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Diseases of Poverty: The Science of the Neglected

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1. Introduction

Diseases of poverty are those diseases identified as affecting the poorest and most disadvantaged populations in the world. Poverty is one of the main risk factors for the conditions, creating exposure to poor water and sanitation; poor nutrition, poor environmental conditions that favour the growth and spread of micro-organisms and vectors that cause and transmit disease; and lack of education and access to appropriate disease prevention, health promotion, treatment and rehabilitative services. Diseases of poverty include for instance, the neglected tropical (communicable) diseases (NTDs) which until relatively recently were considered low priority for both governments and pharmaceutical companies (1–4). Furthermore, diseases of poverty increasingly include the non-communicable diseases (5–7); hypertension, cardiovascular diseases, diabetes and other metabolic diseases and cancers, previously considered diseases of affluence (8–11). While there is some variation in the specific drivers that cause and exacerbate the communicable and non-communicable diseases for the poor, invariably, the processes and context are similar, impeding choices for healthier lifestyles, access to and acceptability and affordability of regular and quality care for chronic conditions and strategies for prevention and health promotion. In turn, affliction with these diseases hinders economic opportunities and development and perpetuates poverty. The disease increases vulnerability and exposure to poverty by increasing household expenditure and decreasing household income.

Through mechanisms provided by the Millennium Declaration and associated Millennium Development Goals, the World Economic Forum, the Global Fund, the Bill and Melinda Gates Foundation and the US President's Emergency Fund for AIDS Relief, the global health community has highlighted the plight of the poor and vulnerable, and gained support to address the major diseases. There is more funding available in global health now than there has ever been before (12–14). Major drug companies have committed to free donation of particular pharmaceuticals in an effort to achieve elimination of a number of diseases (15). The more recent UN Summit on NCDs employed this global advocacy process to elicit support from the highest levels of government to address the growing burden of specific chronic diseases. Critically however, programmes that result from these global health campaigns have historically been characterised largely by disease focused, vertical interventions that treat communities as a collective, providing a large scale clinical intervention. Much less attention is

focused on the more persistent underlying contributors to diseases of poverty – poverty and its other contextual drivers that are intimately interlinked with the diseases and outcomes.

In this discussion paper, we argue that despite the importance of these contextual drivers, they are largely neglected in the science and evidence that contributes to solutions for addressing diseases of poverty. We begin with the premise that there are fundamental differences in the ways that different disciplines conceptualise health, illness and disease. From a biomedical and clinical sciences perspective, diseases of poverty represent 'slugs, bugs and drugs' and present an ideal opportunity for technical fixes. There is robust evidence on the efficacy of these fixes and a strategy based on this evidence presents good value for money(16–20). From the perspective of the social sciences however, there is less of a separation between the person, the human condition, the environment and the disease process. The interest, from a social science perspective is primarily in the social, cultural, environmental and economic drivers of poverty and disadvantage, societal norms that mitigate marginalisation and the ecological factors that determine who becomes ill, what they do about it, and the outcomes of the illness. This would therefore also encompass the contextual factors that would enhance or hinder the delivery of a given biomedical strategy that involves populations. While robust and theoretically grounded, evidence from social science research and solutions that arise from that research may not necessarily present the kinds of context free, quantifiable, linear solutions that are frequently desired under biomedical research models. Similarly, under social science models, a solution that removes proximal causes of suffering without addressing the more distal and complex contextual factors that continue to put populations at risk, may not appear to be a desirable end point for a strategy. In this paper therefore we explore:

1. The contextual factors the define diseases of poverty;
2. The challenges in conceptualising and operationalizing these factors for the purposes of generating evidence;
3. The barriers to the translation of social science generated evidence in global public health; and
4. Some solutions to rebalancing the scientific approaches to neglected.

To address these questions, this report consists of a critical review of the diseases of poverty with a focus on the social, cultural, environmental and other contextual factors that affect risk, exposure, treatment and sequelae. In this context, diseases of poverty refer to the neglected diseases defined as those diseases which (i) have a disproportionate effect on the most disadvantaged sections of the community (the poor and marginalised); and (ii) lack investment in research and development for solutions that are explicitly accessible to the disadvantaged. We then provide a critical analysis of the sciences required to explore the complex nature of neglect in diseases of poverty and offer some suggestions for a broader approach to achieving long term solutions.

