

Study Protocol

Evaluation of safety and efficacy of polyglactin 910 suture in surgical incision closure: clinical study protocol for a randomized controlled trial

Asha Dixit¹, Purnima Nadkarni², Viral Shah³, Bhavi Patel⁴,
Prakash Kumar Turiya⁴, Ashok Thakkar^{4*}

Department of Obstetrics and Gynecology, ¹Dixit Hospital, Vapi, ²21st Century Hospitals, Vapi, ³Shraddha Multispeciality Hospital, Ahmedabad, Gujarat, India

⁴Department of Clinical Research, Meril life Sciences Pvt. Ltd., Vapi, Gujarat, India

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***Correspondence:**

Dr. Ashok Thakkar,

E-mail: ashok.thakkar@merillife.com

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ABSTRACT

Background: Surgical site infection (SSI) occurs in a considerable portion of patients after closure of surgical incision. The newer synthetic absorbable sutures consistently display proven advantages for wound healing over naturally derived suture. The study is planned to evaluate the safety and efficacy of MITSU™ Polyglactin 910 Suture with Coated Vicryl® Polyglactin 910 Suture in a closure of surgical incision.

Methods: This is a prospective, multicentric, post-marketing, randomized, controlled, single-blinded, comparative study in a closure of surgical incision where general soft tissue approximation and/or ligation is required during an elective surgery. Patients are randomized to 1:1 ratio in the test (MITSU Polyglactin 910 Suture) and reference (Coated Vicryl Polyglactin 910 Suture) groups. Patients are monitored for safety and efficacy outcomes, viz. the rate of SSI, hospital length of stay, overall wound dehiscence and any adverse events/serious adverse events at post-procedural, 14 days, 30 days and 6 months of surgery. The rate of SSI for each group will be analyzed using one sided T-test. The effect of type of suture on SSI and overall wound dehiscence will be evaluated with chi-square test. Length of stay in hospital will be evaluated with student's t-test.

Conclusions: The study has been designed to compare the safety and efficacy of MITSU Polyglactin 910 Suture versus Coated Vicryl Polyglactin 910 Suture in a closure of surgical incision.

Trial registration: The trial protocol has been registered with the clinical trial registry of India (CTRI/2017/01/007717; registered on 17/01/2017).

Keywords: Absorbable polyglactin 910 suture, Surgical site infection, Wound dehiscence

INTRODUCTION

Surgical site infection (SSI) makes up the most surveyed and the most frequent type of nosocomial infection, which remains significant concerns for a healthcare services in developing countries according to the World Health Organization.¹ Despite the advances in surgical

techniques and a better understanding of the pathogenesis of wound infection, management of SSI remains a significant burden on healthcare services regarding the morbidity, mortality and economic cost.² The recent studies from India documented 1.6 to 21% SSI rates.^{3,4} The types of suture materials used in any surgical procedure have a significant impact on the occurrence of

SSI.^{5,6} Instead of the prolonged and irrational use of antibiotics, steps towards the improved antimicrobial policy should be undertaken.⁷

Even though the centuries with wound closure biomaterials' practice, the perfect suture for all situations yet not recognized. The chemical nature and physical characteristics of various suture materials are of vital importance in the context of the degree of tissue reactions.⁸ The eventual goal of suture material is to obtain a functional result associated with minimal inflammatory reactions, suture marks that disappears afterward with a cosmetically pleasing outcome.⁹ Significant discomfort experienced by the patients with non-absorbable sutures and it can leave a prominent suture marks on the skin, which can be less satisfactory aesthetic result being perceived by patients.¹⁰ An absorbable suture is a promising option as compared with non-absorbable sutures regarding saving clinical time, reducing patient's anxiety towards postoperative procedures and aesthetic appearance of the surgical site. The absorbable sutures consistently display both theoretically and clinically proven advantages for wound healing over the older, naturally derived sutures.⁸ The coated absorbable polyglactin 910 suture is composed of a polyglactin 910 copolymer (90% glycolide and 10% L-lactide) coated with the mixture of an equal portion of polyglactin 370 and calcium stearate exhibit non-antigenic and non-pyrogenic properties. The suture materials are of fundamental importance in the surgical outcomes. Hence, the present study is to evaluate safety and efficacy of coated synthetic absorbable sterile surgical suture of two different brands (MITSU Polyglactin 910 Suture versus Coated Vicryl Polyglactin 910 Suture) in a closure of surgical incision.

