ENVIRONMENTAL EVIDENCE

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What are the non-food impacts of GM crop cultivation on farmers' health?

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Abstract

Background: With a steady increase in the area cultivated with genetically modified (GM) crops, the impacts of GM crop cultivation are coming under closer scrutiny around the world. The impacts on humans usually refer to possible risks to health occurring as a result of the GM food consumption. Other concerns, such as the claims of human health benefits arising from the cultivation of GM crops via reduced use of pesticides could be considered, if at all, under economic impacts of the technology. Similarly, other human health impacts could occur as a result of a modification of the amount of pesticides residues found in underground water, which could be considered under environmental impacts.

Yet many GM crops are not consumed on-farm, either because they require processing before becoming edible (such as soya bean, cottonseed and oilseed) or because the entire harvest is sold to maximise profits. It would be certainly difficult to demonstrate the importance of GM foods health effects versus the non-food health effects of GM crop cultivation on farmers. However, the non-food health effects, although apparently receiving less attention, deserve a closer look because of their potential economic and environmental links.

Methods/design: The primary research question is: What are the non-food impacts of GM crop cultivation on farmers' health? To address specifically the main research question, the analysis focuses on two related secondary questions: 1) Does the cultivation of GM crops result in a lower number of pesticide-related poisonings? and 2) Does the cultivation of GM crops allow for higher financial resources to be used by farmers to improve their and their family's health status? Further, the review will also evaluate the extent to which information relevant to the two secondary questions is freely-available. The abstracts of non-free articles, alongside their bibliographic details, will be included in a separate table, and if the information supplied would be detailed enough, a summary will be provided. The search and assessment methodologies (especially the search string, inclusion/exclusion criteria, data extraction table, data synthesis and presentation) were adapted following problems overcome, and experience gained, during a scoping search.

Keywords: GM Crops, Farmers, Pesticides, Poisonings, Incomes, Health expenditures

Background

The first GM crop approved for commercialisation was a GM tomato in 1994 in the USA. In 2012 there were 28 countries growing genetically modified (GM) crops on a cumulative area of 170 million hectares, making GM crops the technology with the fastest rate of uptake in modern agriculture [1]. Individual reports have pointed towards an array of socio-economic and environmental advantages derived from such adoption. Apart from an increase in farm income [2], the cultivation of GM crops has been reported to reduce the environmental impact of agriculture through: lowering the amount of pesticides applied [3]; decreasing the amount of fossil fuel consumed and CO_2 emitted as ploughing has been reduced or avoided [4], and; facilitating conservation tillage, resulting in better conservation of agricultural soils [5,6]. Conversely, reports have appeared that indicate that the cultivation of GM crops results in: an increase in the use of pesticides [7]; failures to provide significantly increased yields [8], and; an increase in allergenic and toxic effects [9].

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Within the vast array of impacts ascribed to GM crop cultivation, those pertaining to human health may not be as easily analysed. Effects on human health can be considered separately or included in economic or environmental evaluations [4]. Human health effects may occur broadly as a result of: i) the consumption of GM food [10], ii) the influence of GM crop cultivation on on-farm pesticide use [11] and iii) impacts on overall welfare related to changes in on-farm incomes. For economic benefits, both pecuniary and non-pecuniary effects have been described, with health benefits derived from a reduction in pesticide use amongst the latter [4]. In other instances, impacts on human health were considered under broader environmental impacts, within indicators such as the Environmental Impact Quotient (EIQ) [4].

Further, links between agricultural productivity and health have included health impacts derived from changes in household income and from impacts on agricultural production chains generated by the introduction of new crops [12]. Any modification of household income can affect patterns of spending within the household, including the money available for buying more and/or better food, paying for medical expenses, and saving [12]. The introduction of a new crop can bring changes on consumption patterns of other agricultural commodities, on agricultural practices (e.g. time assigned to on-farm work can interfere with other activities, or an intensification of agriculture practices with heavy use of pesticides and fertilisers which in turn can increase the number of accidents and toxicity from pesticides), and markets (availability of better/worse products than before) [12].

