Reviewer’s report

** General assessment

The authors calculate the burden of MNDs (in particular of IDA, VAD and ZnD), for pre-school children in the Philippines, and they do so by separately estimating medical costs, production losses and intangible costs of these deficiencies, using data from two large representative national surveys, and projecting these costs over the lifetime of a 1-year cohort. The authors find that these costs are substantial, in particular those occurring in the future lifetime of children in the model cohort – and within that cohort among children in lower socio-economic strata. The authors point out the relevance of their findings for the design, evaluation and choice of MN policies in the Philippines. Moreover, the authors do comprehensive sensitivity analyses that clearly highlight what the crucial parameters in their calculations are and how their variation affects the projected results, and in most cases they generate plausible distributions around their main results to illustrate the ranges into which the eventual results are likely to fall. All this work is accompanied by detailed and informative tables and figures. Overall this is a well-done and very interesting study that – once the following comments are addressed – should be published.

** Specific comments

*** Discretionary Revisions (DR) which are recommendations for improvement but which the author can choose to ignore:

DR1 – p. 3, 1st para, ref. 3: This reference is more than 10 years old but it is used to make a statement about the present (“200 million preschool children suffer”). As the authors themselves concede that there has been a decrease in the prevalence of VAD over the previous 10-15 years, at least in the Philippines (p. 22), such old data should perhaps be used with caution. If the authors cannot find a more recent global estimate on the size of VAD as a public health problem, perhaps they want to word their statement more carefully (e.g. “as many as 200 million preschool children could still suffer from vitamin A deficiency”).

DR2 – p. 3, 2nd para, 4th sentence: Why is data on the burden of specific diseases only important for local priority setting? International stakeholders in the field of public health may also find it useful to know in which country which
disease is a particular problem and prioritise their activities accordingly. (Perhaps the authors may want to simply drop the “local”.)

DR3 – p. 3, 4th para, 1st sentence: Perhaps the authors can provide a reference for their statement that MNDs are “still” a “relevant” public health issue in the Philippines? (On p. 22 they state that the prevalence of VAD in the Philippines decreased.) Otherwise the authors may want to word their statement more cautiously (e.g. “in which MNDs are still considered to be a public health issue”).

DR4 – p. 5, Figure 1: DALYs do not measure the “quality” of life lost (even if “quality-adjusted life years” are a closely related concept), but they measure the degree of disability that is imposed by a disease – or, to stick to the idea of “loss”, DALYs measure the degree of functioning that is lost because of a disease. Hence, in the box in the lower right corner, the authors could consider replacing “quality of life lost” in the last bullet point with “loss of normal functioning”.

DR5 – p. 9, 3rd para, last two sentences: The authors may want to move the explanation how they consider expected future productivity increases in their calculation of future “production losses” from the section on discounting up to the actual description of their calculation of these production losses (p. 9, 1st para).

DR6 – p. 20, last para, 2nd sentence: While the authors put the subsequently reported monetary results into context (as percent of GDP or health care spending), the DALYs result are only reported as absolute figures. Perhaps the authors can put these figures into context, too? For instance, how does this loss of DALYs compare to the total burden of disease in the Philippines or to the loss caused by another public health problem? Similarly, to facilitate comparisons across countries with different population sizes, perhaps the authors can report the DALYs results also in a relative measure, such as “DALYs per 100,000 population” as the WHO (2011) does for its DALY estimates?

*** Minor Essential Revisions (MER) such as missing labels on figures, or the wrong use of a term, which the author can be trusted to correct:

MER1 – p. 3, 2nd para, 1st sentence: While there may not be an abundance of studies, perhaps it cannot be said that “little” is known about the economic consequences of MNDs for specific countries, either. In addition to the Global Burden of Disease studies that are mentioned by the authors themselves, for instance the World Bank (1994) did an early assessment of the costs of MNDs in developing countries, Horton and Ross (2003) calculated the economic consequences of IDA in various countries, the Micronutrient Initiative (2004) did estimates for some countries, Stein and Qaim (2007) approximated the costs of MNDs in India, and Ma et al. (2008), Yi et al. (2011) and De Steur et al. (2012) did analyses on MNDs in China that also covered economic and cost aspects. The authors could either simply drop the statement or reformulate it to acknowledge the evidence of the studies so far that indicates that the economic consequences of MNDs can be of considerable magnitude in countries with high prevalence rates.
MER2 – p. 3, 2nd para, ref 12-14: It is unclear how reference 14 (on GDP data) supports the statement that micronutrient interventions are part of the effort to reach the MDGs. References 12 & 13 also seem to argue that MN interventions can be part of the efforts or can contribute to the achievement of the MDGs, rather than stating that they are actually used by UN agencies for this purpose. The authors should check the references and how they support their statement.

