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Does Prophylactic Antibiotic Administration Time Effect Surgical Site Infection Rates in Colorectal Surgery?

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A Major Paper Presented

by

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Abstract

Colorectal surgery is known for having a high risk of surgical site infection (SSI). Prior research has suggested that administering prophylactic antibiotics prior to colorectal surgery may prevent SSI. This led to the question: In adult surgical patients having colorectal surgeries, does prophylactic antibiotic administration time effect surgical site infection rates within 30 days of surgery? A comprehensive literature review was completed followed by a detailed screening for inclusion and exclusion criteria, resulting in a final total of nine studies. Detailed data were collected for each study, followed by completion of critical appraisal checklists appropriate to the study design. Quality of the evidence was assessed across studies. Six of the studies were cohort studies, with only two randomized controlled trials and one systematic review. Results indicated that there is insufficient evidence to support a definite course of action for timing of antibiotic prophylaxis for colorectal surgery. The certified registered nurse anesthetist (CRNA) should be aware of the recommendations to administer antibiotics for colorectal surgery before the surgical incision based on the results of this systematic review as timing of administration can affect SSI rates. It is recommended to carefully consider antibiotic selection and timing when administering antibiotics for colorectal surgery.

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Does Prophylactic Antibiotic Administration Time Effect Surgical Site Infection Rates In Colorectal Surgery?

Background/Statement of the Problem

Surgical wound infections (SSIs) are often preventable. Research reflects a decrease in morbidity and SSI rates in relation to prophylactic antibiotic administration (Gustafsson et al., 2013). In 2013, guidelines for antibiotic prophylaxis were established by the American Society of Health-System Pharmacists (ASHP), the Infectious Disease Society of America (IDSA), the Surgical Infection Society (SIS), and Society for Healthcare Epidemiology of America (SHEA). However, not all institutions and providers follow these same guidelines. Based on the type of surgery, researchers recommend that appropriate antibiotic timing, selection, and route of administration needs further research (Nelson, Gladman, & Barbateskovic, 2014). Colorectal surgery is known for having a high risk of surgical site infection. In a study by Dettenkofer et al. (2002) of perioperative antibiotic prophylaxis for colorectal and hip surgeries, it was found that there was uncertainty related to appropriate timing of perioperative antibiotic administration and its duration. Previous research has shown that giving prophylactic antibiotics prior to colorectal surgery prevents SSIs (Nelson et al., 2014). This lead to the research question: In adult surgical patients having colorectal surgeries, does prophylactic

antibiotic administration time effect surgical site infection rates within 30 days of surgery? The purpose of this systematic review was to examine the relationship between SSI rates and prophylactic antibiotic administration time in adults having colorectal surgeries.

Next, the review of the literature will be presented.

Literature Review

A literature search was conducted using the following key words: “Antibiotic Prophylaxis”, “Colorectal Surgery”, “Timing”, “Surgical Site Infection”, and “Surgical Care Improvement Program”. CINAHL, PubMed, Cochrane, and Google Scholar produced relevant literature for analysis and evaluation. The literature search was limited to studies no older than 15 years. The following research studies have been summarized.

Surgical Site Infections

A SSI is an infection that occurs after surgery in the area of the body where the surgery was performed (Centers for Disease Control and Prevention [CDC], 2012). Surgical site infections can sometimes be superficial and involve only the skin, while other SSIs are more severe and can involve tissues below the skin, organs, or implanted devices (CDC). Surgical site infections have been shown to increase readmission rates, length of stay, and costs for patients (Institute for Healthcare Improvement [IHI], 2012). Surgical site infection prevention measures include appropriate hair removal, use of prophylactic antibiotics, controlled postoperative glucose levels for cardiac patients, and immediate normothermia for colorectal surgery patients post-operatively. If implemented correctly, these measures can drastically decrease the incidence of SSIs (IHI). The

economic costs of SSIs are considerable; however, there are extreme variations in cost between minor superficial infections ranging from less than $400 up to $299,237 for complex infections (Alexander, Solomkin, & Edwards, 2011). In the 1990s, the median cost for hospitalization for SSIs was $7,531 and $3,844 for patients without SSIs. The increase in cost for SSIs was $2,671 for colon surgery (Alexander et al.). A more current study evaluated length of stay and expenses associated with elective colorectal surgery SSIs. It was found that SSI was associated with a $30,000 increase in cost for each hospital discharge (Eagye & Nicolau, 2009).

Surgical Site Infections and Colorectal Surgery

Colorectal surgery is linked with the highest risk of SSI due to the large amount of bacteria in the colon and rectum (Ishikawa et al., 2014). The occurrence of SSIs after colorectal surgery have been reported to range between 5% and 26% (Ishikawa et al.). Ho et al. (2011) noted that among elective procedures, colorectal surgery has the highest occurrence of SSI, with infection rates varying from 3% to 43%, depending on the method of follow-up and SSI definition used (Ho et al.).

Timing and Decreased Incidence of SSI in Colorectal Surgery. Ho et al. (2011) attempted to identify adherence to a set of guidelines for antibiotic administration

and to assess risk for SSIs. It was hypothesized that compliance with the guidelines would decrease the occurrence of SSIs. Six hundred five patients having colorectal surgeries with anastomosis between June 2001 and July 2008 were selected randomly. Data were gathered via a retrospective chart review of patients having surgeries at the New York Presbyterian Hospital and Weill Cornell Medical Center using the CDC definition for SSI. A statistical program known as "STATA/IC" was used for data analysis. The first antibiotic dose was given to 361 patients within 30 minutes of incision, to 202 patients greater than 30 minutes before incision and to 22 patients after incision. Results indicated that increased occurrence of SSIs correlated with early administration of prophylactic antibiotics, specifically greater than 30 minutes prior to incision (OR 1.725, 95% CI 1.147-2.596). Documentation of exact time of administration of antibiotics was not clear if administered before patients arrived in the operating room, which was one of the limitations of this study. Use of bowel preparation and oral antibiotics were not examined in this study and the sample size was small. It was recommended that research be continued in order to improve guidelines for appropriate antibiotic administration timing and repeat dosing for colorectal procedures (Ho et al.).

A review by Gustafsson et al. (2013) examined current recommendations related to perioperative treatment in colorectal surgery based on the Enhanced Recovery After Surgery (ERAS) care pathway. The ERAS Society for Perioperative Care was started by the previous ERAS Study Group and was formed in 2010. The Society aims to improve perioperative care through research, education, and implementation of best practice. The ERAS care pathway includes evidence-based treatments for the perioperative period made into a standardized protocol.

The Gustafsson et al. (2013) review was conducted to identify the most current literature related to appropriate perioperative care for colon surgery. Literature was gathered from Cochrane, EMBASE, and Medline with publications dated from 1966 to 2012. Mainly meta-analyses, randomized controlled trials (RCTs), and large cohort studies were included in this review. The studies were individually analyzed for relevance and further examined by the senior author and committee members of ERAS. Both the Cochrane checklist and the GRADE system were used to assess quality. With a recommendation grade of "high" and an evidence level of "strong", it was found that the most appropriate time to administer intravenous (IV) antibiotics is 30 to 60 minutes prior to the surgical incision for colorectal surgery. One study by Steinberg et al. (2009) was

used to support this recommendation. In this study, the overall association between timing and infection risk was found to be significant (P = 0.04). Infection risk after antibiotic administration within 30 minutes before incision was 1.6% compared with 2.4% associated with antibiotic administration 31 to 60 minutes prior to surgery (odds ratio [OR] 1.74; 95% confidence interval 0.98 –3.04) (Steinberg et al.). However, appropriate timing of oral antibiotic administration prior to colon surgery requires more investigation because the use of oral antibiotics has not been examined without mechanical bowel preparation (Gustafsson et al.).

Timing and Decreased Incidence of SSI in Mixed Surgeries. Another study by Weber et al. (2008) aimed to determine specific information about the most appropriate timing for perioperative antibiotic prophylaxis. Weber et al. organized a prospective observational cohort study at a university hospital where timing of antimicrobial prophylaxis was examined based on SSI occurrence in 3,836 surgeries. Cefuroxime 1.5g IV was administered as a single dose to each patient along with metronidazole 500mg IV for colorectal surgeries. Weber et al. demonstrated a decreased occurrence of SSI rates when cefuroxime and metronidazole were administered 30 to 60 minutes before incision for procedures including colorectal surgery. Analyses showed a significant increase in

the incidence of SSIs when antibiotic prophylaxis was administered during the last half hour of surgery ($P < 0.001$) and during the last 60 to 120 minutes of surgery ($P = 0.035$) as compared with 30 to 59 minutes before surgical incision (Weber et al.). It was concluded that when IV cefuroxime was given for antibiotic prophylaxis, administration 30 to 59 minutes prior to incision is more effective than during the last half hour (Weber et al.).

