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# Projected impact of mandatory food fortification with folic acid on neurosurgical capacity needed for treating spina bifida in Ethiopia

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**Abstract**

Spina bifida, also known as meningomyelocele, is a major birth defect mostly associated with folate deficiency in the mother early in pregnancy. The prevalence of spina bifida is disproportionately high in Ethiopia compared to the global average; about 10,500 liveborn are affected annually. Many affected infants do not receive timely repair surgery. There are a high number of stillbirths, and neonatal, infant, and under-five deaths. Mandatory fortification of staple foods such as wheat and maize flour with folic acid, a B vitamin, is an effective primary prevention strategy for spina bifida. Survival in those with spina bifida increases if neurosurgical intervention is available soon after birth, along with continuous surgical and clinical aftercare throughout the lifespan. Currently, Ethiopia does not have mandatory food fortification for primary prevention or adequate neurosurgical capacity to meet the need to prevent adverse outcomes associated with spina bifida. We present in this paper two concurrent and complementary policy and practice solutions occurring in Ethiopia through global partnerships: (1) capacity-building of neurosurgery care through training programs; and (2) promoting national mandatory folic acid fortification of staples for primary prevention of spina bifida. These two policy and practice interventions ensure all affected infants can receive timely pediatric neurosurgery and sustained surgical aftercare through required neurosurgeon availability, and ensure primary prevention of spina bifida. Primary prevention of spina bifida frees up significant neurosurgical capacity in resource-poor settings that can then be directed to other critical neurosurgical needs thus lowering child mortality and morbidity.

**KEYWORDS**

fortified foods, health policy, maternal child health, neural tube defects, neurosurgery

## 1 | INTRODUCTION

Recent studies in Ethiopia have brought to attention the high prevalence of spina bifida (Berihu et al., 2018; Gedefaw, Teklu, & Tadesse, 2018), a common and major birth defect affecting the spine. Spina bifida is associated with a high risk of stillbirth and neonatal, infant, and under-five mortality, especially in low- and middle-income countries (Blencowe, Kancherla, Moorthie, Darlison, & Modell, 2018). The majority of cases of spina bifida can be prevented with folic acid, a B vitamin, taken by women before and during early pregnancy, and delivered through supplementation by a pill or folic acid fortification of staple foods (Atta et al., 2016). Children born with spina bifida require life-saving surgery within 48 hours after birth; timely surgical closure of the spinal column improves both survival and quality of life (Spina Bifida Association, 2018). Additionally, multiple surgeries for lesion closure, shunt insertion, and shunt revision are required throughout the lifespan to address complications associated with infections and hydrocephaly (Alabi et al., 2018). Without early surgery and repeated surgical and clinical care, infants with spina bifida typically die by one year of age (Watson, Tye, & Ward, 2014).

The global average of spina bifida prevalence is about one in every 1,000 births (Blencowe et al., 2018). Ethiopia reports a prevalence of 6.5 cases of spina bifida (including live and stillborn cases) per 1,000 births (Berihu et al., 2018; Gedefaw et al., 2018). Approximately 50% of all spina bifida cases result in stillbirths in Ethiopia (Berihu et al., 2018). According to the United Nations, Ethiopia has 3.2 million live births each year. With a prevalence of 6.5 live and stillborn spina bifida cases per 1,000 births, each year, the absolute number of cases in the country would be approximately 21,000, of which 10,500 cases would be live born and an additional 10,500 would be stillborn. The World Health Organization (WHO) recommends one neurosurgeon per 100,000 population; this ratio is unmet in many countries, especially in Africa (Park, Johnson, & Dempsey, 2016). Ethiopia currently does not have enough neurosurgeons to meet this benchmark for its population of 112 million, especially for the pediatric neurosurgical needs for spina bifida care (Mukhopadhyay et al., 2019).

Mandatory fortification of staple foods is an effective intervention which reduced live birth prevalence of spina bifida to 0.3 cases per 1,000 births in countries that have effectively implemented food fortification (Atta et al., 2016). Thus, mandatory fortification of staple foods in Ethiopia can reduce the annual number of live births with spina bifida from the current 10,500 cases to about 1,050; or about 9,000 cases will be averted. The residual 1,050 cases would occur in spite of fortification because spina bifida has other less frequent and largely preventable risk factors (e.g., maternal diabetes, maternal exposure to anti-epileptic medications during pregnancy) (Agopian et al., 2013).