Due to this multitude of uncoordinated sources of impacts of GM crop cultivation on human health, it is difficult to obtain a comprehensive overview. In addition, when addressing human health impacts of GM crops, the focus is usually on effects resulting from the consumption of GMOs and GMO-derived agricultural products. The non-food effects on human health are usually ignored. At a first look, this might indicate the need for a systematic mapping for the effects of non-food GM crop cultivation. However, due to the controversy surrounding GM crops, the objectivity of articles analysing the impacts of GM crop cultivation is often questioned. For all the reasons presented above, the systematic review (SR) was chosen therefore as the most appropriate methodology to guide the evaluation of the existing evidence of GM crop non-food effects on human health and/or to point to a gap in knowledge, if that should be the case.

The proposed systematic review will review the impacts of the GM crop cultivation derived from the changes in on-farm pesticide usage and welfare and the resulting effects on health (Figure 1). Farmers, as the primary beneficiaries of GM crop technology to date, represent the population chosen for this study. Farmers are understood as farm owners, farm labourers and agricultural contractors in developing and developed countries. Although GM crops have recently come under scrutiny for their role in food and nutritional security for consumers, comprehensive reviews of the non-food impacts of GM crop cultivation on producers' health are difficult to find. As the focus of the present systematic review will concern non-food impacts on GM crop producers rather than on consumers, this review will not investigate the main health criteria evaluated during the safety assessments of GM foods, such as toxicity, allergenicity, specific nutritional components and nutritional effects associated with genetic modification, the stability of the inserted gene, or any unintended effects resulting from the gene insertion [10]. Further, the contribution of GM crop cultivation to the lowering of greenhouse gas emissions, sometimes considered as an indirect health effect [4], as well as health effects determined by possible pesticide contamination of underground water and improved sanitation will also not be considered during this review.

Objectives

The primary research question is: What are the non-food impacts of GM crop cultivation on farmers' health? To address the main research question, the analysis focuses on two related secondary questions: 1) Does the cultivation of GM crops result in a lower amount of pesticides usage, leading further to a lower number of pesticide-related poisonings? and 2) Does the cultivation of GM crops allow for higher financial resources to be used by farmers to improve their and their family's health status? "Farmers" are to be understood as farm owners, labourers, and agricultural contractors. Both secondary questions look at final outcomes (number of pesticide-related poisonings and health related expenditures) through a well-established pathway, through the presence of intermediary outcomes (amount of pesticides usage and income derived from GM crop cultivation). The main concepts to be addressed in this systematic review ("PE/ICO"; P - Population, E – Exposure/Intervention, C – Comparator, O - Outcome) [13-15] are formulated in Table 1. The review will analyse quantitative articles estimating the extent of non-food health impacts from GM crop cultivation, according to the objective stated above.

Methods/design

Searches

The following combination of keywords and wildcard symbols (*, $), linked with Boolean operators 'AND' and 'OR' will be used to search online databases:

(farmer* OR agric* OR worker OR contractor) AND ((genetic*modif*) OR (genetic*engineer*) OR GE OR transgene* OR herbicide$tolerant OR insect$resistant OR biotech* OR BT OR GM OR stacked$trait*) AND (crop* OR plant* OR flower*) AND (health OR poisoning OR security OR safety OR welfare OR benefit) AND

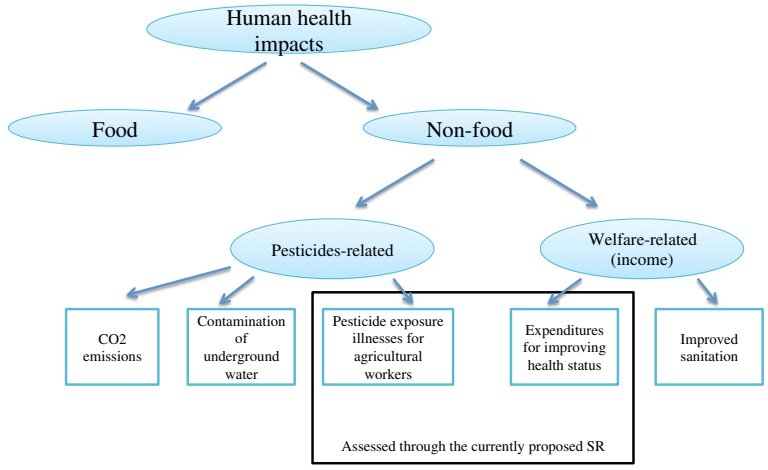

Figure 1 Diagram of human health impacts of GM crop cultivation.