Conversely, several current studies have failed to show decreased incidence of SSI with adherence to SCIP recommendations for prophylactic antibiotic administration time. Pastor et al. (2010) hypothesized that the incidence of SSI would be decreased with the application of SCIP prevention measures. A multidisciplinary team was assembled to put SCIP infection prevention measures into effect and monitor adherence. Study participants included patients having non-emergent colorectal surgeries with an abdominal incision. The sample included 491 patients having surgery at a tertiary institution. Subjects were assigned to either the first 14-month group or the second 14-month group in order to compare and analyze data from each group. Patient characteristics were compared during the two time periods by use of an independent t test for continuous variables and the Pearson test for categorical variables. Compliance and

rate of SSI was determined by linear regression. A P value of <.05 was considered to be statistically significant. This study showed an increase in adherence to SCIP measures but without a decrease in SSI related to compliance for each individual case. A 95% rate of compliance was achieved for timing of antibiotic prophylaxis, identified as starting administration within 60 minutes of surgical incision (P = .002). The SSI rate between groups was similar at 18.9 % and 19.4 %. Overall, there was a 19% rate of SSI after elective colorectal surgery. Compliance with re-dosing of antibiotics was a challenge for prolonged surgery due to a lack of documentation and timing of administration. Antibiotic discontinuation before 24 hours after surgery also remained a challenge. It was recommended that the practice of oral antibiotic prophylaxis and mechanical bowel preparation for colorectal surgery be further researched. The sample size for this study was somewhat small, limiting its application to other populations (Pastor et al.).

In a study by Hawn et al. (2011), SCIP guidelines were implemented and evaluated to determine if following the guidelines would result in a decreased incidence of SSI rates within 30 days of a surgical procedure. Data were gathered from 2005 to 2009 from the National Veterans' Affairs Surgical Quality Improvement Program (VASQIP) on both compliance to SCIP measures and SSI incidence. This was a

retrospective cohort study that also examined adherence to five SCIP measures including timely prophylactic antibiotic administration: SCIP-inf 1. Five types of surgeries including cardiac, colorectal, hip or knee arthroplasty, arterial vascular, and hysterectomy were done at Veterans' Affairs hospitals and included among the 60,853 surgeries used for analysis in this study. Of this number of surgeries, 39,149 surgical cases were evaluated with the measurement of SCIP-inf 1. A total of 15,444 colorectal surgeries were included in this study. The overall SSI rate was 6.2% and 11.3% for colorectal surgeries. After adjusting for the procedure and patient variables, the results indicated that compliance with the SCIP measures did not correlate with a lower incidence of SSI. For the timely antibiotic measure, an adjusted OR was determined to be 0.90 with a 95% CI for 29,042 cases. In addition, this study's VA population was mostly men, which could make a generalization to women difficult (Hawn et al.).

A more recently published study conducted by similar authors focused specifically on timing of surgical antibiotic prophylaxis and included subjects from the same population as in the earlier study. Hawn et al. (2013) aimed to discover the correlation between antibiotic administration time and SSI rates within 30 days postoperatively. The design and database from the previous study were repeated in this

study. There were a total of 34,459 patients having one of the five types of surgery included in this research study. Antibiotics were administered at a median of 28 minutes before surgical incision and 1,497 patients (4.6%) developed an SSI. As compared with procedures with antibiotic administration within 60 minutes before incision, higher SSI rates were present for timing greater than 60 minutes before incision, but not after incision. Generalized additive models (GAMs) were used to determine the correlation between SSI and timing of antibiotic administration. In unadjusted generalized additive models, a significant nonlinear relationship was present between prophylactic antibiotic timing and SSI with timing as a continuous variable ($P = .01$). In generalized additive models adjusted for procedure, patient, and antibiotic variables, no significant correlation between prophylactic antibiotic timing and SSI was seen ($P = 0.26 - 0.85$). This was true for 5,469 colorectal surgeries (adjusted OR 0.7; 95% CI). Therefore, the researchers felt that there was not enough evidence to recommend compliance to this SCIP measure. Based on the findings, it was also stated that there are several variables that could affect timing associated with SSI rates. Researchers should take into account the patient population and antibiotic being used. A limitation of this study was that more men than women were included, so a generalization to women cannot be made. It was

recommended that further research address appropriate antibiotic selection and repeat dosing (Hawn et al.).

Ishikawa et al. (2014) conducted research which closely looked at SSI associated risks for colorectal cancer patients having open surgeries. The purpose of the study was to identify the occurrence and possible determinants of incisional SSI in this population. Data were collected by continuous observation, which was maintained for incisional SSI for one year on surgeries performed in 2009 by an individual colorectal surgeon. The population selected for the study included patients having elective colorectal resections, in which the wound was closed at the end of the procedure. Patients were excluded if the wound was not closed. Also excluded were patients who were having laparoscopy or simple ostomy creation or closure with wedge or segmental resection. This study included a 224 patient cohort, 120 of which were male. A specific form was filled out by the surgeon on incisional SSI for a given patient based on the definition from the Center for Disease Control and Prevention (CDC). Another form was used to identify patient demographics and specified factors possibly associated with incisional SSI. Multivariate analysis was used to analyze the possible reasons for incisional SSI in this population. Assessment of the surgical incisions was done up to a minimum of 30 days

postoperatively. The specific time of antibiotic administration was documented by the anesthesiologist. For all patients included in this study, administration of antibiotics was between 15 and 50 minutes prior to the surgical incision. The onset of incisional SSI was not affected by the timing of preoperative antibiotic administration. There was no significant difference between antibiotic administration 15 to 29 and 30 to 50 minutes prior to incision ($P = 0.773$). Of the 124 patients who received antibiotic prophylaxis, about 29 % developed a SSI. Many confounding variables were minimized because all surgeries were performed by the same surgeon. A study with more subjects is needed in order to provide further evidence on different causes of SSIs (Ishikawa et al.).

Nelson et al. (2014) composed a systematic review in order to examine the relationship between antibiotic prophylaxis and SSI for patients having colorectal surgeries. Cochrane, Embase, and Medline were used to search for relevant evidence. Prophylactic antibiotic treatment done in randomized controlled trials including patients having both emergent and elective colorectal surgeries with SSIs were selected for this review. Data were examined by a single reviewer and then rechecked by another reviewer for SSI. The GRADE system was used to evaluate quality. The review included a total of 260 trials and 43,451 participants. Two related studies compared the

administration of antibiotics before surgery to the administration after surgery and no notable difference was found (risk ratio [RR] 0.67, 95% CI 0.2-2.15). Quality of the review is considered to be high, however its attrition rate presents a limitation across many studies. The authors advise further research on the timing and dosing of oral antibiotics (Nelson et al.).

Across the studies and reviews, there are still many questions to be asked and answered on this topic. It seems that there is much uncertainty in relation to prophylactic antibiotic administration time. The findings suggest that there is no definitive answer to the question of how timing of prophylactic antibiotic administration effects incisional SSI rates.

Next, the theoretical framework guiding this study will be presented.

Theoretical Framework: The Germ Theory

A theoretical framework widely known as The Germ Theory was initially discovered in 1858 by Louis Pasteur (McEwen & Wills, 2011). Louis Pasteur came up with the theory that a certain microorganism could have the ability to cause infection. It was suggested that in order for someone to get an infection, a person first needs to be susceptible to a microorganism. McEwen and Wills explained that someone with an increased risk for infection may be a person with a bad burn due to the loss of skin protection. This theory has been extremely influential in the study of medicine and the prevention of infection for many years. Current application of this theory includes measures to aid in the prevention of infection such as frequent hand washing and antibiotic prophylaxis. It is also used to recognize and control different infectious diseases (McEwen & Wills).

After the proposal of The Germ Theory, Louis Pasteur continued his research further by studying different diseases including cholera, silkworm disease, rabies, and anthrax (Toledo-Pereyra, 2009). He observed the progression of rabies, found a way to vaccinate animals and was successful in creating the first rabies vaccine for humans. A British surgeon named Joseph Lister followed Pasteur's work and was found to have

similar beliefs on surgical infections. He sent Pasteur a letter in 1874 thanking him for his accomplishments with The Germ Theory and explaining how his years of study had saved many lives. Pasteur showed how germs could be detrimental in many different situations including when found in wounds. It has been said that Louis Pasteur gave rise to a surgical revolution. Surgeons today continue to support these fundamentals of surgery, which were largely attributed to the work of Louis Pasteur (Toledo-Pereyra).

Based on the Germ Theory of Disease by Louis Pasteur, Joseph Lister began to use antiseptic techniques for surgery with the use of carbolic acid (Wilson, 1999), which was found to kill microorganisms. Lister further investigated the use of antiseptic dressings in the 1860s. During this time, Lister was able to significantly decrease the mortality rate of patients having amputations. Many people had not initially supported his ideas, but the principles that he proposed became accepted over time. Lister's efforts allowed for the first appropriate and believable implementation of The Germ Theory to manage infectious disease, which advanced the field of surgery (Wilson). Even though asepsis and sterile technique have replaced antisepsis as the main principle in preventing infection, it was Lister’s application of The Germ Theory to surgery that provided the foundation for what surgeons currently do. Through his work, he demonstrated to

physicians and surgeons the necessity of keeping wounds clean and free of contamination. Joseph Lister continues to be an inspiration to surgeons today (Pitt & Aubin, 2012).

The methodology guiding this systematic review will be presented next.

Method

Purpose/Clinical Question/Outcomes Examined

SSIs can often be prevented, however, not all institutions and providers follow the same guidelines for timing of antibiotic prophylaxis. Colorectal surgery is known for having a high risk of surgical site infection (SSI). Based on the type of surgery, researchers recommend that appropriate antibiotic timing, dosing, and selection need further research. The clinical question that was addressed is: "In adult surgical patients having colorectal surgeries, does prophylactic antibiotic administration time effect surgical site infection rates within 30 days of surgery?" The purpose of this research project was to examine the relationship between SSI rates and prophylactic antibiotic administration time in adults having colorectal surgeries.

Inclusion/Exclusion Criteria/Limits

This systematic review included studies involving adult surgical patients having colorectal surgeries with an abdominal incision. All types of studies are included due to the limited amount of research available. The included research must have delineated timing of prophylactic IV antibiotic administration and SSI rates within 30 days of surgery.

