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Research Article

Surgical Site Infection Wound Bundles Should Become Routine in Colorectal Surgery: A Meta-Analysis

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Abstract

Background: Surgical Site Infections (SSI) are a major source of post-operative complications and potentially affect oncological outcomes. Reducing SSI is multi-factorial, best served by the additive affect of individual wound bundle elements. With changing strategies and novel innovations ongoing meta-analyses are needed to inform current practice. This study undertook a meta-analysis of existing wound bundles impact on SSI in colorectal surgery.

Methods: A PROSPERO-registered (ID: CRD42018104923) meta-analysis following Preferred Reporting Items for Systematic Reviews and Meta-Analyses guidelines and using databases PubMed, Scopus and Web of Science, from January 2008 to July 2018, was undertaken. Articles scoring ≥ 17 using Methodological Index for non-randomised Studies (MINORS) criteria were included.

Results: 5,104 articles were reviewed, and 27 studies met inclusion criteria with a total cohort of 23851 patients. Wound bundles significantly decreased SSI rates from 17.5% to 9.7%. Sub-analysis identified greatest impact on superficial SSI (risk reduction of 54%; p<0.00001) and organ-space infections (risk reduction 42%; p=0.0006).Wound bundles also significantly reduced hospital length of stay (MD=−0.79; p<0.00001).

Conclusions: Colorectal wound bundles significantly reduce the risk of SSI and length of hospital stay. They should become routine in colorectal surgery. Future work encompasses the need for standardisation of wound complications, standardised follow-up of patients and internationally agreed research definitions.

Keywords: Care pathway; Colorectal surgery; Surgical site infections; Surgical outcomes; Wound bundles

List of Abbreviations: **ASA:** American Society of Anesthesiologists; **CDC:** Centres for Disease Control and Prevention; **CI:** Confidence Interval; **ECDC:** European Centres for Disease Control and Prevention; **IHI:** Institute of Healthcare Improvement; **MINORS:** Methodological Index for non-randomised Studies; **NSQIP:** National Surgical Quality Improvement Program; **PO:** Per Oral; **PRISMA:** Preferred Reporting Items for Systematic Reviews and Meta-Analyses guidelines; **RR:** Relative Risk; **SSI:** Surgical Site Infection

Introduction

The global impact of Surgical Site Infection (SSI) is increasingly recognised, both in terms of post-operative complications and the effect on patient's outcomes. SSI rates vary internationally, related in part to variable definitions, different populations, co-morbidities and strategies utilised to reduce surgical site infection [1,2]. Surgical site infection may cause distress and inconvenience to patients, delay their discharge, increase risk of incisional hernia and re-admission to hospital [3,4]. Furthermore, the hospital or patients may be financially penalised. Recently the negative oncological impact of SSI is becoming increasingly reported [5-7]. A key to reducing SSI is a team approach, involving all providers, in every phase of care, with a cumulative additive benefit of each aspect in the bundle. A wound bundle, in general, will have more than three components and extend from pre-operative care through to rehabilitation. Newer concepts in colorectal surgery wound care include negative pressure therapy [8] and wound protective devices [9,10].

While several meta-analyses have been performed looking at bundles and surgical site infection, with the exception of Pop-Vicas, et al. [11], most relate to publications and interventions before 2016. The search strategy used in this paper differed from that of Pop-Vicas, et al. [11] in that it used different keywords and databases. This study therefore undertook a meta-analysis of bundle impact on SSI.

Methods

Search Strategy and Study Eligibility

A detailed meta-analysis of the literature was undertaken to incorporate articles relating to colorectal surgery wound care, surgical wound infection, and surgical site care bundles. Existing research optimizing wound care in colorectal surgery was reviewed to determine current bundle strategies to improve wound outcomes. A systematic review and meta-analysis of all published English articles was conducted using PubMed, Scopus, Web of Science and Cochrane electronic databases from 2008 to July 2018. A literature search was conducted using keywords; colorectal surgery, surgical site infections, wound bundles, compliance, care pathway, and surgical outcomes. Additional studies were identified by searching the reference lists of included articles.

Inclusion and Exclusion Criteria

The methods of the analysis and inclusion criteria were specified in advance and registered with the International Prospective Register of Systematic Reviews (PROSPERO) on 23/07/2018. This meta-analysis adhered to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statement. The Centres for Disease Control and Prevention (CDC) definitions for surgical site infection were used. They are classified into superficial, deep or organ/space in this study [12]. A wound care bundle was defined as three or more items combined to reduce wound infection as per the Institute for Healthcare Improvement [13]. For this meta-analysis, only studies with pre- and post-intervention SSI data for colorectal surgery were included, while studies that did not compare results to pre-intervention SSI rates were not included. Non-English articles were not included.

Eligibility Assessment and Data Extraction

Eligibility assessment was performed independently in a blinded standardised manner by two reviewers (DF and CMcI). Disagreements between reviewers were resolved by discussion between the two review authors and if no agreement could be reached, it was planned a third reviewer would decide (AJ), however a third reviewer was not required. Two reviewers (DF and CMcI) independently assessed each published study for the quality of study design by using the Methodological Index for non-randomised Studies (MINORS) score [14]. A MINORS score of ≥ 17 was considered the standard for inclusion. Information was extracted from each included study on SSI classifications, bundle elements, length of stay, bundle adherence rates, study design, country, study length, cohort sizes, and SSI rates pre- and post-intervention. The primary outcome was SSI rates following the use of wound bundles. Secondary outcomes were the effect of individual interventions included in the bundles and the SSI rates for superficial, deep and space organ infections.

Statistical Analysis

For comparison of SSI rates pre-and post-intervention risk ratios (RR) were calculated using Review Manager Version Five (RevMan5). Meta-analyses were performed by computing the RR using Mantel-Haenszel method and both fixed-effect models or random-effects models, depending on the heterogeneity of studies. Heterogeneity was assessed using the I^2 statistic where a value greater than 50% was considered high and a random-effect model was then used to combine variables of interest. RR and 95% Confidence Intervals (CI) for each classification of SSI was calculated, along with the p-value for which a value < 0.05 represented statistical significance. For the analysis of wound bundle elements, individual bundle elements in each study were reported in three phases of care: pre, peri- and post-operative care. However, any perioperative intervention that was only used once was not included in the table and was reported separately. The individual elements of each wound bundle were reviewed, and random-effect models were used to further explore the underlying effects of specific methodological features and intervention aspects of the care bundles on the rate of SSI. Some wound bundle features were identified that may explain some of the heterogeneity in the risk of SSI between studies.

Four studies provided sufficient raw data to carry out a meta-analysis on risk factors for SSI [15-18]. The following risk factors were analyzed: American Society of Anesthesiologists (ASA) physical status, diabetes mellitus and surgical approach (open vs. laparoscopic).

Results

This meta-analysis reviewed 5,104 articles. 46 studies were found to be potentially suitable and 27 studies [19-41] were included in this meta-analysis with a total cohort of 23851 patients (Figure 1).