In this manuscript, we present two concurrent and complementary policy and practice solutions that we are actively advocating in Ethiopia: (1) capacity-building of neurosurgery care through training programs for adequate and timely treatment of spina bifida; and (2) a timeline for promoting national mandatory folic acid fortification of staple foods for primary prevention of spina bifida. The study was not based on a research involving human subjects and hence no patient consent was sought.

## 2 | CAPACITY-BUILDING OF NEUROSURGERY CARE THROUGH TRAINING PROGRAMS IN ETHIOPIA

In 2006, there were two neurosurgeons in Ethiopia. To build further neurosurgical capacity, a training program for neurosurgeons was established at Addis Ababa University (AAU) and Myungsung Christian Medical Center in Addis Ababa. The program was a collaboration between AAU, Haukeland University in Bergen, Norway, and the Foundation for International Education in Neurological Surgery (FIENS). The goal of the program was to provide training by Ethiopians for Ethiopians and to retain them in their country, as validated by a study showing very high retention rates of graduates trained in East and South Africa (Hutch et al., 2017).

Spina bifida and hydrocephalus constitute a large proportion (~40%) of neurosurgical need in Ethiopia (Abebe, Munie, & Bekele, 2011). In 2009, the ReachAnother Foundation (RAF) started work in Ethiopia, providing surgical consultation, training, and advocacy for spina bifida.

In 2011, the first three neurosurgeon trainees graduated from the program that was established in 2006. Zewditu Memorial Hospital in Addis Ababa was designated as the third AAU training hospital. By 2015, the number of neurosurgical graduates in Ethiopia had grown to 15. As more infants received spina bifida surgery and survival improved among those affected, the RAF focus shifted to the need for aftercare and primary prevention of spina bifida. The majority of infants born with spina bifida have normal baseline characteristics and normal urinary tract anatomy at birth, but 90% of cases have problems with neurogenic bladders, which result in subsequent urinary tract infection, renal failure, and death (Tanaka et al., 2019). Studies on mortality among individuals with spina bifida from Ethiopia are lacking. A 10-year follow-up study of surgical cases in

Uganda showed 55% long term survival, 78% of deaths occurred in the first 5 years, and death was attributed to "infection and neglect" (Sims-Williams, Sims-Williams, Kabachelor, Fotheringham, & Warf, 2017). Long-term survival is known to depend on a healthcare infrastructure that provides training programs for aftercare nursing and training of intermittent bladder catheterization to reduce the risks (Sims-Williams et al., 2017). 1n 2017, to build capacity for spina bifida care, RAF designed a Center of Excellence program with six Ethiopian universities (AAU, St. Paul University, Gondar University, Hawassa University, Bahir Dar University, and Mekelle University) and their training hospitals. The aim of the program is for each of these universities to provide complete care for at least 1,000 newborn and re-admitted spina bifida cases per year by 2025. The program creates specialized spina bifida and hydrocephaly teams to provide the complex multispecialty treatment for lifespan care.

By 2019, the AAU had graduated 35 neurosurgeons. Two additional training programs, St. Paul University in Addis Ababa, and Mekelle University in Mekelle, began to further increase the number of neurosurgical graduates. The current annual graduation rate of these training institutions is 12 neurosurgeons. Because neurosurgeons attend to a wide variety of surgical cases and duties, it is expected that even with an increasing number of neurosurgeons graduating from the training programs, the increase in capacity for spina bifida surgeries will be limited to 500 cases per year from 2020 onward.

## 3 | A TIMELINE FOR PROMOTING NATIONAL MANDATORY FOLIC ACID FORTIFICATION OF STAPLE FOODS FOR PRIMARY PREVENTION OF SPINA BIFIDA

Ethiopian national nutrition surveys have established a significant insufficiency of blood folate concentrations in 50–80% of women of reproductive age (Ethiopian Public Health Institute, 2016). The lack of adequate folate in the mother's body before and during early pregnancy is directly associated with the high prevalence of spina bifida noted in the country (Berihu et al., 2018; Gedefaw et al., 2018). To address this issue, Ethiopian neurosurgeons have long advocated for public health interventions to prevent spina bifida. The Society of Ethiopian Neurosurgical Professionals was founded in 2017, expanding advocacy for spina bifida prevention. Food fortification of wheat and maize products with folic acid is an established intervention for preventing spina bifida (Centeno Tablante, Pachón, Guetterman, & Finkelstein, 2019). Wheat flour is consumed by 20% of Ethiopians, mostly urban, and has a potential for fortification. Additionally, iodized salt has a potential for fortification with folic acid, as it has a wider coverage and is consumed in the majority of households, reaching both rural and urban areas of the country (UNICEF, 2019).