Safety objective of the study is overall wound dehiscence for 6 months of the study. Efficacy objectives of the study are the rate of SSI and hospital length of stay (LOS) evaluated for the 6 months follow-up period in a closure of surgical incision where general soft tissue approximation and/or ligation is required during elective surgery with coated polyglactin 910 surgical suture.

METHODS

Experimental design

This is a prospective, multicentric, randomized, controlled, single-blind, non-inferiority, comparative study comparing two coated polyglactin 910 surgical suture in a closure of surgical incision in which 122 subjects will be randomized to 1:1 ratio in the allocated groups (Figure 1).

Setting

The study setting is multicentric, which has three sites in India. The trial is ongoing at the time of publication.

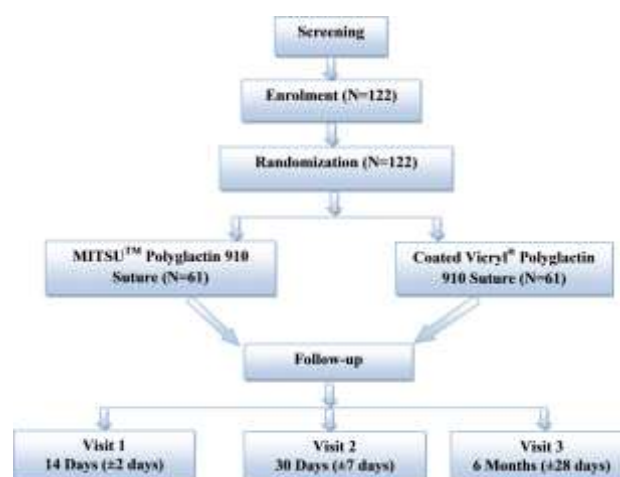


Figure 1: Flow chart of trial participant and timeline.

Participants/eligibility

Inclusion criteria

1. All subjects must be aged ≥ 18 years.
2. Subjects or a legally authorized representative must provide written informed consent prior to any study related procedure.
3. Subjects must schedule for closure of surgical incision where general soft tissue approximation and/or ligation is required during elective surgery by using test (MITSU Polyglactin 910 Suture) and reference (Coated Vicryl Polyglactin 910 Suture) interventions.
4. Subjects must agree not to participate in any other trial or invasive study for 6 months.
5. Subjects must agree to comply with all protocol requirements and protocol specific follow-up visits.

Exclusion criteria

1. Subjects with a history of HIV or any other systemic infections.
2. Subjects who require other emergency operations (major surgical procedure).
3. Subjects with ongoing sepsis or septicemia, ongoing bacterial infection or on antibiotic treatment (other than prophylaxis antibiotics given prior to and post surgery).
4. Subjects with a history of prior surgery within the past one month with SSI.
5. Patients with positive urine pregnancy test other than patient require the gynecological surgical procedure.

Recruitment

The first subject was randomized in January 2017. Total 117 subjects are enrolled in the study and enrollment is still ongoing at the time of publication. Potential subjects to the trial are identified at the time they attend for diagnosis. Subjects who meet selection criteria receive a

brief study presentation and explanation of risk and benefits of a study by an investigator. After selection criteria confirmation, the written informed consent form (ICF) in subject's selected language is obtained for their voluntary participation in the study. Baseline data are collected following consent process during the preoperative period.

Randomization

Subjects are randomized in a 1:1 ratio to each treatment group with PROC PLAN syntax using SAS[®] statistical software, version 9.4 (SAS Institute, Cary, NC). A sufficient number of subjects are recruited according to the sample size calculation to reduce randomization error.

Study treatment and assessment

All the subjects are assessed for eligibility criteria, medical history, and physical examination before the procedure. Demographics, laboratory assessment, vital signs and current medication are recorded during the screening visit. The subjects meeting the eligibility criteria are considered as enrolled in the trial. Subjects who need a closure of surgical incision where general soft tissue approximation and/or ligation is required during elective surgery are randomized in a 1:1 ratio to treatment with either test or reference intervention. Documentation of surgical procedure, any procedural complication, rate of SSI, wound dehiscence and any adverse event/serious adverse event (AE/SAE) are mandatory in all randomized patients. Subjects are continuously monitored clinically, for all local and systemic side-effects at the planned interval for 6 months.