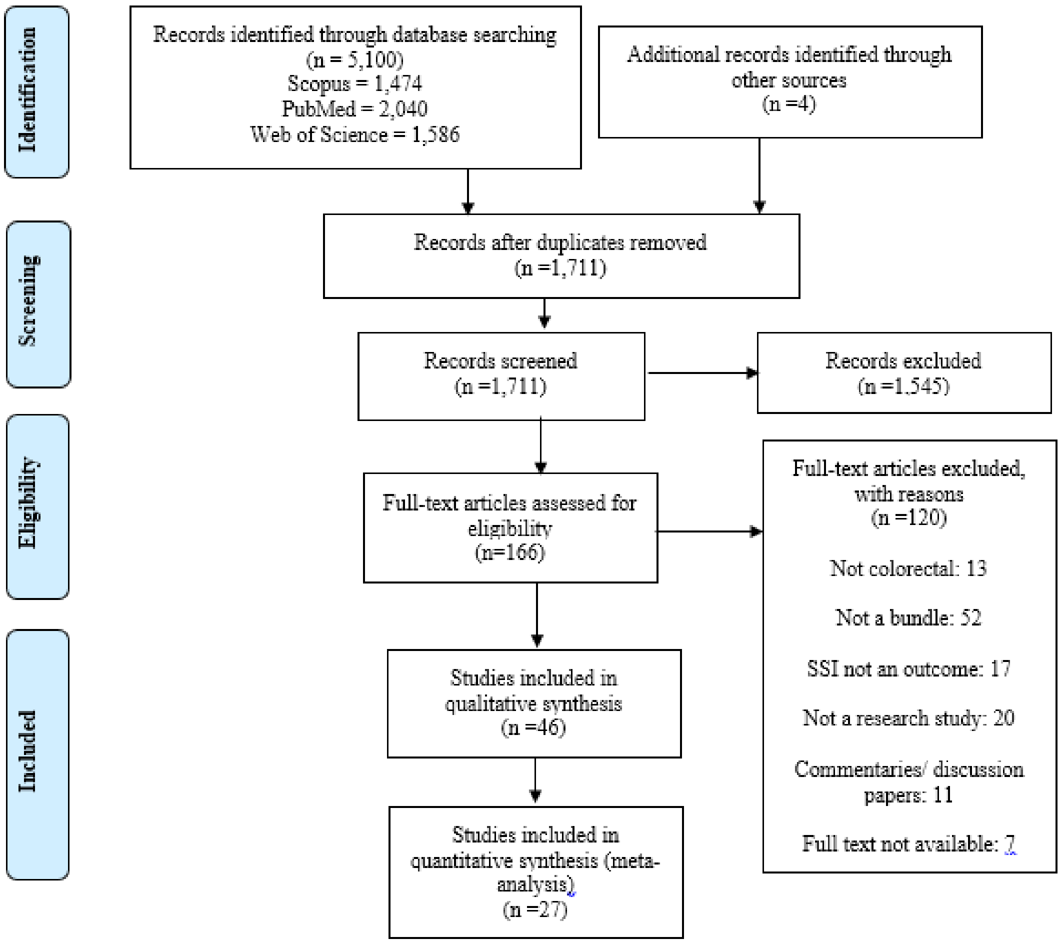

Figure 1: Identification, review and selection of articles included in the meta-analysis for impact of wound bundles on Surgical Site Infections in Colorectal Surgery**.**

19/46 studies were excluded from the meta-analysis: Seven studies stratified cohorts based primarily on compliance in using a bundle [42-48], six did not state colorectal specific SSI rates [49-54], 3 were deemed of low quality [55-57] and three did not provide pre-intervention cohort sizes [58-60]. Characteristics of included studies are shown in Table 1.

Author and year	Country	Study design	Sample group	Data collection period	Sample size baseline	Sample size cohort	SSI definition	Surveillance
Anthony 2011	USA	RCT	colorectal	2 yr, 8 months	97	100	CDC	30 days
Benlice 2016	USA	Cohort	colorectal	1 yr, 1 yr	986	1293	NSQIP	30 days

Bert 2016	Italy	Cohort	colorectal	1 yr	651	671	ECDC	30 days
Bull 2011	Australia	Cohort	colorectal	1yr, 1 yr	180	275	CDC	
Cima 2013	USA	Cohort	colorectal	1 yr, 2 yr	531	198	NSQIP	30 days
Connolly 2016	USA	Cohort	colorectal	3.5 yr, 3.5 yr	379	311	CDC	30 days
Crolla 2012	Netherlands	Cohort	colorectal	1.5 yr, 2.5 yr	394	377	CDC	30 days
Elia-Guedea 2017	Spain	Cohort	colorectal	3 mo, 3.5 mo	70	79	CDC	
Gachabayov 2018	USA	Cohort	colorectal resections	3 yr,3 yr	379	311	CDC	NSQIP
Ghuman 2015	Canada	Cohort	Colon resections		111	103	CDC	
Gorgun 2018	USA	Cohort	Colorectal	1 yr,1 yr	986	1264	NSQIP	30 days
Hewitt 2017	USA	Cohort	colorectal	2 yr, 1 yr	489	212	NSQIP	NSQIP
Hoang 2018	USA	Cohort	colorectal	2 yr, 4 yr	436	459	NSQIP	NSQIP
Keenan 2014	USA	Cohort	Colorectal	3 yr,1.5 yr	212	212	NSQIP	30 days
Keenan 2015	USA	Cohort	Colorectal	16 mo, 20 mo	165	285	NSQIP	
Lutifyya 2012	USA	Cohort	colorectal	4 yr, 1.5 yr	430	195	NSQIP	NSQIP-30 days
Perez-blanco 2015	Spain	Cohort	Colorectal	3 yr, 1 yr	218	124	CDC	
Reames 2015	USA	Cohort	colorectal	2 yr, 2 yr	2604	3119	CDC	
Rencüzoğulları 2018	USA	Cohort	colorectal	30 mo, 18 mo	1408	498	CDC	
Ruiz-Tovar 2018	Spain	RCT	Elective lap CRC cancer	2 yr	99	99	CDC	30 Days
Rumberger 2016	USA	Cohort	Colorectal	1 yr, 10 mo	269	261	CDC	30 days
Schiavone 2017	USA	Cohort	colorectal	1 yr, 1 yr	115	118	CDC	30 days
Tanner 2016	UK	Cohort	Colorectal	6 mo, 6 mo	127	166	HPA	30 days

Tillman 2013	USA	Cohort	colorectal	1 yr, 1 yr	79	104	NSQIP	
Weiser 2018	USA	Cohort	colorectal	10 mo,13 mo	454	616	CDC	30 days
Wick 2012	USA	Cohort	Colorectal	1 yr, 1 yr	278	324	NSQIP	
Yamamoto 2015	Japan	Cohort	Colorectal	3 yr, 2 yr	47	25	CDC	

Table 1: Characteristics of studies used in Meta-analysis.

Wound Bundle and their effect on Surgical Site Infection Rates

Overall SSI Rates: Of the 27 studies included in the meta-analysis two large studies (almost 8000 patients) only reported superficial SSI rates and were not included in the overall SSI rate analysis [39,41]. There was an overall decrease in SSI rates following the implementation of wound bundles (1432/8182 [17.5%] vs 777/8040 [9.7%]). There was significant heterogeneity between trials (I^2=73%) and a random-effects model was used. Despite the heterogeneity there was significant reduction in the risk of SSIs by 46% (RR=0.54; 95% CI, 0.46-0.64; p<.00001, I^2=73%) (Figure 2).

