TRANSDISCIPLINARY INSIGHTS

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HIV-positive men as a key population for fighting HIVDR in Africa

**Jennifer Herrmann^{1,2*}, Jenny Lushaba^{1,3*},
Lotte Michielsen^{1,4*}, Nicklas Quirós^{1,3*}, Robbe
Saesen^{1,5*}, Coenie Louw⁷, Michael R Jordan^{8,9},
Anne-Mieke Vandamme^{1,6,10}, Astrid Van den
Eede¹, Anneleen Kiekens^{1,6,§}**

¹KU Leuven – University of Leuven, Honours Programme Transdisciplinary Insights, Leuven, Belgium;

²KU Leuven – University of Leuven, Master student Biomedical Sciences, Leuven, Belgium;

³KU Leuven – University of Leuven, Master student Philosophy, Leuven, Belgium;

⁴KU Leuven – University of Leuven, Master student Medicine, Leuven, Belgium;

⁵KU Leuven – University of Leuven, Master student Pharmaceutical Sciences, Leuven, Belgium;

⁶KU Leuven – University of Leuven, Department of Microbiology and Immunology, Rega Institute for Medical Research, Clinical and Epidemiological Virology, Leuven, Belgium;

⁷Gateway Health Institute, Pretoria, South Africa;

⁸Tufts University School of Medicine, Boston, USA;

⁹Tufts Medical Center, Boston, USA;

¹⁰Center for Global Health and Tropical Medicine, Unidade de Microbiologia, Instituto de Higiene e Medicina Tropical, Universidade Nova de Lisboa, Lisbon, Portugal.

*These authors contributed equally to the project;

§Email: anneleen.kiekens@kuleuven.be.

Abstract

This article is concerned with transdisciplinarity as a framework for addressing the wicked problem of rising HIV drug resistance (HIVDR) rates in Africa and its implications. According to data published by the Joint United Nations Programme on HIV/AIDS (UNAIDS), even though the number of AIDS-related deaths has declined by 48% between 2005 and 2016, this significant decrease is now threatened by a rise in resistance of HIV to antiretroviral drugs in several regions, including Africa. Through the application of transdisciplinary research methods, the team identified various factors with an impact on HIVDR, of which they found adherence to be the one most reasonable to address in the context of their research project. Subsequently, the team sought to characterise factors influencing non-adherence among HIV+ individuals. By identifying the current state of the problem, existing gaps in knowledge needed to tackle the issue and stakeholders with a pronounced impact on HIV+ individuals' adherence and beliefs, non-governmental organisations and community health workers were established as particularly important actors. As a result of discussions with external experts and a review of the literature, the poor health-seeking behaviour of men, who represent a group particularly challenging to engage, became the focal point of the project. Eventually, investigating the possibility of setting up a health helpline providing

peer-to-peer support to men living with HIV in South Africa was agreed upon as a concrete objective of the project in collaboration with Dr. Coenie Louw of the Gateway Health Institute. The attributes such a helpline would need to be useful and attractive to its target audience will be explored further in the near future by means of interviews with local community health workers as well as through focus group discussions with male HIV+ individuals in South Africa. A transdisciplinary approach to the problem of HIVDR facilitated the sharing of knowledge across multiple disciplines, which in turn facilitated the exchange of thoughts and ideas between students from different academic backgrounds and various stakeholders with expertise relevant to the project.

Key words

HIV, HIVDR, Drug resistance, HIV-positive men, Transdisciplinary methodology, Health helpline, Stakeholders, Stigma, Community health workers

Challenge Statement

A way to understand and prevent HIV drug resistance in Africa

Introduction

Note: *the authors have deliberately chosen to avoid labelling people infected with HIV as ‘patients’ throughout this article, opting instead for the terms ‘HIV+ individuals’ or ‘people living with HIV’. Thereby, they hope to contribute in part to reducing the stigma accompanying positive HIV status by refraining from automatically associating it with disease and suffering.*

