR adults	LCI OR adults	UCI OR adults	OR peds	LCI OR peds	UCI OR peds	OR peds	LCI OR peds	UCI OR peds	OR peds	LCI OR peds	UCI OR peds	OR peds
			.2121	.0056	7.964	.0514	.0029	.9112	.2424	.0266	2.208								
			.393	.1268	1.218	.7867	.4998	1.238	2.002	.7101	5.643								
			.8507	.2769	2.613	2.664	1.693	4.194	3.132	1.122	8.742								

SUPPLEMENTAL TABLE 4 Continued

Review	Title	Comparison	Severe adverse events	sROR		LCI_sROR		UCI_sROR		i2		OR		ped		UCI OR		UCI OR	
				ROR	LCI ROR	UCI ROR	UCI ROR	adults	OR	adults	OR	adults	OR	ped	OR	ped	OR	ped	OR
CD006198	Vaccines for preventing malaria (pre-erythrocytic)	RTS,S vaccine vs control	Malaise	.8777	.2825	2.727	2.15	1.864	1.35	2.573	2.123	2.123	2.123	.7163	6.295				
CD001415	Gabapentin add-on for drug-resistant partial epilepsy	Gabapentin vs placebo	Fatigue	.9883	.1576	6.198	2.166	2.166	1.128	4.158	2.191	2.191	.3939	12.19					
CD002028	Oxcarbazepine add-on for drug-resistant partial epilepsy	Oxcarbazepine in add-on vs placebo	Fatigue	1.337	.4839	3.695	2.151	2.151	1.138	4.068	1.609	1.609	.7288	3.552					
Review	Title	Comparison	Specific adverse signs or symptoms	sROR	LCI_sROR	UCI_sROR	i2												
			Dizziness	.69	.37	1.29	0.000												
CD001909	Lamotrigine add-on for drug-resistant partial epilepsy	Add-on lamotrigine vs placebo	Dizziness	.4971	.1714	1.442	2.603	2.603	1.921	3.527	5.236	5.236	1.888	14.530					
CD002028	Oxcarbazepine add-on for drug-resistant partial epilepsy	Oxcarbazepine in add-on vs placebo	Dizziness	.6964	.2871	1.689	3.383	3.383	2.087	5.484	4.857	4.857	2.311	10.21					
CD004125	Drugs for preventing postoperative nausea and vomiting	Tropisetron vs placebo	Dizziness or vertigo	1.086	.0366	32.24	.3548	.3548	.1246	1.01	.3266	.3266	.013	8.216					
CD001415	Gabapentin add-on for drug-resistant partial epilepsy	Gabapentin vs placebo	Dizziness	1.527	.2339	9.964	2.487	2.487	1.502	4.118	1.629	1.629	.2675	9.925					
CD004052	Valproate for acute mood episodes in bipolar disorder	Valproate vs lithium	Dizziness				2.086	2.086	.5429	8.017									
Review	Title	Comparison	Specific adverse signs or symptoms	sROR	LCI_sROR	UCI_sROR	i2												
			Infections	.62	.27	1.43	0.000												
CD004386	Antibiotic prophylaxis for bacterial infections in febrile neutropenic patients following chemotherapy	Drug vs placebo/no intervention	Infection resistant to drug taken, prophylaxis versus placebo or no intervention or other antibiotic	.4618	.0657	3.245	1.466	1.466	1.019	2.109	3.174	3.174	.4675	21.54					
CD004386	Antibiotic prophylaxis for bacterial infections in febrile neutropenic patients following chemotherapy	Quinolone vs TMP-SMZ	Infection resistant to drug taken, prophylaxis versus placebo or no intervention or other antibiotic	.5278	.103	2.706	.3519	.3519	.1603	.7726	.6667	.6667	.1591	2.793					
CD003038	Beta-lactam versus beta-lactam-aminoglycoside combination therapy in cancer patients with neutropenia	Beta-lactam vs beta-lactam-aminoglycoside combination therapy	Bacterial superinfections	.7408	.2464	2.227	1.075	1.075	.8424	1.373	1.452	1.452	.4962	4.246					