(pesticides OR insecticides OR herbicides OR fungicides OR bactericides OR income OR revenue OR gains OR wage OR profit OR earnings OR livelihood).

The composition of the search string was established as a result of the searches undertaken within the scoping exercise (see Additional file 1). The structure of the search string follows the PICO/PECO structure, albeit in a slightly modified form. For the Intervention/Exposure we chose the GM crop cultivation. Yet we wanted to make sure that the search terms referring to the intervention/exposure could capture only GM crops and not GM insects or animals. As such, we had one parenthesis with synonyms for "GM" and another for "crop".

For the Comparator, we did not include any separate string of key words because it is already included in the Intervention/Exposure section: (crop* OR plant* OR flower*).

The Outcomes were separated between intermediary: (pesticides OR insecticides OR herbicides OR fungicides OR bactericides OR income OR revenue OR gains OR wage OR profit OR earnings OR livelihood) and final outcomes: (health OR poisoning OR security OR safety OR benefit OR welfare OR environment).

The databases will be divided among 3 reviewers so 2 reviewers will search each database. The databases will be searched within title, topics and full text. As some databases do not accept the full search string, searches will be adapted to contain combinations of fewer words (for example, one term from each group within brackets united by an 'AND' operator). As this will be database-specific, the short search strings are not specified *a priori*. Each reviewer will have the operational flexibility to perform their assigned searches using several word combinations, if the full search string did not recover any hits. The primary hits retrieved will be analysed by each reviewer at the title and abstract level, according to the inclusion/exclusion criteria detailed in the specific section below. Each reviewer will register the exact search string used for each database, along with the results and their analyses.

In cases where web searches and databases display large numbers of results in the order of relevance (e.g. Google Scholar) only the first 100 will be checked. When databases that return results of equal relevance (e.g. Web of Knowledge) will retrieve a high number of hits (in the order of thousands) a title search will be performed before an abstract search.

Publication databases

The list was compiled after consulting the Cochrane Handbook for Systematic Reviews of Interventions [16], and further supplemented with additional databases suggested by the reviewers. Some databases for "grey literature" i.e. literature produced on all levels of government, academics, business and industry in print and electronic formats, but which is not controlled by commercial publishers, were also included. All databases are free for public use or can become so following online registration for a free trial.

General databases

BioMed Central- www.biomedcentral.com/browse/journals/

Database of Promoting Health Effectiveness Reviews (DoPHER) - http://eppi.ioe.ac.uk/webdatabases/Intro.aspx?ID = 2

HighWire Press - http://highwire.stanford.edu/

Latin America and the Caribbean (LILACS) - http://lilacs.bvsalud.org/en/

Medical Literature Analysis and Retrieval System Online (MEDLINE) - www.nlm.nih.gov/pubs/factsheets/medline.html

Pubget - http://pubget.com

PubMed Central (PMC) - www.pubmedcentral.nih.gov/

Science Direct - www.sciencedirect.com

Web of Knowledge- http://wokinfo.com/

Table 1 Elements of the systematic review questions

Secondary questions	Subject	Population	Exposure/ Intervention	Outcome	Comparator	Design
Q1: Does the cultivation of GM crops result in a lower number of pesticide-related poisonings?	Non-food health effects of GM cultivation	Farmers (understood as farm owners, farm labourers and agricultural contractors) in developing and developed countries	GM cultivation: any type of GM trait and any type of host crop	**Intermediary:** amount of pesticides usage; **Final:** number of pesticide-related poisonings	Farmers cultivating corresponding conventional non-GM crops (both traditional and organic)	Any study comparing the impacts on human health, before and after cultivating GM crops on the same farm, and between cultivation of GM crops and cultivation of non-GM crops either on the same farm or between different farms, but occurring at the same time
Q2: Does the cultivation of GM crops allow for higher financial resources to be used by farmers to improve their and their family health status?	*Same as above*	*Same as above*	*Same as above*	**Intermediary:** income derived from GM crop cultivation; **Final:** health related expenditures	*Same as above*	*Same as above*

Specialist databases on biotechnology and/or international development. (This list includes sources from academia, industry, as well as civil society)

