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Technology Assessment Unit of the McGill University Health Centre

TAU Annual Report

April 2011 - 2012

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Mission Statement

- To advise the hospital in difficult resource allocation decisions, using an approach based on sound, scientific technology assessments, and a transparent, fair decision-making process.

- To publish its research in peer-reviewed journals when appropriate, and contribute to the training of personnel in the field of health technology assessment.

MUHC TAU Executive Committee

Nandini Dendukuri – Director **Dr. Maurice McGregor - Chairperson**

Committee Members	Discipline
André Bonnici	P & T Committee
Sandra Dial	Clinical Epidemiology
Christian Janicki	Quality Management
Patricia Lefebvre	Quality Management, Risk Management and Performance
Brenda MacGibbon-Taylor	Patients' Committee
Gary Pekeles	Council of Physicians & Dentists
Guylaine Potvin	Multidisciplinary Council
Judith Ritchie	Council of Nurses
Hugh Scott	Consultant (Invited Member)
Gary Stoopler	Administration

Arrivals

Ioana Nicolau, MSc joined our TAU Unit as a Research Assistant in August 2011.

This publication was compiled and edited by Lorraine Mines of the Technology Assessment Unit of the McGill University Health Centre (MUHC TAU). This document is available in PDF format on our website: http://www.mcgill.ca/tau/publications/annual

TAU Reports

NOTE: Projects are researched and drafts prepared by members of the MUHC TAU, referred below as "the authors". They are assisted by expert consultants appointed for each project. Draft reports are then circulated, reviewed, amended and finally approved by the full TAU Policy Committee who thereby become “the authors” of the final report.

The following reports have been completed during the year.

Fiducial Markers (Mini HTA)

Title:	**Fiducial markers for improving treatment margins in radiotherapy for prostate cancer**.
Requestor:	Gary Stoopler, Administrative Director, Surgery, Medicine, Cancer Care, Mental Health & Women’s Health, MUHC
Publication date:	June 16, 2011
Author(s):	Dendukuri, Nandini, Xie, Xuanqian, McGregor, Maurice
Background:	A Fiducial marker is a metallic object inserted in the area of interest (organ or tumor to be treated with radiation therapy) and used as a point of reference to facilitate its visualization by an imaging system. Daily localization of the fiducial markers immediately before radiation therapy delivery allows for correction of inter-treatment organ motion, minimizing geometrical errors when small treatment margins are used.
Conclusion(s):	This intervention will in all probability diminish the risk of radiation damage to bladder and rectum for the approximately 30 patients per year in whom it will be used. The extent of risk reduction cannot be estimated. The estimated budget impact would be

approximately $6,000 per year. It could be carried out without any impact on service, and at insignificant risk to patients.

VerifyNow (Mini HTA)

Title:	**Use of the VerifyNow point of care test to detect non-responsiveness to clopidogrel and aspirin.**
Requestor:	Gary Stoopler, Administrative Director, Surgery, Medicine, Cancer Care, Mental Health & Women's Health, MUHC
Publication date:	July 19, 2011
Author(s):	Xie, Xuanqian, McGregor, Maurice
Background:	VerifyNow is a point-of-care test that can evaluate a patient's response to several antiplatelet inhibitors, including aspirin and thienopyridines. Its purpose is to detect non-responders to antiplatelet medication so that by dose adjustment or change of medication a therapeutic response can be achieve
Conclusion(s):	• The applicant intends to use the VerifyNow test to detect those patients at increased risk of arterial thrombotic events due to Clopidogrel resistance. Patients found to be clopidogrel resistant will be treated with other thienopyridine drugs. • The VerifyNow test is easy to use and is sufficiently accurate for this purpose. • The cost of this intervention for approximately 100 selected patients per year will be approximately $8,400. There will be no increased use of beds or other hospital services. • This intervention will probably result in improved patient outcomes. However, it is an intervention that has not previously been used and its value is still unproven. It should therefore be considered an experimental intervention.

Probiotics

Title: **The use of *Lactobacillus* probiotics in the Prevention of Antibiotic Associated *Clostridium Difficile* Diarrhea. Update**

Requestor: TAU initiative

Publication date: December 19, 2011

Author(s): Sinclair,Alison, Xie, Xuanqian, Dendukuri, Nandini

Background: *Clostridium difficile* diarrhea (CDAD) is the most common nosocomial diarrhea, prolonging hospitalization and for some patients leading to colectomy or death. It is strongly associated with antibiotic use, and has been attributed to perturbation of the normal intestinal biota; for this reason there has been an interest in the effectiveness of live cultures (probiotics) in preventing CDAD. The TAU reviewed the use of probiotics in the prevention and treatment of *Clostridium difficile* associated diarrhea (CDAD) in 2005 and again in 2009. The publication of additional trials prompted a further update and a meta-analysis of *Lactobacillus* probiotics in the prevention of CDAD.