SUPPLEMENTAL TABLE 4 Continued

Review	Title	Comparison	Severe adverse events	sROR		LCI_sROR		UCI_sROR		i2	LCI OR		UCI OR	
				ROR	LCI ROR	LCI ROR	UCI ROR	adults	OR		adults	OR	adults	OR
CD0004052	Valproate for acute mood episodes in bipolar disorder	Valproate vs lithium	Diarrhea	2.801	.085	92.25	92.25	.8131	0%	.2454	2.684	.2903	.0109	7.737
CD0004529	Atovaquone-proguanil for treating uncomplicated malaria	Atovaquone-proguanil vs amodiaquine	Diarrhea	1.591	.5556	4.558	4.558	1.062		.4762	2.367	.6672	.3375	1.319
CD0002028	Oxcarbazepine add-on for drug-resistant partial epilepsy	Oxcarbazepine in add-on vs placebo	Diplopia	.3107	.0363	2.661	2.661	7.954		3.814	16.59	25.6	3.403	192.6
CD0004125	Drugs for preventing postoperative nausea and vomiting	Hyoscine vs placebo	Dry mouth	.0847	.0091	.7863	.7863	1.966		1.341	2.883	23.22	2.585	208.6
CD0003133	Addition of anti-leukotriene agents to inhaled corticosteroids for chronic asthma	Leukotriene receptor antagonists + ICS vs same dose of ICS in symptomatic patients	Elevated liver enzymes	.5563	.0391	7.906	7.906	1.088		.3553	3.334	1.956	.1763	21.7
CD0002314	Anti-leukotriene agents compared to inhaled corticosteroids in the management of recurrent and/or chronic asthma in adults and children	Anti-leukotriene vs inhaled glucocorticoids	Elevated liver enzymes	2.659	.15	47.14	47.14	1.296		.6714	2.5	.4872	.0297	8.002
CD0006198	Vaccines for preventing malaria (pre-erythrocytic)	RTS,S vaccine vs control	Fever	2.818	.9396	8.452	8.452	2.172		.8178	5.767	.7707	.4663	1.274
CD0000059	Clozapine versus typical medication for schizophrenia	Clozapine vs typical antipsychotics	Fits	.3887	.0131	11.51	11.51	1.412		.6989	2.851	3.632	.1321	99.85
CD0003038	Beta-lactam versus beta-lactam-aminoglycoside combination therapy in cancer patients with neutropenia	Beta-lactam vs beta-lactam-aminoglycoside combination therapy	Fungal superinfections	3.598	.1644	78.73	78.73	.6976		.455	1.07	.1939	.0091	4.119
CD0004386	Antibiotic prophylaxis for bacterial infections in afebrile neutropenic patients following chemotherapy	Drug vs placebo/no intervention	Fungal infection, prophylaxis versus placebo or no intervention or other antibiotic	2.925	.2833	30.2	30.2	1.059		.6701	1.674	.3621	.0367	3.573
CD0004405	Corticosteroids for acute bacterial meningitis	Corticosteroids vs placebo	Gastrointestinal bleeding	9.745	.2903	3.271	3.271	1.501		.6973	3.23	1.54	.603	3.932
CD0004405	Corticosteroids for acute bacterial meningitis	Corticosteroids vs placebo	Herpes zoster infection	9.074	.2526	3.26	3.26	1.125		.8245	1.536	1.24	.3587	4.288
CD0003341	High first dose quinine regimen for treating severe malaria	Loading dose vs no loading dose	Hypoglycemia	5.752	.1842	179.6	179.6	3.214		.2982	34.64	.5588	.0464	6.727
CD0003754	Reduced osmolality oral rehydration solution for treating cholera	Reduced osmolality (glucose-based) oral rehydration solution vs standard oral rehydration solution	Biochemical hyponatremia (serum sodium < 130 mmol/L)	1.101	.3362	3.605	3.605	1.571		.932	2.649	1.427	.4921	4.14

