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An update on trends in the types and quality of childhood immunization research outputs from Africa 2011–2017: Mapping the evidence base

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ABSTRACT

Background: Strengthening immunisation programmes in Africa remains a key strategy of improving vaccine coverage. Research plays a vital role in the design and implementation of strategic immunisation plans for improving vaccination coverage, in turn providing context specific evidence to inform policy and practice. We therefore updated an evidence map describing the types and quality of available literature on childhood immunisation in Africa from 2011 to 2017.

Methods: PubMed and Africa Wide databases were searched for English studies on childhood immunisation in Africa published from January 2011 to September 2017. Studies had to be conducted in humans and the reported information needed to be on either: vaccines; immunisation programmes; immunisation policies; or epidemiology of vaccine preventable diseases targeted by Expanded Programme on Immunisation vaccines.

Results: Out of 5567 studies retrieved, 797 studies from 165 journals met the inclusion criteria. During 2011–2017, 42 African countries contributed to research on childhood immunisation. Most studies were carried out in multiple countries (15.1%). Five countries contributed 41% of the total research output. Nigeria and South Africa contributed the highest proportion of studies at 12% and 11.4% respectively. The quantity of research output increased progressively from 2011 to 2015 after which there was a significant decline.

Conclusion: There was a remarkable increase in childhood immunisation research in the period 2011 to 2017 when compared to the initial assessment. However, the reason for decline in research output from 2015 requires further investigation. Most childhood immunisation research was still generated by five countries as previously observed, highlighting the critical need for strategic investment in research capacities and improved collaboration between countries in Africa.

1. Introduction

There are multiple known benefits of childhood immunisation which include reduction of mortality and morbidity, as well as aversion of disability associated with vaccine preventable diseases [1]. The World Health Organisation (WHO) has placed child immunisation as one of the high priority interventions needed to effectively reduce under 5 years old mortality [2]. It is therefore not surprising that childhood immunisation is central to many global initiatives [3–5].

Despite the considerable progress in attaining high childhood immunisation coverage, one out of five children in Africa does

Abbreviations: AU, African Union; GVAP, Global Vaccine Action Plan; JIF, Journal Impact Factor; MeSH, medical subject headings; NIP, National Immunisation Programme; NITAG, National Immunisation Technical Advisory Group; VPD, Vaccine Preventable Diseases.

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not receive these essential vaccines [6,7]. The Expanded Programme on Immunisation (EPI) in African countries has attained significant progress since its establishment in 1974. However, EPI in Africa still faces many challenges including suboptimal funding, poor immunisation data quality, insufficient resources, and vaccines stock outs [8] among others.

Contributions of immunisation research in Africa to the global immunisation research pool have been well described by two past studies [9,10]. Both studies focused on research conducted during a 40-year period starting from 1970 to 2010. Wiysonge et al., conducted a bibliometric analysis that assessed the factors associated with childhood immunisations research productivity in Africa, and found that Africa's contribution was minimal and private funding was positively associated with productivity [10]. Machingaidze et al. assessed the trends, types and quality of childhood immunisation research output in Africa, finding that 48 African countries contributed to childhood immunisation research, and six of these countries (South Africa, The Gambia, Nigeria, Senegal, Guinea-Bissau and Kenya) accounted for over half of the total research outputs [9]. The urgent need for the development of research capacity in low performing countries around Africa was highlighted [9].

Since these two key publications [9,10], a major milestone in global health was reached in 2015 - the end of the Millennium Development Goals [3]. While great strides were made to reduce child mortality by two thirds since 1990 (Goal 4) – this target was not met [3]. As Africa contributes towards the global effort set by the new Strategic Development Goals (Goal 3 in particular) [5], it is important to ensure comprehensive, context-specific, timely research is conducted to inform decisions relating to vaccination programmes on the continent.