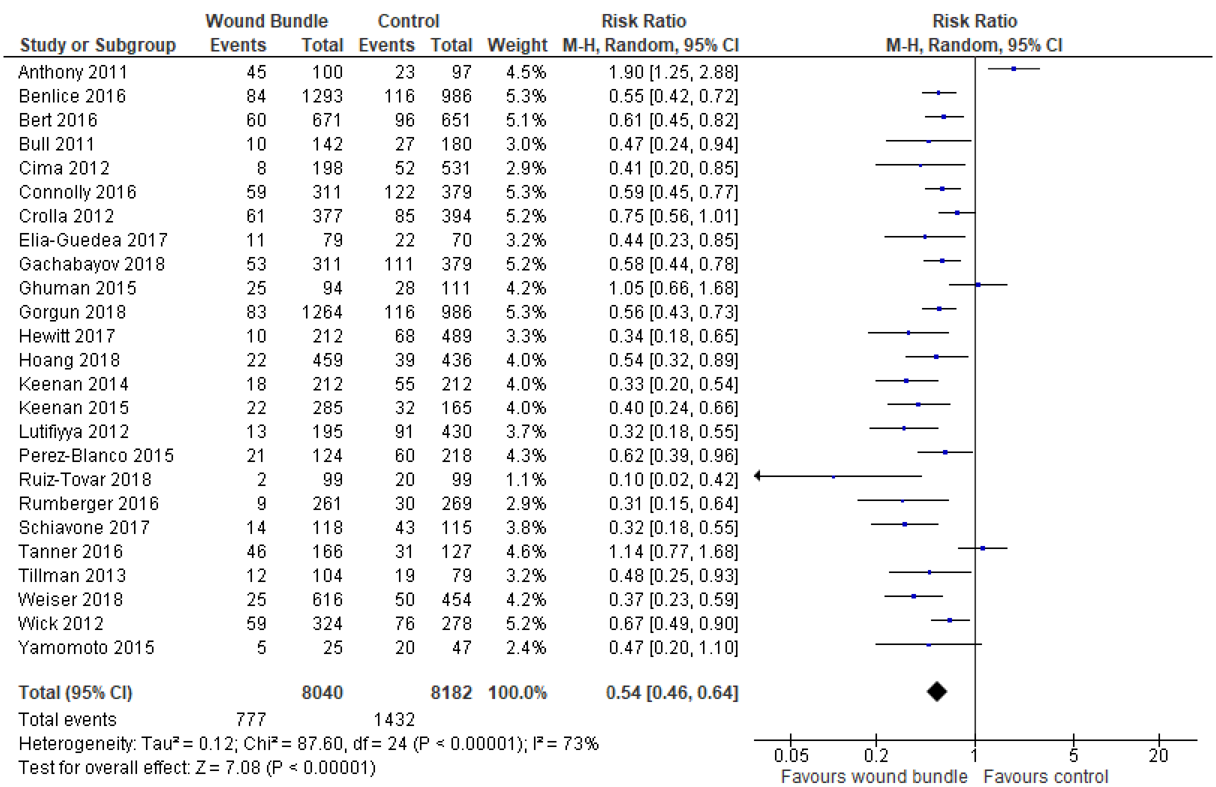

Figure 2: Forest plot: Surgical Care bundles Vs. Control to reduce the risk of Surgical Site Infections.

22 of the 25 studies had a statistically significant decrease in overall SSI rates following bundle implementation [16-20, 22-38]. Two studies showed no effect [21,40] and Anthony, et al. 2011 [15] reported a statistically significant increase in SSI after bundle implementation.

Superficial SSI Rates: Superficial SSI rates were reported in 20 studies with a cohort of 20,806 patients. The meta-analysis showed that wound bundles reduced superficial SSIs by 54% (RR= 0.46; 95% CI, 0.34-0.62; p<.00001, I^2=84%) (Figure 3).

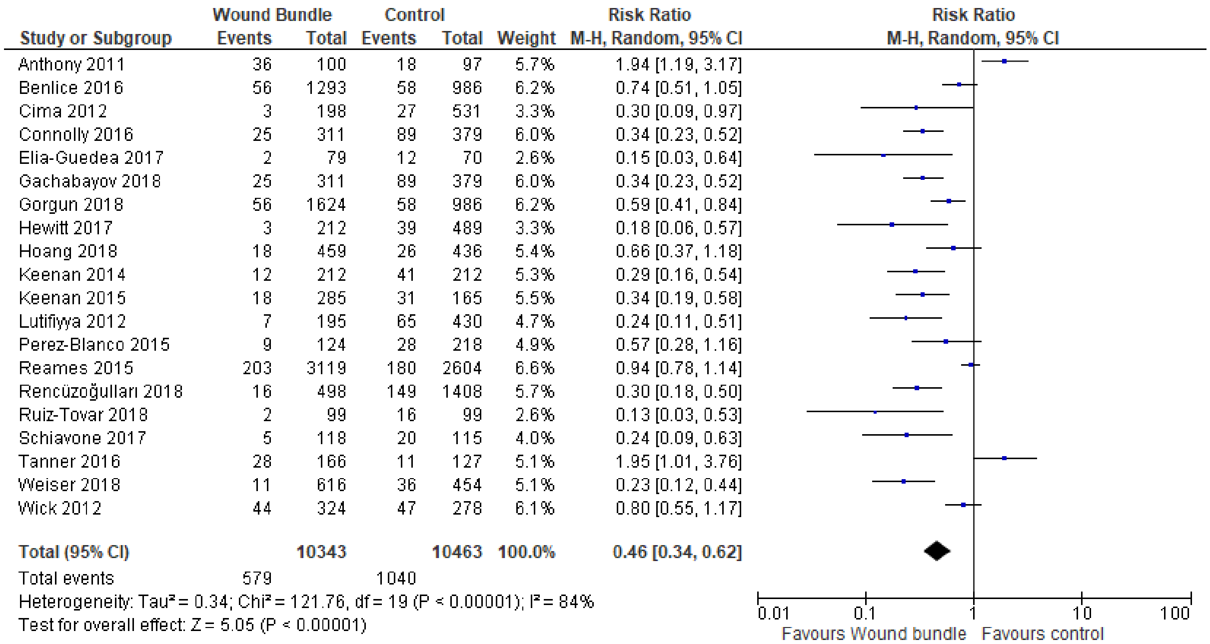

Figure 3: Forest plot: Surgical Care bundles Vs. Control to reduce the risk of Superficial Surgical Site Infections.

Deep SSI Rates: Fifteen studies [16,18,20-22,25,26,28-32,34,36-38] included data on deep SSIs, with only one study [37] showing a statistically significant decrease in deep SSI rates. Overall there was not a statistically significant reduction in the risk of deep SSI and this meta-analysis required a fixed-effect model due to its heterogeneity of I^2=0% (RR=0.76; 95% CI, 0.56-1.04; p= 0.09, I^2=0%) (Figure 4).

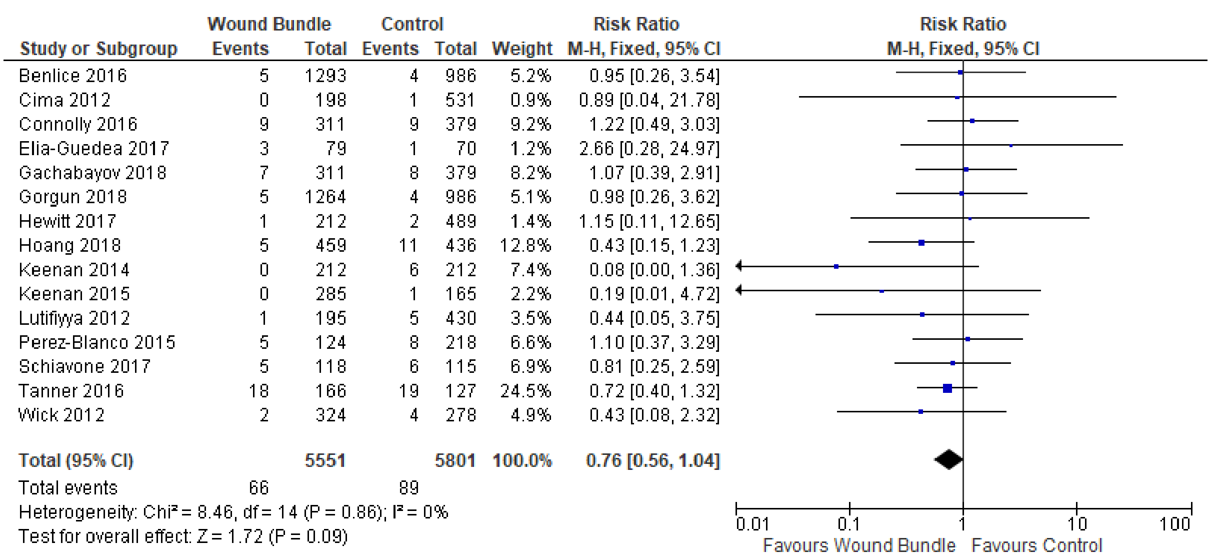

Figure 4: Forest plot: Surgical Care bundles Vs. Control to reduce the risk of Deep Surgical Site Infections.

Organ Space SSI Rates: Sixteen studies [15,16,18,20,22,23,25,27-32,34,36,38] reported organ space SSI rates. The meta-analysis showed a statistically significant reduction in the risk of organ/space SSIs by 42% (RR=0.58; 95% CI, 0.43-0.79; p=.0006, I^2=59%) (Figure 5).