SUPPLEMENTAL TABLE 4 Continued

Review	Title	Comparison	Severe adverse events	sROR		LCI_sROR		UCI_sROR		i2		UCI OR		LCI OR		UCI OR		LCI OR	
				ROR	LCI ROR	UCI ROR	UCI ROR	adults	OR	adults	OR	adults	OR	adults	OR	adults	OR	adults	OR
CD006198	Vaccines for preventing malaria (pre-erythrocytic)	RTS,S vaccine vs control	Injection site pain	1.25	0.73	2	5.62	2.15	0%	5.309	3.862	7.298	1.64	1.045	2.573				
CD004529	Atovaquone-proguanil for treating uncomplicated malaria	Atovaquone-proguanil vs amodiaquine	Insomnia	4.733	.4858		46.11		1.27	.252	6.4	2.683	.0541	1.331					
CD000059	Clozapine versus typical antipsychotics medication for schizophrenia	Clozapine vs typical antipsychotics	Movement disorders	1.525	.0548		42.39		.5083	.3829	.6747	.3353	.0121	9.156					
CD005535	Long-acting beta2-agonists versus placebo in addition to inhaled corticosteroids	Long-acting beta2 vs placebo (both groups receiving similar dose ICS)	Oral thrush	.294	.0354		2.442		1.134	.3848	3.34	3.855	.6245	23.8					
CD003274	Budesonide versus placebo for chronic asthma in children and adults	BUD vs placebo (not on oral steroids)	Oropharyngeal side effects	2.831	.7475		10.72		1.208	.4258	3.43	.4259	.1866	.9767					
CD003558	Inhaled corticosteroids versus sodium cromoglycate in children and adults with asthma	Inhaled corticosteroids vs cromolyn	Oropharyngeal side effects	1.64	.1234		21.79		2.148	.3635	12.69	1.31	.1998	8.585					
CD003901	Regular treatment with long acting beta agonists versus daily regular treatment with short acting beta agonists in adults and children with stable asthma	Regular treatment with LAB2A vs daily regular treatment with SAB2A	Palpitations	1.161	.208		6.48		1.112	.6064	2.041	.9582	.1917	4.788					
CD005535	Long-acting beta2-agonists versus placebo in addition to inhaled corticosteroids	Long-acting beta2 vs placebo (both groups receiving similar dose ICS)	Tachycardia-palpitation	5.281	.2664		104.7		2.539	.8795	7.328	.4808	.0295	7.845					
CD001385	Long-acting beta2-agonists for chronic asthma in adults and children where background therapy contains varied or no inhaled corticosteroid	LAB2A vs placebo	Adverse events - pharyngitis	1.321	.5321		3.28		1.727	.8327	3.581	1.307	.7593	2.25					
CD005161	Cyclosporin versus tacrolimus for liver transplanted patients	Tacrolimus vs cyclosporin	Post transplant lymphoproliferative disease	.0898	.0045		1.799		.4748	.0599	3.767	5.287	.6055	46.17					
CD004529	Atovaquone-proguanil for treating uncomplicated malaria	Atovaquone-proguanil vs amodiaquine	Pruritis	2.524	.0841		75.78		2.878	.1115	74.24	1.14	.4175	3.112					
CD004405	Corticosteroids for acute bacterial meningitis	Corticosteroids vs placebo	Recurrent fever (adverse event)	1.316	.6699		2.587		1.809	.9717	3.369	1.374	1.055	1.79					
CD000059	Clozapine versus typical antipsychotics medication for schizophrenia	Clozapine vs typical antipsychotics	Salivation	.4939	.0626		3.899		5.186	3.832	7.02	10.5	1.36	81.06					
CD006198	Vaccines for preventing malaria (pre-erythrocytic)	RTS,S vaccine vs control	Swelling	.0317	.0012		.8036		.3287	.0134	8.093	10.38	6.689	16.16					

