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Social and Ethical Implications of HIV Cure Research

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Curing HIV: A New Scientific Priority

One of the defining qualities of living with HIV has been that it is incurable, and this basic fact has powerfully formed and disrupted individual, organizational, and institutional identities [1, 2]. But now this basic fact is contested. Today one individual appears to be cured [3, 4]. Several individuals are “post-treatment controllers,” having undetectable viral loads following a period of early antiretroviral therapy [5, 6]. HIV cure research, once unimaginable, is now at the center of public and scientific attention [7]. Curing HIV has become a strategic priority of the International AIDS Society and the National Institute of Allergy and Infectious Diseases at the US National Institutes of Health, spurring the development of global HIV cure collaborations and advancing initial clinical research efforts [8]. On both clinical and public health grounds, the identification of an effective HIV cure would be a great achievement. It could decrease morbidity and mortality associated with HIV infection, paving the way for comprehensive public health control efforts. At the same time, curing HIV is best conceived not simply as an absolute medical victory, but also as a social intervention whose meaning and effects are complex and uncertain.

Intended and Unintended Implications of Cure Research

History demonstrates that the social meaning of a disease – including how it is represented and policies pertaining to its treatment and control – changes dramatically when advances in biomedical research transforms it from incurable to treatable or even curable [9]. Research efforts aspire to the development of effective curative interventions that can be widely implemented in order to significantly reduce the burden of HIV infection. But new disease cures are rarely linear advancements. They are often contested and accompanied by a diversity of unintended consequences. While a completely effective and affordable cure could emerge and contribute to global HIV control, alternatively HIV cure research efforts might fail, leading to distrust and suspicion of researchers and public health authorities among HIV-infected individuals and the general public. Or a cure may be only partially effective or accessible to only a subset of HIV-infected individuals, raising questions of justice and equity. While the history of infectious diseases provides examples of disease eradication (e.g., smallpox), it is also rich with examples of cures, such as those for tuberculosis or syphilis, where the development of a new cure has complex effects on

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overall disease control. A more comprehensive understanding of the social context of curing HIV is fundamental to informing the logistics and implementation of research and programs [10].

Social and Ethical Analyses in HIV Cure Research

Given the complexity of curing diseases generally, and HIV in particular, a comprehensive social and ethical analysis is needed to accompany clinical cure research. Uncertainties about the scientific and social meaning of HIV cure research underline the need to conduct research that is both theoretical and empirical (Table 1). A proactive and multidisciplinary exploration of the social dimensions of an HIV cure can inform the conduct of clinical research studies and perhaps help to ensure that an HIV cure is accurately perceived and appropriately implemented. Conceptual, historical, and ethical analyses of HIV cure research are all important next steps that are briefly described below.

Conceptual analysis of HIV cure research

“Conceptual analysis” is branch of philosophy that examines concepts as holistic entities and constituent parts in order to better understand them [11]. It has great relevance to understanding the concept of an HIV cure. As a starting point, the broader concept of cure is embedded in the history, culture, and sociology of disease. Cure is defined in the Oxford English Dictionary as “to heal (a disease or wound)” or figuratively to “remedy, rectify, or remove (an evil of any kind)” [12]. This second definition implies that the process of cure is a complete removal of disease from the body, an absolute act that leaves the individual free of both symptoms and the pathogen itself. Two things are notable about this concept: its unambiguous positive trajectory (e.g., the idiom “to kill or cure” which means a way of solving a problem that will either fail completely or be very successful) and its finality. Cure is the terminus of physical abnormalities along the trajectory of illness. In this light, cure is inherently aspirational. However, while HIV cure is an appropriate long-term goal and strategic priority, there are many short-term and medium-term goals that will be necessary to achieve in order to develop a cure. A functional cure, defined as symptom control without viral elimination, or post-treatment control may be easier to achieve compared to a complete sterilizing cure. Further development of HIV reservoir biomarkers and animal models are necessary in order to clearly draw the boundaries between these new categories and assess the need for structured treatment interruptions.

Historical analysis of HIV cure research

The historical experience of HIV and cures for other infectious diseases such as syphilis [13] may provide insight into the social context of HIV cure research. HIV cure research could give rise to speculation, distrust and confusion in locations such as South Africa [14], Zambia [14], Zimbabwe [14], the Gambia [15], and Nigeria [16], where purported HIV cures have been discredited in the past. On a positive note, unsuccessful HIV cures reveal how HIV cure projects, even small trials and individual cases, can rapidly raise hopes and galvanize communities [15]. History suggests that efforts to cure sexually transmitted diseases may also result in unexpected synergies. For example, the momentum generated by a new cure for syphilis (penicillin) during the 1940s spilled over into strengthening syphilis

laboratory, diagnostic, and clinical capacity, setting the stage for several large-scale syphilis control programs [17].