Study outcomes

Efficacy outcomes

Efficacy outcomes of the study are the rate of SSI and hospital length of stay evaluated up to 6 months follow-up period in a closure of surgical incision with both coated polyglactin 910 surgical sutures.

The rate of SSI is measured at the time of baseline visit, post-procedural at discharge, 14 days, 30 days and 6-month or any unscheduled visit during the follow-up period of study. The centers for disease control and prevention (CDC) define surgical site infection as, (i) Superficial incisional infection, involving the skin and subcutaneous tissue. These infections may be signaled by localized (Celsian) signs such as redness, heat, pain or swelling at the place of the incision or by the drainage of pus. (ii) Deep incisional infection, affecting the fascial and muscle layers. These infections may be indicated by the occurrence of pus or an abscess, fever with a tenderness of the wound, or a parting of the edges of the incision exposing the deeper tissues. (iii) Organ or space infection involves any components of the anatomy other than the incision that is opened or manipulated during the surgical process, for instance, joint or peritoneum. These

infections may be indicated by the drainage of pus or the formation of an abscess found by histopathological or radiological assessment or during reoperation.

For each patients presenting SSI, its marked relevant symptoms are recorded viz., wound infection, postoperative pain, localized swelling, redness, heat, drainage of pus, fever with a tenderness of wound, formation or presence of abscess, separation of the edges of an incision and any others. Tissue/blood culture and sonography of the patients presenting SSI are performed as per investigator's discretion. If tissue/ blood culture is performed for a patient than, the name of the bacteria/fungi, and any given medication to that patient are recorded. For any performed sonography, its outcome should be mentioned in the document. This outcome was selected as the primary outcome for several reasons. Surgical site infection was the most used primary outcome in reported published trials evaluating and comparing the efficacy of suture materials.^{5, 11-14} Surgical site infection is also a common and major cause of postoperative morbidity, and it contributes greatly to the economic costs of surgical procedures.¹² Among the several risk factors, suture materials might play a significant role in the occurrence of SSI. As we are comparing the efficacy of surgical sutures, SSI stands out as an important outcome of the study.

Hospital length of stay is calculated by subtracting day of admission from the day of discharge. There was a significant difference found in length of hospital stay between patients with a SSI and those without observed in many trials.^{11,12} Serious SSIs can develop from local to systemic infection which leads to extended hospitalization, and increased healthcare expenditure, causing an additional inpatient care cost.¹⁵ With such status, it could be advantageous to record hospital length of stay for evaluation of the efficacy of sutures.

Safety outcomes

Safety outcome of the study is overall wound dehiscence recorded at post-procedure, after 14 days, 30 days, and 6 months or any unscheduled visit during the follow-up period of study. Details of any emergent reoperation required after the occurrence of wound dehiscence is recorded.

Wound dehiscence was defined as an entire wound disruption that needed emergent reoperation. A surgical wound dehiscence impact on mortality and morbidity rates associated with surgeries and contributory to associate psychosocial stressors on individuals and their families.¹⁶ In our study, overall wound dehiscence gives a picture of optimization of patient's postoperative recovery and rehabilitation.

Timelines and follow-up schedule

All patients are followed up for the 6 months period, with each follow-up visits at 14 days (± 2 days), 30 days (± 7

days) and 6-month (± 28 days) following the intervention. Schedule of enrollment, intervention, and assessments are presented in table 1. If a subject is not turning up for follow-up visits, a consecutive attempt should be made by clinical research coordinator to get in contact with the

subject. At follow-up visits, current medications, sonography (if required), tissue culture (if required) and AE/SAE assessment will be done. Physical examination including surgical site examination will be done at each follow-up visit.

Table 1: Schedule of enrollment, intervention and assessments.

Events	Screening	Baseline	At post procedure/ discharge	Follow-up visits		
				14 days (± 2 days)	30 days (± 7 days)	6 months (± 28 days)
Informed consent	×					
Inclusion/Exclusion criteria	×					
Demographics	×					
Medical history	×					
Physical examination	×			×	×	×
SSI		×	×	×	×	×
Laboratory assessment (CBC)	×					
Vital signs	×					
Current medication	×	×	×	×	×	×
Surgical procedure		×				
Ultrasound (sonography)			× ¹	× ¹	× ¹	
Tissue/ blood culture		×	× ¹	× ¹	× ¹	× ¹
AE/SAE assessment		×	×	×	×	×

CBC: complete blood count, SSI: Surgical site infection; ¹Ultrasound (sonography) and/or tissue culture can be done at any point of time during study as per investigator's discretion.

