

**Written in alignment with the PRISMA-P 2015 statement<sup>1</sup> with modifications for a restricted systematic review<sup>2</sup>**

**Title**

Livestock and avermectins in Sub-Saharan Africa: protocol for a restricted systematic review of the impacts on productivity and documentation of resistance

**Registration**

This protocol has not been registered, but the prospective protocol will be published in VTechWorks (<https://vtechworks.lib.vt.edu/>), a publicly available database for Virginia Tech Scholarship

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**Contributions**

CR is leading the protocol development, analyses and dissemination. RZ and CR are first and second reviewers. Both authors will contribute to data interpretation and article drafts. KD is assisting with protocol development and article drafts.

**Support**

The Multicultural Academic Opportunities Program (MAOP) at Virginia Tech

(<https://www.maop.vt.edu/>) provided funding for RZ to work on this review. Neither the MAOP or Virginia Tech played a role in developing the protocol.

## INTRODUCTION

### Rationale

Avermectins are commonly used around the world in cattle, small ruminants, and swine to treat gastrointestinal helminths and ectoparasites. Although there is strong evidence that treating livestock with avermectins to control parasites improves animal productivity, most of the research has been performed in Europe and the United States<sup>3-8</sup>. Location of the research is important, as animal genetics, environmental conditions, and production systems (e.g., intensive vs. extensive) likely influence the relationship among parasite prevalence, impacts on productivity, and follow-on economic consequences of production losses<sup>9</sup>.

Currently, there is significant scientific interest in using ivermectin, a member of the avermectin group, in mass drug administration (MDA) campaigns in livestock as a vector control tool for mosquitoes important in the transmission of human malaria<sup>10</sup>. This interest stems from evidence that mosquitos fed on ivermectin-treated livestock die or exhibit reduced reproductive success<sup>11-13</sup>, thereby serving to reduce the mosquito population. It is expected that humans will benefit due to a reduction in the mosquito population and subsequent lower malaria transmission when ivermectin is given to livestock in areas where malaria vectors exhibit partial zoophagy.

The novel approach of using a pharmaceutical in livestock to control a vector of human disease requires a comprehensive and cross-sectoral approach in estimating intervention costs and benefits. Although from a public health perspective livestock essentially serve as a treated blood source for mosquitoes, treated animals also derive health benefits from the use of ivermectin as an anti-parasitic. Health benefits in livestock translate into increased productivity, which has economic and nutritional benefits for livestock-owners and the community<sup>14,15</sup>. In order to quantify the costs and benefits to the livestock sector of using ivermectin (or other avermectins), it is important to be able to estimate impacts on productivity within the likely settings where ivermectin MDA will be used. Over 90% of malaria deaths occur in Sub-Saharan Africa (SSA)<sup>16</sup>, and field studies using ivermectin in livestock to reduce malaria transmission in humans are planned and underway in several SSA countries.

This review will summarize published research on the effects of avermectins on growth rate, reproductive success, and milk production in cattle and swine in Sub-Saharan Africa (SSA). Results may be used to inform future cost-effectiveness analyses for the addition of ivermectin MDA in livestock to ongoing malaria control programs. Additionally, as avermectin resistance would limit the benefit of using this type of anthelmintic in the livestock sector, this review will summarize information regarding parasitic resistance of importance to livestock in SSA.

### Objectives

To summarize existing evidence on:

1. The effects of avermectins on cattle and swine productivity in SSA; where productivity is defined as growth rate, reproductive success, or milk production (cattle only).
2. The distribution of avermectin resistance in internal and external parasites of cattle and swine in SSA.

## METHODS

### Eligibility criteria

For both objectives, only peer-reviewed articles written in English will be included. Objective-specific criteria are based on the following study characteristics:

#### *Objective 1*

- Population: Cattle and pigs in a Sub-Saharan African country
- Intervention: Use of one of the following avermectins: ivermectin, eprinomectin or doramectin
- Comparison: control group or other class of anti-parasitic
- Outcome: Change in productivity as defined by growth rate, reproductive success, or milk production (cattle only)

#### *Objective 2*

- Population: Cattle and pigs in a Sub-Saharan African country
- Exposure: One of the following avermectins: ivermectin, eprinomectin or doramectin
- Outcome: Avermectin resistance in any internal or external parasite
- Time: Published between the year of 2010-2020

### Information sources

The search will employ topic-based strategies designed for each database with the final search date of June 15, 2020. The following three databases will be used:

- CAB Abstracts from CabDirect
- Scopus
- Agriculture, Life, and Natural Sciences Databases from ProQuest (federated search comprised of databases within Virginia Tech's subscriptions)

### Search strategy

#### *Objective 1:*

Databases:

1. Agriculture, Life, and Natural Sciences Databases from Proquest: "Anywhere" for terms including "Africa"; "Anywhere but Full Text" for all other search terms. Limited to peer-reviewed journal articles published in English.

noft((avermectins OR ivermectin OR eprinomectin OR doramectin OR anthelmintic OR anthelmintics)) AND noft((cattle OR bovine OR cow OR cows OR bull OR bulls OR steer OR heifer OR calf OR calves OR swine OR porcine OR sow OR sows OR gilt OR gilts OR boar OR boars OR piglet OR piglets OR pig OR pigs)) AND ("Sub-Saharan Africa" OR "Sub Saharan Africa" OR "Africa")