	Wound Bundle		Control			Risk Ratio
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Random, 95% CI
Anthony 2011	9	100	6	97	5.3%	1.46 [0.54, 3.93]
Benlice 2016	23	1293	54	986	9.1%	0.32 [0.20, 0.53]
Cima 2012	5	198	27	531	5.6%	0.50 [0.19, 1.27]
Connolly 2016	24	311	23	379	8.5%	1.27 [0.73, 2.21]
Elia-Guedea 2017	6	79	9	70	5.4%	0.59 [0.22, 1.58]
Gachabayov 2018	23	311	18	379	8.2%	1.56 [0.86, 2.83]
Gorgun 2018	22	1264	54	986	9.1%	0.32 [0.19, 0.52]
Hewitt 2017	6	212	29	489	6.1%	0.48 [0.20, 1.13]
Keenan 2014	6	212	11	212	5.4%	0.55 [0.21, 1.45]
Keenan 2015	8	285	10	165	5.8%	0.46 [0.19, 1.15]
Lutifiyya 2012	5	195	21	430	5.5%	0.53 [0.20, 1.37]
Perez-Blanco 2015	7	124	24	218	6.5%	0.51 [0.23, 1.16]
Ruiz-Tovar 2018	0	99	4	99	1.0%	0.11 [0.01, 2.04]
Schiavone 2017	3	118	7	115	3.7%	0.42 [0.11, 1.58]
Weiser 2018	14	616	14	454	7.1%	0.74 [0.35, 1.53]
Wick 2012	13	324	25	278	7.7%	0.45 [0.23, 0.86]
Total (95% CI)		**5741**		**5888**	**100.0%**	**0.58 [0.43, 0.79]**
Total events	174		336			

Heterogeneity: Tau² = 0.21; Chi² = 36.19, df = 15 (P = 0.002); I² = 59%
Test for overall effect: Z = 3.42 (P = 0.0006)

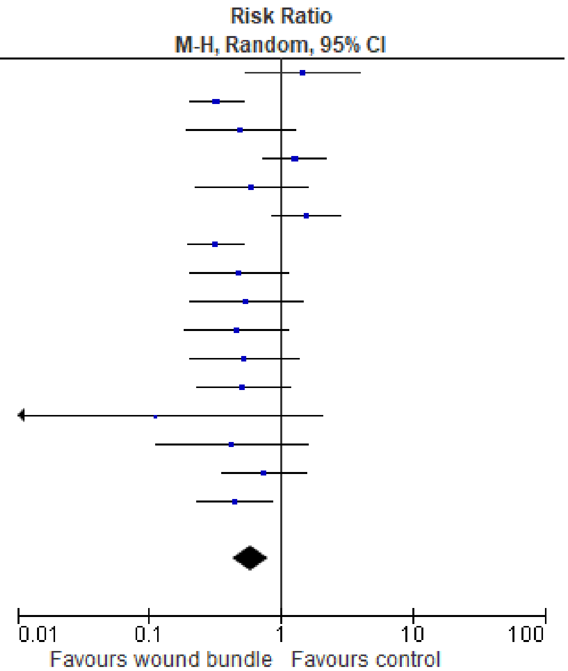

Figure 5: Forest plot: Surgical Care bundles Vs. Control to reduce the risk of Organ Space Surgical Site Infections.

Bundle Elements Results: We identified the following study features that may explain some of heterogeneity in the risk of SSI between studies: the use of Mechanical Bowel Preparation (MBP) and oral antibiotics, wound protectors, instruments for closure, and the implementation of pre-operative shower/wipes with chlorhexidine. Eight studies used both MBP and oral antibiotics. Care bundles including MBP and oral antibiotics had greater risk reduction in SSI then bundles without but the difference was not statistically significant (RR 0.57 vs 0.61, p-value 0.86) (Figure S1).

Study or Subgroup	bundle Events	bundle Total	Control Events	Control Total	Weight	Risk Ratio M-H, Random, 95% CI
3.1.1 MBP with Oral Abx						
Benlice 2016	84	1293	116	986	4.5%	0.55 [0.42, 0.72]
Gorgun 2018	83	1264	116	986	4.5%	0.56 [0.43, 0.73]
Keenan 2014	180	212	55	212	4.5%	3.27 [2.59, 4.14]
Keenan 2015	22	285	32	165	4.0%	0.40 [0.24, 0.66]
Lutifiyya 2012	13	195	91	430	3.9%	0.32 [0.18, 0.55]
Rencüzoğulları 2018	0	0	0	0		Not estimable
Schiavone 2017	14	118	43	114	4.0%	0.31 [0.18, 0.54]
Weiser 2018	25	616	50	454	4.1%	0.37 [0.23, 0.59]
Wick 2012	59	324	76	278	4.5%	0.67 [0.49, 0.90]
Subtotal (95% CI)		**4307**		**3625**	**34.1%**	**0.57 [0.30, 1.09]**
Total events	480		579			
Heterogeneity: Tau² = 0.82; Chi² = 195.97, df = 7 (P < 0.00001); I² = 96%						
Test for overall effect: Z = 1.71 (P = 0.09)						
3.1.2 No MBP and Oral Abx						
Anthony 2011	45	100	23	97	4.2%	1.90 [1.25, 2.88]
Bert 2016	60	671	96	651	4.4%	0.61 [0.45, 0.82]
Bull 2011	10	142	27	180	3.6%	0.47 [0.24, 0.94]
Cima 2012	8	198	52	531	3.5%	0.41 [0.20, 0.85]
Connolly 2016	59	311	122	379	4.5%	0.59 [0.45, 0.77]
Crolla 2012	61	377	85	394	4.5%	0.75 [0.56, 1.01]
Elia-Guedea 2017	11	79	22	70	3.7%	0.44 [0.23, 0.85]
Gachabayov 2018	53	311	111	379	4.5%	0.58 [0.44, 0.78]
Ghuman 2015	25	94	28	111	4.1%	1.05 [0.66, 1.68]
Hewitt 2017	10	212	68	489	3.7%	0.34 [0.18, 0.65]
Hoang 2018	22	459	39	436	4.1%	0.54 [0.32, 0.89]
Perez-Blanco 2015	21	124	60	218	4.2%	0.62 [0.39, 0.96]
Ruiz-Tovar 2018	2	99	20	99	2.1%	0.10 [0.02, 0.42]
Rumberger 2016	9	261	30	269	3.5%	0.31 [0.15, 0.64]
Tanner 2016	46	166	31	127	4.3%	1.14 [0.77, 1.68]
Tillman 2013	12	104	19	79	3.7%	0.48 [0.25, 0.93]
Yamomoto 2015	5	25	20	47	3.2%	0.47 [0.20, 1.10]
Subtotal (95% CI)		**3733**		**4556**	**65.9%**	**0.61 [0.48, 0.76]**
Total events	459		853			
Heterogeneity: Tau² = 0.14; Chi² = 60.33, df = 16 (P < 0.00001); I² = 73%						
Test for overall effect: Z = 4.39 (P < 0.0001)						
Total (95% CI)		**8040**		**8181**	**100.0%**	**0.58 [0.44, 0.76]**
Total events	939		1432			
Heterogeneity: Tau² = 0.41; Chi² = 262.28, df = 24 (P < 0.00001); I² = 91%						
Test for overall effect: Z = 3.95 (P < 0.0001)						
Test for subgroup differences: Chi² = 0.03, df = 1 (P = 0.86), I² = 0%						

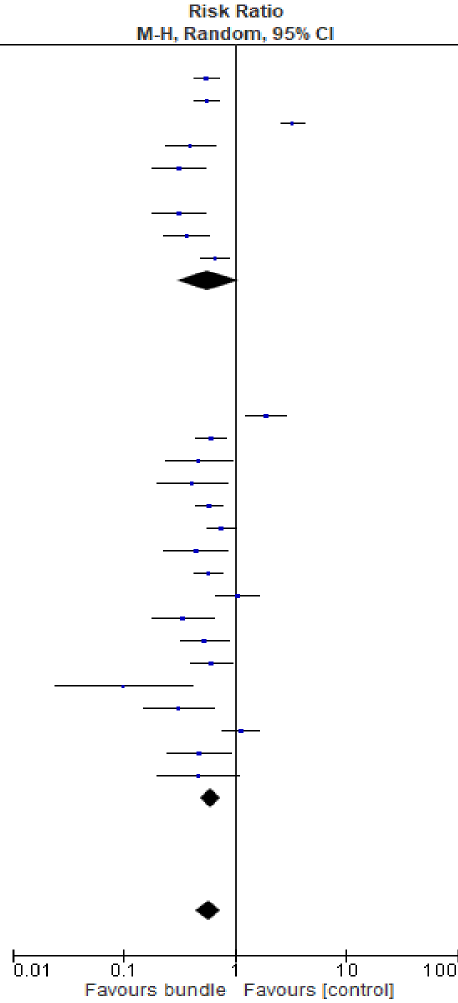

Figure S1: Forest plot: Surgical Care bundles including MBP and Oral Antibiotics Vs. Surgical Care Bundles without.

