Available online at www.sciencedirect.com

ScienceDirect

journal homepage: www.JournalofSurgicalResearch.com

Association for Academic Surgery

Cost-Effectiveness of Exploratory Laparotomy in a Regional Referral Hospital in Eastern Uganda

Nikhil Bellamkonda, BS,[a] *Girish Motwani, MPH,*[b] *Andrew Hyginus Wange, BBA,*[c] *Christopher De Boer, MD,*[b] *Fred Kirya, MBchB, MMed,*[c] *Catherine Juillard, MD, MPH,*[a] *Elliot Marseille, DrPH, MPH,*[b] *Mary Margaret Ajiko, MBchB, MMed,*[c] *and Rochelle A. Dicker, MD*[a,*]

[a] *Department of Surgery, David Geffen School of Medicine, University of California, Los Angeles, California*
[b] *Department of Surgery, Center for Global Surgical Studies, University of California, San Francisco, California*
[c] *Department of Surgery, Soroti Regional Referral Hospital, Soroti, Uganda*

ARTICLE INFO

Article history:
Received 28 February 2019
Received in revised form
26 June 2019
Accepted 16 July 2019
Available online xxx

Keywords:
Health economics
Global surgery
Trauma surgery

ABSTRACT

Background: Surgical disease increasingly contributes to global mortality and morbidity. The Lancet Commission on Global Surgery found that global cost-effectiveness data are lacking for a wide range of essential surgical procedures. This study helps to address this gap by defining the cost-effectiveness of exploratory laparotomies in a regional referral hospital in Uganda.

Materials and methods: A time-and-motion analysis was utilized to calculate operating theater personnel costs per case. Ward personnel, administrative, medication, and supply costs were recorded and calculated using a microcosting approach. The cost in 2018 US Dollars (USD, $) per disability-adjusted life year (DALY) averted was calculated based on age-specific life expectancies for otherwise fatal cases.

Results: Data for 103 surgical patients requiring exploratory laparotomy at the Soroti Regional Referral Hospital were collected over 8 mo. The most common cause for laparotomy was small bowel obstruction (32% of total cases). The average cost per patient was $75.50. The post-operative mortality was 11.7%, and 7.8% of patients had complications. The average number of DALYs averted per patient was 18.51. The cost in USD per DALY averted was $4.08.

Conclusions: This investigation provides evidence that exploratory laparotomy is cost-effective compared with other public health interventions. Relative cost-effectiveness includes a comparison with bed nets for malaria prevention ($6.48-22.04/DALY averted), tuberculosis, tetanus, measles, and polio vaccines ($12.96-25.93/DALY averted), and HIV treatment with multidrug antiretroviral therapy ($453.74-648.20/DALY averted). Given that the total burden of surgically treatable conditions in DALYs is more than that of malaria, tuberculosis, and HIV combined, our findings strengthen the argument for greater investment in primary surgical capacity in low- and middle-income countries.

* *Corresponding author*. Department of Surgery, David Geffen School of Medicine, University of California, 10833 Le Conte Avenue, 72-215 CHS Los Angeles, CA 90095. Tel.: +(310) 825 1485; fax: +(310) 825 0189.
E-mail address: RDicker@mednet.ucla.edu (R.A. Dicker).
0022-4804/$ – see front matter © 2019 Elsevier Inc. All rights reserved.
https://doi.org/10.1016/j.jss.2019.07.037

Introduction

Surgical disease increasingly contributes to global mortality and morbidity, particularly in low- and middle-income countries (LMICs).[1] Estimates suggest that 11% of the entire global burden of disease can be treated with surgery.[2,3] There are an estimated 1.8 million preventable deaths yearly from surgical disease in LMICs. The total burden associated with surgically treatable conditions in LMICs is 401 million disability-adjusted life years (DALYs): more than that of ischemic heart disease, HIV, malaria, and tuberculosis combined.[3,4] The Lancet Commission on Global Surgery projected that between 2015 and 2030, in the absence of urgent scaleup of surgical care, LMICs would face an estimated loss in economic productivity of $12.3 trillion (2010 U S. Dollars) due to surgical conditions, in large part due to injuries.[5]

Surgical care is often perceived to be cost-prohibitive, although there is little data to support this notion.[6] Scaling up basic surgical care (emergency and essential surgical care available at first-level hospitals) could prevent 1.4 million deaths per year in LMICs, including approximately 30 million avertable DALYs per year in sub-Saharan Africa alone.[4] In 2016, O'Neill *et al.* proposed that cesarean delivery, laparotomy, and open treatment of fractures should be standard procedures performed at first-level hospitals.[7] We believe that the argument for investing in surgical capacity building can be further strengthened with concrete data about the cost-effectiveness of these three procedures, known as "Bellwether procedures."