2. The context of diseases of poverty

Most of the conditions identified as diseases of poverty are treatable with currently available drugs. That notwithstanding, prevalence of these conditions remains high and the conditions persist (21). The neglected tropical diseases campaign for instance has relentlessly highlighted the plight of the populations affected by the range of target diseases.

A great deal has been made of stigmatization, disfigurement, persistent poverty, poor maternal and child health outcomes, poor health and education of children caused by infectious diseases (4,22–24). The choice of the word "neglect" is pointed and loaded, forcing us to reflect on our social obligations. Inherent in this campaign strategy is an appeal for the recognition of human suffering and the need for social justice (25).

These issues have been raised time and again by researchers working across the areas of health and human rights, the social determinants of health (26) anthropology and sociology (27–31) to mention a few. At the very least increasing standards of living, provision of the basic human rights of food, shelter, and clothing are definitive interventions towards the elimination of diseases of poverty. The body of evidence that supports the need for structural intervention is significant (32) and is obvious in the lack of these diseases in communities with an even marginally higher socio-economic status than "the bottom billion" (33). Tackling structural problems is harder because the interventions required are more complex; some have suggested too complex to consider (34). However not intervening at these levels increases the futility of current efforts. The re-emergence of diseases that were supposed to have been eradicated 40 years ago (35) is a case in point.

Other vulnerabilities highlighted in diseases of poverty include stigmatisation, social isolation, and disfigurement. These are vulnerabilities that result from social and cultural norms of what is considered normal and who is an acceptable member of the community (28,36,37). The effects of these on health relate to values that are less tangible than disease; equity, opportunity, access - and require intervention at different levels.

The basic concern here is not new and to a significant degree, revisits the major, largely unresolved debates that raged almost 40 years ago between proponents and opponents of Primary Health Care (PHC) (38–40). The critical question is this: does one partition out individual, proximal, biological causes (i.e., the disease) and address them as independent context free problems, or is there a need for a different approach which attempts to address the multiple distal and proximal causes within the context in which they occur? The primary health care debates addressed this question in favour of a disease specific approach with the introduction of Selective Primary Health Care programmes (41), vertical programmes. This establishes the putative 'pro-poor' credentials of diseases of poverty, despite the focus on identifying unabashed medical and technological fixes – the "magical bullet" to combat disease (38).

The contribution of the biomedical technologies cannot be underestimated. However, unless there are also significant interventions to address *health* and *poverty*, and the myriad marginalising factors in the social, cultural, economic, political and physical environments in which affected populations live, there will continue to be neglected people. Even in the research into the NTDs there is a distinct and patent disinterest in the social and contextual (42). Vaccines and drugs do not cure *neglect or poverty* and are not sufficient to rescue the neglected bottom billion from poverty (18).

3. The Implementation gap[1]

Even if it is decided that it would be safe to focus on the health side of the agenda rather than the poverty side, social and environmental (i.e., contextual) concerns cannot be

[1] This section draw significantly on earlier work of the authors and re-presents a number of the ideas without repeated citation, but also extends on some of those ideas(43).

avoided. An almost exclusive focus on the biomedical overestimates the value of the current science, leaving unresolved issues with implementation; that is, embedding a putatively effective intervention in a community. It is, after all, not enough to have the perfect cure if no one in need is able to receive it. Whether an intervention to be implemented in neglected populations has the same benefit in that population as it does in another population is an empirical question.

The randomised control trial (RCT) is widely regarded as the "gold standard" form of scientific evidence for establishing the effectiveness of a treatment (i.e., the cause effect relationship between treatment and cure), with decreasing levels of evidence treated with increasing levels suspicion. The problem with the RCT (and the levels of evidence) is that, in a general sense, and contrary to the expectations of many researchers, an RCT does not show the effectiveness of a treatment. It shows the effectiveness of a treatment in a particular context. Conducting multi-site RCTs, or conducting meta-analyses of multiple RCTs supports the generality of the finding. However, the conclusions about effectiveness can never be made without acknowledging the very controlled nature of experimental studies on which the conclusions about effectiveness are based; and by extension, the limitations imposed on generalising the results into less controlled, more realistic, contexts.