Exclusion criteria included other than adults, colorectal procedures with no incision and evidence of pre-operative infection in any site.

Procedure

Literature search. A comprehensive search of the literature was conducted using the following keywords: "Antibiotic Prophylaxis", "Colorectal Surgery", "Colon Surgery", "Timing", "Surgical Site Infection", and "Surgical Care Improvement Program". CINAHL, PubMed, Cochrane, and Google Scholar were utilized for an in depth literature search. At the end of the database searches, 21 studies were found. Studies were briefly examined to identify which ones best answered the clinical question as guided by Fineout-Overholt, Melnyk, Stillwell, and Williamson (2010a; 2010b; 2010c). Seven studies were retained for data collection as the others did not meet the requirements. The reference list of each study was examined for additional relevant literature. After reviewing the reference lists of each study, two additional studies were obtained, for a total of nine.

Data Collection. Relevant data was collected by using a form created by the researcher (Appendix A). The researcher was guided in the development of a data extraction tool by Fineout-Overholt et al. (2010a; 2010b; 2010c), Parts i-iii. Specifically,

the year, title, author, type of research and journal were recorded in addition to purpose, results, antibiotic administration time, SSI rates, recommendations, and limitations of each study.

Critical Appraisal. A critical appraisal of the literature was completed following guidelines by Fineout-Overholt et al. (2010a; 2010b; 2010c). The rapid critical appraisal began by obtaining full text documents of each study. Each study was reviewed to identify its level of evidence, how well it was performed, and how useful it was to practice. This required use of a critical appraisal guide appropriate for the type of research (Fineout-Overholt et al.). The Critical Appraisal Skills Programme (CASP UK, 2013) Checklists were used as critical appraisal tools. The checklists helped to determine the answers to three broad questions: "Are the results valid?", "What are the results?", and "Will the results help locally?" Specific questions that follow helped the researcher address these issues systematically. The researcher was able to select either, "Yes", "Can't Tell", or "No" in response to each question. Separate checklists were used for different levels of designs, which can be found in Tables 1-3 on the following pages.

Table 1

CASP Systematic Review Checklist

10 Questions			
1). Did the review address a clearly focused question?	Yes	Can't Tell	No
2). Did the authors look for the right type of papers?	Yes	Can't Tell	No
3). Do you think all the important, relevant studies were included?	Yes	Can't Tell	No
4). Did the review's authors do enough to assess the quality of the included studies?	Yes	Can't Tell	No
5). If the results of the review have been combined, was it reasonable to do so?	Yes	Can't Tell	No
6). What are the overall results of the review?			
7). How precise are the results?			
8). Can the results be applied to the local population?	Yes	Can't Tell	No
9). Were all important outcomes considered?	Yes	Can't Tell	No
10). Are the benefits worth the harms and costs?	Yes	Can't Tell	No

(CASP UK, 2013)

Table 2

CASP Randomized Controlled Trial Checklist

10 Questions			
1). Did the trial address a clearly focused issue?	Yes	Can't Tell	No
2). Was the assignment of patients to treatments randomized?	Yes	Can't Tell	No
3). Were patients, health workers and study personnel blinded?	Yes	Can't Tell	No
4). Were the groups similar at the start of the trial?	Yes	Can't Tell	No
5). Aside from the experimental intervention, were the groups treated equally?	Yes	Can't Tell	No
6). Were all of the patients who entered the trial properly accounted for at its conclusion?	Yes	Can't Tell	No
7). How large was the treatment effect?			
8). How precise was the estimate of the treatment effect?			
9). Can the results be applied in your context? (or to the local population?)	Yes	Can't Tell	No
10). Were all clinically important outcomes considered?	Yes	Can't Tell	No
11). Are the benefits worth the harms and costs?	Yes	Can't Tell	No

(CASP UK, 2013)

Table 3

CASP Cohort Study Checklist

10 Questions			
1). Did the study address a clearly focused issue?	Yes	Can't Tell	No
2). Was the cohort recruited in an acceptable way?	Yes	Can't Tell	No
3). Was the exposure accurately measured to minimize bias?	Yes	Can't Tell	No
4). Was the outcome accurately measured to minimize bias?	Yes	Can't Tell	No
5). A. Have the authors identified all important confounding factors? B. Have they taken account of the confounding factors in the design and/or analysis?	Yes	Can't Tell	No
6). A. Was the follow up of subjects complete enough? B. Was the follow up of subjects long enough?	Yes	Can't Tell	No
7). What are the results of this study?			
8). How precise are the results?			
9). Do you believe the results?	Yes	Can't Tell	No
10). Can the results be applied to the local population?	Yes	Can't Tell	No
11). Do the results of this study fit with other available evidence?	Yes	Can't Tell	No
12). What are the implications of this study for practice?			

(CASP UK, 2013)

Quality Assessment. The Critical Appraisal for Summaries of Evidence (CASE) worksheet (Foster & Shurtz, 2013) was used to assess quality of evidence. Summary topic, summary method, summary content, and summary application were reviewed for each study. The CASE worksheet is displayed in Table 4 on the following page (Foster & Shurtz).

Data Synthesis

The CASP checklists (CASP UK, 2013) were used to compare the selected research. Several checklists were utilized by the researcher depending on the type of study being reviewed. As mentioned previously, all types of research were included in the analysis. Consideration of study quality was also included in the data synthesis. Each study was assessed for quality by using the Critical Appraisal for Summaries of Evidence (CASE) worksheets (Table 4). Quality of evidence was compared across studies by utilizing this tool (Foster & Shurtz, 2013).

The results will be presented next, immediately following Table 4.

Table 4

CASE Worksheet

Critical Appraisal for Summaries of Evidence (CASE) Worksheet **Numbers in evaluation correspond with those assigned to articles in data extraction chart**	
Questions	**Evaluation**
Summary Topic	
1. Is the summary specific in scope and application?	Yes- Not completely- No-
Summary Methods	
2. Is the authorship of the summary transparent?	Yes- Not completely- No-
3. Are the reviewer(s)/editor(s) of the summary transparent?	Yes- Not completely- No-
4. Are the research methods transparent and comprehensive?	Yes- Not completely- No-
5. Is the evidence grading system transparent and translatable?	Yes- Not completely- No-
Summary Content	
6. Are the recommendations clear?	Yes- Not completely- No-
7. Are the recommendations appropriately cited?	Yes- Not completely- No-
8. Are the recommendations current?	Yes- Not completely- No-
9. Is the summary unbiased?	Yes- Not completely- No-
Summary Application	
10. Can this summary be applied to your patient(s)?	Yes- Not completely- No-

Results

Overview of and Critical Analysis of Individual Studies

Timing and decreased incidence of SSI in mixed surgeries were examined by Weber et al.[1] (2008; Appendix B), who aimed to determine specific information about the most appropriate timing for perioperative antibiotic prophylaxis. Weber et al. organized a prospective observational cohort study at a university hospital where timing of antimicrobial prophylaxis was examined based on SSI occurrence in 3,836 surgeries. Cefuroxime 1.5g was administered as a single dose to each patient along with metronidazole 500mg for colorectal surgeries. Weber et al. demonstrated a decreased occurrence of SSI rates when cefuroxime and metronidazole were administered 30 to 60 minutes before incision for procedures including colorectal surgery. Analyses showed a significant increase in the incidence of SSIs when antibiotic prophylaxis was administered during the last half hour of surgery ($P < 0.001$) and during the last 60 to 120 minutes of surgery ($P = 0.035$) as compared with 30 to 59 minutes before surgical incision.

As seen in Appendix C (Weber et al.[1]), the critical analysis of this cohort study was positive based on "yes" answers to all questions, except one. A confidence interval was not listed and it was unclear whether the follow-up of subjects was complete enough

because post-discharge monitoring was not performed by outpatient clinics following a standard protocol to assess patients. However, authors do state that due to the three step assessment procedure and high follow-up rates of inpatients and outpatients that the results are likely unbiased.

Pastor et al.[2] (2010; Appendix B) hypothesized that the incidence of SSI would be decreased with the application of SCIP prevention measures. A multidisciplinary team was assembled to put SCIP infection prevention measures into effect and monitor adherence. Study participants included patients having non-emergent colorectal surgeries with an abdominal incision. This study showed an increase in adherence to SCIP measures but without a decrease in SSI related to compliance for each individual case. A 95% rate of compliance was achieved for timing of antibiotic prophylaxis, identified as starting administration within 60 minutes of surgical incision (P = .002). The SSI rate between groups was similar at 18.9 % and 19.4 %. Overall, there was a 19% rate of SSI after elective colorectal surgery.

As seen in Appendix C (Pastor et al.[2]) this cohort study did not list a confidence interval and included a sample size of 491 patients in a small colorectal unit, which limits application to other populations. However, this study had a very positive critical analysis based on the responses seen in Appendix C.

One study by Ho et al.[3] (2011; Appendix B) attempted to identify adherence to a set of guidelines for antibiotic administration and to assess risk for SSIs. It was hypothesized that compliance with the guidelines would decrease the occurrence of SSIs. Six hundred five patients having colorectal surgeries with anastomosis between June 2001 and July 2008 were selected randomly. Results indicated that increased occurrence of SSIs correlated with early administration of prophylactic antibiotics, specifically greater than 30 minutes prior to incision (OR 1.725, 95% CI 1.147-2.596).

This cohort study (Ho et al.[3]) was found to have merit as the critical analysis answers were all "yes" (Appendix C). A confidence interval of 95% was included, so the recommendations may be considered by clinicians such as nurse anesthetists.