Conclusion(s): ***Efficacy***

- In the 7 studies included in the present meta-analysis, the administration of *Lactobacillus* was associated with an average reduction in the relative risk of C difficile of 83% (median pooled RR=0.17 (95% credible interval (CrI) 0.04, 0.42)).
- The number of outcomes in the database was relatively small (17 in the probiotics group and 53 in the placebo group), there was considerable statistical heterogeneity in the RR between studies as well as heterogeneity in the background incidence of CDAD, raising concerns about the generalizability of the median pooled RR to individual studies.
- Bayesian credibility analysis, which tested the robustness of the findings to prior information, showed that even a relatively

weak sceptical prior for the risk ratio produced a posterior distribution for RR that included 1.

- None of the RCTs reported so far have examined outcomes that actually impact hospital costs, e.g. length of stay, among CDAD patients.
- The results of the RCTs conducted so far constitutes suggestive evidence that probiotics based on *Lactobacillus* may be effective in the prevention of CDAD. However, for the reasons stated, the level of evidence is not yet strong enough to determine policy.

Safety

- For patient populations such as those studied in the included randomized controlled trials, in which severely debilitated and immunocompromised patients have been excluded, probiotic therapy appears to be without risk of significant side-effects. However, there have been some case reports of serious side effects in seriously ill patients.

Recommendation(s): Although there is suggestive evidence that probiotics based on *Lactobacillus* may be effective in the prevention of CDAD, the evidence is not strong enough to be the basis for a general policy change. Accordingly, we cannot presently recommend routine use of probiotic *Lactobacillus* in the prevention of CDAD in hospitalized patients receiving antibiotics.

Drug Eluting Stents

Title: **Drug Eluting Stents. What should be the indications for their use at the MUHC?**

Requestor: Gary Stoopler, Administrative Director, Surgery, Medicine, Cancer Care, Mental Health & Women's Health, MUHC

Publication date: December 21, 2011

Author(s): McGregor, Maurice, Sinclair, Alison

Background:

Stents are widely used to maintain patency following coronary angioplasty. In recent years, to reduce the rate of in-stent stenosis, bare metal stents (BMS) have been largely replaced by stents that slowly release anti-fibrotic medication, called drug-eluting stents (DES). Since the cost of a single DES is approximately $900 higher than that of a BMS the choice of which stent is used, is a matter of concern to hospital administrators. As a result of a recently observed increase in stent use, the TAU was requested to develop a list of indications for the use of drug-eluting stents (DES) at the MUHC.

Conclusions/ Recommendation(s):

1. Indications for use of DES

- It is recommended that the recently introduced practice of recording the indications for the use of DES following each procedure be maintained.
- Although the evidence supporting some of the following indications is inconclusive, the preponderance of evidence suggests that use of DES at the MUHC should be restricted to patients with the following indications:
- Patients exhibiting two or three of the following risk factors: diabetes, small vessels (<3 mm diameter), and long lesions (≥20 mm).
- Relief of total chronic coronary occlusion.
- Patients undergoing repeat procedures to relieve in-stent stenosis.
- Patients undergoing multiple stent insertions.
- Interventions in the presence of multivessel disease and/or proximal left main stenosis.

2. Current usage of DES at MUHC.

- The indications currently in effect for the use of DES at the MUHC are largely consistent with the above indications.

- Of 2016 stents used in the budget year 2010-2011, 34% were DES. This is lower than in any other Quebec academic Hospital.

3. **Cost Issues**
   - The gross cost of this intervention in the past budget year was approximately $607,250.
   - Assuming this use of DES resulted in a 5.9% reduction in repeat angioplasty, the net budget impact would be $448,293, and the cost of each repeat procedure would be $10,934.