SUPPLEMENTAL TABLE 4 Continued

Review	Title	Comparison	Severe adverse events	sROR		LCI_sROR		UCI_sROR		i2		OR		pedS	
				ROR	LCI ROR	LCI ROR	UCI ROR	OR adults	OR adults	LCI OR adults	LCI OR adults	UCI OR adults	UCI OR adults	pedS	pedS
CD001417	Topiramate add-on for drug-resistant partial epilepsy	Topiramate vs placebo	Thinking abnormally	.8097	.1413	4.64	7.203	3.353	15.48	8.897	1.852	42.73			
CD001385	Long-acting beta2-agonists for chronic asthma in adults and children where background therapy contains varied or no inhaled corticosteroid	LAB2A vs placebo	Adverse events - throat irritation	1.279	.4101	3.986	1.9	1.115	3.237	1.486	.5443	4.058			
CD003407	Erythropoietin or Darbepoetin for patients with cancer	Erythropoietin or darbepoetin vs placebo	Thrombotic events	.5272	.1022	2.719	1.611	1.265	2.052	3.057	.6033	15.49			
CD002314	Anti-leukotriene agents compared to inhaled corticosteroids in the management of recurrent and/or chronic asthma in adults and children	Anti-leukotriene vs inhaled glucocorticoids	Upper respiratory tract infections	.9648	.6023	1.545	1.013	.6835	1.503	1.05	.8112	1.36			
CD001385	Long-acting beta2-agonists for chronic asthma in adults and children where background therapy contains varied or no inhaled corticosteroid	LAB2A vs placebo	Adverse events - upper respiratory tract infection	.759	.4717	1.221	.9599	.7043	1.308	1.265	.8813	1.814			
CD003559	Anti-IgE for chronic asthma in adults and children (inhaled or oral steroid users)	Subcutaneous Omalizumab + steroid vs placebo + steroid	Urticaria	.1983	.0082	4.786	.683	2.181	2.139	3.445	.1764	67.29			
CD004529	Atovaquone-proguanil for treating uncomplicated malaria	Atovaquone-proguanil vs amodiaquine	Vomiting	1.728	.591	5.05	2.547	1.156	5.615	1.474	.714	3.045			
CD000059	Clozapine versus typical neuroleptic medication for schizophrenia	Clozapine vs typical antipsychotics	Weight gain	.3861	.0601	2.481	1.576	1.11	2.239	4.083	.6569	25.38			
Review	title	comparison	Any discontinuations	sROR		LCI_sROR		UCI_sROR		i2		OR		pedS	
				ROR	LCI ROR	LCI ROR	UCI ROR	OR adults	OR adults	LCI OR adults	LCI OR adults	UCI OR adults	UCI OR adults	pedS	pedS
CD000059	Clozapine versus typical neuroleptic medication for schizophrenia	Clozapine vs typical antipsychotics	Leaving the study early - acceptability of treatment (short term)	.1171	.0089	1.383	.502	.4122	.6112	4.286	.3659	50.2			
CD002217	Phenobarbitone versus phenytoin monotherapy for partial onset seizures and generalized onset tonic-clonic seizures	Phenobarbitone vs phenobarbitone	Time to treatment withdrawal	.1815	.0332	.9923	1.538	1.042	2.268	8.471	1.621	44.26			
CD0003133	Addition of anti-leukotriene agents to inhaled corticosteroids for chronic asthma	Leukotriene receptor antagonists + ICS vs same dose of ICS in symptomatic patients	Overall withdrawals	.5867	.1948	1.767	.8734	6181	1.234	1.489	.5226	4.241			