This updated analysis aims to ascertain the types and quality of childhood immunisations research output on the continent from 2011 to 2017 and compare the results with those previously assessed by Machingaidze et al., (1970 to 2010).

2. Methods

2.1. Search strategy

Two electronic databases; PubMed and Africa Wide were searched for English peer reviewed articles from January 1, 2011 to September 9, 2017. The search strategy from the previous analysis [9] was used (Supplementary file 1). Medical subject headings (MeSH) and free text terms for vaccines, immunisation, children, adolescents, adults and Africa were searched. Reference lists of selected articles were also searched to identify other relevant articles that may have been missed by the search and qualify for the inclusion.

2.2. Study selection

Studies were included if they were: (1) carried out in humans, (2) conducted in Africa and, (3) focused on research outputs on vaccines or immunisation programmes or policies or epidemiology of vaccine preventable diseases (VPDs) targeted by traditional or new EPI vaccines. Studies reporting the epidemiology of VPDs without any reference to a specific vaccine were excluded. Retrieved articles were screened by one reviewer (HEC) and verified by a second reviewer (BMK).

2.3. Data extraction analysis

One reviewer (HEC) extracted data from the included articles using a predesigned MS Excel data extraction form. Data extracted from the included studies consisted of the type of the research (Clinical or Operational), location, period and disease targeted. Verification of the data extraction was carried out by the second reviewer (BMK). Extracted data was imported into STATA v. 14 for analysis. Quantitative results were presented as proportions.

2.4. Quality of studies

The same criterion used for accessing the quality of studies in the previous assessment of the peer-reviewed literature [9] was applied in this updated analysis. The criterion involved the use of Journal Impact Factors (JIFs) to categorize and classify the quality of studies as follows: greater than zero but less than two were considered of 'moderate' quality; two to five were considered of 'good' quality; six to ten and greater than ten were considered of 'very good' and 'excellent' quality respectively.

3. Results

3.1. Literature search

A total of 5567 articles were retrieved from the two databases (PubMed = 4437, Africa Wide = 1130). After duplicates were removed 4876 articles were left for screening. The titles and abstracts of these articles were screened and a further 3390 were excluded. The full text of the remaining 1486 were screened and 1049 met the inclusion criteria. Out of the 1049 included studies, 797 focused on immunisation of children (Fig. 1).

3.2. Quality of research

The 797 studies on childhood immunisation research output were published in a total of 165 peer reviewed journals. We further characterized the 165 journals, based on the JIFs as at 2016. The JIFs ranged from 0.12 to 72.4 [11]. The median JIF was 3 (IQR: 2.27–4.25). Thirty-eight journals where 54 studies were published had missing or no JIFs. One hundred and fifty-three (153) studies published in 54 journals were of moderate quality (JIF > 0 and JIF < 2) whereas 410 studies published in 50 journals were of good quality (JIF > 2 and JIF < 5). Additionally, 120 studies published in 13 journals were of very good quality (JIF > 5 and JIF < 10). The remaining 57 studies published in 10 journals were of excellent quality (JIF > 10).

The highest number of studies (n = 148) were published in the Vaccine journal. The second and third highest number of studies were published in PLoS One (n = 64) and the Journal of Infectious Diseases (n = 54) respectively. Table 1 shows the number of studies published per journal with the corresponding 2016 JIFs. Only the top 10 journals (defined by the highest number of publications) are shown in the table.

3.3. Trend in the number of studies published

There was a gradual increase in childhood immunisation research output from 2011 to 2015 followed by a sharp drop in 2016 and 2017 (Fig. 2). The highest number of studies (n = 154, 19.32%) published in the seven-year period was observed in 2015. The change in the proportion of studies over time was statistically significant (p = 0.004).

