

## Appendix 1 (as supplied by the authors): Estimation of parameters for the model

### *Cohort demographics*

Patients' mean age, sex and area of origin were obtained from clinical records collected at the Mosaic Refugee Health Clinic (MRHC). The age of symptom onset was estimated using a normal distribution that had the same range and standard error described in a longitudinal study of schistosomiasis among expatriates in a non-endemic country.[1]

### *Model probabilities*

The probability of a MRHC patient being infected with schistosomiasis was obtained from data collected from 920 patients at the clinic between 2011 and 2016. Based on other data from the MRHC, patients' acceptance of screening and/or treatment was estimated to be 88%. The probability of being infected with either the hepatosplenic form or the urinary form of the disease was approximated by the following method: using information about geographic distribution of types of schistosomiasis, it was assumed that among patients who develop disease, those from Africa would have a baseline 50% probability of developing hepatosplenic disease, and a 50% probability of developing urinary disease. It was assumed patients from Asia would have a 100% probability of developing hepatosplenic disease.[2] Taking into account the proportion of clinic patients who were from Africa (84%) and Asia (16%), this meant overall patients with disease would have a 58% probability of developing the hepatosplenic form, and 42% probability of developing the urinary form.

Probabilities of progression to various forms of active disease, given infection, were obtained from studies that reviewed the findings of consecutive autopsies in areas where schistosomiasis is endemic.[3-5] Others were obtained from clinicians' descriptions of what proportion of individuals infected with schistosomiasis go on to develop symptoms.[6-9] The probability of pyelonephritis progressing to bacteremia was obtained from a study of catheter-associated urinary tract infections.[10] For probabilistic analysis, the model assigned all progression probabilities a triangular distribution, in which the observed probability was the upper limit of the distribution, and zero was the lower limit.

The sensitivity and specificity of the serologic assay for schistosomiasis was obtained from the website of the National Reference Centre for Parasitology, which performs all the tests in Canada. [11] The probability of cure with praziquantel was obtained from the longitudinal study describe above, and modelled using a normal distribution that had the same mean and standard deviation as reported.[1]

### *Treatment pathways*

It was assumed that certain complications of schistosomiasis would resolve after treatment in hospital, while others would require community follow-up. The first group included: malabsorption; CNS involvement; pyelonephritis; hydronephrosis; and genital infection without secondary infertility.

It was assumed the remaining complications of schistosomiasis would require community follow-up with a family doctor, and in some cases a specialist. These included: ascites; variceal hemorrhage (if the patient survived the first episode of bleeding); pulmonary hypertension; cor

pulmonale; glomerulonephritis; bladder carcinoma, and infertility. For patients who became infertile after a genital infection, it was assumed they would spend 4.1 years being treated. This has been reported as the mean time in treatment for Canadian couples.[12]

### Costs

The costs of hospital treatment were calculated using Alberta Health inpatient care costs for hospitals in Alberta, using case mix groups that most closely approximated different complications of schistosomiasis shown in table 1. [13]

**Table 1) Case mix groups associated with schistosomiasis complications**

<b>Schistosomiasis complication</b>	<b>Case Mix Group</b>	<b>Cost (patients age 18-59)</b>
Pulmonary hypertension	Other lung disease	\$23,637
Genital schistosomiasis	Inflammatory disorder of the female reproductive system	\$4,855
CNS involvement	Infection/Inflammation of the CNS	\$38,009
Cor pulmonale	Heart failure without coronary angiogram	\$12,639
Malabsorption	Other gastrointestinal disorder	\$7,386
Variceal hemorrhage	Gastrointestinal hemorrhage	\$7,821
Bladder carcinoma	Malignant neoplasm of urinary system	\$12,366
Glomerulonephritis	Other disorder of kidney/ureter	\$14,065
Pyelonephritis	Upper urinary tract infection	\$6,070
Bacteremia	Unspecified site infection with intervention	\$62,478
Portal hypertension	Cirrhosis	\$17,280

Prices for praziquantel were obtained from two pharmacies that serve a substantial refugee clientele. In a conversation May 25, 2018 David Brewerton, pharmacist at Luke's Drug Mart in Calgary confirmed the mean dose of praziquantel prescribed to refugees seen at the MRHC clinic during 2017 was 960 mg, or 4.8 tablets. This was rounded to 5 tablets. The price his pharmacy would charge to the IFHP for 5 tabs of praziquantel was \$51.19. In a conversation June 11, 2018, Joel Varsava, pharmacist at Pharmacy in Ottawa confirmed his pharmacy would charge \$44.66 to the IFHP for 5 tablets. The difference in prices was due to differences in markup and dispensing fees. These two prices were treated as upper and lower limits, and the cost of praziquantel was modelled in a uniform distribution between the two.