MER3 – p. 3, 2nd para, 2nd sentence: This sentence seems to suggest that “cost-of-illness” and “burden-of-disease” studies measure the same thing, namely the economic consequences of an illness or a disease. However, while the primary objective of cost-of-illness studies is indeed to quantify the cost of an illness in monetary (i.e. economic) terms, in burden of disease studies the consequences of an illness are measured in terms of the loss of DALYs (i.e. the loss of functioning) that the illness brings about. The authors should clarify these two concepts (or drop the reference to burden of disease studies in this context).

MER4 – p. 5, 1st para, 1st sentence: It is unclear how the “sufficient amount of MNs” is defined. The authors should clarify if this means that all children meet their respective dietary reference intakes? If so, which ones?

MER5 – p. 7, 1st para, 2nd but last sentence: The authors should correct the typo (empty space) in “norm_al range.”

MER6 – p. 15, Table 6: The authors should correct the formatting error in the bottom row (“RR:" instead of “RR of” like in the rows above) and the unintended line break in “Persisten_t” in the header of the fourth column.

MER7 – p. 16, Table 7: The authors should add a colon after “Table 7” as in the captions of all other tables.

MER8 – p. 19, Figure 7: The authors report the impact of variations to various workforce parameters (active workforce participation, age at workforce exit, age of workforce entry), but they do not report their corresponding baseline assumptions anywhere in the study; the authors should do so and also give a brief explanation for their choice.

MER9 – p. 20, last para, 3rd but last sentence: It is unclear whether the 8.5% of total monetary costs relate to public and/or private “spending on health care”? The authors should specify what is included in this spending on health care.

MER10 – p. 33, ref. 41: The authors should correct the typo (D and not J) in the initials of the first author.

MER11 – p. 34, ref. 49: The authors should correct the typo (transposed “co”) in “accounts”, perhaps the authors can also provide a website or more bibliographic details for this reference – with the given information it was not possible to locate this reference online.

*** Major Compulsory Revisions (MCR) which the author must respond to before
a decision on publication can be reached:

MCR1 – p. 5, 1st para, 2nd sentence: The authors state that they build a health economic model, but they do not provide more detailed information on the model and how it is used for the simulations (e.g. formulas, parameters or modelling environment). Perhaps in an appendix, the authors should provide a minimum of information on how the model calculates medical costs, production losses and intangible costs and what parameters it uses. (Some info can be found throughout the paper, but it would be preferable if the authors could consolidate and complement the information to present the model more coherently.)

MCR2: The authors explain how they derive prevalence rates for the MNDs they consider in their study (p. 6/7), and they explain that they use the method of the GBD study to calculate DALYs lost (p. 9). They also explain that for some of the health effects they apply PAF to current prevalence rates to calculate the number of episodes attributable to MNDs (p. 8), but for the other health effects (IDA, stunting) it remains unclear how the authors get the incidence rates that are required for the GBD’s DALYs formula. The authors should explain the conversion from prevalence rates or how they arrive at the incidence rates.