Ethics and HIV cure research

The pursuit of HIV cure research raises a number of important ethical issues [18, 19]. Human research studies on curing HIV introduce ethical challenges related to assessing and communicating the risks and benefits of the research, challenges in participant selection, and therapeutic misconception. First, our understanding of the risks and benefits of individual participation in clinical HIV cure research is rapidly evolving. Small human studies limit the extent to which generalizations can be made about curing HIV. Such early trials may pose serious risks while initially producing little individual or social benefit. Standardized guidelines on how to explain the complexities of HIV cure research to a general audience are needed. Second, participant selection in early HIV cure research raises specific issues of beneficence and justice. Similar to antiretroviral treatment research [20], early trials are likely to involve white, non-marginalized, relatively affluent members of high-income nations and be optimized within those health systems. Access to promising studies or successful cure interventions would likely be available to lower income communities or countries only gradually over time. Finally, therapeutic misconception may be especially prominent in HIV cure research. Therapeutic misconception refers to “when individuals do not understand that the defining purpose of clinical research is to produce generalizable knowledge, regardless of whether the subjects enrolled in the trial may potentially benefit from the intervention under study or from other aspects of the clinical trial” [21]. Cure studies may be marked by a curative misconception among those who are HIV-infected and who hope to permanently rid their bodies of the virus.

Sociological/Normative Analysis

Normative analysis is an investigation of what ought to happen, drawing on theoretical constructs and value propositions. One potentially useful theory in considering HIV cure research is Merton’s theory of “unanticipated consequences of purposive social action” [22]. This sociological theory proposes that social actions could have unintended negative consequences in addition to their desired effects, negative consequences that perversely relate to the desired effects, or unintended positive consequences. This theoretical foundation could provide a richer understanding of the potential implications of HIV cure research. For example, HIV organizations that have exclusively provided HIV services without integration into local health systems may resist the growing momentum to consider curing HIV. Although HIV is increasingly perceived as just another disease, many jobs, careers, and identities are tightly linked with the service structures and research spawned by HIV [23]. At the institutional level, implementation structures that establish a false dichotomy between treatment and cure, similar to the false dichotomy between HIV treatment and prevention in the 1990s [24], could pit these potentially complementary approaches against each other. HIV cure implementation structures that identify individuals with acute HIV infection have inherent public health benefits, but HIV cure research and programs that depend on newly HIV-infected babies could introduce perverse incentives that

are misaligned with global expectations regarding the elimination of mother-to-child HIV transmission.

Conclusion

Thirty years ago, AIDS was a death sentence with no effective medical forms of prevention, treatment, or cure. Its high morbidity, mortality and association with stigmatized sexual and drug-use behaviors led to the rise of HIV exceptionalism, the tendency to treat HIV differently from other diseases. While this arguably was justifiable early in the epidemic [2], over time, a culture of HIV exceptionalism has profoundly shaped public perceptions, law, policy, advocacy, funding priorities, and the structure of health service delivery. How curing HIV either facilitates or hinders the integration of HIV services into routine health systems requires both empirical and theoretical investigation. As a society, we must insist that careful consideration, broad discussion, and clear communication surround the challenges and expectations, benefits and costs, and social and ethical implications of the work to find a cure for HIV.

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Table 1

Social and Ethical Considerations for HIV Cure Research

Cure Research Theme	Analyses	Key Research Questions
Theoretical Research	Conceptual	What is the operational definition of “cure” and other key terms such as “post-treatment controllers” ¹ ?
	Historical	How are previous disease cures relevant or not to curing HIV? What were important positive and negative consequences of efforts to cure other disease? How can history inform our understanding of curing HIV?
	Ethical	What are best ways to assess and convey the uncertain risks and benefits of cure HIV research? What are fair mechanisms to choose sites and participants? How can therapeutic misconception be minimized?
	Sociological/Normative	What is an appropriate theoretical framework to inform HIV cure research? How should cure research affect policy positions regarding HIV treatment and prevention?
Empirical Research	Policy	Who are the key policy stakeholders involved in HIV cure research? What are their perceptions of potential positive and negative implications of curing HIV?
	Anthropological	How do HIV-infected individuals, HIV physicians, and others understand treatment interruptions, risks and benefits, and other components of cure HIV research?
	Community Engagement	What media can be used to enhance conventional community engagement regarding HIV cure research projects?

¹Term used in the VISCONTI trial to refer to individuals who received early HIV treatment and viral load remains undetectable off therapy[6].