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Of Prepositions and Propositions: HIV, Globalization and Topology

By
Mike Michael and Marsha Rosengarten
CSISP, Sociology Department, Goldsmiths, University of London

ABSTRACT

In this paper we explore how two enactments of HIV – the UN’s AIDS Clock and clinical trials for an HIV biomedical prevention technology or pre-exposure prophylaxis (PrEP) - entail particular globalizing and localizing dynamics. Drawing on Latour’s and Whitehead’s concept of proposition, and Serres’ call for a philosophy of prepositions, we use the composite notion of pre/propositons to trace the shifting topological status of HIV. For example, we show how PrEP emerges through topological entwinements of globalizing biomedical standardization, localizing protests against PrEP trials and globalizing ethical principles. We go on to examine how our own analysis manifests a parallel topological pattern in which we deploy a globalizing argument about the localizing of the globalizing found in the AIDS clock and the PrEP trails. Finally, we consider how the movement of ‘topology’ into the social sciences might itself benefit from a topological treatment.

KEYWORDS: HIV, Globalization, Topology, Proposition, Preposition

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Introduction

If topology can be defined in the simplest of mathematical terms as a study of 'the properties that are preserved through deformations, twistings, and stretchings of objects'ⁱ there are clearly numerous ways in which it can be unpacked in its relation to social scientific inquiry (eg DeLanda, 2005; Mol and Law, 1994; Lash and Lury, 2007). For immediate purposes, we note three points that typify our use of topology: space and time are not external frameworks but are emergent; points (which might be entities or events) that are distant can also be proximal (categorically as well as spatially and temporally); and that transformations of the relations between points are not causal or linear, but open and immanent.

In this paper, this characterization of topology affords a number of interesting supplements to the sociological accounting of globalization processes. Firstly, and most obviously, we would argue, that it facilitates exploration of the relation between global and local without tacit recourse to an external framing or parametrization of one by the other that is found in much social science. Instead of accounting for the local in terms of the global, or vice versa, topology resources an analysis in terms of their mutual emergence. We illustrate this through a consideration of the AIDS Clock on the United Nations Population Fund (UNFPA) websiteⁱⁱ that registers the increasing number of people living with HIV worldwide, and the randomized clinical trials (RCTs) of an HIV prevention technology commonly referred to as pre-exposure prophylaxis or PrEP (with its accompanying ethical problematique). Both of these interventions — the clock and the clinical trials — are instantiated or enacted in global terms, that is, on a global register. In part our aim is to trace the topological space in which these interventions, in being enacted as global, are met with, and become mediated by, localizing contingencies which themselves draw from globalizing resources. Here, we make use of Latour's and Serres', respective notions of proposition and preposition because together they are particularly helpful in unravelling the topologies of the AIDS Clock and the PrEP RCTs. By enabling us to see the myriad of entities (eg drugs, bodies, algorithms) that are topologically connected in the AIDS Clock and the PrEP RCTs, these concepts also allow us to address, how the clock and the trials opened *locally* to particular potentialities, notably, their own continued globalization.

Thus, our 'first-order' argument is that the globalizing enactments of HIV can be usefully illuminated through a topological analysis that charts how divergent spatiotemporalities can co-emerge (to open up particular potentialities). Over and above the implications for social scientific understanding of globalization, this argument suggests that existing conceptions of a 'global' epidemic are often ill-

equipped to respond to the topological contingencies that comprise 'their' dynamic.

However, a topological sensibility also allows for a more complex relation to such an analysis – one which reflects upon (or rather inflects with) the enactment of the very categories (of global/local) that the analysis purports to topologize. In a 'second-order' argument around our own analytic engagement with the two forms of HIV intervention, we set out how our own analysis displays topological features parallel to those we unpick in relation to HIV intervention. On this score, again via the work of Serres and Latour, we draw upon and develop the interconnected notions of propositions and prepositions as a means of articulating these complex topologies across 'what is being analysed' (HIV interventions) and 'what constitutes the analysis' (a topological accounting).

Moreover, we go on to situate this point in relation to a proposed 'third-order' argument, namely that we should also consider the application of topology to the relation between the 'disciplines' of social science and topology. This move sensitizes us to the complex dynamics of the interdisciplinary enactment of the global and local, specifically the application and applicability of concepts across disciplines. In other words, we argue that we need to be topologically sensitive to the ordering and disordering entailed in such conceptual exchanges between these disciplines, not least those involving the concept of 'topology'.

In what follows, we begin by separately presenting our two core empirical cases: The AIDS Clock, and accounts of standardized randomized clinical trials and their accompanying ethics, or ethical problematique. We then consider how their attempted global reach weaves into various local contingencies, particularly - localizing critiques that emphasize the conditions of infection and death, and local political protest against the clinical trials. We argue that there are topological interconnections amongst these globalizing and localizing enactments.ⁱⁱⁱ However, we also go on to note how our own critical commentary upon these interconnections is itself topologically related to its subject matter. In the process, we suggest a series of linked conceptual tools for thinking the topological relations enacted both in these empirical relations and in our analytic enactment of them. Finally, we draw out some implications for the response to the HIV epidemic but also for the topologies of 'doing of topology' in social science.