In a study by Hawn et al.[4] (2011; Appendix B), SCIP guidelines were implemented and evaluated to determine if following the guidelines would result in a decreased incidence of SSI rates within 30 days of a surgical procedure. Data were gathered from 2005 to 2009 from the National Veterans' Affairs Surgical Quality Improvement Program (VASQIP) on both compliance to SCIP measures and SSI incidence. This was a retrospective cohort study that also examined adherence to five SCIP measures including timely prophylactic antibiotic administration: SCIP-inf 1. A total of 15,444 colorectal surgeries were included in this study. The overall SSI rate was

6.2% and 11.3% for colorectal surgeries. After adjusting for the procedure and patient variables, the results indicated that compliance with the SCIP measures did not correlate with a lower incidence of SSI. For the timely antibiotic measure, an adjusted OR was determined to be 0.90 with a 95% CI for 29,042 cases.

As seen in Appendix C, this cohort study (Hawn et al.[4]) included a large VA population of mostly men, which limits application to women and the local population, but otherwise the study included a 95% confidence interval and the answers to the critical analysis questions were positive overall.

A more recently published study conducted by similar authors focused specifically on timing of surgical antibiotic prophylaxis and included subjects from the same population as in the earlier study. Hawn et al.[5] (2013; Appendix B) aimed to discover the correlation between antibiotic administration time and SSI rates within 30 days postoperatively. Antibiotics were administered at a median of 28 minutes before surgical incision and 1,497 patients (4.6%) developed an SSI. In generalized additive models adjusted for procedure, patient, and antibiotic variables, no significant correlation between prophylactic antibiotic timing and SSI was seen (P = 0.26 - 0.85). This was true for 5,469 colorectal surgeries (adjusted OR 0.7; 95% CI). Therefore, the researchers stated that there was not enough evidence to recommend compliance to the timely

antibiotic measure.

This cohort study (Hawn et al.[5]) also included a large VA population of mostly men, so it may not be generalized to women (Appendix C). The answers to the critical analysis questions were all "yes" and a 95% confidence interval was listed by the authors.

Ishikawa et al.[6] (2014; Appendix B) conducted research which closely looked at SSI associated risks for colorectal cancer patients having open surgeries. The purpose of the study was to identify the occurrence and possible determinants of incisional SSI in this population. Data were collected by continuous observation, which was maintained for incisional SSI for one year on surgeries performed in 2009 by an individual colorectal surgeon. This study included a 224 patient cohort, 120 of which were male. For all patients included in this study, administration of antibiotics was between 15 and 50 minutes prior to the surgical incision. The onset of incisional SSI was not affected by the timing of preoperative antibiotic administration. There was no significant difference between antibiotic administration 15 to 29 and 30 to 50 minutes prior to incision ($P = 0.773$). Of the 124 patients who received antibiotic prophylaxis, about 29 % developed a SSI.

As seen in Appendix C, the cohort study (Ishikawa et al.[6]) was critically analyzed and answers to the questions were all "yes" with the following exceptions: there was no

confidence interval listed by the authors and the study population was smaller than some of the others, but overall the critical analysis was positive.

Nelson et al.[7] (2014; Appendix B) composed a systematic review in order to examine the relationship between antibiotic prophylaxis and SSI for patients having colorectal surgeries. Cochrane, Embase, and Medline were used to search for relevant evidence. Prophylactic antibiotic treatment administered in randomized controlled trials including patients that had both emergent and elective colorectal surgeries with SSIs were selected for this review. The review included a total of 260 trials and 43,451 participants. Two related studies compared the administration of antibiotics before surgery to the administration after surgery and no notable difference was found (risk ratio [RR] 0.67, 95% CI 0.2-2.15). Two RCTs that were included in this systematic review are described below.

As seen in Appendix C, this systematic review (Nelson et al.[7]) was critically analyzed for strengths and weaknesses. A systematic review is considered the highest level of evidence and this one in particular included the two available RCTs to make recommendations (Tornqvist et al.[8] & Colizza et al.[9]). A 95% confidence interval was included and this review had more strengths than weaknesses as can be seen in Appendix C.

A RCT was completed to study the effect of dosage and duration of antibiotic prophylaxis and to discover if postoperative treatment was as effective as preoperative treatment (Tornqvist et al.[8], 1981; Appendix B). The authors also aimed to find an appropriate method to estimate contamination of the operation area to relate the degree of contamination to sepsis postoperatively. One hundred ninety-six consecutive patients having elective colonic surgery were included and randomized into four groups. All patients underwent mechanical bowel preparation in a standardized manner. Group I received doxycycline 200mg IV 1-1.5 hours preoperatively. Group II received 600mg IV 1-1.5 hours preoperatively. Group III received 600mg IV postoperatively in recovery, 2-5 hours after colon opening. Finally, group IV received 200mg IV 1-1.5 hours preoperatively and once daily during the first three days postoperatively. SSI rates follow: Group I 13%, Group II 7%, Group III 20%, Group IV 19%.

In Appendix C, the critical analysis of this RCT (Tornqvist et al.[8]) can be viewed. Answers to the critical analysis questions were all "yes" except it was unclear whether patients, health workers, and study personnel were appropriately blinded to the trial, which could have impacted the results. A confidence interval is also not listed by the author. Finally, it is unclear whether this study should be applied to the adult patient undergoing colorectal surgery because the results may not be valid if the people included

were not appropriately blinded.

Colizza et al.[9] (1987; Appendix B) conducted a RCT of short term antibiotic prophylaxis with cefuroxime including 52 patients having elective colorectal surgery. The purpose is not stated. Each patient was randomly assigned to either Group A or Group B. Each patient received a total of 5.250 mg of cefuroxime. However, Group A received 750 mg intramuscularly (IM) preoperatively, 750 mg liquid on the fascia before closure of the skin, 750 mg IV right after the end of the procedure and repeated four times every 6 hours. Group B received 750 mg IV right after the end of the procedure and repeated six times every 6 hours. All patients received a standard bowel preparation preoperatively. Wound sepsis was observed in 11.5% of patients in group A and 23% in group B, while other types of sepsis were observed in 34.6% of group A and 11.5% of group B. The results indicated that better control of wound sepsis was seen in group A, while better protection from other infections or complications was seen in group B. Only 52 patients were included in this trial. Group A included more surgeries that had an increased risk of sepsis. Death occurred for 3 patients likely due to anastomotic leakage.

As seen in Appendix C, it was unclear what the study purpose was and whether all participants were treated equally (Colizza et al.[9]). It was also unclear whether patients, health workers, and study personnel were blinded to the trial, which could have

impacted the results. There is no confidence interval listed by the authors. However, the majority of the critical analysis questions were answered, "yes".

Critical Analysis Across Studies

The critical analyses of the studies were positive, but the ability to generalize is limited overall by the cohort study design of many of the studies. All of the cohort studies (Weber et al.[1], Pastor et al.[2], Ho et al.[3], Hawn et al.[4], Hawn et al.[5], & Ishikawa et al.[6]) had positive results related to the critical analysis. However, Pastor et al.[2] included a sample of patients from a small colorectal unit, which could limit application to other populations. Hawn et al.[4] and Hawn et al.[5] included larger sample sizes, however the studies included a VA population of mostly men, so they may not be generalized to women. The systematic review by Nelson et al.[7] based its conclusions on two RCTs included in this review (Tornqvist et al.[8] & Colizza et al.[9]; Appendix C). Tornqvist et al.[8] and Colizza et al.[9] do not list any limitations and the trials were completed in the 1980s. It is also unclear whether patients, health workers, and study personnel were appropriately blinded for these two studies, which could have affected the results. The RCTs are otherwise important to consider due to the level of evidence and the results and recommendations should be considered when making decisions on timing of antibiotic prophylaxis for colorectal procedures. Tornqvist el al.[8] suggested administering a single

preoperative dose of doxycycline 200mg or 600mg IV as the "treatment of choice". Colizza et al.[9] recommended short term antibiotic use, including a preoperative intramuscular (IM) dose, one intraincisionally, and an IV dose every six hours for 24 hours beginning immediately after the procedure to reduce the incidence of sepsis after elective colorectal surgery.

Pastor et al.[2], Ho et al.[3], Ishikawa et al.[6], Nelson et al.[7], Tornqvist et al.[8], and Colizza et al.[9] focused solely on colorectal surgery, whereas the others (Weber et al.[1]; Hawn et al.[4]; Hawn et al.[5]) included other types of surgery in the analyses. Weber et al.[1], Hawn et al.[4] and Hawn et al.[5] have strengths that are due to the large samples studied and the research is current.

All of the studies included addressed a clear and focused issue (Appendix C). For all of the cohort studies, patient recruitment was appropriate and the exposure and outcomes were accurately measured. The follow-up of patients was determined to be long enough and complete enough for all cohort studies except for Weber et al.[1], which was unclear. The important confounding factors were clearly identified and considered in the analysis of all cohort studies except for Pastor et al.[2] The systematic review by Nelson et al.[7] included all of the relevant available evidence in the form of RCTs (Appendix C). Finally, the purpose was clearly stated for all studies except for Colizza et

al.[9] (Appendix B).