Over the past decades, countless initiatives have been undertaken in order to optimise testing, treatment and care for those infected with human immunodeficiency virus (HIV). As a result, the number of deaths attributable to AIDS declined by 48% worldwide in just over a decade, from about 1.9 million in 2005 to 1.0 million in 2016 [1]. Antiretroviral therapy (ART) is a key contributor to this progress, with 60% of HIV+ individuals receiving ART in Eastern and Southern Africa in 2016 [1]. Due to the relatively low costs associated with their use and their sufficient availability, antiretroviral drugs belonging to the class of non-nucleoside reverse transcriptase inhibitors (NNRTI) are currently being used extensively in the first-line treatment of

HIV in a number of African countries [2]. As a result of the occurrence of corresponding mutations in the HIV genome during replication, however, viral resistance to antiretroviral drugs of all currently available classes, commonly referred to as HIV drug resistance (HIVDR), can arise [2], potentially resulting in insufficient viral suppression [2]. In the 2016–2030 period, HIVDR could thereby be responsible for an additional 16% of AIDS-related deaths and an additional 9% of new HIV infections ([3]). In 2017, the World Health Organization (WHO) carried out a systematic review of the literature [2] in order to estimate the prevalence of resistance to NNRTIs amongst adults who had never been exposed to antiretroviral drugs before, also referred to as ‘pre-treatment drug resistance’. Besides, the review described the evolution of pre-treatment drug resistance over the preceding 16 years in resource-limited settings. Over time, significant increases in pre-treatment drug resistance were observed across all low- and middle-income countries, with a particularly alarming estimated annual increase of 29% (95% CI 17–42) and 23% (95% CI 16–29) in Eastern and Southern Africa, respectively. Non-adherence to ART is an important factor contributing to the development of HIVDR. A systematic review of adherence to antiretroviral drugs in Sub-Saharan Africa covering the period between 2002 and 2014 found an average adherence rate of merely 72.9% among HIV+ individuals ([4]). Adherence rates of between 70% and 89% are strongly associated with the occurrence of HIVDR ([5]). Despite its relevance for the problem at hand, the factors contributing to a lack of adherence to antiretroviral therapy remain insufficiently understood.

The pronounced annual increase in the prevalence of HIVDR in several countries, including Eastern and Southern Africa, and its devastating consequences on both individual and public health illustrate the urgent demand for an improved understanding of the causes of HIVDR, including lack of adherence, and for immediate appropriate actions.

In a response to the aforementioned report of the WHO ([2]) and under the assumption that a complex problem such as HIVDR would benefit from a radically novel research approach, Dr. Michael R. Jordan provided a challenge document entitled “A way to understand and prevent HIV drug resistance in Africa.” (*Supplement 1*) to the Honours Programme Transdisciplinary Insights at KU Leuven. In this document, he specifically mentioned adherence to ART

as an important factor in the context of HIVDR. Subsequently, a research team involving students with backgrounds in medicine, biomedical sciences, pharmaceutical sciences and philosophy was put together in order to address the problem in a transdisciplinary manner over a period of 8 months. Thereby, the team built upon the work of the preceding year, during which another student research team had worked on a similar challenge in the context of the Honours Programme Transdisciplinary Insights at KU Leuven. This team had explored the value and acceptability of peer support groups in Dar-es-Salaam, Tanzania, in order to improve HIV treatment adherence [15].

The research undertaken by the student team and presented herein therefore had three main objectives. First of all, the team explored the potential of addressing the problem of HIVDR in a transdisciplinary manner. In this context, the significance of working in a team of students with different backgrounds and of applying established transdisciplinary methodologies to a complex problem such as HIVDR should be analyzed. Secondly, the different factors relevant in the context of HIVDR, including adherence to antiretroviral therapy, should be identified and their potential impact on HIVDR and on each other should be characterized. Thirdly, the team should develop an approach towards the problem of HIVDR based on one or more of the factors previously identified as relevant and targetable.

Methods

During the first 3 months of the project, the team was trained in transdisciplinarity and complexity through various workshops and exercises [15]. Over the course of eleven sessions, the students developed a shared understanding of the HIVDR challenge, identified the latest state of the problem and worked towards parsing its complexity. The aim was to narrow the scope of research down to a particular subtopic by the end of the third month, in order to be able to create an output for the challenge after the 8 months designated for the project.