Exploratory laparotomy has been thought of as a cost-effective surgical procedure that addresses a large public health burden.[8] However, cost-effectiveness estimates for emergency surgical procedures in LMICs, such as exploratory laparotomy, are difficult to find.[9] The 2015 Lancet Commission on Global Surgery found that there is a paucity of adequate cost-effectiveness analyses of surgery in LMICs, and called for further cost and financing focused global surgery research.[10] Moreover, cost-effectiveness analyses of surgical procedures in LMICs are sometimes limited because they rely on estimates from the literature or other nonprimary data sources.[6] In this study, we sought to fill this gap in knowledge by conducting a cost-effectiveness analysis of exploratory laparotomy in a regional referral hospital in Eastern Uganda. We specifically sought to determine the incremental cost-effectiveness ratio of exploratory laparotomies compared with the status quo in this setting, which is alternative medical management with likely poor and probably fatal outcomes.

Methods

Research setting

This prospective observational economic analysis was conducted at Soroti Regional Referral Hospital (SRRH), one of 13 regional hospitals in Uganda, with a catchment area of approximately two million people (about 5% of the Ugandan population). The hospital participates in a countrywide decentralization model. It has 247 beds, serves 21,000 inpatients and 103,000 outpatients yearly, and has one operating theater with three operating tables. There are separate male and female surgical wards, gynecology, and obstetrics wards. The surgical unit of the hospital is staffed by rotating teams of medical officers and six to eight intern doctors. There are one to two attending general surgeons, two attending gynecological surgeons, and three nurse anesthetists.

This study received ethical approval by the Institutional Review Board at the University of California, Los Angeles, and by SRRH. Oral consent was obtained from all patients in their native language before surgery.

Patients

All patients undergoing an exploratory laparotomy between February and April 2017 and between June and December 2018 were included in this study. Both emergency and planned exploratory laparotomy patients were included. There were no exclusion criteria. Basic patient demographics, cause for surgery, and complications were recorded. Postoperative data were collected until discharge or death in the hospital.

Cost data collection

Costs in this study were those incurred by the health provider, SRRH.

Surgical personnel costs

A time and motion analysis was utilized to measure costs associated with staff directly involved in each patient's operation. A data entry form with 10 sequential steps (Table 1) starting from entry to the operating theater to transport back to the ward and theater cleanup was used. Each member of the surgical team was categorized as an attending physician, medical officer, intern, nurse anesthetist, nurse, or theater assistant. The total time taken for each step was recorded and it was noted which members of the surgical team were involved in each step. The total time per personnel were summed to calculate the time each provider spent on the case. We therefore determined and utilized only the specific time personnel spent on each case in our cost calculations. Surgeons' nonoperative time was not included in our calculations.

The total time in person-hours per personnel category was multiplied by their respective hourly wages. To calculate hourly wages, we assumed all personnel salaries were based on a 40-h work week.

Ward personnel costs

Ward personnel costs consisted of nurse staffing wages for the day, evening, and night shifts. The number of nurses per shift was averaged in each ward over the course of the study. The average day, evening, and night shift costs per ward were summed to determine the average staffing cost per day. This was divided by the average daily ward patient count to yield a daily cost per patient, per ward. This was then multiplied by each patient's postoperative length of stay in their respective ward to yield the cost of their time in the ward.

Table 1 – Processes comprising the time and motion analysis.

Stage	Activity	Typical staff
Preoperative	1. Transport to waiting area	Intern, attendants
	2. Time in waiting area	Intern, nurse anesthetists
Surgery	3. Pre-Op: Transport of patient into operating room, position, sterile prep, and draping	Medical officer, intern, nurse anesthetists, nurse assistants
	4. Intra-Op: From incision to start of closing	All OR staff
	5. Closure and extubation	All OR staff
	6. Clean-up and transport to recovery	Intern, nurse anesthetists
Postoperative	7. Write post-op report and orders	Surgeon, medical officer, or intern
	8. Time in recovery area	Intern, nurse anesthetist
	9. Transport to ward and transfer to bed	Attendants
	10. OR cleanup	Theater assistant

OR = operating room.