Withdrawals

The study withdrawal decision must be an independent decision of the subject. Moreover, the investigator may choose to withdraw a patient from the study if follow-up is considered too burdensome for the patient. Early withdrawals will be documented in the case report form (CRF) of the subjects.

Blinding

The study is a single-blinded trial where the subjects are unaware of the studied intervention. It is not possible to blind surgeons in our trial because of the nature of the studied intervention and surgical procedure.

Data management

Data is recorded in the study-specific CRFs via web-program based on the eCRF data capturing system. To maintain the confidentiality of participant's identity, CRFs are identified only by a subject ID and initials. All records that contain subject names or other identifying information are reserved confidential. Data are monitored for quality and consistency by the data managers and any queries/discrepancies raised by the data managers; it will be resolved by the clinical research coordinator and investigator.

Sample size calculation

Reliable data on the usage pattern of both test and reference interventions in reducing SSI were collected at

the selected sites. Assuming a SSI rate of 20% in test intervention and 10.6% in reference intervention followed by two-sided 95% confidence interval with 85% power and a significance level of 5% (0.05) prove non-inferiority (non-inferiority margin 0.09) results into an estimated sample size of 55 subjects for each group in the study. Assuming a discontinuation rate of 10%, the required total recruitment to each group is 61 for 85% power. Therefore we plan to enroll a total of 122 subjects, 61 subjects in each group in the present study.

Statistical analysis

All the statistical analysis will be performed based on the subjects for whom data are available. The socio-demographics and some clinical characteristics will be summarized using descriptive statistics. Continuous variables will be presented as Mean \pm SD, non-continuous as median (IQR) and categorical variable as counts and percentages. Continuous variable follows normal distribution among the group will be compared using Student's t-test and Mann-Whitney U-test who doesn't follow the normal distribution. Categorical variable among groups will be analyzed using Fisher's exact test or chi-square test as appropriate. Efficacy endpoint, i.e. SSI rates for each group, will be summarized by frequency (%) and analyzed using a one-sided T-test to estimate binomial proportion confidence intervals. The effect of type of suture on SSI will be evaluated with the chi-square test and reported with a risk ratio (RR) with 95% confidence interval (CI). Safety endpoints such as overall wound dehiscence will be presented by frequency (%) and analyzed using a chi-square test. Hospital length

of stay will be presented as mean \pm SD and evaluated with student's t-test. Analysis of adverse event will be based on frequency (%) and severity. The P-value less than 0.05 will be considered statistically significant.

Monitoring

Trained and qualified personnel monitor the study throughout its duration by means of personal visits to the investigator's facilities and through other modes of communication. The visits are conducted to evaluate the progress of the study, verify the rights and well-being of the subjects and accuracy of data. A monitoring visit ensures whether the study protocol is being followed properly. Any adverse events/ serious adverse events are recorded and reported according to the adverse event reporting system of the sponsor.

Ethical considerations

Documented approval has been obtained from appropriate independent review board/ independent ethics committee for all three trial sites prior to initiation of the study. The protocol for this study was approved by the local ethical committee at each participating clinical institution. The study is conducted in accordance with ICH-GCP, ISO 14155, Medical device directives, Global harmonization task force and local regulations as well as with the Declaration of Helsinki. Written informed consent must be obtained from each patient before any study-specific procedure takes place. The trial is registered with the clinical trial registry of India with CTRI/2017/01/007717 registration number (<http://ctri.nic.in/Clinicaltrials/advsearch.php>).