In 2019, voluntary fortification of wheat flour with folic acid was authorized in Ethiopia. However, a recent systematic review has shown that mandatory fortification is more effective in reducing the prevalence of spina bifida compared to a voluntary policy (Atta et al., 2016). In 2020, mandatory fortification of wheat flour and cooking oils with folic acid was authorized pending parallel development of regulations and industrial capacity building in Ethiopia. However, iodized salt is consumed by majority of households in Ethiopia (UNICEF, 2019). Salt fortification with iodine and folic acid is technically feasible and demonstrated in the lab. Ethiopia is now conducting feasibility and effectiveness studies before fortification of iodized salt with folic acid can be implemented as a public health intervention. We project these studies to take 3–4 years, and policies for fortification to be initiated by 2025. We expect the large-scale production and scale up will require at least 2 years. Accordingly, mandatory fortification of wheat flour and iodized salt with folic acid is projected to go into effect in 2027 reaching complete effectiveness in 2028.

Figure 1 presents a schematic of: (a) progression of current and future neurosurgical capacity in Ethiopia to provide repair surgery and meet ongoing surgical needs for spina bifida, and (b) progression of primary prevention of spina bifida in Ethiopia through food fortification. Line A plots the annual number of spina bifida cases operated since 2011 and projected cases that will need surgery from year 2020 onwards. The lines $A_1$ and $A_2$ represent, respectively, the number of spina bifida cases needing surgeries in two contrasting scenarios, i.e., without ($A_1$), and with ($A_2$), mandatory folic acid fortification of multiple staples (e.g., wheat flour and salt), projected to start between years 2025 and 2027. The numbers in gray squares indicate the number of trained neurosurgeons in Ethiopia per given year. The neurosurgical capacity grows by 12 neurosurgeons per year from year 2020 onwards. Line P is the current live births with spina bifida in Ethiopia estimated based on the knowledge gained in year 2018 through two hospital-based birth defects surveillance studies, one in an urban and another in a rural area (Berihu et al., 2018; Gedefaw et al., 2018). Line $P_1$ is the projected annual number of liveborn spina bifida cases without fortification at the current prevalence rate (Berihu et al., 2018; Gedefaw et al., 2018). Line $P_2$ is the evidence-based expected projection of the number of liveborn spina bifida cases if Ethiopia implements effective and sustained folic acid fortification between