3.4. Childhood immunisation research output by individual African countries

The included studies were from 42 of the 54 African countries. Out of all the total studies 15.1% (n = 120) were carried out in multiple African countries (Fig. 3). The top five ranking individual

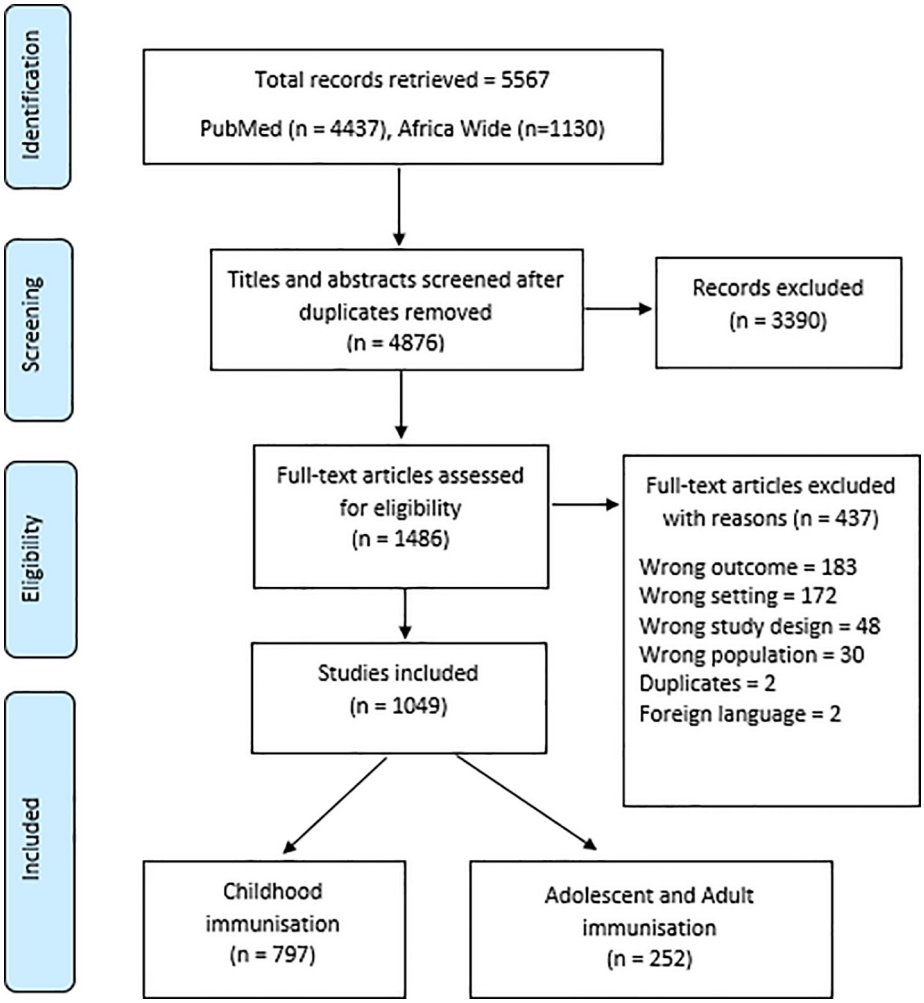

Fig. 1. Flowchart for selection of studies.

Table 1
Top 10 journals with their impact factors.

Journal	Number of studies	2016 Impact Factor
Vaccine	148	3.24
PloS One	64	2.8
Journal of Infectious Diseases	54	6.27
BMC Public Health	41	2.27
Clinical Infectious Diseases	35	8.22
Paediatric Infectious Disease Journal	27	2.49
Pan African Medical Journal	24	0.33
BMC Infectious Diseases	19	2.76
Human Vaccine & Immunotherapeutics	15	1.44
Lancet Infectious Diseases	11	19.86