DISCUSSION

Surgical patients commonly acquire postoperative "irritative fever," followed by pus drainage from their incisions, overwhelming sepsis, and many a time death, before the mid-19th century.¹⁷ Whether a practitioner is managing a complex trauma or a minor incision, there is always a need for surgical closure.¹⁸ Suturing is an ancient technique used by physicians for at least 4000 years now. Sutures constitute the largest groups of biomaterials used as implants in a human body, having a huge market all over the world. Over the years, surgical suture materials have matured as core products in the new era of medical industry.¹⁹

Suture material is an operator reliant variable, and playing essential role in wound infection.¹⁸ Joseph Lister in late 1860s, introduced the principles of antisepsis after that postoperative infectious morbidity decreased substantially.¹⁷ Improved operating room ventilation, sterilization method, surgical techniques, and availability of antimicrobial prophylaxis have been adapted as the several new advances in infection control practices. Surgical site infection still remnants and has a significant impact on morbidity and mortality among hospitalized

patients which may be due to evolvement of antibiotic resistant pathogens and increased numbers of debilitating surgical patients. Any foreign body including suture material may trigger inflammation at the surgical site and increases the probability of SSI.¹⁷ According to the various reported studies, significant differences were found in the SSI rates when different suture materials were used.^{9,20}

In the early 1970s, with the development of the synthetic absorbable polymer, polyglycolic acid, the new era of absorbable polymeric sutures was started which got extraordinary commercial success.¹⁹ Now a day, absorbable sutures have become a treatment of choice over non-absorbable sutures. Still, the efficacy and safety of absorbable sutures greatly depend on the chemical nature and physical characteristics.⁸ Polyglactin 910 copolymer (90% glycolide and 10% L-lactide) coated with polyglactin 370 and calcium stearate exhibits non-antigenic and non-pyrogenic properties which can be beneficiary in reducing rates of SSI. The only concern is an absorbable suture cannot be recommended where extended approximation of tissues under stress is required.

There are remarkable studies available evaluating clinical outcomes of Coated Polyglactin 910 Sutures. Ford et al. evaluated the intra-operative handling and wound healing characteristics of coated vicryl polyglactin 910 Suture compared with other suture in a total of 147 patients. They reported excellent score (59%) for overall intra-operative handling and placid wound healing parameters with Coated Vicryl Polyglactin 910 Suture.²¹ Out of 376 patients, SSI occurred in 24 (6%) patients who were treated with Vicryl Polyglactin 910 Suture in a sternal wound closure study.²² Another study of Vicryl Polyglactin 910 Suture in the appendectomy patients reported 8% (4 of 50 patients) SSI rate.¹¹ Several other studies were performed to evaluate the Coated Vicryl Polyglactin 910 Suture, but the evaluation of safety and efficacy of new MITSU polyglactin 910 suture in surgical incision is not reported yet. It is best to evaluate the treatment effectiveness of MITSU polyglactin 910 suture in randomized control trial against the traditional Coated Vicryl Polyglactin 910 Suture. The random allocation of the test and reference interventions is only way to ensure that observed outcome can actually be attributed to the effectiveness of the investigated products and not to any immaterial factors.²³ The results of this study will compare the test and reference polyglactin 910 suture for their safety and efficacy in a closure of the surgical incision by using appropriate statistical tests. The insignificant difference between the outcomes of both the polyglactin 910 suture will prove the non-inferiority of MITSU polyglactin 910 Suture compared to traditional Coated Vicryl Polyglactin 910 Suture. A suture being an important factor for the success of the surgical procedure, the study is intended to assist a rational choice of suture in medical practice, depending on price, efficacy, and safety.

Funding: Meril Life Sciences Pvt. Ltd. is the sponsor of the MITSU™ Polyglactin 910 Suture study

Conflict of interest: None declared

Ethical approval: The study was approved by the Institutional Ethics Committee (No ECR/663/Inst/GJ/2014, ECR/663/inst/GJ/2014 and ECR/147/Inst/GJ/2013)