It was necessary to estimate costs of laboratory testing using estimates from labs in countries other than Canada. All testing for schistosomiasis is done at Canada's National Reference Centre for Parasitology (NRCP), however the NRCP could not provide the authors with an estimate of the cost of testing, nor does the NRCP charge clients for schistosomiasis testing. However, in a conversation on February 1, 2018 the laboratory director, Dr. Momar Ndao, suggested the true cost to the lab would be comparable to what it is for other national laboratories. The authors contacted two laboratories. In an email sent May 24, 2018, Jayne Jones of the Liverpool School of Tropical Medicine confirmed the internal cost of the ELISA assay for schistosomiasis at the School's laboratory was £35.71. In an email sent June 13, 2018, the department of public inquiries for the CDC's Division of Parasitic Diseases and Malaria confirmed the internal cost of the same assay at its laboratory was \$67.00 USD. These amounts were converted to Canadian dollars. These two prices were treated as upper and lower limits,

and the cost of the schistosomiasis screening test was modelled in a uniform distribution between them.

There are no published studies of ongoing per-patient care costs for specific complications of schistosomiasis, in Canada or comparable countries. So resource use for community follow-up was estimated, where possible, using published estimates of the cost of care for conditions that were similar to complications of schistosomiasis. Costs published in prior years were adjusted to 2019 dollars using the Consumer Price Index.[14] These are summarized in table 1. We could not identify a published estimate of the cost of long-term follow-up of esophageal varices, so we modelled the cost based on the recommendations of a clinical care guideline. It was assumed patients would require only 1 visit per year each with their family and specialist physicians. It was also assumed they would require the minimum drug therapy recommended in the management guideline. These are summarized in table 2.

Table 1) Estimates of cost of care for certain conditions

Schistosomiasis complication	Analogous condition	Adjusted annual cost	Reference
Infertility	Infertility	\$16,181	[15]
Bladder cancer	Bladder cancer	\$23,612	[16]
Portal hypertension	Decompensated cirrhosis	\$2,776	[17]
Cor pulmonale	Congestive heart failure	\$1,627	[18]
Pulmonary hypertension	Pulmonary hypertension	\$245	[19]
Variceal hemorrhage	See tables 2 & 3	\$909	[20-24]

Table 2) Guideline-based care for community follow-up of variceal hemorrhage

Condition	Annual visits	Medications	Annual Tests & Procedures*	Reference
Variceal hemorrhage	Family physician, gastroenterologist	Propanolol 200 mg po daily	CBC, electrolytes, esophagogastrosocopy	[20, 21]

\*CBC = complete blood count

For follow-up of varices, the following costs were applied to the guideline recommendation.

Table 3) Costs used to estimate follow-up care

Item	Cost	Reference
Family physician visit	\$51.37	[22]
Consult – gastroenterologist	\$119.96	[22]
Propanolol 200 mg per day	\$0.26	[23]
Complete Blood Count	\$8.27	[24]
Electrolytes	\$7.76	[24]
Esophagogastrosocopy	\$572.27	[22]

### *Survival times*

The base life expectancy used in the model was derived from the Canadian life table published by Statistics Canada in 2015.[25] A study of mortality rates among Canadian refugees shows they are lower than for average Canadians, with a standardized mortality ratio of 0.48 for men and 0.58 for women [26]. To allow for the lower annual mortality observed among refugees, annual mortality rates were multiplied by the mean SMR of 0.53. To calculate life expectancies for patients with complications of schistosomiasis, survival times for different complications were extrapolated from several studies that followed patients’ survival with portal hypertension, pulmonary hypertension, cor pulmonale, glomerulonephritis, or bladder cancer.[27-31] Using Stata 15 software, different hazard functions (Gompertz, Exponential,

Lognormal, Loglogistic and Weibull) were fit to survival study data.[32] Akaike and Bayes information criteria were used to choose which function types had the best fit to the data for each disease. The hazard functions for each disease were then extrapolated fifty years forward. For each condition, a life table was constructed by incorporating the calculated disease-specific hazard functions into the modified Statistics Canada life table, following a method published elsewhere.[33] In a given year of life, the table used either the baseline risk of death, or the disease-specific risk of death, whichever was greater. Disease-specific life expectancies for patients were then obtained from each life table.

### Utilities

Utility weights for all health states, except infertility, were calculated following the method described by Sullivan *et al.* [34] For each condition, utility decrements were subtracted from the mean utility weight (0.88) for adults age 35-49. Additional decrements were subtracted for individuals with multiple comorbid conditions. Because Sullivan *et al* do not describe disease states that precisely match different complications of schistosomiasis, states that were analogous to complications of schistosomiasis were used. The disutility for infertility was obtained from a separate study.[35] These are described in table 5.