2. CAB Abstracts: "All fields" for terms including "Africa"; "abstract only" for all other search terms. Limited to journal articles published in English

(ab:((avermectins OR ivermectin OR eprinomectin OR doramectin OR anthelmintic OR anthelmintics)) AND ab:((cattle OR bovine OR cow OR cows OR bull OR bulls OR steer OR heifer OR calf OR calves OR swine OR porcine OR sow OR sows OR gilt OR gilts OR boar OR boars OR piglet OR piglets OR pig OR pigs) ) AND (("Sub-Saharan Africa" OR "Sub Saharan Africa" OR "Africa")) AND ( ((item-type:("Journal article" ) ) ) (sc:( "CA" ) ) ) (language:( "English" ) ) ) )

3. Scopus: "ALL" for terms including "Africa"; "Title, Abstract, and Keywords" for all other search terms. Limited to journal articles published in English.

TITLE-ABS-KEY((avermectins OR ivermectin OR eprinomectin OR doramectin OR anthelmintic OR anthelmintics) AND (cattle OR bovine OR cow OR cows OR bull OR bulls OR steer OR heifer OR calf OR calves OR swine OR porcine OR sow OR sows OR gilt OR gilts OR boar OR boars OR piglet OR piglets OR pig OR pigs)) AND ALL(("Sub-Saharan Africa" OR "Sub Saharan Africa" OR "Africa")) AND ( LIMIT-TO ( SRCTYPE,"j" ) ) AND ( LIMIT-TO ( DOCTYPE,"ar" ) ) AND ( LIMIT-TO ( LANGUAGE,"English" ) )

#### Objective 2:

##### Databases:

1. Agriculture, Life, and Natural Sciences Databases from Proquest with VA Tech Access: "Anywhere" for terms including "Africa"; "Anywhere but Full Text" for all other search terms. Limited to peer-reviewed journal articles published between 2010 – 2020, in English.

noft((cattle OR bovine OR cow OR cows OR bull OR bulls OR steer OR heifer OR calf OR calves OR swine OR porcine OR sow OR sows OR gilt OR gilts OR boar OR boars OR piglet OR piglets OR pig OR pigs)) AND noft((avermectins OR ivermectin OR eprinomectin OR doramectin OR anthelmintic OR anthelmintics) ) AND noft((resistance OR "anthelmintic resistance")) AND ("Sub-Saharan Africa" OR "Sub Saharan Africa" OR "Africa")

2. CAB Abstracts: "All fields" for terms including "Africa"; "abstract only" for all other search terms. Limited to journal articles published between 2010 – 2020, in English.

((ab:((cattle OR bovine OR cow OR cows OR bull OR bulls OR steer OR heifer OR calf OR calves OR swine OR porcine OR sow OR sows OR gilt OR gilts OR boar OR boars OR piglet OR piglets OR pig OR pigs) ) AND ab:((avermectins OR ivermectin OR eprinomectin OR doramectin OR anthelmintic OR anthelmintics)) AND ab:((resistance OR "anthelmintic resistance")) AND (("Sub-Saharan Africa" OR "Sub Saharan Africa" OR "Africa")) AND ( ((sc:( "CA" ) ) ) ) yr:[2010 TO 2020])) AND ( ((item-type:("Journal article" ) ) ) (sc:( "CA" ) ) ) )

3. Scopus: "ALL" for terms including "Africa"; "Title, Abstract, and Keywords" for all other search terms. Limited to journal articles published in English. Included articles published between 2010 – 2020 in the title/abstracts review.

TITLE-ABS-KEY((cattle OR bovine OR cow OR cows OR bull OR bulls OR steer OR heifer OR calf OR calves OR swine OR porcine OR sow OR sows OR gilt OR gilts OR boar OR boars OR piglet OR piglets OR pig OR pigs) AND (ivermectins OR ivermectin OR eprinomectin OR doramectin OR anthelmintic OR anthelmintics) AND (resistance OR "anthelmintic resistance")) AND ALL(("Sub-Saharan Africa" OR "Sub Saharan Africa" OR "Africa")) AND ( LIMIT-TO ( SRCTYPE,"j" ) ) AND ( LIMIT-TO ( DOCTYPE,"ar" ) ) AND ( LIMIT-TO ( LANGUAGE,"English" ) )

## Study records

### *Data Management:*

Records will be managed through Mendeley, reference management software (<https://www.mendeley.com>).

### *Selection process:*

RZ will be the primary reviewer and CR will be the secondary reviewer. All returned results will be reviewed for inclusion using title and abstract, with a full review performed when it is unclear from the title and abstract if the publication meets the inclusion criteria, or if there is a disagreement between reviewers. Disagreements between the reviewers will be discussed until consensus is reached. When reviewers identify a review article related to the topics of interest, they will also review the bibliography to identify any relevant papers missed with the initial search.

### *Data collection process:*

Using a standardized form, data extraction will be performed by RZ with random spot checks for verification by CR.

## Data items

Data extracted will include the following:

*Objective 1:* year of publication, country/countries where data were collected, study design, species investigated, ivermectin used, productivity outcome measured, effect of treatment.

*Objective 2:* year of publication, country/countries included, species investigated, ivermectin used, species of parasites demonstrating resistance, method/s used for evaluating resistance.

## Data synthesis

Data will be summarized in table format, with a written narrative synthesis of findings.

## References

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