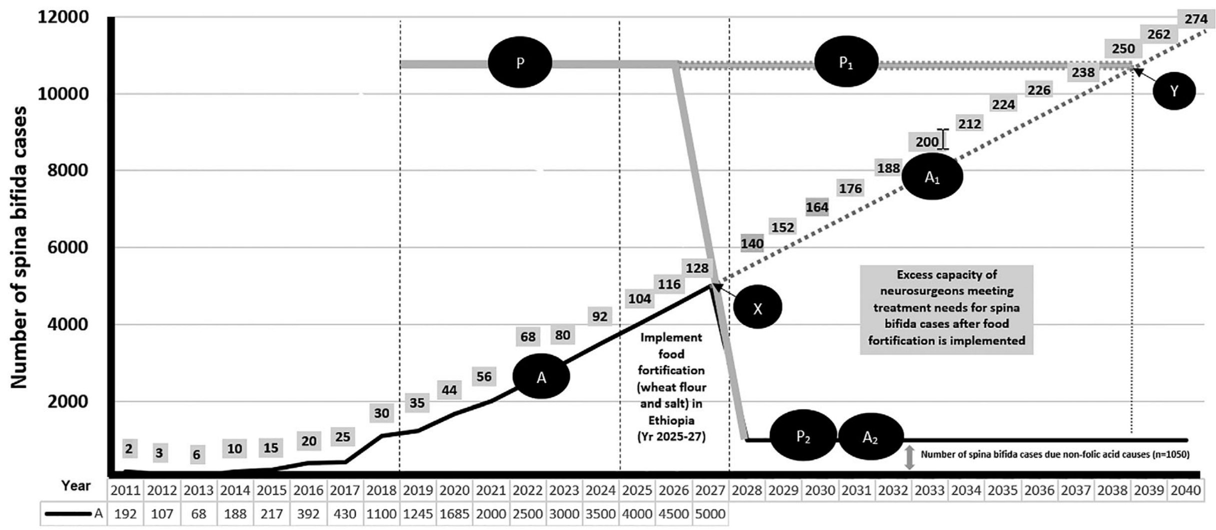


**FIGURE 1** Number of live born spina bifida cases in Ethiopia, and met and unmet need for neurosurgical repair of spina bifida by age 1 year, with and without folic acid fortification, years 2011–2040. Line A = Number of live born spina bifida cases who receive(d) repair surgery for spina bifida within the first year of life in Ethiopia annually from years 2011 to 2027. Line $A_1$ = Without folic acid fortification, the number of live born spina bifida cases who will receive repair surgery for spina bifida within the first year of life in Ethiopia annually from years 2028 to 2040. Line $A_2$ = With folic acid fortification, the number of live born spina bifida cases ($n$ = 1,050 cases each year) who will receive repair surgery for spina bifida within the first year of life in Ethiopia annually from years 2028–2040. Line P = Line P is the number of live births affected by spina bifida in Ethiopia at the prevalence rate of 3.25 cases per 1,000 births (approximately10,500 spina bifida-affected live births). Line P starts in year 2018 as evidence of prevalence was first generated in Ethiopia through two publications in 2018.[1,2] Prior to 2018, there was no published study on the estimate for live birth prevalence of spina bifida. Line $P_1$ = Without folic acid fortification, $P_1$ is the number of live births affected by spina bifida in Ethiopia at the prevalence rate of 3.25 cases per 1,000 births (approximately 10,500 spina bifida-affected live births). Line $P_1$ starts in year 2018 as evidence of prevalence was first generated in Ethiopia through two hospital-based surveillance studies in 2018.[1,2] Line $P_2$ = With folic acid fortification, $P_2$ is the number of live births affected by spina bifida in Ethiopia at a reduced prevalence rate of 0.3 cases per 1,000 births (or 1,095 spina bifida-affected live births based). This prevalence level is based a systematic review and meta-analysis of prevalence of spina bifida in countries with effective mandatory folic acid fortification programs.[4] Node X = If folic acid fortification was implemented and achieved effectiveness in Ethiopia between years 2025 and 2027, the node X will be the point of time when the number of live born cases of spina bifida in Ethiopia needing repair surgery will meet the need with adequate number of neurosurgeons available to conduct repair surgery within first year of birth. Thus, node X is assumed to be achieved in year 2028. Node Y = If folic acid fortification is not implemented in Ethiopia, and the status quo persists, the node Y will be the point of time when the number of live born cases of spina bifida in Ethiopia needing repair surgery will be met with adequate number of neurosurgeons available to conduct repair surgery within first year of life. Thus, node Y is assumed to be achieved in year 2038. Number = Number of neurosurgeons available per given year

years 2025 and 2027, and the policy reaching complete effectiveness by 2028.

The two scenarios presented in Figure 1:

a. *Without fortification*: Maintaining status quo, with no fortification in Ethiopia, the liveborn cases of spina bifida will remain at 10,050 per year. Under this circumstance, the neurosurgical capacity will not be adequate to repair every liveborn with spina bifida in Ethiopia until year 2038, indicated by node Y. For almost two decades before that point, there will be a high proportion of spina bifida cases that will not receive life-saving surgery within 48 hours of birth (as recommended) due to an unmet need of neurosurgeons. During this period, almost all untreated infants will die before one year of age. Additionally, due to this lack of neurosurgical capacity, it will not be possible to meet the need for repeat surgeries or aftercare of future complications for individuals with spina bifida.
b. *With fortification*: Assuming mandatory folic acid fortification of wheat flour and salt is initiated in years 2025–2027 in Ethiopia, reaching maximal effectiveness in 2028 by reaching a majority of women of reproductive age, the number of cases of spina bifida needing surgery and the number of neurosurgeons available will converge in year 2028, indicated by node X on the Figure. The post-fortification era reduction in the annual prevalence of spina bifida will result in about 1,050 new cases per year, and capacity of neurosurgeons will meet the need for both initial repair surgery of all liveborn cases, as well as for

sustained aftercare throughout the lifespan. Fortification will free up significant neurosurgical care capacity that can be directed to other critical neurosurgical needs, lowering child mortality and morbidity.