Fourteen studies implemented pre-operative shower/wipes with chlorhexidine gluconate. There was a greater risk reduction in SSI in care bundles using chlorhexidine gluconate than bundles without but the difference was not statistically significant (RR 0.51 vs 0.62, p-value 0.31) (Figure S2).

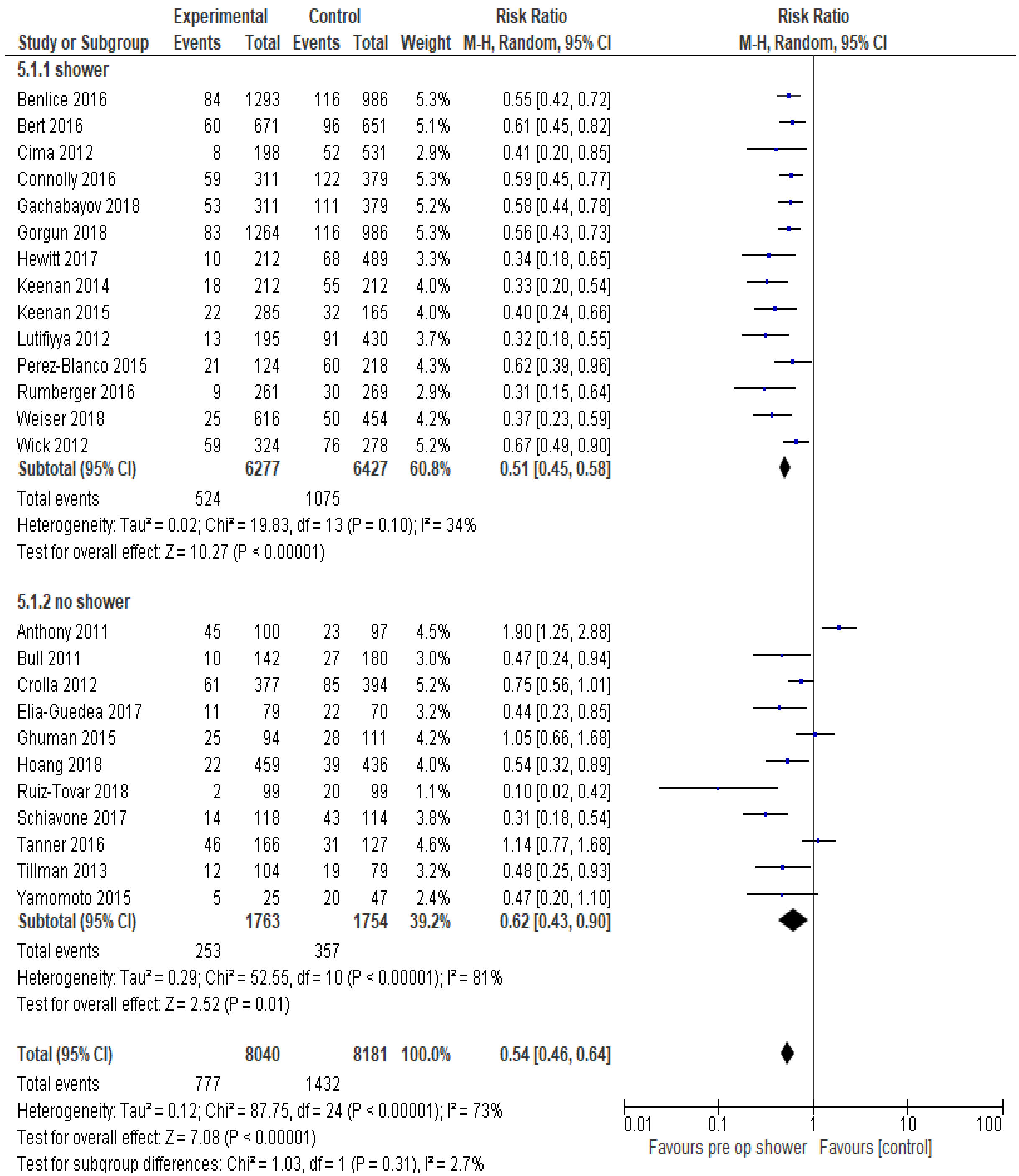

Figure S2: Forest plot: Surgical Care bundles including CHG shower/wipes Vs. Surgical Care Bundles without.

12 studies reported outcomes of a dedicated wound closure instrument tray. There was a greater risk reduction in SSI in care bundles using wound closure tray (RR 0.47 vs 0.74, p-value 0.05) (Figure S3).

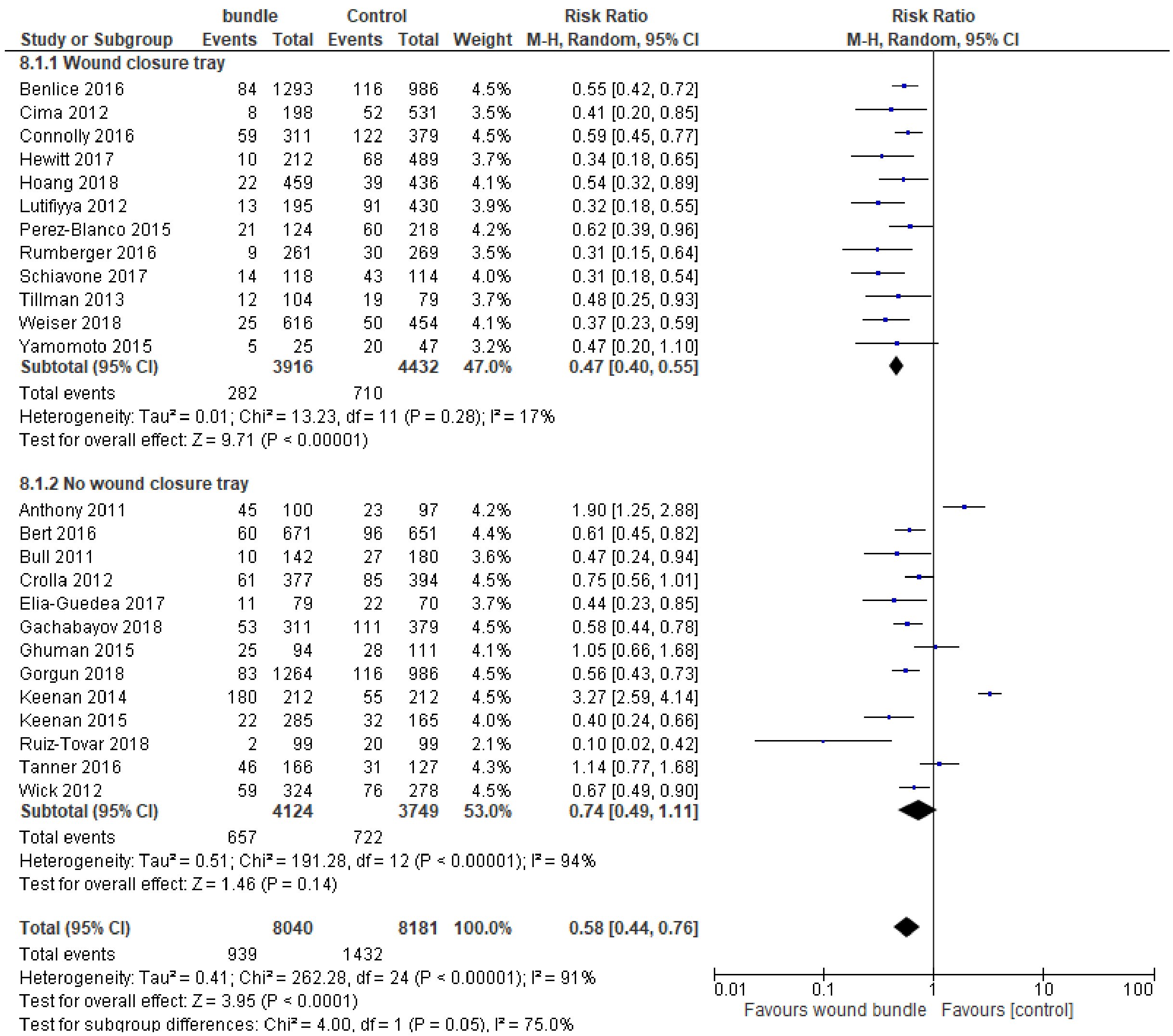

Figure S3: Forest plot: Surgical Care bundles including dedicated wound closure tray Vs. Surgical Care Bundles without.