SUPPLEMENTAL TABLE 4 Continued

Review	Title	Comparison	Severe adverse events	sROR		LCI_sROR		UCI_sROR		i2		OR		UCI OR		pedts	
				ROR	LCI ROR	UCI ROR	UCI_sROR	adults	OR	adults	adults	OR	pedts	adults	OR	pedts	adults
CD001769	Phenytoin versus valproate monotherapy for partial onset seizures and generalized onset tonic-clonic seizures	Valproate vs phenytoin	Time to withdrawal of allocated treatment (all seizures)	.6826	.1981	2.352	2.15	.5582	1.378	.8177	.3512	1.904					
CD003615	Oxcarbazepine versus phenytoin monotherapy for epilepsy	Oxcarbazepine vs phenytoin	Discontinuation of allocated treatment	.8032	.3081	2.094	2.973	1.635	2.973	2.036	9627	4.305					
CD005535	Long-acting beta2-agonists versus placebo in addition to inhaled corticosteroids	Long-acting beta2 vs placebo (both groups receiving similar dose ICS)	Total # withdrawals	.9651	.7685	1.212	.8566	.7693	.8566	.7971	.6521	.9744					
CD004386	Antibiotic prophylaxis for bacterial infections in febrile neutropenic patients following chemotherapy	Quinolone vs TMP-SMZ	Side effects requiring discontinuation were not described in details	.9754	.1495	6.362	.7886	.4877	.7886	.5	.0816	3.063					
CD001385	Long-acting beta2-agonists for chronic asthma in adults and children where background therapy contains varied or no inhaled corticosteroid	LAB2A vs placebo	Withdrawals (all reasons)	.9895	.6869	1.426	.9517	.9009	.9517	9.104	.6346	1.306					
CD005533	Combination of inhaled long-acting beta2-agonists and inhaled steroids versus higher dose of inhaled steroids in children and adults with persistent asthma	LABA + ICS vs higher dose ICS	Total # withdrawals	1.204	.5478	2.648	1.009	.9094	1.009	.755	.3458	1.646					
CD002314	Anti-leukotriene agents compared to inhaled corticosteroids in the management of recurrent and/or chronic asthma in adults and children	Anti-leukotriene vs inhaled glucocorticoids	Overall withdrawals	1.586	.6208	4.053	1.571	1.353	1.571	.8533	.3379	2.154					
CD001911	Carbamazepine versus phenytoin monotherapy for epilepsy	Carbamazepine vs phenytoin	Discontinuation of allocated treatment	1.634	.7468	3.577	1.712	1.151	1.712	.7042	.3584	1.384					
CD001415	Gabapentin add-on for drug-resistant partial epilepsy	Gabapentin vs placebo	Withdrawals	1.716	.6973	4.224	2.498	1.513	2.498	.7653	.4073	1.438					
CD001909	Lamotrigine add-on for drug-resistant partial epilepsy	Add-on lamotrigine vs placebo	Withdrawal from treatment for any reason	2.122	.9818	4.585	1.881	1.314	1.881	.6191	.313	1.224					
CD005161	Cyclosporin versus tacrolimus for liver transplanted patients	Tacrolimus vs cyclosporin	Withdrawals from treatment for any reason	2.165	1	4.294	.9077	.7098	.9077	.3279	.173	.6215					
CD001417	Topiramate add-on for drug-resistant partial epilepsy	Topiramate vs placebo	Withdrawals	11.5	.52	254.4	3.716	2.411	3.716	.2096	.0098	4.498					

SUPPLEMENTAL TABLE 4 Continued

Review	Title	Comparison	Severe adverse events				i2															
			sROR	LCI	sROR	UCI	sROR	LCI	sROR	UCI												
			1.25	0.73	2.15	0%																
			ROR	LCI	ROR	UCI	ROR	LCI	ROR	UCI	ROR	LCI	ROR	UCI	ROR	LCI	ROR	UCI	ROR	UCI		
			adults	adults	adults	adults	adults	adults	adults	adults	adults	adults	adults	adults	adults	adults	adults	adults	adults	adults		
			ped	ped	ped	ped	ped	ped	ped	ped	ped	ped	ped	ped	ped	ped	ped	ped	ped	ped		
Review	Title	Comparison	sROR	LCI	sROR	UCI	sROR	LCI	sROR	UCI	sROR	LCI	sROR	UCI	sROR	LCI	sROR	UCI	sROR	LCI	sROR	UCI
			88	70	1.11	32.2%																
CD0002152	Routine anticonvulsants for treating cerebral malaria	Phenobarbitone vs placebo or nothing	.2521	.1012	.6279	.6019	.3254	1.113	2.388	1	4.686	0.000										
			Analysis 1.1. Comparison 1 Phenobarbitone compared to placebo or nothing, Outcome 1 Death within 6 months in all trials.																			
CD0001319	Colloid solutions for fluid resuscitation	Hydroxyethyl starch vs albumin or plasma protein fraction	.3157	.0521	1.913	.9612	.7504	1.231	3.045	.5112	18.14											
			Analysis 1.1. Comparison 1 Albumin or PPF versus HES, Outcome 1 Death.																			
CD0000196	Corticosteroids for acute traumatic brain injury	Any steroid administered in any dose against no steroid	.3203	.0103	9.947	1.174	1.074	1.284	3.667	.1182	113.7											
			Analysis 1.1. Comparison 1 Any steroid administered in any dose against no steroid, Outcome 1 Death at end of follow up period.																			
CD0001385	Long-acting beta2-agonists for chronic asthma in adults and children where background therapy contains varied or no inhaled corticosteroid	LAB2A vs placebo	.4351	.0169	11.19	1.337	.8475	2.109	3.073	.1234	76.52											
			Analysis 2.5. Comparison 2 Studies with parallel group design: withdrawal & safety outcomes, Outcome 5 Death (all cause) - SMART all participants.																			
CD0000527	Artemisinin derivatives for treating severe malaria	Any artemisinin drug vs quinine	.5162	.342	.779	.4886	.3639	.6562	.9467	.7104	1.262											
			Analysis 1.1.5 Comparison 1 Artemisinin drug vs quinine, Outcome 1 Mortality (any artemisinin drug)																			
CD0004386	Antibiotic prophylaxis for bacterial infections in febrile neutropenic patients following chemotherapy	Drug vs placebo/no intervention	.6084	.1765	2.083	.7108	.5475	.923	1.172	.351	3.915											
			Analysis 1.1. Comparison 1 All-cause mortality, Outcome 1 drug vs placebo/no intervention.																			
CD0004405	Corticosteroids for acute bacterial meningitis	Corticosteroids vs placebo	.9238	.6292	1.356	.924	.7023	1.216	1.000	.7645	1.309											
			Figure 9. Forest plot of comparison: 1 All patients, outcome: 1.1 Mortality.																			
CD0001208	Human albumin solution for resuscitation and volume expansion in critically ill	Supplemental albumin vs control	.931	.7222	1.2	1.013	.9062	1.133	1.088	.8661	1.367											
			Analysis 1.1. Comparison 1 supplemental albumin, Outcome 1 deaths.																			