In what follows, a timeline of the Honours Programme Transdisciplinary Insights and the respective accomplishments is provided. A summary of the process can be found in *Figure 1*, and the different aspects of this figure are described in more detail below.

In session 1, the team members were introduced to each other and to the challenge as submitted by the stakeholder, Dr. Michael R. Jordan. In session 2, the

Figure 1: Schematic representation of the process of actor identification and knowledge acquisition.

team attended the ‘Co-creation of Knowledge’ workshop by Professor Marc Craps, a Belgian organisational psychologist and anthropologist, who lectures at KU Leuven and has experience in multi-actor collaboration and transdisciplinary research. The purpose of this session was to introduce the students to the principles of transdisciplinarity and to the idea of wicked problems ([6]). In session 3, the team interviewed Dr. Michael R. Jordan and Moses Supercharger over Skype. Dr. Michael R. Jordan is an American physician in the Division of Infectious Diseases and Geographic Medicine at Tufts Medical Center, an assistant professor of medicine at Tufts University School of Medicine and a consultant for the World Health Organisation. The team contacted him to discuss the submitted challenge and to determine his expectations towards and his precise role in it. Moses Supercharger is a Ugandan musician living with HIV, who uses music to raise awareness and aims at de-stigmatising people living with HIV. The purpose of this interview was to enable the team to develop a better understanding of what it is like to live with HIV in a sub-Saharan society today. In session 4, the team discussed the existing literature on HIVDR. Moreover, the students were formally introduced to systems mapping as a way to visualize complex problems and to the exercise of the ‘10 Reflective Steps’ (cf. *infra*) ([7]). Subsequently, the students were given a list of potential stakeholders relevant in the context of the challenge and were invited to research which experts they would like to interview.

In session 5, the ‘Actor Constellation Game’ ([8]) was carried out; this is a tool useful for defining the most important actors influencing a certain wicked problem. First, the team agreed on a central question. Subsequently, potential actors were written down on labels and positioned around this central question. The closer the labels were thereby placed to the question, the more influence the respective actors were deemed to exert in the framework, while the distance between two labels reflected the strength of the underlying association. At the end of the session, various actors were assigned to the students for them to conduct online research on those actors. In session 6, a second round of the Actor Constellation Game was performed. At the same time the team conducted an online phone interview with Dr. Fausta Mosha and Dr. Raphael Z. Sangeda. Dr. Mosha is a Tanzanian medical microbiologist and epidemiologist working for the Tanzanian Ministry of Health and Social Welfare. She has also been the director of the National Public Health Laboratory since 2010. Dr. Raphael Z. Sangeda is a Tanzanian bioinformatician and senior lecturer in the Department of Pharmaceutical Microbiology at the Muhimbili University of Health and Allied Sciences. The purpose of the interview was to provide the students with an insight into the epidemiology of HIVDR and its implications on public health. The students also asked for Dr. Mosha’s and Dr. Sangeda’s expert opinion on potential solutions to tackle HIVDR. Ultimately, the students were invited to discuss the ‘10 Reflective Steps’ ([7]) online, which challenged the students to analyse their work up to that point.

In session 7, the team discussed the usefulness of narrowing their scope of research down to non-governmental organizations (NGOs) and community health workers (CHWs) as a result of their preceding research (see results). They attended a presentation on the ‘3 Types of Knowledge’ and were invited to perform the corresponding exercise ([9]). The purpose of this exercise was twofold: on the one hand, it was supposed to shed light on the team’s current position with regard to the project; on the other hand it was meant to support the team in reaching a decision about suitable next steps. In session 8, the team discussed the results of the research the individual team members had carried out in the context of the exercise on the ‘3 Types of Knowledge’. Afterwards, they conducted an interview with Prof. Eric Van Wijngaerden, Rita Verstraeten and Dr. Marie-Pierre de Béthune. Prof. Van Wijngaerden is a Belgian

infectious disease specialist and a professor of medicine at KU Leuven. Mrs Verstraeten is a Belgian specialized nurse at the AIDS reference centre of the University Hospital Leuven. Dr. de Béthune is a Belgian HIV virology consultant. The interviewees shared their experiences with health care provider-patient relationships in the context of HIV and African societies. They supported the students in understanding the problem of HIVDR from a patient’s perspective. In session 9, the team attended a lecture on the societal impact of social mass media by Prof. Steven Eggermont. The content of the session invited the team to reconsider the role of social media when tackling the problem of HIVDR. In session 10, the team attended a workshop on systems mapping, during which the students were familiarized with tools used to visualize complex problems. In session 11, the team discussed the progress achieved over the past months and possible ways to proceed.