MCR3: In their calculation of future “production losses” (p. 9, 1st & 3rd para, also see DR5), the authors assume that future productivity increases (only) in line with the average growth rate of real GDP per capita between 1990 and 2011. This is almost certainly an underestimate as it ignores any kind of dynamic and multiplier effects: In the past national income growth was bogged down (at least in part) because MNDs were so prevalent, i.e. once MNDs are eradicated and this brake on national growth is removed, productivity should rise much faster. (For instance, Fogel (2004) suggests that 30% of the growth in British per capita income over the last two centuries was due to better nutrition – incl. micronutrients, such as iodine, iron and folate. Likewise, the Commission on Macroeconomics and Health of the WHO (2001) expects that the economic benefits of better health develop in a dynamic fashion (and not linear) because improved health should help spur economic growth. And, using a modelling approach, Anderson et al. (2005) show how the health-enhancing attributes of rice that is enriched with provitamin A (Golden Rice) would boost the productivity of unskilled workers among Asia’s poor.) As the authors’ own sensitivity analysis shows, the choice of the real income growth rate has a considerable effect on the final estimate of future production losses (p. 19, Figure 7). Therefore, the authors could think about how to take such dynamism into account when computing future production losses or when doing their sensitivity analyses (also see MCR6 below); at the very least the authors should include a discussion of this issue into their section on “Strengths and limitations (p. 21/22).

MCR4 – p. 9, 1st para, last sentence: The authors explain that whereas current production losses are valued with SES specific incomes, future losses are all valued with an average income. That is, as the authors explain in the discussion of the “strengths and limitations” of their study (p. 21/22), without MNDs a child of a poor household would have the same future productivity – which they equate with income – as a child of a wealthier household. They justify this assumption
with “the uncertainty of the long-term development of a rapidly evolving emerging country”. However – contrary to this assumption of vertical social mobility and the disregard of SES-specific determinants of income other than MNDs – there is agreement that inequality remains a challenge in the Philippines (ADB 2009, World Bank 2010, Inquirer 2011). It seems to be a very strong assumption that current inequality will have given way to full social mobility by 2025 (which should be about the time the children who were 1 year old in 2008 enter the labour market; also see MER8). In line with what they do for current production losses, perhaps the authors can base future production losses on suitably adjusted SES specific incomes and have two lines in Table 10 (p. 18), one for production losses under the current “equal” scenario and one for an “unequal” scenario? Otherwise the authors should at least include a discussion of this issue and the likely distribution of future production costs across SES into their section on “Strengths and limitations (p. 21/22).

MCR5 – p. 9, 2nd para, last sentence: It seems the quantification of both “production losses” and “intangible costs” amounts to double counting, at least to some extent. Even if a direct monetary quantification of DALY (or QALY) losses can be criticised, as the authors point out (p. 9, 2nd para, last sentence, ref. 32), this is done routinely for pragmatic reasons (Hirth et al. 2000, WHO 2001, Eichler et al. 2004, Zimmermann and Qaim 2004, Stein and Qaim 2007, Braithwaite et al. 2008, Towe 2009, Cressey 2009, Brent 2011), i.e. one could argue that there is an overlap between production losses and DALY losses. Therefore the authors should clarify throughout the text that these two measures are _alternative_ ways of quantifying the cost/burden of MNDs.

MCR6 – p. 9, 3rd para, 2nd sentence: Perhaps the authors can add a reference that supports their claim that a discount rate of 3% is “widely accepted” for cost-of-illness studies? In the literature a much wider range of possible discount rates is discussed, which especially in developing countries can be as high as 10% (Zhuang 2007, WHO 2008, Gauvreau 2011, Dhaliwal et al. 2012). The authors do carry out a sensitivity analysis that includes varying the interest rate (p. 19) and, as they also show in Figure 7, future production losses are most affected by deviations of the discount rate, so this is an important parameter. However, in their sensitivity analysis the authors vary the discount rate only by 20%, i.e. they consider discount rates in the range of 2.4-3.6%. While a discount rate of 2.4% is probably a very low estimate, compared to 10% a rate of 3.6% can hardly be considered a sufficiently large deviation. The authors should run their sensitivity analyses with a much larger increase of the interest rate – one that is in line with the larger values that are suggested in the literature for discount rates in developing countries. While a largely ad hoc variation of plus/minus 20% is fine for parameters where there is no additional information on the possible range of the true value, in the case of the discount rate (or the future productivity growth, also see MCR3), this assumption needs to be adjusted and the sensitivity analysis should reflect the possible range of values a parameter could have.