SUPPLEMENTAL TABLE 4 Continued

Review	Title	Comparison	Severe adverse events	sROR		LCI_sROR		UCI_sROR		i2		OR		LCI OR		UCI OR	
				ROR	LCI ROR	UCI ROR	LCI ROR	UCI ROR	adults	OR	adults	OR	adults	OR	adults	OR	adults
CD004269	Prophylactic platelet transfusion for haemorrhage after chemotherapy and stem cell transplantation	Prophylactic platelet transfusion versus non prophylactic or therapeutic transfusion	Analysis 1.1. Comparison 1 Prophylactic platelet transfusion versus non prophylactic or therapeutic transfusion, Outcome 1 Mortality from all causes.	1.027	.1057	9.977	2.15	0%	1.071	.1502	7.642	1.043	.3522	3.278			
CD002314	Anti-leukotriene agents compared to inhaled corticosteroids in the management of recurrent and/or chronic asthma in adults and children	Anti-leukotriene vs inhaled glucocorticoids	Analysis 1.66. Comparison 1 Anti-leukotriene (AL) vs. Inhaled glucocorticoids (in HFC-BDP equivalent), Outcome: Death.	1.036	.0112	96.24	3.115		3.115	.1263	76.81	3.006	.1222	73.97			
CD005161	Cyclosporin versus tacrolimus for liver transplanted patients	Tacrolimus vs. Cyclosporin	Analysis 1.1. Comparison 1 Tacrolimus vs. Cyclosporin, Outcome 1 Mortality	1.056	.369	3.025	.812		.812	.6647	.992	.7686	.2737	2.159			
CD003407	Erythropoietin or Darbepoetin for patients with cancer	Erythropoietin or darbepoetin vs placebo	Analysis 5.1. Comparison 5 Overall Survival, Outcome 1 Overall survival updated review (unadjusted results).	1.07	.1479	7.748	1.051		1.051	.9729	1.135	.9818	.1358	7.096			
CD003108*	Cotrimoxazole prophylaxis for opportunistic infections in adults with HIV (combined with pediatric CD003508)	Cotrimoxazole vs control	Analysis 1.1. Comparison 1 Cotrimoxazole vs control, Outcome 1 Death.	1.175	.7427	1.858	.638		.638	.4812	.8459	.5431	.3783	.7797			
CD003038	Beta-lactam versus beta-lactam-aminoglycoside combination therapy in cancer patients with neutropenia	Beta-lactam vs beta-lactam-aminoglycoside combination therapy	Analysis 11.1. Comparison 11 Adults vs. children, Outcome 1 All cause mortality.	1.238	.5158	2.974	.91		.91	.7355	1.126	.7348	.3142	1.719			
CD000033	Barbiturates for acute traumatic brain injury	Barbiturate vs control	Analysis 1.1. Comparison 1 Barbiturate vs control, Outcome 1 Death at the end of follow up.	1.287	.3856	4.292	1.287		1.287	.6356	2.604	1.000	.3764	2.657			
CD001090	Intravenous immunoglobulin for treating sepsis and septic shock	IVIg vs placebo or no intervention	Analysis 1.1.(1-2) Comparison 1 IVIG versus placebo or no intervention, Outcome 1 All-cause mortality by type of IVIG, random effects. [ONLY SUBTOTALS] (Polyclonal IVIG: adults ; neonates)	1.445	.9415	2.217	.9003		.9003	.8105	1.000	.6252	.4115	.9438			
CD003341	High first dose quinine regimen for treating severe malaria	Loading dose vs no loading dose	Analysis 1.1. Comparison 1 High first (loading) dose compared with no loading dose, Outcome 1 Death.	1.661	.0653	42.24	.9375		.9375	.0537	16.37	.5645	.1242	2.566			