The intention to treat (ITT) analysis of RCTs is a partial acknowledgement of the problems of context. In the simplest kind of RCT, patients are randomly allocated to a treatment or a control (non-treatment / "usual treatment") group. Imagine that some people who were allocated to the treatment group ended up receiving no treatment – just like the control group. Under the ITT analysis, one analyses the results of the intervention as if all the people allocated to the treatment group, even those who did not receive treatment, did end up receiving treatment. This can seem somewhat counter-intuitive. Why would one analyse data counter to the reality of what happened? The analysis, however, establishes the effectiveness of a policy, i.e., an intention to treat patients in a particular way. The biological efficacy of the treatment should have already been established in early stage trials, and not be in doubt. The ITT analysis established the effectiveness of a treatment policy in a particular clinical setting.[2]

The use of community-based trials, and 'less rigorous' forms of effectiveness study try to capture the likely context in which an intervention might actually be employed; and to some degree they support the generalisation of the findings. A caveat, however, always remains, because study sites are inevitably different from sites that do not fall under the scrutiny of researchers. The context of the research study is not the context in which most lives are lived. The generalisation of the conclusions from the research study site to the populations that do not live under those conditions goes beyond the science.

The philosopher of science Nancy Cartwright raised points relevant to this argument in other branches of science. The issue is about what one knows in a general sense from doing scientific research. One of her points was that what one knows, relates to the context in which the research was conducted. Two illustrative examples of hers relate to the electronic transistor and to a leaf blowing in an alley. Consider the first example of the electronic transistor; a device used to regulate the flow of electricity. The basis of the transistor is grounded in quantum physics – a

[2] Interestingly, DDR recently read a description of statistical techniques to avoid the ITT analysis, so that the "true" effect of the intervention could be estimated. This presupposes that the idea of a true effect devoid of a context in which a treatment is applied makes any sense – which seems very doubtful.

theory that is free of contextual considerations. This means that a transistor works the same in New York, Bogotá, and Ouagadougou. When you start your laptop computer, which has millions of transistors, you do not first have to find out where to make contextual adjustments to the transistors. Superficially the science under-pinning the transistor looks to provide the very kinds of context-free insight that real science is all about.

On reflection the context-free nature of the findings are superficial. It is not the case that the transistor works in all contexts; rather, industrial manufacturing processes have been developed which make sure that the context within the transistors' housings remain the same without regard to where the transistors are. In effect, manufacturers have learned to create miniature, identical, controlled environments, with a fixed context of operation that conforms to an idealised model. The quantum effects work reliably and consistently within the bounds of the miniature environment, but without the same certainty outside that environment.

The second example is of a leaf. Science and engineering has provided significant insights into aerodynamics. We have instrumentally valuable theories that predict airflow and lift. Empirical work in wind tunnels, computer simulation efforts and theoretical advances allow for very precise predictions to be made about how aircraft will behave under a range of plausible environmental conditions. Predicting the path, however, that a leaf will follow when blown down an alley is beyond us. The idealised understanding that we have of aerodynamics allows us to frame and control the context of the science that is done. Aircraft wings are crafted so that they maximise our predictive capacity, and conform to our understandings of the laws of aerodynamics. When we cannot control the context of the science, however, what we actually know becomes far less impressive.

These observations are not pedantry, and they do not belittle the science that allows us to fly aircraft and build computers. What they do suggest, however, is that our science works because we know and understand the context in which it is applied. With a change in context, the success of the science is less certain. When developing health interventions, we do not have the luxury of constructing the context to suit the kinds of interventions or designing the intervention to work in a single context. Rather, we need to engage in the type of science that embraces interventions that are contextually appropriate.