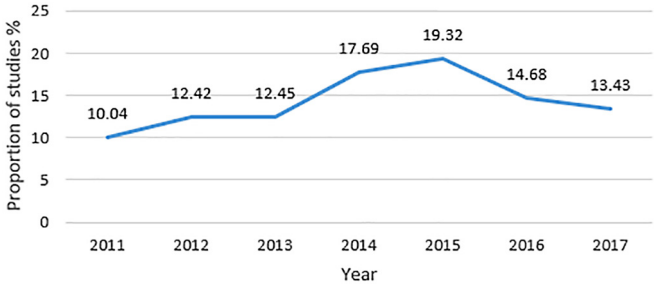

Fig. 2. Trend in the number of published studies.

countries with the greatest childhood immunisation research output were: Nigeria (n = 96, 12%); South Africa (n = 91, 11.4%); Kenya (n = 61, 7.6%); Guinea Bissau (n = 42, 5.2%) and The Gambia (n = 38, 4.7%) (Fig. 4).

3.5. Classification of the childhood immunisation research outputs

3.5.1. Type of study

There were more clinical studies (n = 425, 53.3%) than operational studies (n = 372, 46.7%) (Table 2). Among the clinical studies, most of the outputs, 196 (46.1%) were on the burden of disease or epidemiology of vaccine preventable diseases. Other types of clinical studies, 174 (41%) were either on mortality or assessment of immune response to vaccines or adverse events following immunisation. The last 55 (12.9%) clinical studies were grouped as phase I to IV clinical trials.

For the types of studies classified as operational, the categorization was as follows: 314 (84.4%) were on programme management; 41 (11%) on finance and finally, 17 (4.6%) on policy.

3.5.2. Vaccine preventable diseases

Looking at the distribution of diseases, a quarter (n = 206, 25.8%) of all the studies focused on a cluster of diseases targeted