Subglottic Secretion Drainage

Title:	**Subglottic Secretion Drainage Endotracheal Tubes for Prevention of Ventilator-Associated Pneumonia.**
Requestor:	Gary Stoopler, Administrative Director, Surgery, Medicine, Cancer Care, Mental Health & Women's Health, MUHC
Publication date:	January 19, 2012
Author(s):	Xie, Xuanqian, Nicolau, Ioana, McGregor, Maurice, Dendukuri, Nandini
Background:	Ventilator-associated pneumonia (VAP) is a common nosocomial infection in mechanically ventilated patients. Intubation with a modified endotracheal tube (ETT) that allows subglottic secretion drainage (SSD) may reduce incidence of VAP. The Technology Assessment Unit was asked to evaluate the efficacy, cost and cost-effectiveness of such a device in reducing the risk of VAP in the adult intensive care units of the McGill University Health Centre (MUHC). The incidence rate of VAP in the Royal Victoria Hospital was 8.3 per 1000 ventilator days for the year 2010-2011(5). This is higher than the VAP rate of 5.4 per 1000 ventilator days published by the National Nosocomial Infections Surveillance (NNIS) Systems Report in the United States(6), based on voluntary reports from participating hospitals. The TAU was

approached by Gary Stoopler , Administrative Director of the Medical Mission, MUHC, to evaluate the utility of SSD ETT in reducing the VAP rate at the MUHC, and the costs associated with its use.

Conclusion(s):

- Twelve of 14 randomised controlled trials found a statistically significant reduction of VAP or early onset of VAP associated with use of SSD ETT. The average reduction based on all 14 studies is 47% (95% credible interval 36%, 53%).
- The possibility cannot be excluded that this benefit might be the result of bias or confounding due to other therapeutically effective co-interventions. Thus, further more methodically rigourous trials are very desirable.
- In spite of this, until stronger evidence is available, the available evidence of benefit is sufficiently convincing to serve as the basis for MUHC policy in the case of this relatively low-cost, apparently harmless intervention**.**
- Based on the efficacy as defined in this study, application of this technology to an estimated 500 patients per year would result in:
  - Prevention of 20 cases of VAP per year.
  - An estimated reduction in ICU occupancy due to VAP of 86 bed days (95% credible interval 65 days, 103 days), with an equivalent increase in the number of other patients treated.
  - The budget impact of this intervention (the cost of the necessary equipment) would be $9,250.

Recommendation(s): SSD ETT is an efficacious intervention that should be approved for use in those patients who are expected to be mechanically ventilated in the ICU for at least 3 days.

BinaxNow

Title:	**The clinical effectiveness and cost of a pneumococcal urine antigen immunochromatographic test (BinaxNOW Streptococcus pneumoniae) in the diagnosis of community acquire Streptococcus pneumoniae pneumonia in patients admitted to hospital.**
Requestor:	Dr Vivian Loo (Chief of the Department of Microbiology of the MUHC) and Marty Teltscher (Microbiologist and Infectious Disease Consultant, Lachine Campus of the MUHC
Publication date:	January 31, 2012
Author(s):	Sinclair, Alison, Xuanqian, Xie, Dendukuri, Nandini
Background:	BinaxNOW *Streptococcus pneumoniae* (BinaxNOW-SP) is an immunochromatographic test for the presence of *Streptococcus pneumoniae* (SP) coat antigen. Applied to an initial urine sample, it can suggest a diagnosis of SP infection within an hour or less, in contrast to cultures, which may take 24 hours or more. BinaxNOW-SP is believed to have higher sensitivity than blood culture and is expected to increase the percentage of patients who receive a precise bacteriological diagnosis. This has the potential to permit the use of narrower-spectrum antibiotic therapy, and in turn reduce risk of antibiotic resistance or *Clostridium difficile* associated diarrhea. The Technology Assessment Unit (TAU) was requested to evaluate clinical effectiveness and cost effectiveness of BinaxNOW-SP in the diagnosis of community acquired pneumonia (CAP) in patients admitted to the MUHC.
Conclusion(s):	• There is currently no evidence that the introduction of BinaxNOW-SP influences physicians' prescribing habits. Observational studies examining this question were inconclusive. • Our meta-analysis shows that addition of BinaxNOW-SP to the diagnostic work-up of patients with suspected CAP may,

in addition to providing an earlier bacteriological diagnosis, result in an increase in the percentage of SP pneumonia cases diagnosed by 30% (95% CrI 17%, 41%). This would be, accompanied by a smaller increase in the percentage of false-positive cases 3% (95% CrI 0%, 7%). Note that the credible intervals around these estimates are very wide due to the heterogeneity in sensitivity and specificity estimates across individual studies.