In the fourth month of the project, two members of the team conducted interviews with experts in South Africa:

- Prof. Tulio de Oliveira: South African bioinformatician, director of the KwaZulu-Natal Research and Innovation Sequencing Platform (KRISP), professor at the University of KwaZulu-Natal (UKZN) and at the Centre for the Aids Programme of Research in South Africa (CAPRISA);
- Prof. Salim Abdool Karim: South African infectious disease specialist, epidemiologist, professor of global health at Columbia University and Pro Vice-Chancellor (Research) at the University of KwaZulu-Natal (UKZN);
- Prof. Deenan Pillay: Director of the Africa Health Research Institute and professor of virology at University College London (UCL);
- Dr. Coenie Louw: South African physician, founder of the NGO Gateway Health Institute.

The transcripts of these interviews were passed on to the entire team and enabled the team to further narrow down their scope of research and to identify a subtopic of HIVDR, which was subsequently addressed primarily through literature research for the remainder of the project.

Results

Through online research, discussions with experts and exercises in transdisciplinary thinking, a myriad of

different and interconnected factors mutually influencing both the rise of HIVDR in Africa as well as each other were identified, a non-exhaustive list of which is provided in *Table 1*. The embeddedness of the problem of HIVDR into this dynamic network of factors thus indeed renders it a ‘wicked problem’ ([6]). Problems of this type are inherently difficult to formulate, as a thorough understanding of them can be reached only once all potential solutions are considered. To identify, for example, the relevance of stigmatization to the rising rates of HIVDR requires widening of the scope of the problem, and with each proposed effort to reduce stigmatization the issue of HIVDR becomes clearer in return. Tackling one issue contributing to a wicked problem can thereby actually magnify it via underlying interdependencies with other causes. For instance, if one were to try to solve the problem of HIVDR by launching public awareness campaigns to increase the knowledge about its potential health repercussions, this could result in new-found feelings of animosity towards people living with HIV among the general population, thereby worsening stigmatization. Wicked problems like HIVDR have no straightforward solutions, and there is no clear-cut way to assess the impact of measures intended to mitigate them. This

also implies that there is no point at which one can reasonably state that the problem is solved. Solutions are never all-encompassing and due to time and/or budget constraints, one often has to settle for a solution that is simply ‘good enough’.

In the present case, poor adherence to treatment was finally identified as the most feasible factor for the team to address meaningfully within the foreseen timeframe of the challenge. By their very nature, wicked problems span many different fields of expertise, and therefore require a transdisciplinary approach.

Actor Constellation Game

The final outcome of the Actor Constellation Game demonstrated that the team should focus on NGOs and CHWs, a lay group of (mostly) volunteers who provide basic healthcare to their community. CHWs represent the direct connection between formally trained and remunerated healthcare staff at specialized centres and the people living with HIV in rural areas. Other actors that were taken into consideration were nurses, doctors and media. With regard to nurses and doctors, the team concluded that they were already suffering from a heavy workload and

Infrastructure	
Drug Stock-Outs	Insufficient transport systems undermining a consistent supply of medication in rural areas
Insufficient Access to Care	Large distances between clinics and homes of HIV+ individuals and insufficient time for visits to clinics due to employment
Healthcare System	
Drug Stock-Outs	Poorly funded and/or organized healthcare systems unable to provide sufficient medication
Insufficient Availability of Medical Staff	Severe shortage of medical professionals, resulting in overworked doctors and nurses lacking time to provide sufficient information to patients
Awareness and Personal Behavior	
Lack of Education	Insufficient public knowledge and awareness about HIVDR
Illusion of Being Well	Refusal of HIV+ individuals to take medication due to absence of obvious symptoms
Absence of Safe Sex	Low use of safe sex methods facilitating the spread of drug resistant viruses
Psychosocial Factors	
Stigmatization	Avoidance of or discontinuation of treatment due to feelings of shame and/or fear of becoming an outcast
Lack of Trust	Distrust in conventional medicine paralleled by deeply rooted trust in traditional healers
Association with Homosexuality	Reluctance of governments to address HIVDR due to its association with (morally condemned or illegalized) homosexuality