Currently, neurosurgeons are the de facto caregivers for spina bifida and hydrocephalus in Ethiopia. However, the most effective management of spina bifida is achieved through integrated multi-specialty "Spina Bifida Teams". These teams are actively being developed in Ethiopia, and will significantly improve neurosurgical care and its availability in the future. Neurosurgical care networks such as the International Society for Pediatric Neurosurgery, Cure Neuro, and InterSurgeon are also expanding in the country.

In conclusion, our solutions to address spina bifida issue in Ethiopia include increasing neurosurgical capacity, and simultaneously implementing mandatory fortification of staple foods with folic acid. There is a fierce sense of urgency for food fortification among the Ethiopia's neurosurgeons. Assuming the need for 2 hours of surgery and 2 hours of aftercare by the neurosurgeon per each case of spina bifida, primary prevention through mandatory fortification will save or avoid the need for 37,800 hours (10,500 expected cases without folic acid intervention minus 1,050 observed case after folic acid intervention = 9,450 averted cases and surgeries × 4 hour/surgery = 37,800 averted surgical hours that open up for other surgical care) of neurosurgical care per year in Ethiopia. This is equivalent to about 19 full time equivalent (FTE) (1 FTE = 2,000 surgical care hours) neurosurgeon years. If we further assume that each case requires one additional neurosurgical procedure, the total savings will double to 38 FTE years. This saved time is considerable and can be devoted to other urgent neurosurgical care in the country. Coincidentally, this FTE number is equal to the total number neurosurgeons trained in the first 13 years of training at AAU, and perfectly illustrates the powerful effect of food fortification on neurosurgery manpower capacity. There is a movement among international neurosurgery organizations to make folic acid fortification of staple foods a top priority for meeting the need for and improving the quality of neurosurgical care worldwide (Rosseau, 2020). This effort is in line with the WHO's 2030 Sustainable Development Goals (SDG) to achieve health, welfare, and economic growth, especially in low- and middle-income countries, where more neurosurgeons are urgently needed to meet the capacity for spina bifida care. Mandating folic acid fortification of staple foods, Ethiopia will prevent at least 10,000 infant deaths associated with spina bifida annually, along with an approximately equal number of spina bifida-associated stillbirths (Dixon, Kancherla, Magana, Mulugeta, & Oakley Jr, 2019). Using the solutions presented in this paper for spina bifida prevention and care, Ethiopia can reach their Every Newborn Action Plan goals for stillbirth prevention, and SDG for neonatal- and under-five mortality prevention (Dixon et al., 2019). Our proposed strategy can be applied in many other countries where there is a high prevalence of spina bifida, and no effective fortification programs for primary prevention of these cases.

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## CONFLICT OF INTEREST

The authors have no financial relationships relevant to this article to disclose.

## DATA AVAILABILITY STATEMENT

Data sharing not applicable - no new data generated and the article describes entirely theoretical concepts.

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## REFERENCES

Abebe, M., Munie, T., & Bekele, A. (2011). Pattern of neurosurgical procedures in Ethiopia: Experience from two major neurosurgical centres in Addis Ababa. *East and Central African Journal of Surgery*, *16*(1), 104–110.

Agopian, A. J., Tinker, S. C., Lupo, P. J., Canfield, M. A., Mitchell, L. E., & National Birth Defects Prevention Study. (2013). Proportion of neural tube defects attributable to known risk factors. *Birth Defects Research. Part A, Clinical and Molecular Teratology*, *97*(1), 42–46. https://doi.org/10.1002/bdra.23100

Alabi, N. B., Thibadeau, J., Wiener, J. S., Conklin, M. J., Dias, M. S., Sawin, K. J., & Valdez, R. (2018). Surgeries and health outcomes among patients with spina bifida. *Pediatrics*, *142*(3), e20173730. https://doi.org/10.1542/peds.2017-3730

Atta, C. A., Fiest, K. M., Frolkis, A. D., Jette, N., Pringsheim, T., St Germaine-Smith, C., … Metcalfe, A. (2016). Global birth prevalence of spina bifida by folic acid fortification status: A systematic review and meta-analysis. *American Journal of Public Health*, *106*(1), e24–e34. https://doi.org/10.2105/AJPH.2015.302902

