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Pediatricians as champions for ending folic acid-preventable spina bifida, anencephaly globally

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Pediatricians as champions for ending folic acid-preventable spina bifida, anencephaly globally

Timothy G. Singer MD, MS[1], Vijaya Kancherla, PhD[2,3], Godfrey P. Oakley Jr., MD, MSPM, FAAP[2,3,4]

Authors:
1. Department of Neurosurgery, George Washington University School of Medicine and Health Sciences, Washington, D.C., USA
2. Department of Epidemiology, Emory University Rollins School of Public Health, Atlanta, GA, USA
3. Center for Spina Bifida Prevention, Department of Epidemiology, Emory University Rollins School of Public Health, Atlanta, GA, USA
4. Department of Pediatrics, Emory University School of Medicine, Atlanta, GA, USA

Address correspondence to:
Timothy G. Singer, MD, MS
Department of Neurological Surgery
The GW School of Medicine & Health Sciences
2150 Pennsylvania Avenue, NW, Suite 7-420
Washington, DC 20037
Email: tgsinger@gwu.edu
Phone: +1 202-741-2712
Fax: +1 202-741-2742

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Abbreviations:
GAPSBi-F: Global Alliance for Prevention of Spina Bifida-F (Folic acid)
SBA: spina bifida and anencephaly
SBA-F: folic acid-preventable spina bifida and anencephaly
WHA: World Health Assembly

Author contributions

Dr. Singer, Dr. Kancherla, and Dr. Oakley conceived of and drafted the original manuscript and provided critical revisions.

Pediatricians have a long history of championing highly effective public health programs that have improved the lives of children around the world. Now, pediatricians have another unprecedented opportunity to champion primary prevention of spina bifida and anencephaly (SBA) globally. Thirty years ago, the British Medical Research Council's landmark randomized trial established that adequate intake of folic acid consumption by mothers before and during early pregnancy is the most effective public health strategy for preventing the majority of SBA cases, known as SBA-F (F indicates folic acid-preventable SBA).(1) As of 2020, about 60 countries have mandatory policies for staple food fortification with folic acid, due to which about 25% of global cases of preventable SBA-F are prevented.(2) While mandatory fortification benefits some countries, many countries in Europe, Asia and Africa lag behind in SBA-F prevention by not investing in this proven public health intervention.(2)

At the May 2022 World Health Assembly (WHA) meeting, the Columbian government agreed to champion the passage of a resolution to promote global prevention of SBA-F. The proposed resolution calls for adoption by all member states of folic acid fortification of commonly consumed staple foods. Essential to passage of the resolution will be the votes by member-nation delegates. We encourage pediatricians in all countries, and their local, national and international pediatric organizations, to help delegates to the WHA understand the potential benefit to the health of children everywhere if the resolution is passed.

There is extensive literature from which pediatricians can draw to advocate for primary prevention of SBA-F.(2) First, there is a large burden of preventable SBA worldwide that needs to be addressed urgently. A systematic review and meta-analysis by Blencowe et al. estimated that about 213,800-322,000 pregnancies are affected annually with SBA globally.(3) This is comparable to the number of babies affected by poliomyelitis before the implementation of

global polio vaccine programs. Further, about 50% of SBA-affected pregnancies result in elective terminations or stillbirths, and about 75% of affected live-born children die before reaching five years of age.(3) We note that these modeled estimates on the burden of SBA are based on conservative assumptions in countries without birth defects surveillance systems; however, they serve as best available data until all countries prioritize population-based surveillance and achieve robust tracking of all pregnancy outcomes to understand the total prevalence of birth defects. Second, prevention is feasible and proven. Mandatory folic acid fortification of commonly consumed staple foods has been repeatedly shown to be the most effective solution to prevent SBA-F, and associated disability and mortality.(4) Further, a systematic review of the effectiveness of folic acid fortification has reported a significantly lower prevalence of spina bifida in countries with mandatory fortification compared to countries with voluntary fortification or no fortification policy.(4) Third, there is a strong economic incentive for governments to adopt folic acid fortification. When implemented well, especially in low- and middle-income countries, fortification is shown to save $957 USD per death averted and $15 USD per disability-adjusted life year averted from SBA-F.(5) Thus, folic acid fortification serves as a proven, feasible, and cost-effective strategy for countries to meet their 2030 Sustainable Development Goals in promoting health for all, and reaching newborn and under-five child mortality prevention goals.

Equipped with the evidence above, we encourage pediatricians to:

1. Champion the benefits of the WHA resolution on folic acid fortification to their respective WHA delegations.
2. Champion sustainable folic acid fortification programs once implemented in their countries.