Agricultural Biotechnology Network in Africa (ABNETA) - http://abneta.org/

African Centre for Biosafety (ACBIO) - www.acbio.org.za

AgBioForum - www.agbioforum.org/

Bibliosafety database - http://bibliosafety.icgeb.org/=

CropLife International - http://croplife.intraspin.com/BioTech/

Greenpeace - www.greenpeace.org/international/en/publications/

International Food Policy Research Institute (IFPRI) - www.ifpri.org/

International Service for the Acquisition of Agri-biotech Applications (ISAAA) - www.isaaa.org

Monsanto - www.monsanto.com/products/Pages/biotech-technical-publications.aspx

Search engine

Google Scholar - http://scholar.google.com

Other

PhD and Masters theses:

ProQuest (Dissertations & Theses, Dissertations & Theses (PQDT) A&I, Sociology, Sociological Abstracts) - www.proquest.co.uk/en-UK/

In addition, the cited literature of 5-10 reviews found through the search process will be searched as well.

Article screening

Study inclusion/exclusion criteria

The following criteria will be applied to each study to determine its suitability for further inclusion:

Language: English.

Timeline: Published after 1994 - the year when the first GM crop was commercially cultivated (on-going research not included)

Population: Farmers (understood as farm owners, farm labourers and agricultural contractors) in developing countries and developed countries

Exposure/Intervention: GM cultivation: any type of GM trait and any type of host crop

Comparator: Non-GM crop cultivation (both traditional and organic)

Outcomes: intermediary outcomes (amount of pesticides usage and income derived from GM crop cultivation) and final outcomes (number of pesticide-related poisonings and health related expenditures).

Screening process

Lists will be made with articles that have been analysed by reviewers at title and abstract level and found to correspond to the inclusion/exclusion criteria, and hence to be included in the next step. A Cohen Kappa test will be undertaken to verify consistency of assessment between reviewers, with a threshold of 0.6. A lower result would indicate that inclusion/exclusion criteria should be clarified. A final list (Tier 1 list) will be compiled for the full-text screening stage. The articles that will enter the list will include all articles identified by each reviewer as qualifying according to the inclusion/exclusion criteria, regardless if they are in agreement with the second reviewer or not. This measure should eliminate the reviewer bias and help retain articles, when in doubt about their relevance, until examined at full text.

The articles on the Tier 1 list will be divided among 3 reviewers who will then undertake a full text analysis with the inclusion/exclusion criteria. If the Cohen Kappa test above had a result of over 0.6, then a second reviewer will randomly check 10% of the abstracts allocated for each reviewer. If the Cohen Kappa test had a result below 0.6, then the articles will be divided among 3 reviewers with each article checked by 2 reviewers, after which a Cohen Kappa test will be performed again with the same stipulations as for the previous step.

The result of this analysis (Tier 2) should be a series of tables: a table for articles not relevant to the criteria, duplicates, and ex-ante studies; a table with reviews; a table with articles for which full text was not found even after contacting the authors; and a table of articles that after a full text analysis are evaluated as qualifying for data extraction.

Potential effect modifiers and reasons for heterogeneity

Potential effect modifiers and reasons for heterogeneity have been established following discussions amongst the reviewers. The modifiers have been categorised into larger groups, each with several subgroups, as follows:

1. Type of intervention (GM crops):
   1.1. Number of crops analysed
   1.2. Type of crops
   1.3. Type of trait introduced
   1.4. Type of pesticide(s) applied
2. Context:
   2.1. Country
   2.2. Location
   2.3. Agro-ecological climate
   2.4. Weather
   2.5. Pest pressure
   2.6. Irrigated/rain-fed
3. Farm and Farmer profiles:
   3.1. Age
   3.2. Gender
   3.3. Education
   3.4. Farm size
   3.5. Areas cropped to GM/non-GM

3.6. Use of pesticide protective measures (if relevant)
4. Institutional context:
   4.1. Agricultural subsidies
   4.2. Agricultural credits
   4.3. Price control policies
   4.4. Agricultural extension services
5. Study design:
   5.1. Methodology employed
   5.2. Frequency and period of data collection
   5.3. Sample size

Data extraction

Studies reported in articles selected after full text screening will undergo data extraction. The data retrieved will be recorded on tables of which the template is presented in Table 2. The list of included articles will be divided among 3 reviewers, with 25% of data extraction tables randomly checked by a second reviewer.

Study quality assessment

After analysing several sources from the theoretical literature for SR [13-16], as well as related SR [17,18] and based on the present potential effect modifiers, a set of 8 questions requiring dichotomous answers (yes/no) were developed to assess the quality of the articles.