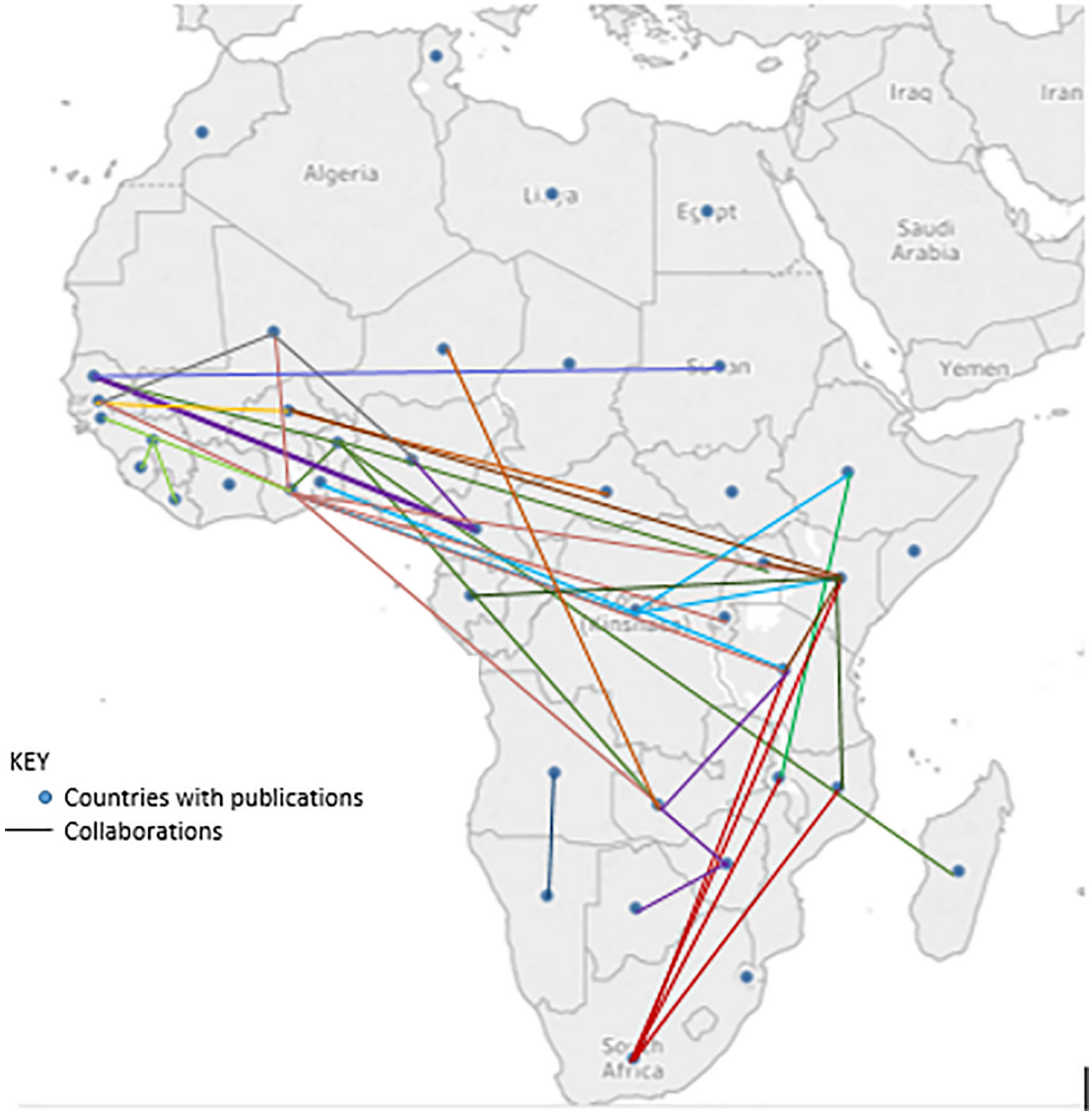

Fig. 3. Collaboration between African countries for research on childhood immunisation.

by the EPI -BCG, polio, diphtheria, tetanus, pertussis, hepatitis B, measles, haemophilus influenza. Nineteen (2.3%) studies targeted two or three diseases while the most frequent single disease studies were on pneumococcal disease (n = 76, 8.6%) measles (n = 73, 9.1%), polio (n = 72, 9%) %), diarrhoea (n = 68, 8.5%), malaria (n = 53, 6.6%), tuberculosis (n = 51, 6.3%), meningitis (n = 46, 5.7%), hepatitis B (n = 29, 3.3%), cholera (n = 13, 1.6%) and influenza (n = 13, 1.6%). Other diseases reported at much lower numbers were yellow fever, typhoid, ebola, HIV, rubella, onchocerciasis, non-typhoidal salmonella, schistosomiasis.

4. Discussion

This analysis found that between 2011 and September 2017, 42 African countries, led by Nigeria and South Africa contributed to research on childhood immunisation. There were more clinical studies carried out than operational studies. Most studies focused on the EPI as a unit and pneumococcal disease. The quantity of childhood immunisation research output increased progressively from 2011 to 2015 after which there was a sharp and significant decline.

Between 1970 and 2010, South Africa had the highest number of publications followed by Nigeria [9]. Post-2010 we observe that Nigeria now tops the publication list followed by South Africa. These two countries remain the leading contributors of childhood immunisation research output on the continent. The high research productivity by Nigeria and South Africa has been attributed to better access to financial and skilled human resources for research [9,10]. Only five countries accounted for 41% of the total childhood immunisation research output in Africa – an observation made in the previous analysis [9] and indicates little improvement within countries. However, there was an encouraging finding; 15% of the childhood immunisation research outputs were from collaboration of multiple African countries. As previously suggested [9], leveraging on countries with greater research productivity and infrastructure can help to bridge the gap. Such a collaborative network would help the efficiency of individual countries to identify bottle necks in EPI and implement appropriate corrective interventions without always having to conduct extensive primary research, saving both time and limited resources.