Table 1. Selection of factors relevant in the context of HIVDR.

that it would be neither feasible nor desirable to further expand their scope of work. With respect to media, recent literature ([10]) suggests that the public is already fed up with the myriad of messages and campaigns aiming at boosting HIV awareness. Therefore, the media are not likely to constitute an effective channel to reach out to communities. In the discussion with Dr. Marie-Pierre de Béthune, one of the team's external experts, she stressed the importance of working with an already existing local partner or structure, which was a clear affirmation of the outcome of the results of the Actor Constellation Game.

10 Reflective Steps

The results of the '10 Reflective Steps' exercise are shown in *Figure 2*. In a first step, the team divided the research question into four separate questions:

- What are the different **factors** influencing HIVDR?
- What are the **relationships** between those factors (i.e. mutually reinforcing, counteracting, etc.)?
- How could one **support** HIV+ individuals in taking their drugs properly?
- What is the relevance of **stigmatization** in HIV drug resistance and how can one contribute to reducing it?

1. Formulate your research question.

- What are the different **factors** influencing HIVDR?
- What are the **relationships** between the factors (i.e. mutually reinforcing, counteracting, etc.)?
- How could we support HIV+ individuals in taking their drugs properly?
- What is the relevance of **stigmatization** in HIV drug resistance and how can we reduce it?

Is the research basic, applied or transdisciplinary?

This is a **transdisciplinary** research question, as it deals with a **societally relevant wicked problem** requiring input from many different fields of knowledge (biomedicine, sociology, human behaviour...). We will tackle it as a student team with different academic backgrounds.

2. Formulate the societal problem you want to help solve.

The bigger picture: What is the **impact** of increasing HIV drug resistance in general?

We attempt, firstly, to understand, and secondly, to solve the problem of **stigmatization**, given the increase in HIV drug resistance (HIVDR). HIVDR can develop because of bad adherence to drugs. Bad **adherence** is a societal problem. On the other hand, the development of severe HIVDR might lead to the societal problem of having a lot of hard-to-control HIV cases, which will put a huge burden on public health.

3. Specify the stage of the policy cycle.

- **Problem framing:** What exactly has an influence on HIV+ individuals who do not take their drugs properly? How can we act upon these different (f)actors?
- **Policy development:** Create a **complexity map** with the different (f)actors influencing drug adherence. Develop a differentiated model of care to act upon these (f)actors.
- **Implementation:** Implement differentiated model of care.
- **Evaluation:** Does the implementation of the differentiated model of care improve drug adherence among people living with HIV?

We are still in the 'problem framing' and to a certain extent also the 'policy development' stage. Research around this topic all seems to be quite recent and there does not appear to be a general consensus among different groups in society about how the problem should be defined, let alone which kind of solution should be implemented. For example, HIV+ individuals feel that their doctors do not explain the consequences of taking drugs incorrectly enough, while the doctors themselves will probably tell you there is not enough time to do this and the responsibility should be transferred to someone else.

4. Clarify the form of knowledge required.
So far we have been focusing a lot on systems knowledge and a little bit on target knowledge , but as time progresses we should shift our knowledge frame and work more on the target and transformation knowledge. The transformation knowledge seems like the key to really understanding the problem and tackling it efficiently as it connects the other two knowledge types.
5. Identify relevant disciplines and societal actors.
Disciplines: What we have: biomedical sciences, medicine, pharmacy, philosophy What we still need: engineering, marketing, psychology, economics, architecture Societal actors: People living with HIV, doctors, nurses, NGOs, religious leaders, family, friends, government... (see Actor Constellation Game)
6. Position disciplines and societal actors in relation to the research question.
<i>Please refer to the Actor Constellation Game.</i>
7. Carry out an actor constellation game.
<i>Please refer to the Actor Constellation Game.</i>
8. Clarify disciplines' and societal actors' expected contributions.
–
9. Plan the functional-dynamic interaction.
–
10. Think about main lessons learned.
–

Figure 2: 10 reflective steps and state of progress after the first semester. Steps 8, 9 and 10 were not discussed by the team and are thus left blank.