- Assuming that BinaxNOW-SP does influence prescribing practice, our cost-analysis showed that the addition of BinaxNOW-SP to the work-up will result in an incremental net cost of $36.2 (95% CrI $35.7, $36.6) per patient in a regular ward and $3.7 (95% CrI -$10.6, $14.6) per patient in the ICU, despite cost-savings from using targeted treatment. It should be noted that our estimates ignore the possible decrease in cost due to reduced risk of nosocomial infections. Cultures will continue to be required to provide information about antibiotic resistance.
- For 1700 patients with pneumonia (estimated admissions to MGH and RVH over one year), assuming that 170 (10%) required ICU admission, that represents a budget impact of $56,022 (95% CrI $52,938,$58,342). Assuming test results determine prescribing practices, this would result in the targeted treatment of 457 patients.
- The limited evidence available suggests that this change of therapy would produce no measurable benefit to the individual patient. We do not presently have the information to quantify the indirect benefits of improved antibiotic stewardship.

Recommendation(s): We recommend that Binax-NOW not be used in the routine testing of patients suspected of community acquired pneumonia. Any use that takes place should be carried out within a protocol, to be

determined by the Departments of Microbiology and Infection Control, with the objective of defining the value of this test. This issue should be reviewed in one year at which time usage and value of this test should be reviewed.

Diffusion

- Our reports are indexed in the international database for the Center for Reviews and Dissemination, York University, UK. http://www.crd.york.ac.uk/crdweb/
- Our reports are diffused from our website (www.mcgill.ca/tau) . Between April 1, 2011 and March 31, 2012 our website received approximately 124,000 hits.
- Our reports are also now circulated to all members of the McGill RUIS.

TAU Related Activities

Dr. Dendukuri represents TAU at quarterly meetings of hospital-based technology assessment units in Quebec that are organized at INESSS.

Dr. McGregor is a regular contributor to the Executive Training for Research Application (EXTRA) program for health executives.

Presentations

Dendukuri, N. “Bayesian meta-analysis of diagnostic test accuracy in the absence of a gold standard reference test”. 32nd annual conference of the International Society of Clinical Biostatistics, Ottawa. August 2011.

Dendukuri, N. “Est-ce qu’un test de l’antigneurinaire peut ameliorer le diagnostic de la pneumonie acquise dans la communauté accrotre l’utilisation des antibiotiques cibles? Une revue systematique de la preuve”. Atelier enjeux et pratiques, Institut nationale d’excellence en santé et en services sociaux (INESSS),Montreal. February 2012.

McGregor M, Xie X, Dendukuri N. The use of quality instruments to weight evidence from RCTs
CADTH 2011 Symposium, Vancouver. April 4, 2011.

Xie X, McGregor M, Dendukuri N. Negative Pressure Wound Therapy. Is it effective? CADTH 2011 Symposium. Vancouver. April 4, 2011

Sinclair A, Xie X, Dendukuri N. The use of probiotic lactobacillus in the prevention of Clostridium difficile diarrhea in adult inpatients receiving antibiotics. 2011 CADTH Symposium. Vancouver. April 4, 2011

Dendukuri N, Pan I. Efficacy of a Gentamicin-loaded collagen sponge for surgical site infection prophylaxis in cardiac and colorectal surgery. 2011 CADTH Symposium. Vancouver. April 4, 2011

Xie X, Nicolau I,McGregor M, Dendukuri N. Subglottic Secretion Drainage Endotracheal Tube for Prevention of Ventilator-Associated Pneumonia (poster). 2012 CADTH Symposium,
Ottawa. April 15-17, 2012

Sinclair A, Xie X, Dendukuri N. Diagnosis of Streptococcus pneumoniae infection in community acquired pneumonia by BinaxNOW® urine test: diagnostic meta-analysis in the absence of a perfect reference standard (poster) 2012 CADTH Symposium, Ottawa. April 15-17, 2012

McGregor M. The connect between wait times, sustainability and HTA. Health Care, Technology and Place (HCTP). Symposium on: The Career of Health Technology: Perspectives
on Innovation, Assessment, and Use. Toronto. March 24, 2011.

McGregor M. HTA in the Canadian Healthcare System. CADTH Science Week. Ottawa. Oct. 11,2011

McGregor M. HTA From a Local Perspective. The Hospital. PATH Institute Policy Forum. Toronto. October 21, 2011

McGregor. M. HTA. What is it? Why do we need it?. MentecNorth. Annual Conference. Montréal. April 18, 2012.