Key Comparisons Across Studies: The CASE Worksheet

Key aspects of a comparison across the studies are discussed below and can be found in Appendix D. Based on comparison across the included studies using the CASE worksheet (Foster & Shurtz, 2013), it was found that for all studies the summaries were specific in both scope and application. The authors were identifiable and transparent; however, the editors of the summaries were only transparent for Pastor et al.[2], Ho et al.[3], Hawn et al.[5], Ishikawa et al.[6], and Nelson et al.[7]. The research methods for most studies were found to be comprehensive and transparent (Weber et al.[1]; Pastor et al.[2]; Ho et al.[3]; Hawn et al.[4]; Hawn et al.[5]; Ishikawa et al.[6]; Nelson et al. [7]) but not all (Tornqvist et al.[8] & Colizza et al.[9]). The evidence grading system was found to be transparent and easily understood for all studies included.

Summary content was assessed by identifying and confirming clear recommendations at the end of each study. Recommendations were clearly stated in the majority (Weber et al.[1]; Ho et al.[3]; Hawn et al.[4]; Ishikawa et al.[6]; Nelson et al.[7]; Tornqvist et al.[8]) but not all (Pastor et al.[2]; Hawn et al.[5]; Colizza et al.[9]). All studies except the RCTs by Tornqvist et al.[8] and Colizza et al.[9] included current recommendations. All summaries except that of Hawn et al.[5] were determined to be unbiased.

As a group, the results of the quality assessment are overall consistent, however the cohort design of many of the studies limits the ability to generalize. Overall, several summaries can be applied to the adult undergoing colorectal surgery with an incision (Weber et al.[1], Ho et al.[3], Ishikawa et al.[6]). These cohort studies are specific in scope and application, the research methods are clear, recommendations are clear and appropriately cited, and the results can be applied to the studied population based on the results of the CASE worksheet (Appendix D). The results of the three cohort studies (Weber et al.[1], Ho et al.[3], Ishikawa et al.[6]) will be discussed in further detail in the summary and conclusions section. Summaries that can be partially applied are Pastor et al.[2], Hawn et al.[4], Hawn et al.[5], Nelson et al.[7], Tornqvist et al.[8], and Colizza et al.[9]. Pastor et al.[2] did not list clear recommendations, included a sample from a small colorectal unit, and is limited to generalization due to the study design. There was also a change in antibiotic prophylaxis selection during the study, which could have impacted the results of the study (Appendix B). Hawn et al.[4] and Hawn et al.[5] are both cohort studies, which limits the ability to generalize due to the design of the studies. The studies also included a large VA population of mostly men, which limits application to women (Appendix D). The systematic review by Nelson et al.[7] based its conclusions on the two available RCTs (Tornqvist et al.[8] & Colizza et al.[9]) which did not prove to be of great quality based on

the results of the CASE worksheet (Appendix D). However, Tornqvist et al.[8] and Colizza et al.[9] are considered to be a higher level of evidence than the previous cohort studies.

Next, the summary and conclusions will be presented.

Summary and Conclusions

Colorectal surgery is known for having a high risk of surgical site infection. Surgical site infections can often be prevented; however, not all institutions and providers follow the same guidelines for timing of antibiotic prophylaxis. Previous research suggested that administering prophylactic antibiotics prior to colorectal surgery may prevent SSIs. This led to the research question: "In adult surgical patients having colorectal surgeries, does prophylactic antibiotic administration time effect surgical site infection rates within 30 days of surgery?" The purpose of this systematic review was to examine the relationship between SSI rates and prophylactic antibiotic administration time in adults having colorectal surgeries.

This systematic review included studies involving adult surgical patients having colorectal surgeries with an abdominal incision. All study designs were included due to the limited amount of research available. The included research must have delineated timing of prophylactic IV antibiotic administration and SSI rates within 30 days of surgery. Exclusion criteria included other than adults, colorectal procedures with no incision and evidence of pre-operative infection in any site.

A comprehensive search of the literature was conducted using the following keywords: "Antibiotic Prophylaxis", "Colorectal Surgery", "Colon Surgery", "Timing",

"Surgical Site Infection", and "Surgical Care Improvement Program". The search engines CINAHL, PubMed, Cochrane, and Google Scholar were utilized. At the end of the database searches, 21 studies were found; these were examined to determine eligibility. Seven studies were retained for data collection and the reference list of each study was examined for additional relevant literature. After reviewing the reference lists of each study, two additional studies were obtained, for a total of nine.

Relevant data were collected by using an extraction form created by the researcher. The researcher was guided in the development of a data extraction tool by Fineout-Overholt et al. (2010a). A copy of the data extraction form is illustrated in Appendix A. Next, a critical appraisal of the literature was completed following guidelines by Fineout-Overholt et al. (2010a; 2010b; 2010c). Each study was reviewed to identify its level of evidence, how well it was performed, and how useful it was to practice. This required use of a critical appraisal guide appropriate for the type of research (Fineout-Overholt et al.). The Critical Appraisal Skills Programme (CASP UK, 2013) Checklists were used as critical appraisal tools (Appendix B). The checklists helped to determine the answers to three broad questions: "Are the results valid?", "What are the results?", and "Will the results help locally?" Specific questions that follow helped the researcher address these issues systematically. The researcher was able to

select either, “Yes”, “Can’t Tell”, or “No” in response to each question. Separate checklists were used for different levels of designs, which can be found in the Tables 1-3 above. The Critical Appraisal for Summaries of Evidence (CASE) worksheet (Foster & Shurtz, 2013) was used to assess quality of evidence across the studies. Summary topic, summary method, summary content, and summary application were reviewed for each study (Appendix D).

Limitations of this systematic review were based on the available evidence, which were mostly cohort studies. First, there was very little level I or II evidence. Though a systematic review was included in this research, it only included two RCTs which were quite dated and did not include all of the important considerations based on the results shown in Appendix C. There were no limitations noted by authors of either of the RCTs. One of the trials (Colizza et al.[9]) did not include the purpose of carrying out the experiment. In another study (Weber et al.[1]), confounding of findings by unmeasured variables could not be ruled out completely due to the observational nature of the study. Some of the studies included more men than women (Hawn et al.[4] & Hawn et al.[5]) making the generalization to women more difficult.

In conclusion, three summaries were identified that can be cautiously applied to the adult undergoing colorectal surgery (Weber et al.[1], Ho et al.[3], Ishikawa et al.[6]). These

cohort studies are specific in scope and application, the research methods are clear, recommendations are clear and appropriately cited, and the results can be applied to the studied population based on the results of the CASE worksheet (Appendix D). Weber et al.[1] demonstrated a decreased occurrence of SSI rates when cefuroxime and metronidazole were administered 30 to 60 minutes before incision for procedures including colorectal surgery. Analyses showed a significant increase in the incidence of SSIs when antibiotic prophylaxis was administered during the last half hour of surgery and during the last 60 to 120 minutes of surgery as compared with 30 to 59 minutes before surgical incision. As seen in Appendix C (Weber et al.[1]), the critical analysis of this cohort study was positive based on "yes" answers to all questions, except one. The research method was found to be comprehensive and transparent and the evidence grading system was found to be easily understood.

The cohort study by Ho et al.[3] (2011) attempted to identify adherence to a set of guidelines for antibiotic administration and to assess risk for SSIs. Results indicated that increased occurrence of SSIs correlated with early administration of prophylactic antibiotics, specifically greater than 30 minutes prior to incision. This cohort study was found to have merit as the critical analysis answers were all "yes" (Appendix C). A confidence interval of 95% was included, so the recommendations may

be considered by clinicians.

Ishikawa et al.[6] (2014) conducted research which closely looked at SSI associated risks for colorectal cancer patients having open surgeries. For all patients included in this study, administration of antibiotics was between 15 and 50 minutes prior to the surgical incision. The onset of incisional SSI was not affected by the timing of preoperative antibiotic administration. There was no significant difference between antibiotic administration 15 to 29 and 30 to 50 minutes prior to incision. Of the 124 patients who received antibiotic prophylaxis, about 29 % developed a SSI. As seen in Appendix C, the cohort study was critically analyzed and answers to the questions were all "yes" with the following exceptions: there was no confidence interval listed by the authors and the study population was smaller than some of the others, but overall the critical analysis was positive.

Results indicated that there is insufficient evidence to support a definite course of action for timing of antibiotic prophylaxis for colorectal surgery at this time. Further randomized controlled trials are needed. The certified registered nurse anesthetist (CRNA) should be aware of the recommendations to administer antibiotic prophylaxis for colorectal surgery before the surgical incision based on the results of this systematic review as timing of administration can affect SSI rates. It is recommended to carefully

consider antibiotic selection and timing when administering antibiotics prophylactically for colorectal surgery.

Next, the recommendations and implications for advanced nursing practice will be presented.

Recommendations and Implications for Advanced Nursing Practice

Ultimately, the aim in relation to surgeries, including colorectal surgeries, should be to administer antibiotics at the optimal time despite practical difficulties (Weber et al.[1]). Oral antibiotic prophylaxis and mechanical bowel prep for colorectal surgery should also be further researched (Pastor et al.[2]). Appropriate antibiotic selection and timing of administration for prophylaxis are believed to be important factors to decrease the likelihood of SSI elective colorectal surgery with intestinal anastomosis (Ho et al.[3]). Although the SCIP measures are best practices and should continue, using them to direct patients to high and low performing hospitals is not appropriate and could be misleading (Hawn et al.[4]). In addition, the authors of one study (Hawn et al.[5]) concluded that there was not enough evidence to support compliance to the SCIP measure for timing of antibiotic prophylaxis (administration within 60 minutes of surgical incision). It is also important to consider the many variables that can affect timing of antibiotic prophylaxis such as patient population, antibiotic selection, and repeat dosing (Hawn et al.[5]). A single preoperative dose of Doxycycline has been recommended as the choice treatment for antibiotic prophylaxis to decrease the infection rate in colon surgery; however, this study is dated and should be repeated with a larger sample size and consideration of all

confounding factors (Tornqvist et al.[8]). Short term prophylactic cephalosporin administration also may be helpful in decreasing the incidence of sepsis after elective colorectal surgery (Colizza et al.[9]). The differences in results of research on this topic may be due to the population of patients selected rather than the type of antibiotic used (Colizza et al.[9]).