MCR7 – p. 13, last para, 2nd sentence: The authors explain that they exclude
xerophthalmia and blindness as health consequences of VAD in their calculations, because these conditions would no longer be observed in the Philippines. The authors should provide a reference in support of their claim. (While these studies refer to the 1990s, for instance Pedro et al. (2004) found that the prevalence of VAD in the Philippines rose after the introduction of a universal vitamin A capsule distribution programme in 1993, and Dawe et al. (2002) suggested that the coverage of the distribution programme fell after 1997 once it was not integrated any longer in polio immunisation efforts, which means VAD could have further increased; for more on VA interventions in the Philippines also see Fiedler et al. (2000).)

MCR8: In this context (MCR7), one interesting question is to what extent the disappearance of more severe VAD-related eye problems may be due to past and current VA interventions. Therefore,

(a) the authors should provide an overview of the MN interventions in the Philippines that were in place during 2008 and the preceding years at the national or regional levels and discuss their possible impact (perhaps as part of the “Background on p. 3/4), and

(b) the authors should add the costs for these programmes to the calculation of the “direct medical costs” (p. 8) as without these interventions/costs the economic and health consequences of MNDs in the Philippines would be bigger.

MCR9: The authors only have children as target group and consider “low physical activity” due to IDA as a temporary effect (p. 15, Table 6) that does not contribute to production losses (p. 13, Figure 4). However, Stein et al. (2005), on whose work the authors also build for some of their assumptions, suggest that low (or “impaired”) physical activity due to IDA should also be considered in adults (even if the prevalence of IDA is typically much smaller, especially in men). In the literature there are many examples for the reduction of productivity/earnings of labourers due to IDA (e.g. rubber tappers or tea pickers; see Haas and Brownlie (2001) for a review). Hence, by ignoring the production losses due to IDA in adults, the authors underestimate the cost of IDA. While it is difficult to say what the prevalence of IDA will be in the model cohort when its members reach working age, in the authors’ current calculations a prevalence rate of zero is implied. Instead (in a sensitivity analysis), the authors could use current IDA prevalent rates in adults of working age to estimate a maximum of the production losses due to low physical activity later on in life. Otherwise the authors should at least include a discussion of this issue into their section on “Strengths and limitations” (p. 21/22) and highlight that their current results underestimate the cost of IDA. (Similarly, the authors did not include maternal mortality as an outcome of IDA, which also means their results underestimate the cost of IDA.)

MCR10 – p. 14, 1st para & p. 15, Table 6, last row: The authors state that they exclude an effect of ZnD on mortality in their analysis. However, the authors do include an effect of ZnD on diarrhoea and respiratory diseases. As these health outcomes of ZnD can be fatal, it is unclear why or how ZnD should have no effect on mortality. It is also not entirely clear how the authors model the influence of
MNDs (all combined?) on “all-cause mortality” (p. 14, 2nd para). The authors should expand their explanation of the all-cause mortality calculations and how the contribution of ZnD to fatal cases of diarrhoea and respiratory diseases is (not) considered. It seems that the authors did a calculation in which they included ZnD-related mortality that produced very different results, i.e. costs that were 20-30% higher (p. 21, 1st para, last sentence). This is an important impact of a change in an assumption and the authors should discuss this impact more explicitly in the section on the results of the sensitivity analysis on p. 19 (also see MCR3 & MCR6).

MCR11 – p. 17, 1st para, 1st sentence: The authors should explain what “dollars” they use. From the list of abbreviations and the tables it seems they use US Dollars (and not, for instance, International Dollars that would reflect the purchasing power parity of costs incurred in the Philippines), and presumable they use 2008 as base year, but this should be stated explicitly.

* References


Level of interest: An article whose findings are important to those with closely related research interests
Quality of written English: Acceptable

Statistical review: No, the manuscript does not need to be seen by a statistician.

Declaration of competing interests:

I declare that I have no competing interests. However, for the sake of transparency I want to point out that in the past I worked with the International Rice Research Institute in Los Baños on “Golden Rice” (www.irri.org/goldenrice). This rice, which is enriched with provitamin A, is developed with the goal of helping control vitamin A deficiency in rice-eating populations in developing countries; one possible target country for the introduction are the Philippines. The development of Golden Rice is a humanitarian undertaking and not for profit, and I have nothing to gain or to lose from a possible introduction.