REFERENCES

- World Health Organization, Global guidelines for the prevention of surgical site infection. World Health Organization, 2016.
- Valecha SM, Saswade MN. An original research paper on incidence and risk factors for surgical site infections following major abdominal surgeries in obstetrics and gynaecology. *Int J Reprod Contracept Obstetr Gynecol*. 2017;6(5):1859-63.
- Shah S, Singhal T, Naik R. A 4-year prospective study to determine the incidence and microbial etiology of surgical site infections at a private tertiary care hospital in Mumbai, India. *Am J Infection Control*. 2015;43(1):59-62.
- Ramasubramanian V, Iyer V, Sewlikar S, Desa A. Epidemiology of healthcare acquired infection—An Indian perspective on surgical site infection and catheter related blood stream infection. *Indian J Basic Applied Med Res*. 2014;3:46-63.
- Hoshino S, Yoshida Y, Tanimura S, Yamauchi Y, Noritomi T, Yamashita Y. A study of the efficacy of antibacterial sutures for surgical site infection: a retrospective controlled trial. *Int Surg*. 2013;98(2):129-32.
- Jung KH, Oh SJ, Choi KK, Kim SM, Choi MG, Lee JH, et al., Effect of triclosan-coated sutures on surgical site infection after gastric cancer surgery via midline laparotomy. *Ann Surg Treatment Res*. 2014;87(6):311-8.
- Negi V, Pal S, Juyal D, Sharma MK, Sharma N. Bacteriological profile of surgical site infections and their antibiogram: A study from resource constrained rural setting of Uttarakhand State, India. *J Clin Diagnos Res*. 2015;9(10):DC17.
- Greenberg JA, Clark RM. Advances in suture material for obstetric and gynecologic surgery. *Reviews Obstetr Gynecol*. 2009;2(3):146.
- Kundra R, Newman S, Saithna A, Lewis AC, Srinivasan S, Srinivasan K. Absorbable or non-absorbable sutures? A prospective, randomised evaluation of aesthetic outcomes in patients undergoing elective day-case hand and wrist surgery. *Ann R Coll Surg Engl*. 2010;92(8):665-7.
- Guyuron B, Vaughan C. A comparison of absorbable and nonabsorbable suture materials for skin repair. *Plastic Reconst Surg*. 1992;89(2):234-6.
- Mingmalairak C, Ungbhakorn P, Paucharoen V. Efficacy of antimicrobial coating suture coated polyglactin 910 with triclosan (Vicryl plus) compared with polyglactin 910 (Vicryl) in reduced surgical site infection of appendicitis, double blind randomized control trial, preliminary safety report. *Med J Med Assoc Thailand*, 2009;92(6):770.
- Galal I, El-Hindawy K. Impact of using triclosan-antibacterial sutures on incidence of surgical site infection. *Am J Surg*. 2011;202(2):133-8.
- Justinger C, Moussavian MR, Schlueter C, Kopp B, Kollmar O, Schilling MK. Antibiotic coating of abdominal closure sutures and wound infection. *Surgery*. 2009;145(3):330-4.
- Chen SY, Chen TM, Dai NT, Fu JP, Chang SC, Deng SC, et al. Do antibacterial-coated sutures reduce wound infection in head and neck cancer reconstruction? *Eur J Surg Oncol (EJSO)*, 2011;37(4):300-4.
- Mingmalairak C. Antimicrobial sutures: new strategy in surgical site infections. *Science against Microbial Pathogens: Communicating Current Research and Technological Advances: Formatex Research Center*. 2011: 313-323.
- Sandy-Hodgetts K, Carville K, Leslie GD. Determining risk factors for surgical wound dehiscence: a literature review. *Int Wound J*. 2015;12(3):265-75.
- Mangram AJ, Horan TC, Pearson ML, Silver LC, Jarvis WR. Guideline for prevention of surgical site infection, 1999. *Am J Infection Control*. 1999;27(2):97-134.
- Katz S, Izhar M, Mirelman D. Bacterial adherence to surgical sutures. A possible factor in suture induced infection. *Ann Surg*. 1981;194(1):35.
- Pillai CKS, Sharma CP. Absorbable polymeric surgical sutures: chemistry, production, properties, biodegradability, and performance. *J Biomaterials App*. 2010;25(4):291-366.
- Nakamura T, Sato T, Takayama Y, Naito M, Yamanashi T, Miura H, et al. Risk factors for surgical site infection after laparoscopic surgery for colon cancer. *Surgical infections*. 2016;17(4):454-8.
- Ford HR, Jones P, Gaines B, Reblock K, Simpkins DL. Intraoperative handling and wound healing: controlled clinical trial comparing coated VICRYL® Plus antibacterial suture (coated polyglactin 910 suture with triclosan) with Coated VICRYL® suture (coated polyglactin 910 suture). *Surgical Infections*. 2005;6(3):313-21.
- Fleck T. Triclosan-coated sutures for the reduction of sternal wound infections: economic considerations. *Ann Thoracic Surg*. 2007;84(1):232-6.
- McLeod RS. Issues in surgical randomized controlled trials. *World J Surg*. 1999;23(12):1210-4.

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