Based on the results of this review, there are various recommendations related to timing of antibiotic prophylaxis for colorectal surgery. There is not enough evidence to support a definite course of action for timing of antibiotic prophylaxis at this time. It is recommended by several authors that further research be conducted in the form of RCTs. A study with a larger sample size is necessary to provide evidence of risk factors for surgical site infection after open colorectal surgery (Ishikawa et al.6). Modification of existing recommendations on timing of surgical antibiotic prophylaxis may be necessary.

The CRNA should be aware of the recommendations for appropriate antibiotic prophylaxis for colorectal surgery as timing of administration can affect SSI rates. Surgical site infections can also be very costly and timing of antibiotic prophylaxis can be a contributing factor. At this time, is it recommended to follow the current policies of each institution related to the timing of administration of antibiotic prophylaxis for colorectal surgery. It is necessary for the CRNA to be considerate of and be educated on

antibiotic selection and patient population when administering antibiotics prophylactically for colorectal surgery. For example, some antibiotics like vancomycin need to be administered over a longer period of time and started much earlier than other antibiotics.

The CRNA is responsible to check the surgeon's antibiotic orders in the patient's chart and make sure the antibiotic is available. The appropriate antibiotic dose must then be administered according to the institution's policy. Education should be completed during clinical training related to antibiotic selection, administration time, and dosing for this type of surgery. It is the responsibility of the CRNA to remain current in practice and up-to-date in regard to evidence-based practice changes.

Further research is needed related to antibiotic administration time, route of administration, re-dosing, and antibiotic selection in this and other patient populations. Randomized controlled trials are critically needed to address the questions that remain. Finally, the CRNA has the knowledge and skills to be actively involved in clinical trials and to become actively involved in professional organizations that have the ability to impact available research funding and relevant policy agendas.

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Appendix A

Extraction Form
Title of Study:
Author(s):
Type of Research:
Journal and Year:
Purpose:
Antibiotic Administration Time(s):
Surgical Site Infection Rate:
Author Noted Limitations:
Recommendations:
Results:

Appendix B

Extraction Form
Title of Study #1- The Timing of Surgical Antimicrobial Prophylaxis
Author(s): Walter P. Weber, MD., Walter R. Marti, MD, FACS, Marcel Zwahlen, PdD, Heidi Misteli, MD, Rachel Rosenthal, MD, Stefan Reck, MD, Philipp Fueglistaler, MD, Martin Bolli, MD, Andrej Trampuz, MD, Daniel Oertli, MD, FACS, & Andreas F. Widmer, MD
Type of Research: Prospective Observational Cohort Study
Journal and Year: Annals of Surgery, 2008
Purpose: To obtain precise information on the best time window for surgical antimicrobial prophylaxis.
Antibiotic Administration Time(s): 0-14 minutes before, 15-29 minutes before, 30-44 minutes before, 45-59 minutes before, 60-74 minutes before, and 75-120 minutes before.
Surgical Site Infection Rate: 4.7% (180 of 3,836)
Author Noted Limitations: Not high level evidence, a prospective cohort study exploring a consecutive series of surgeries. Residual confounding of findings by unmeasured factors cannot ever be ruled out entirely in observational studies. The optimal time for antibiotic prophylaxis may not be generalized to all antimicrobials or antibiotics.
Recommendations: Modify existing recommendations of timing of surgical antibiotic prophylaxis. The aim should be to apply prophylaxis at the optimal time, despite practical difficulties. Administer Cefuroxime 30-59 minutes before incision.
Results: 180 Surgical Site Infections (SSIs) out of 3,836 procedures. Lowest rate of SSI was when antibiotic administration was 30-74 minutes before surgery. Cefuroxime as a prophylactic antibiotic administered 30-59 minutes before incision is more effective than during the last ½ hour.

Appendix B

Extraction Form
Title of Study #2- An Increase in Compliance With the Surgical Care Improvement Project Measures Does Not Prevent Surgical Site Infection in Colorectal Surgery
Author(s): Carlos Pastor, M.D., Avo Artinyan, M.D., Madhulika G. Varma, M.D., Edward Kim, M.D., Laurel Gibbs, M.T., Julio Garcia-Aguilar, M.D., Ph.D.
Type of Research: Prospective Cohort Study
Journal and Year: Diseases of the Colon & Rectum, 2010
Purpose: To test the hypothesis that an increased compliance with quality process measures decreases the rate of SSIs in patients having colorectal surgeries.
Antibiotic Administration Time(s): Within 1 hour of incision (SCIP process measure)
Surgical Site Infection Rate: 99 patients (19%) developed SSI out of 491 patients
Author Noted Limitations: Small sample size of 491, small colorectal unit, limits application to other populations, and compliance was already relatively high before the start of the study. There was a change in antibiotic prophylaxis selection during the study.
Recommendations: Oral antibiotic prophylaxis and mechanical bowel prep for colorectal surgery should be further researched. More realistic expectations recommended.
Results: Increased compliance with the SCIP measures does not result in decreased SSI rates. 99 patients with SSIs (19%)

Appendix B

Extraction Form
Title of Study #3- Antibiotic Regimen and the Timing of Prophylaxis Are Important for Reducing Surgical Site Infection after Elective Colorectal Surgery
Author(s): Vanessa P. Ho, Philip S. Barie, Sharon L. Stein, Koiana Trencheva, Jeffrey W. Milsom, Sang W. Lee, and Toyooki Sonoda
Type of Research: Retrospective Review-prospective database of a random sample
Journal and Year: Surgical Infections, 2011
Purpose: To determine compliance with an antibiotic administration protocol including regimen, initial dose, timing, and redosing. A second aim is to determine the risk of SSI associated with each of the previous measures.
Antibiotic Administration Time(s): Greater than 30 minutes prior to incision, within 30 minutes of incision, and after the incision.
Surgical Site Infection Rate: 76 patients (12.6%) superficial or deep incisional SSI, 54 patients (8.9%) organ/space SSI. Overall SSI rate- 21.5%
Author Noted Limitations: Retrospective nature, bowel preparation unknown for each patient, small sample size of 605 patients, administration by anesthesiologists instead of nurses to decrease SSI incidence for the study.
Recommendations: Future research should continue to focus on optimal prophylaxis regimens and timing. Changes in clinical outcomes should be followed with the implementation of quality control measures.
Results: Overall SSI rate- 21.5%. Increased occurrence of SSI with administration of prophylactic antibiotics greater than 30 minutes before incision.

Appendix B

Extraction Form
Title of Study #4- Surgical Site Infection Prevention: Time to Move Beyond the Surgical Care Improvement Program
Author(s): Mary T. Hawn, MD, MPH, Catherine C. Vick, MS, Joshua Richman, MD, PhD, William Holman, MD, Rhiannon J. Deierhoi, MPH, Laura A. Graham, MPH, William G. Henderson, MPH, PhD, & Kamal M.F. Itani, MD
Type of Research: Retrospective Cohort Study
Journal and Year: Annals of Surgery, 2011
Purpose: To evaluate whether the SCIP improved SSI rates using national data at the patient level for both SCIP adherence and SSI occurrence.
Antibiotic Administration Time(s): Administration within 60 minutes of incision (120 minutes for Vancomycin and Fluoroquinolones).
Surgical Site Infection Rate: 6.2%
Author Noted Limitations: Evaluation of VA population, mainly men, so may not be generalized to women. Limited ability to measure “secular effects” of the program prior to its implementation at the VA.
Recommendations: Although the processes measured are best practices and should continue, using them to discriminate between high and low performing hospitals is not recommended.
Results: Implementation of the SCIP infection prevention measures did not improve the rate of SSIs. Using these measures to send patients to high quality hospitals could be misleading.

Appendix B

Extraction Form
Title of Study #5- Timing of Surgical Antibiotic Prophylaxis and the Risk of Surgical Site Infection
Author(s): Mary T. Hawn, MD, MPH, Joshua S. Richman, MD, PhD, Catherine C. Vick, MS, Rhiannon J. Deierhoi, MPH, Laura A. Graham, MPH, William G. Henderson, MPH, PhD, Kamal M.F. Itani, MD
Type of Research: Retrospective Cohort Study
Journal and Year: JAMA, 2013
Purpose: To determine whether prophylactic antibiotic timing is associated with surgical site infection (SSI) occurrence.
Antibiotic Administration Time(s): 16-23 minutes before incision for colorectal surgeries, within 60 minutes, greater than 60 minutes.
Surgical Site Infection Rate: 4.6% (1,497 cases developed an SSI)
Author Noted Limitations: More men than women included in the study, so generalization to women may not apply.
Recommendations: Further research is needed on antibiotic selection and repeat dosing. Not enough evidence to recommend compliance to the SCIP measure for timing of antibiotic prophylaxis. Several variables can affect timing including patient population and antibiotic choice.
Results: 4.6 % or 1,497 out of 32,459 patients developed a SSI. There were higher SSI rates when antibiotic was administered greater than 60 minutes prior to incision, but not after incision. It was determined that there was no significant association between prophylactic antibiotic timing and SSI.