Over the past seven years more clinical studies than operational studies were carried out as opposed to the similar ratio of studies reported before 2011 [9]. The clinical studies focused mostly on the

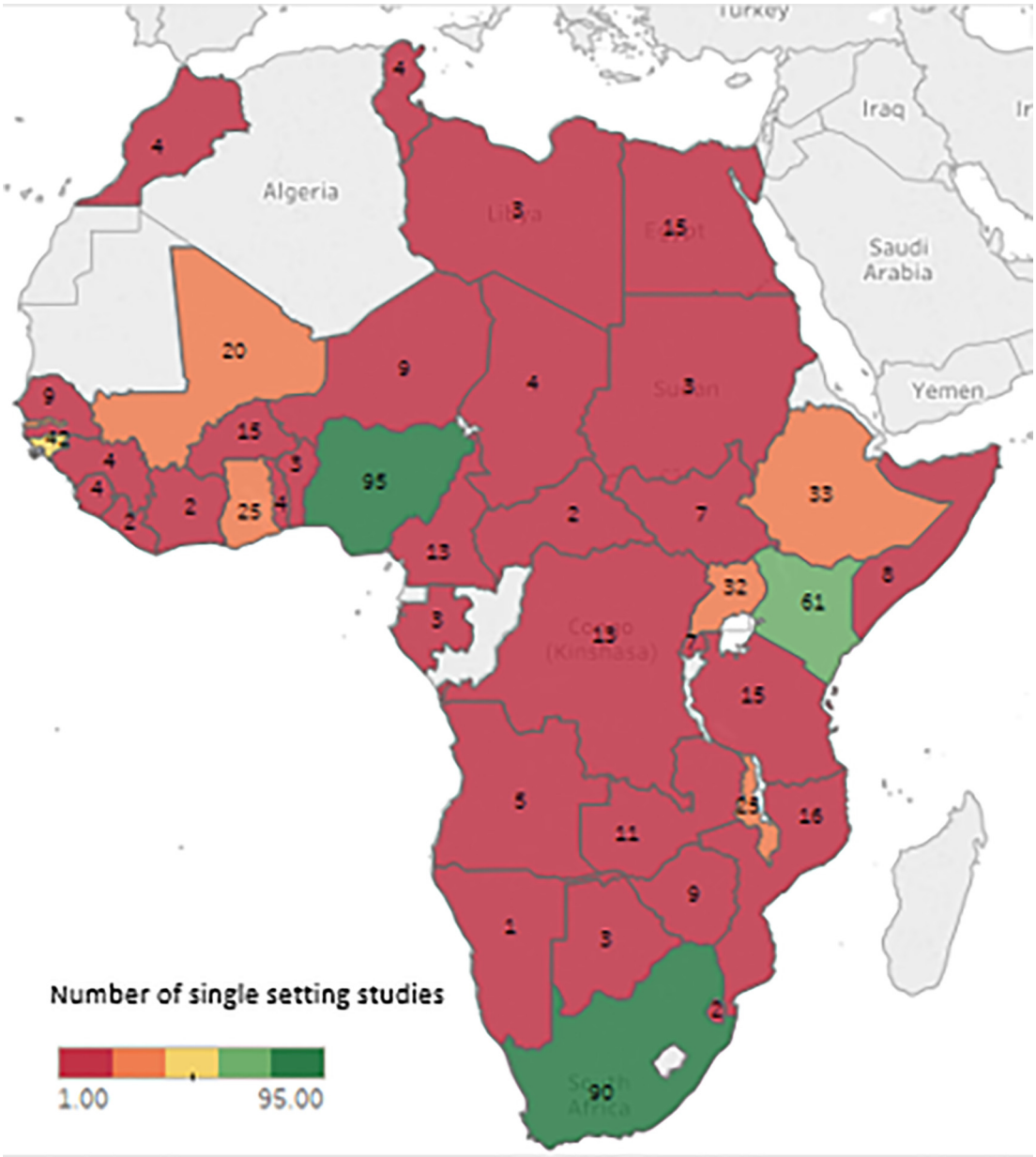

Fig. 4. Distribution of immunisation publications across Africa.