Table 5) Disease states and associated utility decrements

Schistosomiasis complication	Analogous health state	Disutility	Standard error	Reference
CNS involvement	Acute cerebrovascular disease	0.0483	0.0009	[34]
Cor pulmonale	CHF, nonhypertensive	0.0546	0.0010	[34]
Malabsorption	Other gastrointestinal disorders	0.0315	0.0005	[34]
Variceal hemorrhage –	Gastric ulcer	0.0269	0.0002	[34]
Glomerulonephritis	Other diseases of the kidney	0.0544	0.0011	[34]
Ascites	Other liver diseases	0.0184	0.0013	[34]
Pulmonary hypertension	Other lung disease	0.0428	0.0002	[36]

Infertility	Infertility	0.070	-	[35]
Bladder carcinoma	Unspecified neoplasm	0.0174	0.0001	[36]
Pyelonephritis	Other diseases of the kidney	0.0544	0.0011	[34]
Genital schistosomiasis	Other female genital disorders	0.015	0.0007	[34]

With the standard errors shown above, disutilities were modelled in a gamma distribution using the methods of moments, following the recommendation of Briggs, Claxton and Sculpher. [37]

## References

- 1 Whitty, C.J., et al., Presentation and outcome of 1107 cases of schistosomiasis from Africa diagnosed in a non-endemic country. *Trans R Soc Trop Med Hyg*, 2000. 94(5): p. 531-4.
- 2 WHO. Schistosomiasis Fact Sheet. 2017 January 2017 [cited 2017 July 3]; Available from: <http://www.who.int/mediacentre/factsheets/fs115/en/>.
- 3 Smith, J.H., et al., A Quantitative Post Mortem Analysis of Urinary Schistosomiasis in Egypt. *The American Journal of Tropical Medicine and Hygiene*, 1974. 23(6): p. 1054-1071.
- 4 Cheever, A.W. and Z.A. Andrade, Pathological lesions associated with schistosoma mansoni infection in man. *Transactions of the Royal Society of Tropical Medicine and Hygiene*, 1967. 61(5): p. 626-639.
- 5 Gelfand, M., et al., Distribution and extent of schistosomiasis in female pelvic organs, with special reference to the genital tract, as determined at autopsy. *Am J Trop Med Hyg*, 1971. 20(6): p. 846-9.
- 6 Prata, A., Infection with *S. mansoni*, in *Schistosomiasis: Epidemiology, Treatment and Control*, P. Jordan and G. Webbe, Editors. 1982, William Heinemann Medical Books: London. p. 105-127.
- 7 Reboucas, G., Clinical aspects of hepatosplenic schistosomiasis: a contrast with cirrhosis. *Yale J Biol Med*, 1975. 48(5): p. 369-76.
- 8 Saad, A.M., et al., Oesophageal varices in a region of the Sudan endemic for *Schistosoma mansoni*. *Br J Surg*, 1991. 78(10): p. 1252-3.
- 9 Andrade, Z.A., The situation of hepatosplenic schistosomiasis in Brazil today. *Memórias do Instituto Oswaldo Cruz*, 1998. 93: p. 313-316.
- 10 Stamm, W.E., Catheter-associated urinary tract infections: epidemiology, pathogenesis, and prevention. *Am J Med*, 1991. 91(3b): p. 65s-71s.