1. Did the study include more than one study area (country/region within a country)?
2. Were the farmers randomly selected?
3. Did the study include data from more than one year?
4. Did the sources of data rely on written records?
5. Were there any measures in place to deal with attrition?
6. Did the study test differences between GM adopters and non-adopters?
7. Did the study test if the farmers' use of pesticides protective measures was related to the pesticides-related poisonings?
8. Did the study include confounding variables in the calculation of farmers' income?

The overall purpose of the quality assessment is to show strong causality, both for the intermediary and final variables. We need to account that not all questions are relevant for all articles; 7 questions are relevant for each secondary research question. As such, each Yes answer will receive a score of 1, while a No will receive a score of 0. An average score will be calculated for each study. Below 0.28 the study will have a high susceptibility to bias; between 0.28 and 0.71 will have a medium susceptibility to bias; and over 0.71 will have a low susceptibility to bias.

Table 2 Template of data extraction table (modified after scoping exercise)

Revision date:
Name of person filling the form:
Notes:
ID of the form (usually name of the first author and year of publication):
Author(s) of the study and affiliations:
Title
Publication type:
Journal:
Funding agency:
Type of intervention (GM crops)
• Number of crops analysed
• Type of crops
• Type of trait
• Type of pesticides applied
Context
• Country
• Location
• Agro-ecological climate
• Weather
• Pest pressure
• Irrigated/rain-fed
Farm and farmer profiles
• Age
• Gender
• Education
• Farm size
• Area cultivated with GM/non-GM
• Use of pesticide protective measures (if relevant)
Institutional context: subsidies, credits, price control policies, extension services
• Agricultural subsidies
• Agricultural credits
• Price control policies
• Agricultural extension services
Study design
• Methodology employed
• Frequency and period of data collection
• Sample size
Intermediate outcomes
1. Q1: Pesticide usage
2. Q2: Household income
Final outcomes
• Q1: Number of pesticide-associated illnesses
• Q2: Health-related expenditure

The best quality articles will be those that: include more than one study area; the farmers are randomly selected; include data from more than one year; the sources of data rely on written records; contain measures to deal with attrition; test differences between GM adopters and non-adopters; determine that the farmers' use of pesticides protective measures is not related to the pesticides-related poisonings; include confounding variables in the calculation of farmers' income.

Data synthesis and presentation

As the scoping exercise study indicated a heterogeneous set of methodologies and results, a narrative synthesis will be made of the data i.e. the findings will be summarised and described, with no meta-analyses undertaken. Studies found through the scoping exercise show a high degree of variability in methodologies, crops and contexts employed, making the data unsuitable for a meta-analysis [16]. Two tables will be constructed to summarize findings, based on the existing data extraction tables, one for each secondary research question. Summary tables will contain the article ID as given in the data extraction tables, bibliographic references, context of intervention (country/region), methodological design, intermediary and final outcomes, as well as the overall score and the main sources of bias as reported by the quality assessment. The low and medium susceptibility to bias articles for each of the research questions will be analysed separately from the high susceptibility to bias ones. Descriptive statistics showing the countries in which research was undertaken, the types of crops, types of traits, types of pesticides applied, characteristics of the farms and farmers studied, as well as the institutional context will also be provided.

Additional file

Additional file 1: Scoping exercise.

Abbreviations

ICGEB: International Centre for Genetic Engineering and Biotechnology; GM: Genetically modified; GMO: Genetically modified organism; SR: Systematic review; CEE: Collaboration for Environmental Evidence; EPPI-Centre: Evidence for Policy and Practice Information and Coordinating Centre; PMC: PubMed Central; ABNETA: Agricultural Biotechnology Network in Africa; ACBIO: African Centre for Biosafety; IFPRI: International Food Policy Research Institute; ISAAA: International Service for the Acquisition of Agri-biotech Applications; PQDT: ProQuest Dissertations & Theses; DoPHER: Database of Promoting Health Effectiveness Reviews; LILACS: Latin America and the Caribbean; MEDLINE: Medical Literature Analysis and Retrieval System Online.

Competing interests

The authors declare that they have no competing interests. The systematic review is funded by the ICGEB, both from its core funding, as well as from various external funds raised by its Biosafety Unit.

Authors' contributions

All authors participated in the drafting, revision and approval of the manuscript.

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