Appendix B

Extraction Form
Title of Study #6- Incisional Surgical Site Infection after Elective Open Surgery for Colorectal Cancer
Author(s): Kosuke Ishikawa, Takaya Kusumi, Masao Hosokawa, Yasunori Nishida, Sosuke Sumikawa, and Hiroshi Furukawa
Type of Research: Prospective Surveillance Study
Journal and Year: International Journal of Surgical Oncology, 2014
Purpose: To clarify the incidence and risk factors of incisional SSI in patients having elective open surgery for colorectal cancer.
Antibiotic Administration Time(s): 15-29 minutes before incision and 30-50 minutes before incision
Surgical Site Infection Rate: 33 patients diagnosed with incisional SSI (14.7%)
Author Noted Limitations: Need larger study/cohort
Recommendations: A study with more subjects is necessary to provide evidence of risk factors for incisional SSI
Results: 224 patients were evaluated, 33 patients had incisional SSI (14.7%). No significant difference between administration of antibiotics 15-29 minutes or 30-50 minutes before incision in the development of incisional SSI.

Appendix B

Extraction Form
Title of Study #7- Antimicrobial Prophylaxis for colorectal surgery
Author(s): Richard L. Nelson, Ed Gladman, and Marija Barbateskovic
Type of Research: Systematic Review
Journal and Year: Cochrane Database of Systematic Reviews, 2014
Purpose: To establish the effectiveness of antimicrobial prophylaxis for the prevention of surgical wound infection in patients undergoing colorectal surgery.
Antibiotic Administration Time(s): Before surgery and after surgery
Surgical Site Infection Rate: Not listed. See included RCTs for SSI rates (Tornqvist et al., 1981; Colizza et al., 1987).
Author Noted Limitations: Only two randomized controlled trials (RCTs) included to support recommendations (1980s), weak RCTs according to authors.
Recommendations: See RCTs for recommendations (Tornqvist et al., 1981; Colizza et al., 1987)
Results: No notable difference was found in antibiotic administration before or after surgery.

Appendix B

Extraction Form
Title of Study #8- Single dose doxycycline prophylaxis and peroperative bacteriological culture in elective colorectal surgery
Author(s): A. Tornqvist, G. Ekelund, A. Forsgren, L. Leandoer, S. Olson, and I. Ursing.
Type of Research: Randomized Controlled Trial
Journal and Year: British Journal of Surgery, 1981
Purpose: 1- To study the effect of dosage and duration of antibiotic prophylaxis and to discover if postoperative treatment was as effective as preoperative treatment. 2- Find an appropriate method to estimate contamination of the operation area to relate the degree of contamination to sepsis/infection postoperatively.
Antibiotic Administration Time(s): 1: 200mg IV 1-1.5 hours preoperatively; 2: 600mg IV 1-1.5 hours preoperatively; 3: 600mg IV postoperatively in recovery 2-5 hours after colon opening; 4: 200mg IV 1-1.5 hours preoperatively and every day during the first 3 days postoperatively.
Surgical Site Infection Rate: Group 1: 13%, Group 2: 7%, Group 3: 20%, Group 4: 19%
Author Noted Limitations: None listed by authors
Recommendations: A single preoperative dose of doxycycline 200mg or 600mg IV is recommended as the “treatment of choice”. A single administration of doxycycline considerably reduces the infection rate in colon surgery.
Results: SSI rates- Group 1: 13% with 1 anastomotic dehiscence with wound rupture, Group 2: 7%, Group 3: 20% with 1 anastomotic dehiscence, Group 4: 19% with 2 anastomotic complications; 1 fatal. Two deaths overall with no signs or symptoms that could be attributed to administration of doxycycline.

Appendix B

Extraction Form
Title of Study #9- Short-Term Prophylaxis with Cefuroxime in Colorectal Surgery for Cancer
Author(s): S. Colizza, M.D., S. De Fazio, M.D., A. Addari, M.D., R. Grande, M.D., and G. Cucchiara, M.D.
Type of Research: Randomized Controlled Trial
Journal and Year: Journal of Surgical Oncology, 1987
Purpose: Not stated
Antibiotic Administration Time(s): Group A: 750mg IM preoperatively, 750mg topically before skin closure, and 750mg IV immediately after surgery and repeated every 6 hours x 4. Group B: 750mg IV immediately after surgery and repeated every 6 hours x 6 (only postoperatively administered).
Surgical Site Infection Rate: "Wound Sepsis"-several types Wound Sepsis: Group A- 11.5%, Group B- 23%; Other Types: Group A- 34.6%, Group B- 11.5%
Author Noted Limitations: None described by authors.
Recommendations: Short term cephalosporin use may be helpful in reducing the incidence of sepsis after elective colorectal surgery. Differences in research on this topic (results) may be due to the selection of patients rather than type of antibiotic used.
Results: Overall operative mortality= 5.7% or 3 cases (not statistically significant). Additional antibiotics were given to 7 patients from Group A and 4 patients from Group B (also not significant). Short term prophylactic cephalosporins can be useful in decreasing the incidence of sepsis after elective colorectal surgery. Treatment A: Better control of wound sepsis. Treatment B: Better protection from other infections/complications-significantly less infectious complications than Group A.

Appendix C

CASP Cohort Study Checklist- Study #1 (Weber et al., 2008)

12 Questions			
1). Did the study address a clearly focused issue?	**Yes**	Can't Tell	No
2). Was the cohort recruited in an acceptable way?	**Yes**	Can't Tell	No
3). Was the exposure accurately measured to minimize bias?	**Yes**	Can't Tell	No
4). Was the outcome accurately measured to minimize bias?	**Yes**	Can't Tell	No
5). A. Have the authors identified all important confounding factors? B. Have they taken account of the confounding factors in the design and/or analysis?	**Yes** **Yes**	Can't Tell Can't Tell	No No
6). A. Was the follow up of subjects complete enough? B. Was the follow up of subjects long enough?	Yes **Yes**	**Can't Tell** Can't Tell	No No
7). What are the results of this study? **SSI rate 4.7% (180 of 3,836)**			
8). How precise are the results? **No CI given**			
9). Do you believe the results?	**Yes**	Can't Tell	No
10). Can the results be applied to the local population?	**Yes**	Can't Tell	No
11). Do the results of this study fit with other available evidence?	**Yes**	Can't Tell	No
12). What are the implications of this study for practice? **The aim should be to administer antibiotic prophylaxis at the optimal time, despite practical difficulties. When cefuroxime is given for antibiotic prophylaxis, administration 59 - 30 minutes prior to incision is more effective than giving it during the last half hour.**			

(CASP UK, 2013)

Appendix C

CASP Cohort Study Checklist- Study #2 (Pastor et al., 2010)

12 Questions			
1). Did the study address a clearly focused issue?	**Yes**	Can't Tell	No
2). Was the cohort recruited in an acceptable way?	**Yes**	Can't Tell	No
3). Was the exposure accurately measured to minimize bias?	**Yes**	Can't Tell	No
4). Was the outcome accurately measured to minimize bias?	**Yes**	Can't Tell	No
5). A. Have the authors identified all important confounding factors? B. Have they taken account of the confounding factors in the design and/or analysis?	Yes **Yes**	**Can't Tell** Can't Tell	No No
6). A. Was the follow up of subjects complete enough? B. Was the follow up of subjects long enough?	**Yes** **Yes**	Can't Tell Can't Tell	No No
7). What are the results of this study? **99 patients (19%) developed SSI out of 491 patients. This study showed an increase in adherence to SCIP measures but without a decrease in SSI related to compliance for each individual case.**			
8). How precise are the results? **No CI listed**			
9). Do you believe the results?	**Yes**	Can't Tell	No
10). Can the results be applied to the local population?	**Yes**	Can't Tell	No
11). Do the results of this study fit with other available evidence?	**Yes**	Can't Tell	No
12). What are the implications of this study for practice? **The practice of oral antibiotic prophylaxis and mechanical bowel preparation for colorectal surgery should be further researched. The sample size was somewhat small, limiting its application to other populations. Other variables such as supplemental oxygen need to be included in future research.**			

(CASP UK, 2013)

Appendix C

CASP Cohort Study Checklist- Study #3 (Ho et al., 2011)

12 Questions			
1). Did the study address a clearly focused issue?	**Yes**	Can't Tell	No
2). Was the cohort recruited in an acceptable way?	**Yes**	Can't Tell	No
3). Was the exposure accurately measured to minimize bias?	**Yes**	Can't Tell	No
4). Was the outcome accurately measured to minimize bias?	**Yes**	Can't Tell	No
5). A. Have the authors identified all important confounding factors? B. Have they taken account of the confounding factors in the design and/or analysis?	**Yes** **Yes**	Can't Tell Can't Tell	No No
6). A. Was the follow up of subjects complete enough? B. Was the follow up of subjects long enough?	**Yes** **Yes**	Can't Tell Can't Tell	No No
7). What are the results of this study? **76 patients (12.6%) with superficial of deep incisional SSI; 54 patients (8.9%) with organ/space SSI. Total = 21.5%** **Increased occurrence of SSI with administration >30 minutes of incision.**			
8). How precise are the results? **95% CI**			
9). Do you believe the results?	**Yes**	Can't Tell	No
10). Can the results be applied to the local population?	**Yes**	Can't Tell	No
11). Do the results of this study fit with other available evidence?	**Yes**	Can't Tell	No
12). What are the implications of this study for practice? **The goal of antibiotic prophylaxis for surgery is to maintain an adequate and appropriate level of antibiotic exposure during the procedure. Future research should focus on optimal antibiotic prophylaxis regimens and timing as it is crucial to prevent SSIs in elective abdominal colorectal surgery.**			