At a recent scientific meeting on community directed ivermectin distribution program for the control of Onchocerciasis, a report was presented from Nigeria where the intervention was not achieving the results anticipated given known effectiveness and the reported high coverage of ivermectin. When the gap between coverage and results was investigated, the evaluation team found that the villagers were receiving the ivermectin; however, instead of taking the tablets themselves, they were distributing them among their cattle. The villagers had decided that the economic benefit of a healthy herd far out-weighted the health loss they faced by failing to treat their personal affliction with onchocerciasis.

The science had shown that ivermectin was a clinically effective approach to onchocerciasis control in one context. Community-based trials confirmed the effectiveness after scaling up the intervention in another context (44); and the economic analysis showed that it was cost-effective (45,46). This was the 'truth' as revealed by the science of fixed contexts. The reality, however, was that the effectiveness of the intervention depended on a range of contextual factors – such as competing economic incentives. Having located the research in fixed (or well regulated) contexts, the likely variability of outcome that occurs in the wilds of real life, did not enter into any decisions about effectiveness.

There are two important corollaries to this. The first: imagine two interventions both of which are significantly more effective than no treatment. Furthermore, in clinical trials researchers have established that intervention A is significantly more effective than intervention B (i.e., $A > B > 0$). When the context changes from the controlled research environment to point of implementation, the apparent magnitude of the effect of the interventions can reverse, with intervention B having a greater effect than intervention A (i.e., $B > A > 0$ or $B > A = 0$). This will occur if, at the stage of implementation, the more effective A cannot be embedded in the community.

The second corollary, which is an extension of the first, is that interventions that seem to be cost-ineffective in one context maybe the cost-effective interventions in another context, and the cost-effective intervention in another context will be the cost-ineffective intervention in this context. Continuing to use interventions A and B, following the effectiveness studies, the economic analysis established that A is more cost-effective than B. However, on implementation, when A fails to achieve any community up-take, B becomes the more cost-effective of the interventions. The implications of this are hard to under-estimate.

Decision making based on effectiveness and cost-effectiveness, which is a rational approach to the optimal allocation of scarce resources, may fail dramatically if the information on which the decision is based comes from the partial science of fixed contexts.

As Allotey et al. observed (p.3), effectiveness is regarded as the appropriate end point for most intervention research. But knowing that a treatment is effective in routine clinical care is not enough, particularly in resource poor settings (i.e., the settings of the neglected). The goal must be the sustainable adoption of the intervention by the health systems and the target population, and not simply the establishment of effectiveness in a monitored clinical population. In other words, an intervention must become embedded; firmly integrated as part of the health system and the health culture of the disease endemic setting. It must be available, acceptable, accessible and affordable to those who need it; used appropriately, and become a part of the disease prevention, treatment seeking culture.

Biomedical research is neither intended to address nor capable of addressing questions about implementation. Thus, not only is the value of the biomedical research limited by our lack of research on the contextual effects associated with implementation, it is also outside the expertise of those scientists to address the issues.

4. The science of the neglected

To this point we have argued that the approach to the neglected diseases has leveraged the idea of the vulnerable and neglected population to advance an argument for providing additional resources to the biomedical scientists so that they can develop cures for neglected diseases – "vaccines against poverty". We then discuss the evidence about social vulnerability to disease, and the possibility of social interventions that address more distal causes of disease – intervening before the biomedical concerns arise. Finally we argued that the focus on proximal interventions is based on a flawed notion of the under-lying science and the generality of that science. In effect we argue for the development of contextually relevant science capable of accounting for social and environmental factors affecting the implementation of interventions.

What is missing from our discussion is (i) the research that supports the implementation of proximal cures, and (ii) the research that supports distal interventions that change the social

vulnerability of neglected populations to disease. The obvious place to look for this research is in the social sciences literature, or the intersection between the clinical, biomedical, and social sciences literature.

In a bibliometric analysis of four diseases of poverty (chikungunya, dengue, leishmaniasis, and onchocerciasis) we found that social sciences contribute to less than 2% of the published research (42). That was a generous counting of the social sciences contribution. The research that was funded was generally insipid, because it was there to act as a hand-maiden for biomedical research, never intended to support a research agenda of implementation or distal intervention. And the lack of a social sciences research agenda has a negative impact on the value of the biomedical research that is conducted, and limits our options for intervention to proximal cures.