Additionally, they characterized the type of research required to address HIVDR as transdisciplinary, since the rise of HIVDR in sub-Saharan Africa can be considered a wicked problem, as explained before. Wicked problems by definition cover many different areas of knowledge and thus suggest a transdisciplinary approach.

The concrete societal problem the team intended to contribute towards solving was further explored in the second step. By focusing on stigmatization and bad adherence to therapy, the team assumed it would be able to contribute towards resolving the issue of rising HIVDR rates in sub-Saharan Africa during the limited time frame of the project.

The third step involved thinking about the problem in terms of the four stages of the policy cycle. In the first stage, the problem could be framed with regard to the factors that may help to explain why some people living with HIV would not take their medication properly. In the second stage, a complexity map of these factors could then be made and a differentiated model of care could be developed in order to act upon them. The third and fourth stages, both of which relate to the question of how to actually implement and evaluate the said model, could not be described in detail yet at the respective point in time.

Step 4 pertained to the '3 Types of Knowledge' (cf. infra). The team discovered that until that point they

had mainly been gathering systems knowledge, i.e. knowledge about the problem as it presents itself at the present time. They also realized that target knowledge, referring to knowledge about the problem as it should be, would become more important to them as the challenge progressed. Transformation knowledge, which allows the bridging of the gap between the other two types of knowledge, was identified as the key to understanding and approaching the problem.

In step 5, the team reflected on the disciplines and societal actors they would require in order to be able to tackle the problem efficiently. They concluded that, while some disciplines (philosophy, biomedical sciences, medicine, pharmacy) were well represented within the group, they still lacked input from other disciplines (engineering, marketing, psychology, economics, architecture). The relevant societal actors were further analysed

during the previously described Actor Constellation Game (step 6 and step 7). The team left out the final three steps at the time of performing this exercise.

3 Types of Knowledge

The results of the ‘3 Types of Knowledge’ exercise are shown in Figure 3. As discussed above, three different types of knowledge relating to the problem can be distinguished. The team reflected on each of them in the context of the two stakeholders they had deemed most feasible to engage with during the remainder of the project, namely NGOs and CHWs. For each type of knowledge several questions were formulated, which would allow the group to acquire the knowledge needed from the respective stakeholders. These questions can be found in Figure 3.

Figure 3: 3 Types of Knowledge and state of progress after the first semester.

Further research and formulation of hypothesis

Following the ‘Actor Constellation Game’ and the exercises on the ‘10 Reflective Steps’ and the ‘3 Types of Knowledge’, the team researched what local NGOs in Africa were concerned with and how they contribute towards improving adherence to ART. Of particular importance was the finding that the majority of NGOs were mainly or exclusively focusing on women. Women face a particularly high burden of HIV, with the rate of infection among girls and young women being twice as high as that among age-matched boys and men ([11]). In addition, the rate of pre-treatment drug resistance without ever having been exposed to antiretroviral therapy is twice as high among women than men ([2]). These findings resulted in the team’s hypothesis that next to resistance resulting from taking ART as prevention of mother to child transmission, a considerable proportion of HIV-positive women might have become infected with an already resistant virus.

Literature research and discussions with multiple stakeholders and experts suggested that men have a higher tendency than women to be in denial about their HIV status and frequently blame their female partners for their infection ([12]). They seek treatment late and consequently often present with advanced disease ([13]). Therefore, men are not only less likely to receive timely HIV treatment in the first place, but also tend to adhere poorly to their prescribed therapeutic regimen. Keeping in mind the study of Sethi et al. (2003), which draws attention to the bell-shaped relationship between adherence and resistance development ([5]), the team hypothesised that male HIV+ individuals could be an important carrier population for drug-resistant HIV.