SUPPLEMENTAL TABLE 4 Continued

Review	Title	Comparison	Severe adverse events	sROR		LCI_sROR		UCI_sROR		i2	OR		LCI OR		UCI OR	
				ROR	LCI ROR	UCI ROR	LCI ROR	UCI ROR	adults		adults	adults	adults	adults	adults	adults
CD002045	Hypertonic versus near isotonic crystalloid for fluid resuscitation in critically ill patients (Trauma)	Hypertonic vs isotonic crystalloid	Analysis 1.1.1 Comparison 1 Hypertonic versus isotonic crystalloid, Outcome 1 Death. (trauma) [ONLY SUBTOTALS]	1.25	0.73	2.15	0%									
CD000345	Sequential combination of glucocorticosteroids and alfa interferon versus alfa interferon alone for HBeAg-positive chronic hepatitis B	Glucoc + IFN vs control + IFN	Analysis 1.1. Comparison 1 Glucoc + IFN versus Control + IFN (overall analyses at maximal follow-up), Outcome 1 Mortality.	5.066	.2145	119.6	.7816	.4635	1.318	.1543	.0068	3.488				
CD003133	Addition of anti-leukotriene agents to inhaled corticosteroids for chronic asthma	Leukotriene receptor antagonists + ICS vs same dose of ICS in symptomatic patients	Analysis 1.25. Comparison 1 Leukotriene Receptor Antagonists (LTRA) + ICS vs. same dose of ICS in SYMPTOMATIC patients, Outcome 25 Death.				.3463	.014	8.556							
CD003992	Oral versus intravenous antibiotic treatment for febrile neutropenia in cancer patients	Oral vs intravenous antibiotic therapy	Analysis 1.1. Comparison 1 Oral vs. intravenous antibiotic therapy, Outcome 1 Mortality.				1.007	.4437	2.286							
CD003039	Colony stimulating factors for chemotherapy induced febrile neutropenia	Colony stimulating factor + antibiotics vs antibiotics alone	Analysis 1.1. Comparison 1 CSF + ATB vs ATB alone, Outcome 1 Mortality.				.7009	.428	1.148							
CD000059	Clozapine versus typical medication for schizophrenia	Clozapine vs typical antipsychotics	Analysis 2.1. Comparison 2 CLOZAPINE versus TYPICAL ANTIPSYCHOTICS - TREATMENT RESISTANT SCHIZOPHRENIA, Outcome 1 Death.				.637	.2022	2.007							

Abbreviations: LOI, low 95% confidence interval; OR, odds ratio (experimental vs control intervention); UCI, high 95% confidence interval; ROR, relative Odds ratio of Adults vs. Children (per each individual meta-analysis); sROR, summary Relative Odds Ratio of Adults vs Children (across all meta-analyses)

Footnote: Highlighted are the results that were statistically significant for any of the following: sROR (across all meta-analyses per harm/harm-related endpoint); ROR (for each individual meta-analysis of the OR in adult studies vs. the OR in pediatric studies); OR adults (OR of the experimental vs control intervention in the meta-analysis of adult studies); OR peds (OR of the experimental vs. control intervention in the meta-analysis of pediatric studies)

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