Supply and medication costs

All disposable supplies used during surgery, such as sutures, gauze, nasogastric tubes, and abdominal mops, were recorded on the time and motion form. No specific instrument sets or specialized tools, such as staplers for bowel anastomoses, are utilized in this setting. All intravenous anesthetics, medications, and fluids used were also recorded. Postoperative medications through each patient's stay were also recorded. The cost per unit of each supply and medication was obtained from a 2014 Uganda National Medical Stores cost list. Uganda National Medical Stores is the government organization mandated to procure, store, and distribute medications and consumable health-related items to all government hospitals, such as SRRH. The total medication and supply costs were summed and then averaged across every study patient.

Administrative and ancillary staff costs and other costs

SRRH administrative and ancillary staff costs were estimated using the patient-day equivalents method.[11] The total daily salary for all administrative and ancillary staff was divided by the average number of patients in the hospital each day to yield the daily cost per patient. This was then multiplied by the number of days the study patient stayed in the ward.

Janitorial and maintenance staff costs were included in the above calculations. Costs for water and electricity were omitted from this study. Although the billing department was able to provide a net hospital cost, they were unable to isolate usage rates of the operating theater. Dividing the total cost among each patient in the hospital, the variable number of their family/attendants living on the hospital grounds, and the hospital staff yielded a daily value on the order of a fraction of a cent. Thus, water and electricity costs were not included.

Disability-adjusted life years averted

DALYs averted were calculated based on expert opinions that presenting conditions would be fatal without surgery. All patients were assigned postoperative disability weights based on the opinions of two experienced surgeons to account for potential complications. The DALYs averted are a function of the age-specific life expectancy for each patient. To see whether our results were sensitive to assumptions about survival in the absence of exploratory laparotomy, a second cost-effectiveness ratio (CER) was calculated with a conservative assumption that all patients receiving an operation for appendix-related conditions received no survival benefit for surgery, such that these cases had zero DALYs averted. Additional CERs were calculated with the even more conservative assumptions that in addition to appendix surgery, all obstetrics/gynecology (OB/GYN), bowel obstruction, and trauma patients had zero DALYs averted.

Finally, to see whether our calculations were sensitive to assumptions on surgical personnel salaries, we also calculated CERs where the salaries of attending physicians, medical officers, and interns were doubled.

We used a 3% discount rate in our calculations, which is the rate that has been recommended and used by many other studies.[12,13]

Results

Patient characteristics and diagnoses

Over the study period, 103 patients were enrolled. Fifty-six were female and 47 were male, with a median age of 32 (interquartile range = 20, 45.5; Table 2). Nineteen patients were under 18 y old. There were 12 (11.7%) deaths while in the hospital, and eight postoperative complications. There were no reoperations. The most common diagnosis (33 patients, 32.1%) was intestinal obstruction (Table 3). This included obstructions secondary to adhesions, volvulus, and congenital band anomalies. Fifteen patients (14.6%) had an obstetric/gynecological condition, including ectopic pregnancies, uterine fibroids, and an invasive mole.

Costs

Surgical personnel costs accounted for 24.4% of the total surgical costs. The mean total surgical person-hours per case

Table 2 – Descriptive patient data.

Total patients (*n*)	103
Male	47
Female	56
Age range	3 wk-82 y
Mean age	32 y (IQR: 20, 45.5)
Children (<18)	19
Deaths	12
Complications	8
Average LOS (d)	6.73 (SD: 1.37)

IQR = interquartile range; LOS = length of stay; SD = standard deviation.

was 601.2 min. The mean surgical personnel cost per case was $18.43 (Table 4). When involved in a case, the average time spent by an attending physician was 117 min, a medical officer 137 min, a first assist intern 136 min, a nurse anesthetist 128 min, an operating room nurse 128 min, and a theater assistant 143 min. An attending physician on average cost $9.43 per patient, a medical officer $5.09, an intern $2.86, a nurse anesthetist $4.07, an operating room nurse $3.07, and a theater assistant $2.54. Attending physicians were involved in 54.4% of procedures.