burden of diseases targeted for eradication and elimination. As the set date for polio eradication approaches, efforts are being put in place to ascertain that countries remain polio free and transmission ends in endemic areas [12]. The same can be said for measles which is targeted for elimination in 2020 [13]. Before 2011, childhood immunisation research outputs classified as clinical studies were mostly phase I to IV clinical trials. Both epidemiological studies and clinical trials are necessary and complementary. An increase in clinical trials would be a reflection of a stronger and more robust research environment.

For the operational studies, we observed a low output for studies on policy (4.6%) which is less than what was observed between 1974 and 2010 period (18%) [9]. New or revised policies are needed for the achievement of National Immunisation Programme (NIP) goals. New or revised immunisation policies will address the increasing demands of challenges such as introducing new vaccines, vaccine safety concerns, expansion of vaccination schedules to older age groups among others.

Countries are encouraged by WHO to establish or strengthen National Immunisation Technical Advisory Group (NITAGs) to guide policy on immunisation by providing decision makers with evidence-informed recommendations [2]. As of 2017, NITAGs have been established in <25% of African countries [14]. While it is important not to recreate the wheel and NITAGs can make use of programmatic evidence generated from other parts of the world that can be generalised, some challenges such as understanding vaccine-seeking behaviour and challenges linked to the efficiency of the local health system are unique and require a tailored approach. Strategic investment in research aimed at answering specific questions should be guided by the changing field of vaccinology. The leaders of EPI, with advisory support from NITAGs, should constantly use the research outputs to improve their understanding of the functioning of the national EPI and broader health system.

Financing remains an integral part of immunisation programmes and health systems. We observed a 2-fold increase in studies on financing as compared to the 1974 to 2010 period. Most

Table 2
Classification of studies.

Type of study	Number of studies n, (%)
Clinical	**425**
AEFI	23 (5.4)
Epidemiology/Burden of disease	196 (46.1)
Immune response	141 (33.2)
Mortality	10 (2.4)
Trial (Phase I-IV)	55 (12.9)
Operational	**372**
Policy	17 (4.6)
Finance	41 (11)
Programme management	
• Vaccine coverage	155 (41.7)
• Service delivery	31 (8.3)
• Logistics	16 (4.3)
• Management	7 (1.9)
• Communication	18 (4.8)
• Advocacy	34 (9.1)
• KAP (Knowledge, attitudes and practices)	40 (10.8)
• Integration of other services into EPI	13 (3.5)

African countries still depend on the Global Alliance for Vaccines and Immunisation (GAVI) for support and this support is temporary [15]. While private or donor funds are essential in improving vaccine coverage in Africa, adequate local research on financing is necessary so that when GAVI support ends, national governments will have identified alternate sustainable sources to finance and mange the EPI. In 2014, African governments agreed to spend 1% of the national gross domestic product on research but this has not been implemented by all countries as a result of multiple reasons such as competing national budget expenses [16]. Country ownership and political support for EPI is essential if the immunisation gains made to date in the African region are to be sustained [17]. Private-public partnerships such as the partnership that led to the manufacture of the meningitis vaccine at a cost of $0.50 per dose are proof that such partnerships are a critical component in helping vaccines become more affordable as African governments take on more financial responsibility in the near future [18].

Turning to the specific areas of research, many studies focused on the EPI as a unit however, pneumococcal disease was the most studied disease. Machingaidze et al., reported measles as the most studied disease between the 1974 and 2010 period despite pneumonia being the leading cause of infant mortality by the 2000s [9]. With the elimination of measles underway and a drop in mortality caused by the disease, focus has since shifted to pneumococcal disease which is still the leading cause of infant mortality in Africa [19]. As predicted by Machingaidze et al., we observed a 7-fold increase in research targeting diarrheal disease as compared to the 1974–2010 period [9]. The shift in research focus shows that research is being driven by the burden of disease on the continent. Similarly, during the 1974–2010 period, there were no studies carried out on malaria but the advances of malaria vaccine research in the diaspora have led to the establishment of malaria vaccine research in Africa.