9 studies reported outcomes of wound bundles that included wound protectors. There was no greater risk reduction in SSI in these care bundles than bundles without wound protectors (RR 0.69 vs 0.54, p-value 0.44) (Figure S4). Analyses of wound bundle elements are shown in supplementary Tables S1-S2.

Study or Subgroup	Bundle Events	Bundle Total	Control Events	Control Total	Weight	Risk Ratio M-H, Random, 95% CI
9.1.1 Bundle with Wound Protector						
Anthony 2011	45	100	23	97	4.2%	1.90 [1.25, 2.88]
Benlice 2016	84	1293	116	986	4.5%	0.55 [0.42, 0.72]
Connolly 2016	59	311	122	379	4.5%	0.59 [0.45, 0.77]
Gachabayov 2018	53	311	111	379	4.5%	0.58 [0.44, 0.78]
Gorgun 2018	83	1264	116	986	4.5%	0.56 [0.43, 0.73]
Hewitt 2017	10	212	68	489	3.7%	0.34 [0.18, 0.65]
Keenan 2014	180	212	55	212	4.5%	3.27 [2.59, 4.14]
Keenan 2015	22	285	32	165	4.0%	0.40 [0.24, 0.66]
Rumberger 2016	9	261	30	269	3.5%	0.31 [0.15, 0.64]
Subtotal (95% CI)		**4249**		**3962**	**38.1%**	**0.69 [0.39, 1.20]**
Total events	545		673			
Heterogeneity: Tau² = 0.69; Chi² = 199.29, df = 8 (P < 0.00001); I² = 96%						
Test for overall effect: Z = 1.32 (P = 0.19)						
9.1.2 Bundle without Wound Protector						
Bert 2016	60	671	96	651	4.4%	0.61 [0.45, 0.82]
Bull 2011	10	142	27	180	3.6%	0.47 [0.24, 0.94]
Cima 2012	8	198	52	531	3.5%	0.41 [0.20, 0.85]
Crolla 2012	61	377	85	394	4.5%	0.75 [0.56, 1.01]
Elia-Guedea 2017	11	79	22	70	3.7%	0.44 [0.23, 0.85]
Ghuman 2015	25	94	28	111	4.1%	1.05 [0.66, 1.68]
Hoang 2018	22	459	39	436	4.1%	0.54 [0.32, 0.89]
Lutifiyya 2012	13	195	91	430	3.9%	0.32 [0.18, 0.55]
Perez-Blanco 2015	21	124	60	218	4.2%	0.62 [0.39, 0.96]
Ruiz-Tovar 2018	2	99	20	99	2.1%	0.10 [0.02, 0.42]
Schiavone 2017	14	118	43	114	4.0%	0.31 [0.18, 0.54]
Tanner 2016	46	166	31	127	4.3%	1.14 [0.77, 1.68]
Tillman 2013	12	104	19	79	3.7%	0.48 [0.25, 0.93]
Weiser 2018	25	616	50	454	4.1%	0.37 [0.23, 0.59]
Wick 2012	59	324	76	278	4.5%	0.67 [0.49, 0.90]
Yamomoto 2015	5	25	20	47	3.2%	0.47 [0.20, 1.10]
Subtotal (95% CI)		**3791**		**4219**	**61.9%**	**0.54 [0.44, 0.67]**
Total events	394		759			
Heterogeneity: Tau² = 0.11; Chi² = 43.41, df = 15 (P = 0.0001); I² = 65%						
Test for overall effect: Z = 5.68 (P < 0.00001)						
Total (95% CI)		**8040**		**8181**	**100.0%**	**0.58 [0.44, 0.76]**
Total events	939		1432			
Heterogeneity: Tau² = 0.41; Chi² = 262.28, df = 24 (P < 0.00001); I² = 91%						
Test for overall effect: Z = 3.95 (P < 0.0001)						
Test for subgroup differences: Chi² = 0.58, df = 1 (P = 0.44), I² = 0%						

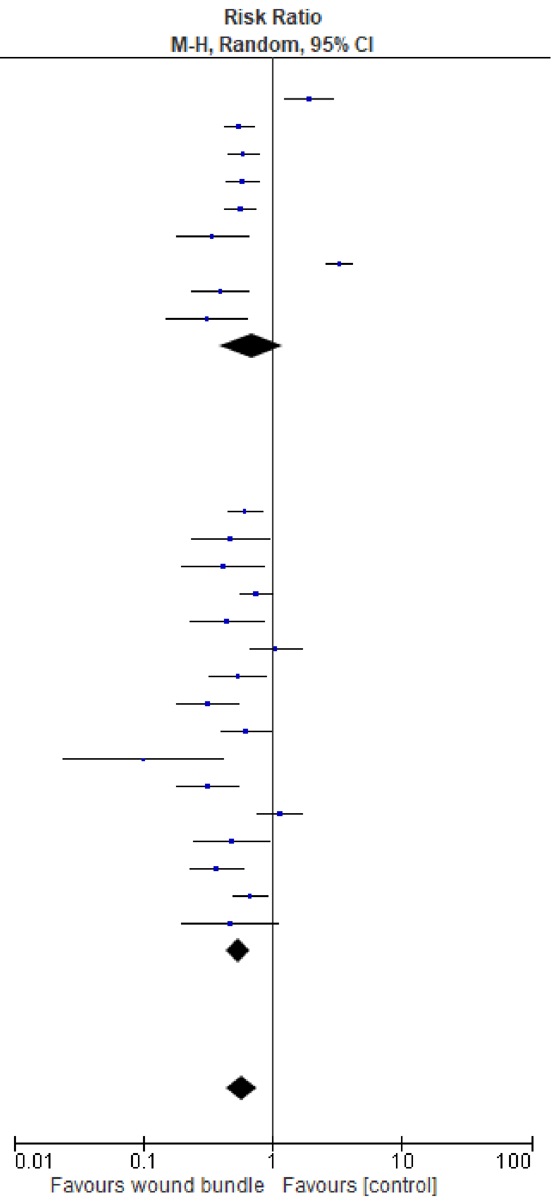

Figure S4: Forest plot: Surgical Care bundles including wound protector Vs. Surgical Care Bundles without.

Author and Year	Preoperative CHG Wipes/ Shower	Risk assessment for SSI	Pre-operative infection screen	Smoking Cessation	Omission of Mechanical Bowel Preparation	Bowel preparation with oral antibiotics	Mechanical Bowel preparation	Pre-operative glycemic screen/ control	preoperative normothermia	Pre-operative Checklist	Pre-operative patient education
Anthony 2011					✓				✓		
Benlice 2016	✓					✓	✓				
Bert 2016	✓										
Bull 2011								✓	✓		
Cima 2012	✓										✓
Connolly 2016	✓										
Crolla 2012									✓		
Elia-Guedea 2017											
Gachabayov 2018	✓						✓	✓		✓	
Ghuman 2015											
Gorgun 2018	✓					✓	✓				
Hewitt 2017	✓		✓	✓		✓		✓	✓	✓	
Hoang 2018						✓		✓			
Keenan 2014	✓					✓	✓	✓			✓
Keenan 2015	✓					✓	✓	✓			
Lutifiyya 2012	✓			✓		✓	✓	✓	✓		✓
Perez-Blanco	✓							✓			
Reames 2015											
Rencüzoğulları 2018						✓	✓				
Ruiz-Tovar 2018							✓				
Rumberger 2016	✓							✓			
Schiavone 2017						✓	✓	✓			
Tanner 2016	✓ **		✓					✓			
Tillman 2013											
Weiser 2018	✓	✓				✓	✓				
Wick 2012	✓					✓	✓				
Yamamoto 2015											

Table S1: Study and their Preoperative Interventions.