Future perspectives

In January 2018, after 4 months of working on the project, the team got in contact with Dr. Coenie Louw and his associates at the Gateway Health Institute in South Africa. Dr. Louw is working on a health helpline targeting girls and young women who are disproportionately affected by HIV ([14]). When the team’s research topic was presented to Dr. Louw, the conclusion was reached that it would be valuable to look into the possibility of setting up peer-to-peer support via

phone for HIV+ men in particular. Such a call service could answer any questions they might have about HIV and encourage them to seek medical care and to stick to their prescribed treatment. The group committed to researching the recommended attributes a health helpline would need to have in order for it to be attractive and useful from the point of view of male HIV+ individuals by conducting qualitative research by means of interviews with CHWs and via focus group discussions with men living with HIV in South Africa. The results of this research will be published in a second abstract.

Discussion

By tackling the problem of HIVDR in a transdisciplinary way, the team was able to combine the ideas of students from different academic backgrounds with the expertise of various stakeholders and societal actors. As the ‘wicked problem’ of HIVDR is an issue with many underlying complexities, this approach made it possible effectively to frame and analyse the problem by connecting established knowledge on the development of HIVDR with the practical experience of HIV+ individuals and healthcare professionals.

By employing a transdisciplinary methodology, the team was able to identify a variety of factors potentially relevant in the context of HIVDR and to narrow the scope of its research to factors deemed relevant, targetable and desirable to be targeted. As a result, it decided to focus its efforts around NGOs and CHWs in Africa. Furthermore, through online research and discussions with experts, it became evident over the course of the project that men living with HIV represent a key population for efforts to curb the development of HIVDR and are also particularly difficult to reach. As a result of the knowledge the team had acquired during the course of the project, it was able to link this finding with an idea for a potential partial solution to the problem of HIVDR. Through a collaboration with the Gateway Health Institute in South Africa, the team will finally contribute to the evidence-based design of a health helpline aiming at reaching male HIV+ individuals.

Supplementary materials

Supplement 1: Dr Michael R. Jordan. 2017. “A way to understand and prevent HIV drug resistance in Africa.”

Supplement 2: Video of the project presentation at the ‘Facing the Future’ Symposium

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Supplement 1: Revised Challenge document

In 2016, the “original” challenge was researched by a team of students of this same honours programme, and their insights were published (Dehens et al., 2017). As a result of those efforts, the here listed “revised” challenge document was submitted in 2017. It is this revised challenge document that was the start of the efforts of the new team in 2018, whose results are published in this report.

Revised Challenge 2017

15th September 2017

Challenge Submitter: Dr. Michael Jordan and Anneleen Kiekens based on (Dehens et al., 2017)

Name of the Challenge: A way to understand and prevent HIV drug resistance in Africa

Could you please state a specific challenge, problem or question?

This challenge focuses on HIV drug treatment in Africa. As of December 2016, 19.5 million people are receiving antiretroviral therapy (ART) for the treatment of HIV infection. Some level of HIV drug resistance (HIVDR) is inevitable and expected to emerge and be transmitted in populations infected with HIV and receiving ART. However, recent data suggest an increase in levels of HIVDR to a point that there may be increased mortality and or morbidity. In recent documents, WHO reports that in Africa, the continent most heavily affected by HIV, levels of HIVDR are increasing (WHO, 2017a). This may be in part due to drug stock outs; difficulty in programs in retaining the patients; problems in communication due to low quality of patient-provider relationship, amongst other reasons. WHO also states that increasing HIVDR may jeopardize the success of HIV treatment and the broader HIV response (WHO, 2017b).

Data show that though African HIV patients are medicated according to accepted guidelines, many still do not follow their therapy plan correctly. WHO's global report on early warning indicators of HIVDR, based on data from cohorts receiving ART between 2004 and 2014 in 59 countries and 12 000 clinics, states that high levels of appropriate antiretroviral (ARV) drug prescriptions were given (WHO, 2016). Over 99% of prescribed regimens were according to national or international HIV treatment guidelines. Global levels of loss to follow-up (LTFU) at 12 months during the same period averaged 20%, exceeding the WHO-recommended target of 15%. Moreover, global levels of LTFU increased significantly over time, from 11.9% in 2004 to 24.5% in 2012 ($p < 0.001$). Globally, retention on ART at 12 months averaged only 73.5% amongst clinics, falling short of the WHO-recommended target of 85% or above. Estimates of retention varied considerably across regions. This suggests that the number of people not taking their prescribed drugs on a regular basis is on the rise.