Ward personnel costs accounted for 20.4% of the total costs. The mean ward personnel cost was $15.41. This was directly correlated to the patient's length of stay. The median length of stay in the hospital was 6 d (interquartile range = 4, 8). In general, daily ward costs for female patients were greater than for male patients because of higher nurse to patient ratios in the female wards. The average daily staffing cost per patient in the male surgical ward was $1.87, $2.46 in the female surgical ward, $2.57 in the obstetrics ward, and $3.40 in the gynecology ward.

The cost of medications was 21.4% of the total costs. The average medication cost per patient was $16.15. This included both intraoperative and postoperative medications. The medication used most was metronidazole (1027 total doses), followed by ceftriaxone (409 total doses), normal saline (394 total doses), and tramadol (322 total doses). Supply costs accounted for 19.7% of the total cost. The average supply cost per operation, which included sutures, gauze, catheters, and other miscellaneous items was $14.86. The largest surgical supply cost was for sutures.

The administrative and ancillary support staff cost per patient was $10.64, 14.1% of the average total surgical cost.

Cost per DALY averted

The mean total cost of exploratory laparotomy was $75.50. The average number of discounted DALYs averted was 18.51. The average cost per DALY averted was $4.08.

In the scenario where all appendix-related cases received no survival benefit, the CER calculated was $4.69/DALY averted. With the assumption that all OB/GYN-related cases additionally had zero DALYs averted, the CER was $5.74/DALY averted. Finally, with the even more conservative assumption that there was no survival benefit derived from any bowel obstruction case, the CER was $11.06/DALY averted and $13.70/DALY averted if all trauma cases were also assumed to have no survival benefit.

Under the assumption that all cases had a survival benefit, if the salary of attending physicians was doubled, the average cost per DALY averted was $4.36. If salaries of medical officers and interns were doubled in addition to this, the average cost per DALY averted was $4.72.

Discussion

In this study, we estimated the costs associated with and cost-effectiveness of conducting exploratory laparotomy in Eastern Uganda. To our knowledge, this was the first study to define the costs and cost-effectiveness of this procedure in an LMIC setting.

Surgical personnel costs were the largest single contributor to overall costs. A shortage of surgeons in the country demands that medical trainees provide the bulk of care at government hospitals.[14] Uganda has less than one trained surgeon, anesthesiologist, and obstetrician per 100,000

Table 3 – Length of stay and mortality by cause of surgery (*n* = 103).

Cause of surgery	Frequency (%)	Length of stay (d) Mean (SD)	Mortality Frequency (%)*
Bowel obstruction	33 (32%)	7.24 (3.21)	5 (15%)
Appendix	11 (11%)	8.09 (2.77)	0
Gut perforation	6 (6%)	5.33 (2.16)	2 (33%)
Intussusception	11 (11%)	6.73 (6.99)	0
Penetrating trauma	4 (4%)	5.00 (2.83)	1 (25%)
Mass/tumor	5 (5%)	9.00 (8.51)	0
OB/GYN condition	15 (15%)	4.20 (1.37)	1 (7%)
Blunt trauma	5 (5%)	5.60 (2.51)	1 (20%)
Other	13 (13%)	7.92 (7.25)	2 (15%)

SD = standard deviation.
* The percentages in this column represent the percentage of cases that died linked to the indicated cause of surgery.

Table 4 – Average costs and surgical personnel time per case (n = 103).

Cost	USD per case	Time (min)
Ward personnel	15.41	
Medications	16.15	
Supplies	14.86	
Administrative	10.64	
Surgical personnel* costs	18.43	
Consultant	9.43	117.2
Medical officer	5.09	137.3
First assist intern	2.86	135.7
Second assist intern	2.46	116.6
Nurse anesthetist	4.07	128.3
OR nurse	3.07	127.8
Theater assistant	2.54	142.7
Total	75.50	

OR = operating room.
* Not all surgical personnel roles were involved in every case.

population.[15] This forced reliance on trainees helps contain personnel costs. At SRRH the interns are provided with housing near the hospital, eliminating housing expenses. Drugs are bought in bulk by the Ministry of Health and supplied to each hospital, minimizing medication costs. The absence of specialized instruments—compared with expensive implants/tools used in more subspecialized surgeries—also helps to contain the cost of laparotomy compared with other types of surgery.[11,16]