Selected Peer-Reviewed Publications Related to Technology Assessment Activities (* denotes students and staff)

Loo V, Bourgault A-M, Poirier L, Lamothe F, Michaud S, Turgeon N, Toye B, Beaudoin A, Frost EH, Gilca R, Brassard P, **Dendukuri N**, Beliveau C, Oughton M, Brukner I, Dascal A. Host and Pathogen Determinants of C. difficile Infection and Colonization. New England Journal of Medicine, 365(18): 1693-1703, 2011

Dendukuri N, *Wang L, Hadgu A. Evaluating diagnostic tests for Chlamydia trachomatis in the absence of a gold-standard: A comparison of 3 statistical methods. Statistics in Biopharmaceutical Research, 3(2): 385-397, 2011

Steingart KR, Flores LL, **Dendukuri N**, *Schiller I, Laal S, Ramsay A, Hopewell PC, Pai M. Commercial serological tests for the diagnosis of active pulmonary and extrapulmonary tuberculosis: An updated systematic review and meta-analysis. 8(8): e1001062, 2011

Flores LL, Steingart KR, **Dendukuri N**, *Schiller I, Minion J, Pai M, Ramsay A, Henry M, Laal S. Antigen detection tests for the diagnosis of tuberculosis: A systematic review and meta-analysis. Clinical and Vaccine Immunology, 18(10): 1616-1627, 2011

*DeGroot J, **Dendukuri N**, Moons K, Brophy J. Adjustment for selection bias in meta-analysis of diagnostic tests. American Journal of Epidemiology, 175(8): 847-53, 2012

Hadgu A, **Dendukuri N**, *Wang L. Evaluation of Screening Tests for Chlamydia Trachomatis: Bias Associated with the Patient Infected Status Algorithm. Epidemiology, 23: 72-82, 2011

René P, Frenette CP, *Schiller I, **Dendukuri N**, Brassard P, Fenn S, Loo VG. Comparison of Eight Commercial Enzyme Immunoassays for the Detection of Clostridium difficile from Stool Samples. Journal of Clinical Microbiology, 73:94-96, 2012

Dendukuri N, *Schiller I, Joseph L, Pai M. Bayesian meta-analysis of the accuracy of a test for tuberculous pleuritis in the absence of a gold-standard reference. Biometrics, doi: 10.1111/j.1541-0420.2012.01773.x, 2012 (Epub ahead of print)

Awards

Dendukuri N, *Wang L, Hadgu A. Evaluating diagnostic tests for Chlamydia trachomatis in the absence of a gold-standard: A comparison of 3 statistical methods. Statistics in Biopharmaceutical Research, 3(2): 385-397, 2011 Statistical Science Award (Theoretical Category) from Centers for Disease Control, United States, 2012

Hadgu A, **Dendukuri N**, *Wang L. Evaluation of Screening Tests for Chlamydia Trachomatis: Bias Associated with the Patient Infected Status Algorithm. Epidemiology, 23: 72-82, 2011 Charles C. Shepard in the Data Methods and Study Design category from Centers for Disease Control, United States 2012

The 2011 Dr. Jill M. Sanders Award of Excellence in HTA Canadian Agency for Drugs and Technology in Health. Recipient: **Dr. Maurice McGregor**. 2011 CADTH Symposium. Vancouver. April 4, 2011

Grants

Principal Investigator: .**Dr Nandini Dendukuri ,** CIHR “Statistical methods for meta-analysis of tuberculosis diagnostic studies” (Co-Principal Investigator: Madhukar Pai). Total amount: $282,798. 2011-2014

Co-Investigator: Dr. Nandini Dendukuri. CIHR “Methods to measure (and measures of) the (actual)mortality reductions produced by cancer screening” (Principal Investigator: James Hanley). Total amount: $188,250, 2011-2014

Postscript

The TAU attempts to adjust the services we offer to conform to the resources available in a transparent, logical, fair, and consistent fashion. While some of our recommendations have not supported the acquisition of a technology, and have thus "saved money", others have supported new developments because they have identified the benefits, and found them to be sufficient to justify the increased expenditure. Our sincere thanks are due to the many members of the MUHC who have assisted with data collection, to those who have served as Consultants, and to the members of the Committee who have dedicated many hours to the consideration of these problems. *Maurice McGregor*.

December, 2012