The unique perspective of pediatricians as the providers of life-saving clinical care to children with spina bifida will be essential for passage of the WHA resolution. Several organizations have already made great progress to amplify the voices of pediatricians and other pediatric specialists, and these efforts should be further built upon leading up to a possible vote on the WHA resolution as soon as May 2023. The Global Alliance for Prevention of Spina Bifida-F (GAPSBi-F), formed in 2017, and has been spearheaded by pediatric neurosurgeons and supported by the Center for Spina Bifida Prevention at Emory University. GAPSBi-F aims to address primary prevention of spina bifida occurring due to maternal folate inadequacy. In addition to pediatric neurosurgeons, GAPSBi-F members include pediatricians, urologists, epidemiologists, food fortification experts, and patient groups. GAPSBi-F collectively advocates for the prevention of SBA-F and has been actively involved in promoting the publication of the WHA resolution on folic acid fortification. Importantly, the International Federation for Spina Bifida and Hydrocephalus, representing people with spina bifida and their families, is working closely with GAPSBi-F. In addition, resources to equip pediatricians in their advocacy are available through the Food Fortification Initiative, Nutrition International, Global Alliance for Improved Nutrition, International Federation for Spina Bifida and Hydrocephalus, and the Emory University Center for Spina Bifida Prevention, among others. With support from pediatricians across the globe, policy makers will get the message of the need to take timely, action-oriented measures to prevent SBA-F, beginning with passage of the WHA resolution and implementation of folic acid fortification programs in their countries.

Critically, passage of the WHA resolution alone, without the funding to implement fortification, would not yield the desired prevention of SBA-F. Therefore, to jumpstart action towards building national folic acid fortification programs, pediatricians, collaborating with

health economists, can convince policy makers to allocate needed funding to implement and sustain effective fortification in their countries when such a policy is lacking or is not working as intended. In addition to the references in this writing, the organizations listed also have resources available for the strong economic case underlying the need for fortification programs.

From the bedside to the WHA, pediatricians are champions locally, nationally, and globally for children with spina bifida. Their voices are essential to raise awareness and move policy makers to take action to achieve universal mandatory food fortification with folic acid and prevent SBA-F globally.

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1. Department of Neurosurgery, George Washington University School of Medicine and Health Sciences, Washington, D.C., USA
2. Department of Epidemiology, Emory University Rollins School of Public Health, Atlanta, GA, USA
3. Center for Spina Bifida Prevention, Department of Epidemiology, Emory University Rollins School of Public Health, Atlanta, GA, USA
4. Department of Pediatrics, Emory University School of Medicine, Atlanta, GA, USA

Address correspondence to:
Timothy G. Singer, MD, MS
Department of Neurological Surgery
The GW School of Medicine & Health Sciences
2150 Pennsylvania Avenue, NW, Suite 7-420
Washington, DC 20037
Email: tgsinger@gwu.edu
Phone: +1 202-741-2712
Fax: +1 202-741-2742

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Dr. Singer, Dr. Kancherla, and Dr. Oakley conceived of and drafted the original manuscript and provided critical revisions.

Pediatricians have a long history of championing highly effective public health programs that have improved the lives of children around the world. Now, pediatricians have another unprecedented opportunity to champion primary prevention of spina bifida and anencephaly (SBA) globally. Thirty years ago, the British Medical Research Council's landmark randomized control trial established that adequate intake of folic acid consumption by mothers before and during early pregnancy is the most effective public health strategy for preventing the majority of SBA cases, known as SBA-F (F indicates folic acid-preventable SBA).(1) As of 2020, 58 countries have mandatory policies for staple food fortification with folic acid, due to which about 22% of global cases of preventable SBA-F are prevented.(2) While mandatory fortification benefits these 58 countries, over 100 other countries, many in Europe, Asia and Africa lag behind in SBA-F prevention by not investing in this proven public health intervention.(2)

At the May 2022 World Health Assembly (WHA) meeting, the Colombian government agreed to champion the passage of a resolution to promote global prevention of SBA-F. This resolution calls for the adoption by all member nations of folic acid fortification of commonly consumed staple foods. We are optimistic that the resolution will be considered for a vote by the full WHA at the upcoming meeting in May 2023. A majority of the member nation delegates must vote in favor for passage of the resolution. We encourage pediatricians in all countries (with and without fortification policies), and their local, national and international pediatric organizations, to help their national delegates to the WHA understand the potential benefit to the health of children everywhere if the resolution is passed.