Such evidence of poor adherence to therapy as described above is indeed a major factor associated with the development of HIVDR. Of note is the finding that the adherence-resistance-development curve is bell-shaped, with peak selection for resistance to ARV between 70%-89% adherence rates (Sethi et al., 2003). This means that no resistance develops in individuals whom either have very poor adherence or have excellent adherence ($\geq 95\%$) (Harrigan et al., 2005). In spite of that, average adherence rates of only 72.9% are reported (Heestermaans et al., 2016). The rate of development of HIV drug resistant strains through suboptimal adherence has been shown to be different for each class of drugs (Kan et al., 2017). These findings suggest the need to aim for nothing less than excellent adherence.

However there is more to HIVDR than low therapy adherence and all its related factors. For example the types of drugs that are available, the specifics of the local health care approach and even factors that are at first sight unrelated, like religion, can play a role in HIVDR (Sangeda, 2013; Mosha, 2014). As many of these factors leading to HIVDR are not known yet, it might be interesting to identify them and determine their interaction with each other. Through the creation of a HIVDR complexity map the true nature of the problem might become more visible, facilitating the solution searching process.

To increase adherence and availability of ART some studies have developed a ‘differentiated model of care’ (Decroo, 2017). Any change in health care approach leading to less work load for the doctors and/or centering the care around the patients themselves can be seen as a differentiated model of care.

Differentiated care models can vary from the patient simply skipping the long waiting line when going for a drug refill, to patients joining a peer support group where they can give each other psychological and logistic support. Several forms of differentiated care models have been implemented in different locations in Africa, in a way that patients have the choice to follow or not follow the alternative model available in their treatment center. However ideally, a differentiated model of care should offer several options so that the patient can choose the one closest to his or her needs and expectations, leaving room for change when the patient’s situation changes over time. Moreover such a model should be adaptive to change in, for example, drug landscape, or economic situation, in order to be sustainable overtime.

Would you like to add some objectives to that challenge?

The research group is asked to identify the factors influencing HIVDR and how they are connected to each other. For this purpose causal loop diagrams or other visualization tools might be appropriate. The group will conduct a case study in Dar es Salaam, Tanzania, with local people to characterize factors influencing HIV drug resistance and ways to improve them. Through a series of case studies and conversations with patients, doctors, nurses, health care providers, general public and community members, the group should suggest steps that can be taken to prevent HIV drug resistance in the form of an adaptive model of care.

The way to progress from here would be to study the existing differentiated models of care to analyse their strengths and weaknesses, and how principles of resilience can be built into such models of care. The group could search for reports on ways to implement differentiated models of care, especially in the context of HIV in Africa. The group project could proceed by adapting such a differentiated model of care based on the HIVDR complexity map. Ultimately, the adaptive model of care case-study will no doubt be helpful in seeking to find new and innovative ways to prevent HIV drug resistance and to identify previously unknown factors that can be implemented in the HIVDR complexity map.

Could you please let us know the context of the challenge and why you think this challenge is relevant to a transdisciplinary research team?

WHO has drafted a 2017–2021 action plan to reduce HIV drug resistance in developing countries, outlining a collective strategy, including surveillance activities, service delivery interventions, diagnostic strengthening, and enabling mechanisms. These cover several disciplines in various domains of science. This action plan outlines the problems, the goals and the possible steps to take. However, this action plan is not detailed with regard to specific local situations that can vary widely. Though the WHO action plan describes local enabling mechanisms, it would be interesting to see these mapped for a particular case study, and whether what WHO described is possible and sufficient for that particular case study. For this purpose, the transdisciplinary research team could make a significant contribution.

References

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Supplement 2: Video of the project presentation at the ‘Facing the Future’ Symposium (9th of May 2018)

The Honour Programme organized a symposium on 9 May 2018, during which all teams were presenting their results so far. This video was made during the presentation of the team that worked on the here presented HIVDR challenge.