- 11 NRC. Immunodiagnostic Services. 2018 [cited 2018 May 22]; Available from: [www.mcgill.ca/tropmed/services/national-reference-centre-parasitology/immunodiagnostic-service](http://www.mcgill.ca/tropmed/services/national-reference-centre-parasitology/immunodiagnostic-service).
- 12 Collins, J.A., E.A. Burrows, and A. Willan, Infertile couples and their treatment in Canadian academic infertility clinics, in Royal Commission on New Reproductive Technologies, Treatment of Infertility: Current Practices and Psychological Implications. 1993, Ministry of Supply and Services Canada: Ottawa. p. 243.
- 13 Alberta Health. Hospital Inpatient Care Costs. Available from: [http://www.ahw.gov.ab.ca/IHDA\\_Retrieval/redirectToURL.do?cat=201&subCat=770](http://www.ahw.gov.ab.ca/IHDA_Retrieval/redirectToURL.do?cat=201&subCat=770)
- 14 Statistics Canada. Table 18-10-0005-01 Consumer Price Index, annual average, not seasonally adjusted. [cited 2020 May 9]; Available from: <https://www150.statcan.gc.ca/t1/tbl1/en/tv.action?pid=1810000501>
- 15 Collins, J.A., The cost of infertility diagnosis and treatment in Canada in 1995. Human Reproduction, 1997. 12(5): p 951-958.
- 16 De Oliveira, C., et al, Estimating the cost of cancer care in British Columbia and Ontario: a Canadian inter-provincial comparison, 2017. 12(3): p. 95-108
- 17 Krajden, M., et al, Health care costs associated with Hepatitis C: a longitudinal cohort study. Can J Gastroenterol, 2010. 24(12): p. 717-726
- 18 Cui Y., Economic evaluation of Manitoba health lines in the management of congestive heart failure, 2013. 9(2): p 36-50.
- 19 Coyle, K., et al., Cost effectiveness of first-line oral therapies for pulmonary arterial hypertension: a modelling study. Pharmacoeconomics, 2016. 34: p. 509-520.
- 20 Garcia-Tsao, G., et al., Portal hypertensive bleeding in cirrhosis: Risk stratification, diagnosis, and management: 2016 practice guidance by the American Association for the study of liver diseases. Hepatology, 2017. 65(1): p. 310-335.
- 21 European Association for the Study of the Liver, EASL Clinical Practice Guidelines: Vascular diseases of the liver. J Hepatol, 2016. 64(1): p. 179-202.
- 22 Alberta Health Care Insurance Plan: Schedule of Medical Benefits. [Internet] 2018; Available from: <https://open.alberta.ca/publications/somb-2017-04-01>.
- 23 Alberta Drug Benefit List. 2018; Available from: <https://www.ab.bluecross.ca/dbl/publications.html#dbl>.
- 24 Schedule of Benefits for Laboratory Services. [Internet] 2017; Available from: [http://www.health.gov.on.ca/en/pro/programs/ohip/sob/lab/lab\\_mn.pdf](http://www.health.gov.on.ca/en/pro/programs/ohip/sob/lab/lab_mn.pdf).
- 25 Statistics Canada. Life Tables, Canada, Provinces and Territories (2010-2012, no. 6). 2017 [cited 2017 July 8]; Available from:

[http://www.statcan.gc.ca/access\\_acces/alternative\\_alternatif.action?loc=/pub/84-537-x/2016006/2016006-eng.xlsx](http://www.statcan.gc.ca/access_acces/alternative_alternatif.action?loc=/pub/84-537-x/2016006/2016006-eng.xlsx).

- 26 Gold, J., et al., Disparities in mortality patterns among Canadian immigrants and refugees, 1980-1998: results of a national cohort study. *Journal of Immigrant Health*, 2005. 7(4): p. 221-231.
- 27 Heaf, J., H. Løkkegaard, and S. Larsen, The epidemiology and prognosis of glomerulonephritis in Denmark 1985–1997. *Nephrology Dialysis Transplantation*, 1999. 14(8): p. 1889-1897.
- 28 Oswald-Mammosser, M., et al., Prognostic Factors in COPD Patients Receiving Long-term Oxygen Therapy: Importance of Pulmonary Artery Pressure. *Chest*, 1995. 107(5): p. 1193-1198.
- 29 Ehdaie, B., et al., Comparative Outcomes of Pure Squamous Cell Carcinoma and Urothelial Carcinoma With Squamous Differentiation in Patients Treated With Radical Cystectomy. *The Journal of urology*, 2012. 187(1): p. 74-79.
- 30 Opitz, C.F., et al., Pre-Capillary, Combined, and Post-Capillary Pulmonary Hypertension: A Pathophysiological Continuum. *Journal of the American College of Cardiology*, 2016. 68(4): p. 368-378.
- 31 Siramolpiwat, S., et al., Idiopathic portal hypertension: natural history and long-term outcome. *Hepatology*, 2014. 59(6): p. 2276-85.
- 32 StataCorp, Stata Statistical Software. 2017, StataCorp LLC: College Station, TX.
- 33 Gaitatzis, A., et al., Life expectancy in people with newly diagnosed epilepsy. *Brain*, 2004. 127(Pt 11): p. 2427-32.
- 34 Sullivan, P.W., W.F. Lawrence, and V. Ghushchyan, A National Catalog of Preference-Based Scores for Chronic Conditions in the United States. *Medical Care*, 2005. 43(7): p. 736-749.
- 35 Scotland, G., et al., Minimising twins in in vitro fertilisation: a modelling study assessing the costs, consequences and cost–utility of elective single versus double embryo transfer over a 20-year time horizon. *BJOG: An International Journal of Obstetrics & Gynaecology*, 2011. 118(9): p. 1073-1083.
- 36 Sullivan, P.W. and V. Ghushchyan, Preference-Based EQ-5D Index Scores for Chronic Conditions in the United States. *Medical Decision Making*, 2006. 26(4): p. 410-420.
- 37 Briggs, A., Sculpher, M., and Claxton, K., Decision modelling for health economic evaluation. 2006, Oxford University Press.