There is extensive literature from which pediatricians can draw to advocate for primary prevention of SBA-F which has been summarized in a recent call to action for the WHA resolution.(3) First, there is a large burden of preventable SBA-F worldwide that needs to be

addressed urgently with about 213,800-322,000 pregnancies that are affected annually with SBA globally.(4) Of the pregnancies that are affected, about 50% result in elective terminations or stillbirths, and of the affected babied that are born alive, 75% die before reaching five years of age.(4) These estimates are based on conservative assumptions, and while they serve as best available data, they underestimate the true burden of these birth defects until all countries prioritize population-based surveillance and achieve robust tracking of all pregnancy outcomes to understand the total prevalence of birth defects. Yet, for context, according to the World Health Organization (https://www.who.int/news-room/fact-sheets/detail/poliomyelitis), the current number of preventable SBA-F cases globally is comparable to the number of babies affected by poliomyelitis before the implementation of global polio vaccine programs. Second, prevention of SBA-F is proven and highly feasible. Mandatory folic acid fortification of commonly consumed staple foods has been repeatedly shown to be the most effective solution to prevent SBA-F, and associated disability and mortality.(5) Additionally, countries with mandatory folic acid fortification have significantly lower prevalence of spina bifida compared to countries with voluntary fortification or no fortification policy.(5) Third, there is a strong economic incentive for governments to adopt folic acid fortification. When implemented well, especially in low- and middle-income countries, fortification is shown to save $957 USD per death averted and $15 USD per disability-adjusted life year averted from SBA-F.(6) Thus, folic acid fortification serves as a proven, feasible, and cost-effective strategy to help countries to meet their 2030 Sustainable Development Goals in promoting health for all, and reaching newborn and under-five child mortality prevention goals.

Equipped with the evidence above, we encourage pediatricians to:

1. Champion the benefits of the WHA resolution on folic acid fortification to their respective WHA delegations.
2. Champion sustainable folic acid fortification programs in their countries *now*.

The unique perspective of pediatricians makes them very effective science-based champions for both passage of the WHA resolution and folic acid fortification in their own countries. Several organizations have already made great progress to amplify the voices of pediatricians and other pediatric specialists, and these efforts should be further built upon leading up to a possible vote on the WHA resolution in May 2023. The Global Alliance for Prevention of Spina Bifida-F (GAPSBi-F), formed in 2017, has been spearheaded by pediatric neurosurgeons and supported by the Center for Spina Bifida Prevention at Emory University. GAPSBi-F aims to address primary prevention of spina bifida occurring due to maternal folate inadequacy. In addition to pediatric neurosurgeons, GAPSBi-F members include pediatricians, urologists, epidemiologists, food fortification experts, and patient groups. GAPSBi-F collectively advocates for the prevention of SBA-F and has been actively involved in promoting support for a WHA resolution on folic acid fortification. Importantly, the International Federation for Spina Bifida and Hydrocephalus, representing people with spina bifida and their families, is working closely with GAPSBi-F. In addition, resources to equip pediatricians in their advocacy are available through the Food Fortification Initiative (www.ffinetwork.org), Nutrition International (www.nutritionintl.org), Global Alliance for Improved Nutrition (www.gainhealth.org), International Federation for Spina Bifida and Hydrocephalus (www.ifglobal.org), and the Emory University Center for Spina Bifida Prevention (www.preventspinabifida.org), among others. With support from pediatricians across the globe, policy makers will get the message of the need to take timely, action-oriented measures to prevent SBA-F, beginning with passage of the WHA

resolution and implementation of folic acid fortification programs in their countries. In addition to the references in this writing, the organizations listed also have resources available for the strong economic case underlying the need for fortification programs.

Critically, passage of the WHA resolution alone, without effective implementation and periodic monitoring and evaluation of fortification, would not yield the desired prevention of SBA-F. Therefore, to jumpstart action towards building national folic acid fortification programs, pediatricians, collaborating with health economists, can convince policy makers to allocate needed funding to implement and sustain effective fortification in their countries when such a policy is lacking or is not working as intended. This funding can support advocates championing for required folic acid fortification in places where fortification policy is still met with challenges. Further, this appropriation can assist the food industry (e.g., grain milling) to implement and sustain effective fortification with built-in quality control processes. Finally, funds can be allocated for governments to monitor the effectiveness of fortification through periodic biomarker surveys of blood folate concentrations in reproductive-aged women and for setting up surveillance systems for SBA-F prevalence.

From the bedside to the WHA, to sustainable fortification in their countries, pediatricians can be effective science-based champions locally, nationally, and globally for children living with spina bifida as well as for primary prevention of this condition where possible. Their critical voices can move policy makers to implement universal mandatory food fortification with folic acid to prevent SBA-F globally.

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