To say that the social sciences have been totally overlooked in the global health efforts would however be inaccurate. The value of the social sciences up until now, however, is qualified. In the area of NTDs, evidence from anthropological studies on stigmatization, the lived experiences of patients disfigured by diseases such as leprosy, yaws, onchocerciasis and filariasis, and the effects of these on health seeking, access to and quality of care, have been used particularly to support advocacy (4,18,28,53,24,54,55). The research that explores the reasons for the failures of programmes for instance is not insubstantial. Anthropological research has provided data on the importance of cultural and social constructions of illness and disease. We have some understanding of the different levels of practitioners, how and why they might be consulted and their role (or lack thereof) within a formal health system. There is evidence from the social sciences of the complexities and pathways to health seeking, the economic and social drivers, the effects of gender and other social determinants. Health economics has shed light on willingness of patients or clients to pay for different types of health services, interventions and pharmaceuticals; and the local market forces that hinder or enable distribution of and access to health services and pharmaceuticals. Health services and health systems research provides rigorous data on the socio-economic and political context in which local, national and global health policy supports (or otherwise) disease control programs.

In broad terms however, social science research in this area has to date focused largely on the evaluation of the implementation process and on factors that will enhance community participation in community based programs (56). Both the process and the outcome indicators therefore relate to the administration of treatment and where appropriate, a short term reduction in NCDs. In other words these approaches to 'deploying' the social sciences are rather utilitarian and often tokenistic (43). The consequences to this are the often questionable quality of the social science evidence generated. Implementation research for instance, if well designed and implemented has the potential to contribute significantly to disease control efforts – however it is an area of research that is poorly funded (43) The problem arises often because social scientists are invited onto teams to undertake specific research projects rather than being a conceptual part of the planning of the intervention (27)

To obtain the higher objective of improving the health and reducing vulnerabilities, it is important for researchers, policy makers and funding agencies to broaden the perspective on the range of research that is needed to address neglected diseases of neglected populations, and to rethink the types of integrated interventions and the nature of evidence to show effectiveness. There is a need to refocus on the health of neglected populations - health as an enabling process (38) - and not merely removing disease.

Critical opportunities are missed through the lack of integration of data from the social science disciplines. Health and illness are social constructs and as such, the disciplines and theories that help us to make sense of these issues should be as much a part of the agenda as pharmaceutical developments. It is tragic, for instance that so much is made of the suffering of patients of neglected tropical diseases, but there is little if any evidence in the funded programmes that addresses how families and communities affected by these diseases could be supported to deal with the social and economic sequelae. Studies of outbreaks of infectious diseases in South East Asia also highlight the almost exclusive disease focus of public health interventions and the total neglect of the mental health and social and economic consequences of these interventions (described as social chaos) on the populations affected (57). To address these issues would require a more complex understanding of the community and its dynamics and the broader political context in which the affected populations live.

Studies in gender for instance have produced frameworks that facilitate the integration of gender across programmes. Similar approaches have been suggested for use with the social sciences (27,43,57,58)

5. Alternative models

There are essentially two issues that are conflated in the advocacy and the current approach to diseases of poverty. The first is the focus on neglect and vulnerabilities – as highlighted above, a significantly complex issue which we, as global health professionals, have an obligation to address (47). These issues cannot however, be fully addressed by vertical programmes. The second is the specific issue of disease which forms an important part of the factors which may be the cause of, but also exacerbate and sustain poverty and vulnerability. This issue is the focus of vertical programmes (41). Interventions to address these two issues should clearly not be mutually exclusive, but often are.

The question of which general approach is better does depend on the expected outcomes but may of course be empirical. Assuming that the expected goal, as most global health programs stipulate, is the improvement of the health of populations, how would a poverty reduction, empowerment, equity based development programme fare against a preventive chemotherapy programme for instance, or one that combined approaches. Studies that test this empirically are rarely designed, in part because the different interventions seek different outcomes. Vertical programmes measure success in terms of reductions in the occurrence of specific diseases. Contextually based, comprehensive programmes count some broader measure of well-being as the desirable outcome. However it is difficult to imagine that there would be no value added to ensuring that the pieces lock together seamlessly. Programmes that privilege longer term improvements in the living conditions over merely achieving significant coverage of mass drug administration have shown a greater impact in rescuing communities and tackling concerns about neglected diseases and neglected populations (48). These tend to be smaller programmes, with significant input from communities and do not operate under the pressures of reporting to funders. Furthermore, when the outcomes of such programmes are published, the robustness of the 'evidence' is often questioned because they were not designed as 'empirical' studies (4,49–51).