Author and Year	Peri-op Glycemic control	Hair removal with clippers	Skin Preparation with CHG in alcohol	Antibiotic prophylaxis <60 minutes before surgery	Antibiotic re-dose within 2-4 hours if required	Intra-operative normothermia	Wound protectors	Triclosan Sutures	Double gloving	Glove and/or Gown change	New wound closure tray	Suction tip change and wound washout	Limited OR Traffic	Antibiotic irrigation of Abdomen	redraping/ draping	Supple-mental Oxygen	Checklist fulfilment
Anthony 2011				✓		✓	✓									✓	
Benlice 2016				✓			✓			✓		✓					
Bert 2016		✓		✓		✓											
Bull 2011	✓			✓		✓									✓	✓	
Cima 2013			✓	✓	✓					✓	✓						
Connolly 2016	✓	✓	✓	✓		✓	✓			✓	✓		✓				
Crolla 2012		✓		✓		✓							✓				
Elia-Guedea 2017				✓	✓					✓	✓		✓				
Gachabayov 2018		✓	✓			✓	✓			✓	✓		✓		✓		✓
Ghuman 2015							✓			✓	✓				✓		
Gorgun 2018			✓	✓			✓			✓	✓	✓					
Hewitt 2017	✓	✓	✓	✓		✓	✓			✓	✓			✓	✓	✓	✓
Hoang 2018	✓	✓		✓	✓	✓					✓					✓	
Keenan 2014			✓	✓		✓	✓			✓	✓		✓				
Keenan 2015			✓	✓		✓	✓			✓	✓						
Lutifiyya 2012	✓	✓	✓	✓	✓	✓			✓							✓	
Perez-Blanco	✓		✓	✓	✓	✓				✓							
Reames 2015	✓	✓		✓		✓											
Rencüzoğulları 2018				✓			✓										
Ruiz-Tovar 2018			✓	✓		✓		✓	✓					✓			✓

Rumberger 2016		✓	✓	✓	✓	✓										✓	
Schiavone 2017	✓		✓	✓	✓					✓	✓						
Tanner 2016	✓	✓	✓	✓		✓									✓		
Tillman 2013	✓	✓		✓		✓											
Weiser 2018	✓	✓		✓	✓	✓					✓						
Wick 2012			✓			✓				✓	✓						
Yamamoto 2015				✓	✓			✓	✓								

Table S2: Study and their Intraoperative Interventions.

Length of Stay Results: There were seven studies that included data on the length of hospital stay in both pre-intervention and post-intervention cohorts [18,22,23,25,27,31,34]. The mean difference between the length of hospital stay pre- and post-intervention was calculated in a meta-analysis. Two studies [22,34] provided the mean and standard deviation (mean ± SD) for the number of hospital days. The other five studies provided the median with either the full range or interquartile range. For these five studies [18,23,25,27,31], the mean ± SD were calculated from the data provided, according to calculations set out in the following studies: Hozo, et al. (2005) [61], Luo, et al. (2017) [62] and Wan, et al. (2014) [63]. This is based on an assumption of normal distribution in these studies. There was a statistically significant mean difference between the two groups in favour of the wound bundle (MD=−0.79; 95% CI: −1.10 to -0.49; p<0.00001) (Figure S5).

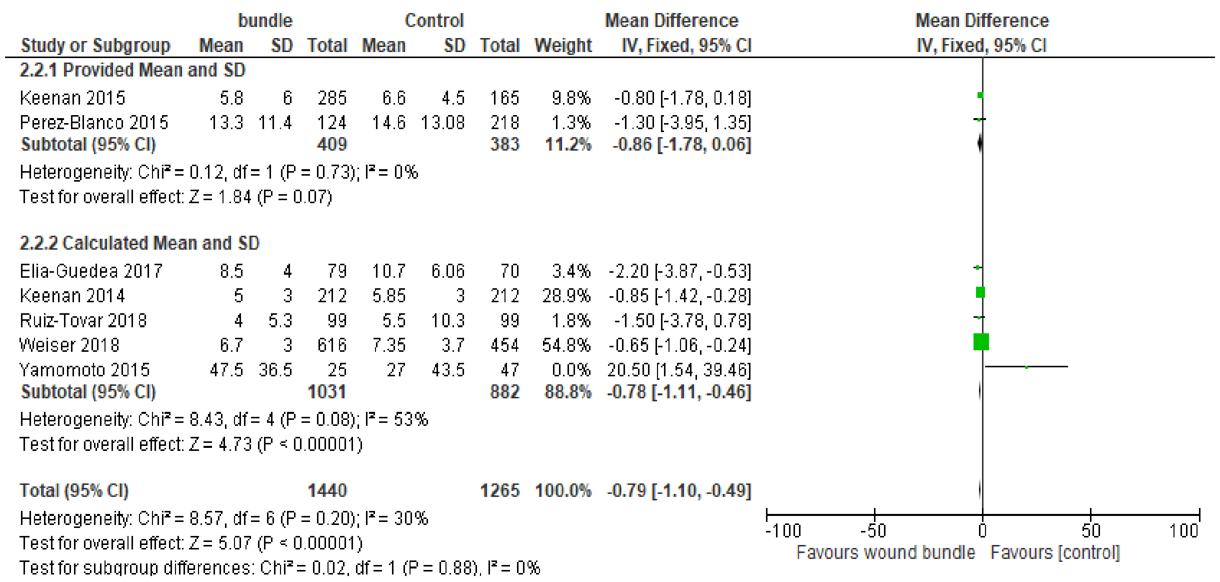

Figure S5: Forest plot: Surgical Care bundles Vs. Control to reduce the length of hospital stay after colorectal surgery

Risk Factor Results: Four studies provided sufficient raw data to carry out a meta-analysis on risk factors for SSI [18,20,23,30]. The American Society of Anaesthesiologists Physical Status classification ≥III was found to be a significant preoperative risk factor (OR=1.66, CI=1.32-2.09, p<0.0001) (Figure S6).

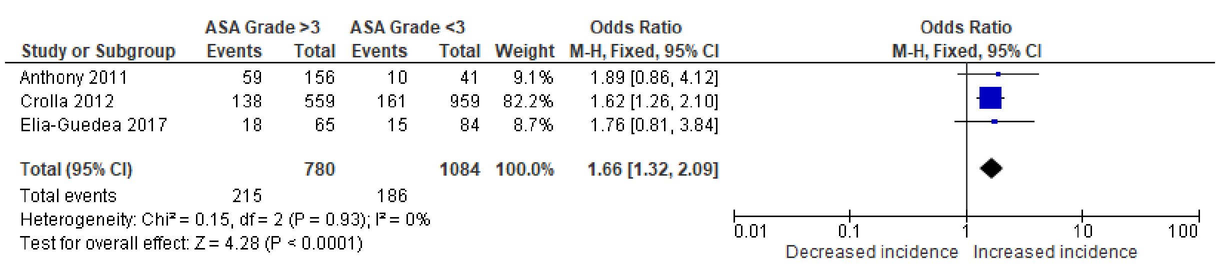

Figure S6: Forest plot: ASA Grade >III Vs. ASA Grade <III.

A meta-analysis of diabetes was also carried out which showed a statistically insignificant decrease in SSI in patients with diabetes mellitus (OR=.40, CI=.12-1.33, p=0.13) (Figure S7).

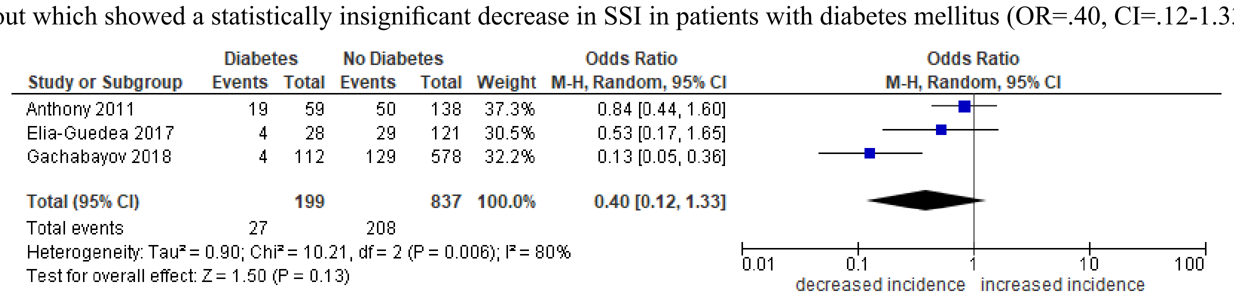

Figure S7 : Forest plot : Diabetes Mellitus Vs. Non-Diabetes Mellitus.