(CASP UK, 2013)

Appendix C

CASP Cohort Study Checklist- Study #4 (Hawn et al., 2011)

12 Questions			
1). Did the study address a clearly focused issue?	**Yes**	Can't Tell	No
2). Was the cohort recruited in an acceptable way?	**Yes**	Can't Tell	No
3). Was the exposure accurately measured to minimize bias?	**Yes**	Can't Tell	No
4). Was the outcome accurately measured to minimize bias?	**Yes**	Can't Tell	No
5). A. Have the authors identified all important confounding factors? B. Have they taken account of the confounding factors in the design and/or analysis?	**Yes** **Yes**	Can't Tell Can't Tell	No No
6). A. Was the follow up of subjects complete enough? B. Was the follow up of subjects long enough?	**Yes** **Yes**	Can't Tell Can't Tell	No No
7). What are the results of this study? **Implementation of the SCIP infection prevention measures did not improve the rate of SSI. SSI rate at 30 days = 6.2%** **11.3% for colorectal surgeries**			
8). How precise are the results? **95% CI**			
9). Do you believe the results?	**Yes**	Can't Tell	No
10). Can the results be applied to the local population?	Yes	**Can't Tell**	No
11). Do the results of this study fit with other available evidence?	**Yes**	Can't Tell	No
12). What are the implications of this study for practice? **Using the SCIP measures to send patients to high quality hospitals could be misleading. Be aware only VA population and mostly male patients included, so may not be generalized to women.**			

(CASP UK, 2013)

Appendix C

CASP Cohort Study Checklist- Study #5 (Hawn et al., 2013)

12 Questions			
1). Did the study address a clearly focused issue?	**Yes**	Can't Tell	No
2). Was the cohort recruited in an acceptable way?	**Yes**	Can't Tell	No
3). Was the exposure accurately measured to minimize bias?	**Yes**	Can't Tell	No
4). Was the outcome accurately measured to minimize bias?	**Yes**	Can't Tell	No
5). A. Have the authors identified all important confounding factors? B. Have they taken account of the confounding factors in the design and/or analysis?	**Yes** **Yes**	Can't Tell Can't Tell	No No
6). A. Was the follow up of subjects complete enough? B. Was the follow up of subjects long enough?	**Yes** **Yes**	Can't Tell Can't Tell	No No
7). What are the results of this study? **1,497 patients (4.6%) developed a SSI. No significant association between prophylactic antibiotic administration time and SSI.**			
8). How precise are the results? **95% CI**			
9). Do you believe the results?	**Yes**	Can't Tell	No
10). Can the results be applied to the local population?	Yes	**Can't Tell**	No
11). Do the results of this study fit with other available evidence?	**Yes**	Can't Tell	No
12). What are the implications of this study for practice? **Be aware only VA population of mostly men included so may not be able to generalize to women. Not enough evidence available to recommend compliance to the SCIP measure for timing of antibiotic prophylaxis. Several variables can affect timing including patient population and antibiotic used.**			

(CASP UK, 2013)

Appendix C

CASP Cohort Study Checklist- Study #6 (Ishikawa et al., 2014)

12 Questions			
1). Did the study address a clearly focused issue?	**Yes**	Can't Tell	No
2). Was the cohort recruited in an acceptable way?	**Yes**	Can't Tell	No
3). Was the exposure accurately measured to minimize bias?	**Yes**	Can't Tell	No
4). Was the outcome accurately measured to minimize bias?	**Yes**	Can't Tell	No
5). A. Have the authors identified all important confounding factors? B. Have they taken account of the confounding factors in the design and/or analysis?	**Yes** **Yes**	Can't Tell Can't Tell	No No
6). A. Was the follow up of subjects complete enough? B. Was the follow up of subjects long enough?	**Yes** **Yes**	Can't Tell Can't Tell	No No
7). What are the results of this study? **33 patients were (14.7%) diagnosed with incisional SSI. There was no significant difference between administration 15 - 29 minutes and 30 - 50 minutes before incision in the development of SSI (P = 0.773).**			
8). How precise are the results? **No CI listed for this measure.**			
9). Do you believe the results?	**Yes**	Can't Tell	No
10). Can the results be applied to the local population?	**Yes**	Can't Tell	No
11). Do the results of this study fit with other available evidence?	**Yes**	Can't Tell	No
12). What are the implications of this study for practice? **A larger study is necessary to provide definitive evidence of risk factors for incisional SSI.**			

(CASP UK, 2013)

Appendix C

CASP Systematic Review Checklist- Study #7 (Nelson et al., 2014)

10 Questions			
1). Did the review address a clearly focused question?	**Yes**	Can't Tell	No
2). Did the authors look for the right type of papers?	**Yes**	Can't Tell	No
3). Do you think all the important, relevant studies were included?	**Yes**	Can't Tell	No
4). Did the review's authors do enough to assess the quality of the included studies?	Yes	**Can't Tell**	No
5). If the results of the review have been combined, was it reasonable to do so?	**Yes**	Can't Tell	No
6). What are the overall results of the review? **Two small studies (RCTs) compared giving antibiotics before or after surgery and no significant difference was found.**			
7). How precise are the results? **RR 0.67, 95% CI**			
8). Can the results be applied to the local population?	**Yes**	Can't Tell	No
9). Were all important outcomes considered?	**Yes**	Can't Tell	No
10). Are the benefits worth the harms and costs?	**Yes**	Can't Tell	No

(CASP UK, 2013)

Appendix C

CASP Randomized Controlled Trial Checklist- Study #8 (Tornqvist et al., 1981)

11 Questions			
1). Did the trial address a clearly focused issue?	**Yes**	Can't Tell	No
2). Was the assignment of patients to treatments randomized?	**Yes**	Can't Tell	No
3). Were patients, health workers and study personnel blinded?	Yes	**Can't Tell**	No
4). Were the groups similar at the start of the trial?	**Yes**	Can't Tell	No
5). Aside from the experimental intervention, were the groups treated equally?	**Yes**	Can't Tell	No
6). Were all of the patients who entered the trial properly accounted for at its conclusion?	**Yes**	Can't Tell	No
7). How large was the treatment effect? **SSI rates measured--Group I: 13% (6/47); Group II: 7% (3/42); Group III: 20% (7/35); Group IV: 19% (8/42). Total SSI rate--15% (24/166)**			
8). How precise was the estimate of the treatment effect? **No confidence limits, no statistical results listed.**			
9). Can the results be applied in your context? (or to the local population?)	Yes	**Can't Tell**	No
10). Were all clinically important outcomes considered?	**Yes**	Can't Tell	No
11). Are the benefits worth the harms and costs?	**Yes**	Can't Tell	No

(CASP UK, 2013)

Appendix C

CASP Randomized Controlled Trial Checklist- Study #9 (Colizza et al., 1987)

11 Questions			
1). Did the trial address a clearly focused issue?	**Yes**	Can't Tell	No
2). Was the assignment of patients to treatments randomized?	**Yes**	Can't Tell	No
3). Were patients, health workers and study personnel blinded?	Yes	**Can't Tell**	No
4). Were the groups similar at the start of the trial?	**Yes**	Can't Tell	No
5). Aside from the experimental intervention, were the groups treated equally?	Yes	**Can't Tell**	No
6). Were all of the patients who entered the trial properly accounted for at its conclusion?	**Yes**	Can't Tell	No
7). How large was the treatment effect? **SSI rates measured--Wound Sepsis: Group A 11.5% (3/26), Group B 23% (6/26). Other Sepsis: Group A 34.6% (9/26), Group B 11.5% (3/26).**			
8). How precise was the estimate of the treatment effect? **No CI listed. Statistical significance of wound sepsis P < 0.01, other sepsis P < 0.001**			
9). Can the results be applied in your context? (or to the local population?)	Yes	**Can't Tell**	No
10). Were all clinically important outcomes considered?	**Yes**	Can't Tell	No
11). Are the benefits worth the harms and costs?	**Yes**	Can't Tell	No

(CASP UK, 2013)

Appendix D

CASE Worksheet: Comparison Across Studies

Critical Appraisal for Summaries of Evidence (CASE) Worksheet **Numbers in evaluation correspond with those assigned to articles in data extrapolation chart**	
Questions	**Evaluation Studies 1 - 9**
Summary Topic	
1. Is the summary specific in scope and application?	Yes-1,2,3,4,5,6,7,8,9 Not completely- No-
Summary Methods	
2. Is the authorship of the summary transparent?	Yes-1,2,3,4,5,6,7,8,9 Not completely- No-
3. Are the reviewer(s)/editor(s) of the summary transparent?	Yes-2,3,5,6,7 Not completely- No-1,4,8,9
4. Are the research methods transparent and comprehensive?	Yes-1,2,3,4,5,6,7, Not completely-8,9 No-
5. Is the evidence grading system transparent and translatable?	Yes-1,2,3,4,5,6,7,8,9 Not completely- No-
Summary Content	
6. Are the recommendations clear?	Yes-1,3,4,6,7,8 Not completely-2,5,9 No-
7. Are the recommendations appropriately cited?	Yes-1,3,4,6,7,8 Not completely-2,5 No-9
8. Are the recommendations current?	Yes- 1,2,3,4,5,6,7 Not completely- No-8,9
9. Is the summary unbiased?	Yes-1,2,3,4,6,7,8,9 Not completely-5 No-
Summary Application	
10. Can this summary be applied to your patient(s)?	Yes-1,3,6 Not completely-2,4,5,7,8,9 No