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The Impact of Folic Acid Food Fortification on Global Incidence of Neural Tube Defects: Systematic Review, Meta-Analysis and Estimate of Preventable Cases.

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INTRODUCTION: Folic acid intake has been proven to reduce the risk of neural tube defects (NTDs), including spina bifida and anencephaly, which belong to the most common birth defects, occurring in approximately 1/1000 births. Despite this evidence, folic acid food fortification (FAFF) has not been universally adopted due to concerns regarding adverse health effects; concerns which have been largely disproven in recent research.

Objective: To assess the global impact of FAFF on the incidence of NTDs and to estimate the number of potentially preventable NTD cases through implementation of FAFF worldwide.

METHODS: A systematic literature search identified studies reporting NTD incidence rates (IR) ($n = 163$). Included studies were assessed for quality according to the Centers for Review and Dissemination (CRD) guidelines. A random-effects meta-analysis was conducted to estimate the global IR of NTD without FAFF, and the effect size of FAFF. In a multivariate meta-regression analysis we determined if pre-FAFF incidence rates can predict the effect size of FAFF in the corresponding populations. The number of cases with NTDs that could be prevented globally through worldwide mandatory FAFF was calculated using birth data obtained from the United Nations population division.

RESULTS: Incidence of NTDs among studies including only live births ranged between 3.8/10,000 (United States) to 82.1/10,000 (India) with an overall IR of 14.1/10,000 (CI = 12.3–16.1). FAFF reduced the incidence of NTDs by 37% (IR Ratio: 0.63 CI = 0.57–0.69; $I^2 = 89.3\%$). The IR before FAFF was significantly associated with the effect size of FAFF ($P = 0.03$). We estimate, using recent world population data and information on countries legislation to mandate FAFF, roughly 70,000 preventable births with NTDs.

CONCLUSIONS: Recent research has shown the benefits of FAFF to outweigh the possible risks. Our results suggest that FAFF would prevent a large number of NTD cases, especially in low income countries, and that worldwide adoption of mandatory FAFF should be considered.