Another meta-analysis was carried out on open surgical approach vs. laparoscopic approach which showed an increased incidence in SSI in open approach however it was statistically insignificant. (OR=1.41, CI=.65-3.08, p=0.38) (Figure S8).

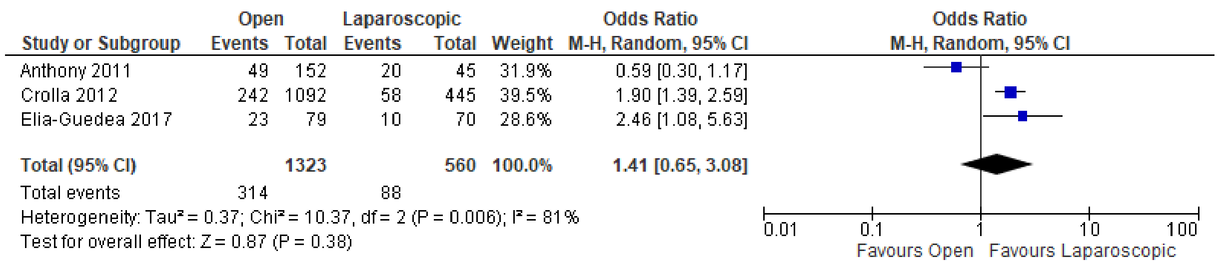

Figure S8: Forest plot: Open Approach Vs. Laparoscopic Approach.

A number of studies had insufficient data for forest plot analysis. Bert, et al. [17] reported the following significant risk factors for SSIs; intervention technique (endoscopic vs. open) (OR, 2.07; CI, 1.25-3.62), ASA score ≥ 3 (OR, 1.80; CI, 1.26-2.57), urgent procedures (OR, 1.81; CI, 1.22-2.66) and contamination class ≥3 (OR, 2.32; CI, 1.62-3.31). Ghuman, et al. [40] found that smoking (OR, 3.75; CI, 1.54-9.13; p = 0.004), diabetes mellitus (OR, 2.75; CI, 1.28-5.95; p = 0.009), and incision location (OR, 1.37; CI, 1.04-1.83; p = 0.03) were significant risk factors. Hewitt, et al. [26] reported that using a laparoscopic approach is a significant factor in reducing SSI (OR, .43; CI, .24-.77). Rencuzogullari, et al. [39] reported that open surgical approach (OR, 2.15; CI, 1.27-3.60; p=0.004), wound class III-IV (OR 13.2; 95% CI, 8.36-21.0; p<0.001) and BMI (OR 1.30; 95% CI, 1.14-1.49; <0.001) were found to be independent risk factors for SSI occurrence.

Discussion

This meta-analysis evaluated the efficacy of wound bundles in SSI reduction, based on a ten-year literature review, yielded 27 publications meeting quantitative criteria. Two were RCT and 25 were retrospective cohort studies. The overwhelming evidence supports the use of wound bundles, even with the recognised heterogeneity of the studies. Surgical site infection, including superficial, deep and organ space, is one of the most common complications following open and colorectal cancer surgery [64]. At the outset, there is a global challenge in relation to the definition and heterogeneity of both superficial and deep SSIs. The lack of standardization of wound event reporting is common both in colorectal and other areas of surgery [65]. DeBord, in an editorial review of the issue, looks at the concept of proposals to classify surgical site events and surgical site occurrences requiring procedural interventions [66]. Of the 27 papers used in our meta-analysis, 15 papers used the Centres for Disease Control and Prevention (CDC) definitions for SSI [12]. A further ten papers used the National Surgical Quality Improvement Program (NSQIP) which uses the CDC definition for the types of SSI. The two remaining papers used the European ECDC definition which is again the CDC definition.

Definitions and reporting of surgical site occurrences, first defined by the Ventral Hernia Working Group (VHWG) in 2010 [67] to include seroma, wound dehiscence, and enterocutaneous fistula have not been widely adopted thus far [66]. Only one study, Anthony et al. 2011, showed an increase in SSIs following application of wound bundles, which may have been due to their failure to include mechanical bowel preparation or oral antibiotic preparation.

There is a significant increase in SSI rate in urgent or emergency procedures due to a myriad of confounding factors such as poor preoperative preparation and both clean contaminated and dirty operations [17,68,69]. Watanabe, et al. [70] have suggested that in cases of colon perforation with generalised contamination, delayed primary skin closure or leaving an incision open to heal by secondary intention should be considered. This is increasingly challenged by more use of comprehensive wound bundles that include wound irrigation and incisional negative pressure therapies [71]. However, despite this, a significant proportion of dirty wounds (without fasciitis) are not closed primarily. In a study by Alkaaki, et al. [72], more than half (30/55 [54%]) of the infected patients in their study underwent emergency surgery and they found that emergency surgery increased the risk of SSI fivefold compared to elective surgery. Ensuring strict adherence of preventative wound bundles, especially in emergency procedures, may see a very significant reduction in SSI globally. Successful implementation of clinical guidelines to reduce hospital acquired infections is challenging. Some have evolved using protocol-driven reduction [73] and others have looked at multiple different implementation strategies [74]. The Institute of Healthcare Improvement (IHI) developed a concept of bundles. A bundle generally uses more than three evidence-based measures which implemented together are more effective than in isolation. Recently, Tomsic, et al. suggested that bundle size itself is important and in their analysis suggested that a bundle with more than eleven items have additional stand-alone benefit in surgical site reduction [75]

In our meta-analysis we identified that surgical site infections were significantly reduced with the use of wound bundles. With sub-analysis of SSI into superficial SSI, deep SSI and organ space SSI, there were differences in outcome. Superficial SSI and organ space SSI were significantly reduced by the bundle, whereas there was only a trend for deep SSI. The reason for this is not entirely clear and may relate to the variability in bundle elements used. Many studies did not use negative wound pressure dressings. Recently, Murphy and colleagues [76] in Canada identified that negative pressure in the Neptune study had no associated effect on SSI. They report a very high SSI rate, approaching 32-34%. However, in their study they did not report or use any wound bundle. This may account for the failure to obtain a significant reduction in infection. Ideally, bundles target areas for reduction in variation in the delivery of care focusing on three key phases pre-operative, intra-operative and post-operative. Bundles should not just involve the patient but also their family. Pop-Vicas and colleagues [11] published a recent meta-analysis on colorectal bundles for surgical site infection prevention in the journal of Infection Control and Hospital Epidemiology. Multiple papers on the same topic are important to reinforce an important clinical issue. Given the potential implications in terms of cost, prolonged hospital stay, patient discomfort, and the potential adverse oncological and survival effects of both superficial and deep SSI, it is important that surgeons and those involved in the primary care of colorectal cancer and colorectal benign patients implement aspects of care bundles that are proven.

Wound protectors are commonly used in colorectal surgery and are recommended in open abdominal surgery in the ACS and SIS Guidelines [60]. However, there are some conflicting results on this in the literature [60,77-79]. The combination of MBP and antibiotic (PO) preparation is recommended for all elective colectomies according to ACS and SIS guidelines [77]. Other surgical techniques such as quilting or killing the dead space to reduce seroma and the use of subcuticular suturing should be looked at with increasing evidence that these may reduce wound infection rates [80,81]. This paper did not specifically look at laparoscopic versus open colorectal surgery and this is something that will need to be done into the future, stratifying cohorts or having separate or comparative studies [82]. Although we found that colorectal wound bundles significantly reduce the risk of SSI and length of hospital stay our study has several limitations. Firstly the vast majority of the included studies were retrospective cohort studies with heterogeneous interventions; no assessment of risk of bias was carried out. Secondly the primary outcome measure of SSI does not have a specified length of follow-up. Thirdly only four studies provided sufficient raw data to carry out a meta-analysis on risk factors for SSI; a small number of patients were included in each analysis. In addition, the effect on wound bindle efficacy in patients with immune compromise, or ongoing Covid infection has not been widely studied.

Conclusion

This meta-analysis has identified significant reductions in wound infections with implementation of wound bundles. As Surgeons we have the responsibility to ensure we routinely use wound bundles which should become routine in colorectal surgery. Future work encompasses the need for standardisation of wound complications, standardised follow-up of patients and internationally agreed research definitions.

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