Berihu, B. A., Welderufael, A. L., Berhe, Y., Magana, T., Mulugeta, A., Asfaw, S., & Gebreselassie, K. (2018). High burden of neural tube defects in Tigray, northern Ethiopia: Hospital-based study. *PLoS One*, *13*(11), e0206212. https://doi.org/10.1371/journal.pone.0206212

Blencowe, H., Kancherla, V., Moorthie, S., Darlison, M. W., & Modell, B. (2018). Estimates of global and regional prevalence of neural tube defects for 2015: A systematic analysis. *Annals of* *the new York Academy of Sciences*, *1414*(1), 31–46. https://doi.org/10.1111/nyas.13548

Centeno Tablante, E., Pachón, H., Guetterman, H. M., & Finkelstein, J. L. (2019). Fortification of wheat and maize flour with folic acid for population health outcomes. *The Cochrane Database of Systematic Reviews*, *7*(7), CD012150. https://doi.org/10.1002/14651858.CD012150.pub2

Dixon, M., Kancherla, V., Magana, T., Mulugeta, A., & Oakley, G. P., Jr. (2019). High potential for reducing folic acid-preventable spina bifida and anencephaly, and related stillbirth and child mortality, in Ethiopia. *Birth Defects Research*, *111*(19), 1513–1519. https://doi.org/10.1002/bdr2.1584

Ethiopian Public Health Institute. (2016). *Ethiopian national micronutrient survey report*. Retrieved from https://www.ephi.gov.et/images/pictures/download2009/National_MNS_report.pdf.

Gedefaw, A., Teklu, S., & Tadesse, B. T. (2018). Magnitude of neural tube defects and associated risk factors at three teaching hospitals in Addis Ababa, Ethiopia. *BioMed Research International*, *2018*, 4829023. https://doi.org/10.1155/2018/4829023

Hutch, A., Bekele, A., O'Flynn, E., Ndonga, A., Tierney, S., Fualal, J., … Erzingatsian, K. (2017). The brain drain myth: Retention of specialist surgical graduates in east, central and southern Africa, 1974-2013. *World Journal of Surgery*, *41*(12), 3046–3053. https://doi.org/10.1007/s00268-017-4307-x

Mukhopadhyay, S., Punchak, M., Rattani, A., Hung, Y. C., Dahm, J., Faruque, S., … Park, K. B. (2019). The global neurosurgical workforce: A mixed-methods assessment of density and growth. *Journal of Neurosurgery*, 1–7. https://doi.org/10.3171/2018.10.JNS171723 Advance online publication.

Park, K. B., Johnson, W. D., & Dempsey, R. J. (2016). Global neurosurgery: The unmet need. *World Neurosurgery*, *88*, 32–35. https://doi.org/10.1016/j.wneu.2015.12.048

Rosseau, G. (2020). Global Neurosurgery, WHO and the growing Global Surgery Movement. Retrieved from https://aansneurosurgeon.org/inside-neurosurgeon/global-neurosurgery-who-and-the-growing-global-surgery-movement/.

Sims-Williams, H. J., Sims-Williams, H. P., Kabachelor, E. M., Fotheringham, J., & Warf, B. C. (2017). Ten-year survival of Ugandan infants after myelomeningocele closure. *Journal of Neurosurgery. Pediatrics*, *19*(1), 70–76. https://doi.org/10.3171/2016.7.PEDS16296

Spina Bifida Association. (2018). Guidelines for the care of people with spina bifida. Retrieved from https://www.spinabifidaassociation.org/wp-content/uploads/Guidelines-for-the-Care-of-People-with-Spina-Bifida-2018.pdf.

Tanaka, S. T., Paramsothy, P., Thibadeau, J., Wiener, J. S., Joseph, D. B., Cheng, E. Y., … Baum, M. A. (2019). Baseline urinary tract imaging in infants enrolled in the UMPIRE protocol for children with spina bifida. *The Journal of Urology*, *201*(6), 1193–1198. https://doi.org/10.1097/JU.0000000000000141

UNICEF. (2019). Iodized salt consumption. Retrieved from https://data.unicef.org/resources/dataset/iodized-salt-consumption/.

Watson, J. C., Tye, G., & Ward, J. D. (2014). Delayed repair of myelomeningoceles. *World Neurosurgery*, *81*(2), 428–430. https://doi.org/10.1016/j.wneu.2013.01.022

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