Most patients were under 40 y old, at an age of economic viability. Although this study did not take into account the economic impact averted by surgery, without surgical treatment, the disproportionate loss of young and productive individuals can have a notable impact on patients' families and communities. There is a palpable burden placed on individuals and households, especially in lower economic strata.[17] On a broader scale, surgical conditions could reduce LMICs' annual GDP growth by almost 2% by 2030. Without investment in surgical services, LMICs are projected to lose up to $12.3 trillion in lost economic productivity between 2015 and 2030.[10]

Our data show that in the context of other common global health interventions, exploratory laparotomies are highly cost-effective. This includes bed nets for malaria prevention ($6.48-22.04/DALY averted), tuberculosis, tetanus, diphtheria, pertussis, measles, and polio vaccines ($12.96-25.93/DALY averted), and HIV treatment with multidrug antiretroviral therapy ($453.74-648.20/DALY).[6,18] These data are consistent with existing data on the cost-effectiveness of surgery in LMICs. Similar CERs have been reported with inguinal hernia repair at $12.88/DALY averted in Ghana, cesarean delivery at $18 and appendectomy at $36 in Guinea, and cataract repair at $5.06 in Nepal.[19-21]

In light of the 2015 World Health Assembly Resolution 68.15, it is critical that the cost-effectiveness of general surgery procedures such as exploratory laparotomy is recognized.[22] Mock *et al.* designated exploratory laparotomy within a category of surgical procedures that have a large public health burden, have high treatment success, and are feasible to promote globally.[8] Economic analyses like this, in tandem with WHA68.15, further exemplify how surgery has increasingly little reason to be the "neglected stepchild of global health."[6,23]

This study had several limitations. It was a single-center study, and generalization of our findings may therefore be limited. In addition, there was unreliable reporting on inhaled anesthetic (halothane) and oxygen usage by nurse anesthetists, and thus these costs were not included. Each halothane canister cost $15.30 and was used until completion for multiple surgical procedures. As such, their inclusion in our cost calculations would have a negligible effect. Equipment costs were also not included given that there are no specific surgery kits and that instruments are used far beyond their expected longevity. While a follow-up survey was conducted, we did not incorporate estimations of costs associated with follow-up care or returns to hospital because of the low volume of participants. Lack of follow-up likely also underestimates true mortality and complication rates. Finally, although we assumed all personnel were paid a fixed salary for a 40-h work week, if they actually work significantly more or less than 40 h every week the hourly wages we used in our calculations will not be accurate and this inevitably affects our CER. We attempted to address this potential limitation by doing additional cost analyses in which we doubled the salaries of surgical personnel. Even in these analyses, we found that the CER remained favorable.

Conclusions

This study found the cost-effectiveness ratio of exploratory laparotomy to be $4.08 per DALY averted in the Ugandan context, and provides information on the direct medical costs associated with the procedure. Although there was already reason to believe that laparotomies are an important procedure to be available in this setting, our findings further strengthen the case for building and supporting capacity for these surgeries. This study can serve to advocate for increased funding toward delivery of surgical care commensurate with the surgical disease burden in this setting.

Acknowledgment

This work was supported by the UCLA Center for World Health and the UCSF Center for Global Surgical Studies.

Authors' contributions: N.B., G.M., C.D.B., C.J., E.M., M.M.A., and R.A.D. were responsible for study concept and design. N.B., C.D.B., and A.H.W. were responsible for acquisition and interpretation of data under the supervision and support of G.M., F.K., C.J., E.M., M.M.A., and R.A.D. N.B. and G.M. drafted the initial manuscript with critical revision by A.H.W., F.K., C.J., E.M., M.M.A., and R.A.D. All authors have given final approval and agree to be accountable for all aspects of the work.

Disclosure

The authors report no proprietary or commercial interest in any product mentioned or concept discussed in this article. The authors have no competing interests to declare.