We observed a large increase in the childhood immunisation research outputs produced between 2011 and 2017. Most countries have increased their research output and this is likely to have been spurred by the African Union's (AU) call to boost research on the continent in line with the Science Technology and Innovation Strategy for Africa-2024 [16]. Between 2011 and 2013 there was a progressive increase in research output followed by a sharp increase from 2013 to 2015 then a sharp decline. The first sharp increase from 2013 to 2014 was driven by a surge in polio research. This period corresponds to the time when countries were preparing for the switch from trivalent oral polio vaccine (OPV) to bivalent OPV and the introduction of inactivated polio vaccine (IPV) into routine immunisation in order to prevent vaccine derived polio type 2 [12]. The second increase from 2014 was driven by pneumococcal disease research. Interestingly, the observed decline in research output from 2015 to 2017 coincides with the end of the MDGs and start of the SDGs. Implementation of both the IPV switch and introduction of PCV into EPI schedules was underway and this may have contributed to the decline as countries focused on implementation. However, this is speculation on the part of the authors and needs to be further investigated.

Using the same measure for the quality of studies as the previous study, most of the included studies were of good quality. The top 10 journals with the most publications differed from those in the previous analysis except for Vaccine Journal and Journal of Infectious Diseases. The South African Medical Journal which had the highest number of publications in the previous analysis was not among the top ten ranking journals in this one. This is likely due to the fact that during the period covered in the first analysis, South Africa had the highest research output, with South African Medical Journal (SAMJ) serving as a local and accessible journal to researchers. We noticed a shift to more specialised and international journals.

Similar limitations to those highlighted in the previous analysis were observed [9]. Firstly, only two databases were searched thus studies not indexed in these databases were missed. However, PubMed is held as a reliable representative source for peer-reviewed publications, with Africa-wide ensuring that additional journals not indexed in PubMed can also be captured. Secondly, only articles written in English were included. Studies published in the other official languages on the continent (French, Spanish, Portuguese) were missed. Thirdly, journal impact factors were used as proxies to measure the quality of individual studies. While journal impact factors are not the most ideal measure for research quality, they provide a fair measure as they combine the number of times a journal has been cited in the past year, as well as a yearly measure of the comparative importance of a journal in relation to other journals in its field.

5. Conclusion

Vaccine and immunisation research in Africa over the past seven years has increased greatly compared to the previous decades. This increase in research forges a way towards the achievement of the sixth strategic objective (for country, regional and global research and development innovations to maximize the benefits of immunization) of the Global Vaccine Action Plan. The research which is mostly clinical has been driven by the burden of disease on the continent. Despite the high research output, research is still lagging in key areas such as finance and policy which are key areas necessary for the achievement of SDGs. Moreover, only a handful of countries continue to generate the majority of the research output highlighting the critical need for strategic investment in research capacities and improved collaboration between countries in Africa. As 2024, which is the deadline for Africa to transition into an innovation-led, knowledge-based economy is only six years away, countries should take advantage of the strategic plan [18] laid by the AU to improve research on the African continent.

Data statement

The datasets used and/or analysed during the current study are available from the corresponding author on reasonable request.

Conflict of interest

The authors declare that we have no conflict of interests.

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None.

Author contributions

GDH, SM and CSW conceived the study. ECH conducted the search, data extraction and analysis with supervision from BMK and GDH. ECH wrote the first draft of the manuscript together with SM and BMK. All authors reviewed all versions and approved the final draft.

Appendix A. Supplementary material

Supplementary data to this article can be found online at https://doi.org/10.1016/j.jvacx.2018.100001.

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