There are data that could arguably have the potential to provide a proxy indication of how the different approaches measure up. We know for instance that significant funds have been invested into global public health most of which have gone into vertical programmes dealing with the big three and more recently, the neglected tropical diseases (13,52). Data

are also available on investments into other programmes designed to meet the other millennium development goals, which also address the vulnerabilities highlighted by the neglected disease advocates. A cost effectiveness analysis of these investments could technically provide an indication of what a dollar could purchase per intervention type. However the success of programmes still tends to be measured often by their coverage rather than by longer term outcomes, and in global health, seldom by improvements in the levels of poverty and broader development. Reasons for this include the time limited nature of programmes; the discipline focus of people involved in programmes, that is health sector and therefore the disease focus – lack of capacity to design the relevant research, monitoring and evaluation tools that would allow a focus that were any broader.

To focus on the addressing neglect and vulnerabilities from a health perspective would require a different way of conceptualising the link between poverty, health and disease, acknowledging the complexities and developing appropriate and realistic solutions. This would mean more than a simple combination of individual supplementary (vertical) programmes. It would also necessarily require a redefinition of outcomes and successes, working to a longer time frame than is currently adhered to in disease based vertical programmes. A detailed discussion is beyond the scope of this paper.

6. Conclusion

Diseases of poverty represent a rich and dynamic interplay between the context of people's lives and the disease process. The interaction is complex and evolves within a social and cultural context as much as it does within a physical and biological context. Understanding this complex dynamic is crucial for the sustainable management of diseases of poverty. The evidence from the health literature, however, is that there is little investigator driven social science research to speak of in the diseases of poverty, and a similarly poor presence of interdisciplinary science. Without this, our understanding and management of diseases of poverty is inevitably reduced to a strategy that relies on a repetitive, reductionist flat-world science to overcome an acknowledged complex system.

The research to address neglected diseases of poverty needs more sophisticated funders and priority setters. Pharmaceuticals (including vaccines) are critical, but they are not the only solutions, and their final application is not in flat worlds. Their application is in complex dynamic worlds in which pathologies evolve to exploits the social nature of humans. Our current understanding of the dynamic, and our understanding of how to develop sustainable approaches to disease management are poor. There are no research templates to overcome this, and the silos of current science into the diseases of poverty have discouraged the development of genuinely interdisciplinary research.

As a major recommendation there is a need to reconceptualise the outcomes for addressing vulnerability and the addressing the health needs of the neglected, poor, disenfranchised and dispossessed. Recognising that the challenges cannot be reduced to simplistic biomedical solutions is a first step. Global public health is ideally placed to bring together the different disciplines to engage in these developments.

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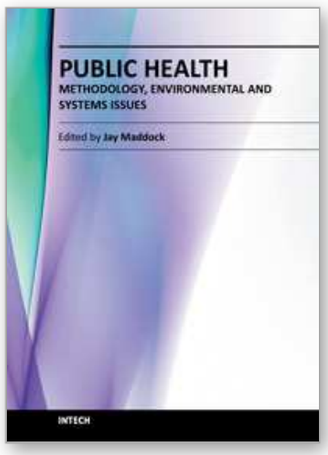

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Public health can be thought of as a series of complex systems. Many things that individual living in high income countries take for granted like the control of infectious disease, clean, potable water, low infant mortality rates require a high functioning systems comprised of numerous actors, locations and interactions to work. Many people only notice public health when that system fails. This book explores several systems in public health including aspects of the food system, health care system and emerging issues including waste minimization in nanosilver. Several chapters address global health concerns including non-communicable disease prevention, poverty and health-longevity medicine. The book also presents several novel methodologies for better modeling and assessment of essential public health issues.

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