REFERENCES

1. Meara JG, Hagander L, Leather AJM. Surgery and global health: a Lancet commission. *Lancet*. 2014;383:12–13.
2. Ozgediz D, Jamison D, Cherian M, McQueen K. The burden of surgical conditions and access to surgical care in low-and middle-income countries. *Bull World Health Organ*. 2008;86:646–647.
3. Debas HT, Gosselin R, McCord C, Thind A. Surgery. In: *Disease Control Priorities in Developing countries*. Washington, DC: The International Bank for Reconstruction and Development/The World Bank; 2006.
4. Bickler SN, Weiser TG, Kassebaum N, et al. *Global burden of surgical conditions*. In: *Essential Surgery: Disease Control Priorities*. 3rd ed 1. Washington (DC): The International Bank for Reconstruction and Development/The World Bank; 2015.
5. Meara JG, Leather AHL. *Global surgery 2030 investing in surgical and anaesthesia care*; 2015. http://docs.wixstatic.com/ugd/346076_23b4c3a24c594888a8f0e077195dc5d8.pdf. Accessed January 25, 2019.
6. Chao TE, Sharma K, Mandigo M, et al. Cost-effectiveness of surgery and its policy implications for global health: a systematic review and analysis. *Lancet Glob Health*. 2014;2:e334–e345.
7. O'Neill KM, Greenberg SLM, Cherian M, et al. Bellwether procedures for monitoring and planning essential surgical care in low- and middle-income countries: caesarean delivery, laparotomy, and treatment of open fractures. *World J Surg*. 2016;40:2611–2619. https://doi.org/10.1007/s00268-016-3614-y.
8. Mock C, Cherian M, Juillard C, et al. Developing priorities for addressing surgical conditions globally: furthering the link between surgery and public health policy. *World J Surg*. 2010;34:381–385.
9. Prinja S, Nandi A, Horton S, Levin C. Costs, effectiveness, and cost-effectiveness of Selected surgical procedures and Platforms 18. *Essential Surgery: Disease Control Priorities*. 2015;1:317–338.
10. Meara JG, Leather AJM, Hagander L, et al. Global Surgery 2030: evidence and solutions for achieving health, welfare, and economic development. *Lancet*. 2015;386:569–624.
11. Kramer EJ, Shearer DW, Marseille E, et al. The cost of intramedullary nailing for femoral shaft fractures in dar es salaam, Tanzania. *World J Surg*. 2016;40:2098–2108.
12. Siegel JE, Weinstein MC, Russell LB, Gold MR. Recommendations for reporting cost-effectiveness analyses. *J Am Med Assoc*. 1996;276:1253–1258.
13. Lea RA. World development report 1993: "investing in health. *Forum Dev Stud*. 1993.
14. Ozgediz D, Galukande M, Mabweijano J, et al. The neglect of the global surgical workforce: experience and evidence from Uganda. *World J Surg*. 2008;32:1208–1215.
15. Holmer H, Lantz A, Kunjumen T, et al. Global distribution of surgeons, anaesthesiologists, and obstetricians. *Lancet Glob Health*. 2015;3:S9–S11.
16. Warf BC, Alkire BC, Bhai S, et al. Costs and benefits of neurosurgical intervention for infant hydrocephalus in sub-Saharan Africa. *J Neurosurg Pediatr*. 2011;8:509–521.
17. El Tayeb S, Abdalla S, Heuch I, Van den Bergh G. Socioeconomic and disability consequences of injuries in the Sudan: a community-based survey in Khartoum State. *Inj Prev*. 2015;21:e56–e62.
18. Laxminarayan R, Chow J, Shahid-Salles SA. Intervention cost-effectiveness: overview of main messages. In: *Dis Control Priorities Developing Countries*. 2nd ed. Washington (DC): World Bank; 2006.
19. Shillcutt SD. Cost-effectiveness of groin hernia surgery in the Western region of Ghana. *Arch Surg*. 2010;145:954.
20. Jha P. The cost-effectiveness of forty health interventions in Guinea. *Health Policy Plan*. 1998;13:249–262.
21. Marseille E. Cost-effectiveness of cataract surgery in a public health eye care programme in Nepal. *Bull World Health Organ*. 1996;74:319–324.
22. World Health Organization. *WHA 68.5 | SIXTY-EIGHTH WORLD HEALTH ASSEMBLY: Strengthening emergency and essential surgical care and anaesthesia as a component of universal health coverage*; 2015. http://apps.who.int/gb/ebwha/pdf_files/WHA68/A68_R15-en.pdf?ua=1. Accessed February 12, 2019.
23. Farmer PE, Kim JY. Surgery and global health: a view from beyond the OR. *World J Surg*. 2008;32:533–536.