Gloablizing Registers of HIV

The AIDS Clock

On visiting the AIDS Clock at United Nations Population Fund (UNFPA) website, one is met with a large digital readout at the head of the page. To the left of this, scroll two texts: 'Every 16 seconds, another person dies of AIDS' then 'That leaves:' The readout (standing at around 35,400,000) changes upwards by one every few seconds. To the right is the text: 'People living with HIV'. Beneath this is a map of the world divided into countries, and in the top right hand corner of

the map is a small panel divided into three bars. On the uppermost is the text: 'RESIZE THE MAP'; the middle reads: 'All countries resize relative to number of people with HIV'; the bottom simply says 'Play'. On pressing 'Play' the map morphs from the familiar projection of countries into a configuration in which, as the accompanying texts states: 'The area of a country now represents the number of people living with HIV'. As the cursor is moved over each territory, a figure appears along with the name of each country. Most immediately prominent are South Africa (5.7 million), India (2.5 million) and Nigeria (2.6 million), though these numbers do not seem to be proportional to the resized national territories (for instance India and South Africa take up roughly the same area). In addition, with the pressing of 'Play' a drop down menu appears which lists such options as 'Regional Info', 'Relative to Population' and 'About HIV/AIDS'. Following the 'Relative to Population' option allows one to see the percentage of people infected with HIV for each country (where data is available), for example, Swaziland, 26.1%. At the bottom of the webpage is a section providing further resources: Fast Facts, links to the 2008 Report on global AIDS epidemic, a Media Kit, a Download of Fast Fact Powerpoint slides, for instance.

The AIDS Clock described above is a relaunch of a clock originally unveiled in public lobby of the United Nations in New York in 1997. This travelled as an exhibition (eg to Toronto, the Hague) before being redesigned as a web-based advocacy tool in 1999. The current incarnation entailed a recalibration in accordance with the new epidemiological data presented in UNAIDS' 2006 Report on the Global AIDS Epidemic. A press release from the UNFPA states, the clock's mission is: 'to present the world with a powerful symbol of the epidemic's scale and the urgent response it demands'. Moreover, "The AIDS Clock reminds us of how pressing our work is", said UNFPA Executive Director Thoraya Ahmed Obaid. "Behind each number is a face, a family and a circle of loved ones who are also affected. Our goal is to slow down, and eventually turn back the AIDS Clock. Preventing HIV is the key". As 'a multimedia advocacy tool' the clock also 'inks to regional figures, fact sheets and epidemiology trends, based on information provided by UNAIDS. It also provides links, amongst others, to some of the major campaigns that work to spread awareness of the issue and mobilize effective responses'.^{iv} As we have noted, clicking on various sections of the map, reveals more complex epidemiological accounts of how and where infections occur and which, in turn, generates a significantly resized map. Yet, crucially, all this (partial) difference feeds into a single clock figure that, as with the original clock, aims to allow people 'to comprehend, in a visual and visceral way, the scale of the epidemic'.^v

Randomized Clinical Trials and their Ethical Problematique

The epidemiological mapping depicted in the AIDS Clock aims to trigger a heightened sense of urgency to the issue of global prevention, drawing attention through the menu embedded in the map to how different epidemiological groups experience higher HIV incidence. Since the introduction of antiretroviral HIV drug therapies and their capacity to slow viral replication and therefore the onset of

AIDS (acquired immune deficiency) resulting from HIV infection, randomized clinical trials (henceforth RCTs) have been conducted to establish the efficacy of using the same drugs for prevention purposes (Paidan et al., 2008). Not unlike other areas of the biological sciences, RCTs are generally seen as the gold standard in testing pharmaceuticals in general, and HIV treatments/pharmaceutical prophylactics in particular (Paidan et al., 2010).^{vi} Indeed, RCTs are regarded as ethical in themselves as the following quote, from leading practitioners in the field, illustrates:

In clinical medicine, the randomized controlled trial is considered the best way of measuring the efficacy of interventions because of its ability to minimize bias and avoid false conclusions. Random assignment of individuals to different treatment groups is the best way of achieving a balance between groups for the known and unknown factors that influence outcome. This may seem to run counter to the traditional medical model of the doctor deciding which treatment is best for each patient, but it is considered ethical only when there is genuine uncertainty about which treatment to offer. By the same token, failure to tackle genuine uncertainty about treatments through randomized controlled trials can be considered unethical because it allows ineffective or harmful treatments to continue unchecked. (Stephenson and Imrie, 1998: 611).

The trialing of antiretroviral drugs for prevention follows many years of testing their efficacy against viral replication in HIV positive populations (thereby preventing the onset of acquired immune deficiency syndrome and inevitable death) and, importantly, evidence of their efficacy in preventing vertical transmission of the virus from mother to baby in pregnancy and during the birth (Paidan et al., 2008: 586). Of the trials underway, we want to focus on those assessing the efficacy of an orally ingested, systemic form of pre-exposure prophylaxis — a daily pill — that operates over the entire body via the bloodstream. This sort of microbicide stands in contrast to topical microbicides, for example, a gel containing the same drugs but applied to a specific body surface (vaginally or rectally).

PrEP trials — in the same manner as other HIV biomedical prevention trials — depend on the likelihood that a high number of participants will be exposed to HIV (usually through unprotected sexual intercourse) during the course of the trial.^{vii} This means that most trials are conducted where HIV prevalence and incidence is high, features of the epidemic that are prominent in low and middle income countries where effective forms of non-biomedical prevention (promotion of the male condom) has either not been instituted or instituted inappropriately for the specific cultural context (Piot et al., 2008). Without rehearsing the complexities of HIV prevention, it is possible to state that the conditions giving rise to HIV vulnerability and attractive for conducting randomized clinical trials are, also, the very conditions that may be exacerbated by such trials. Inadequate health and medical infrastructure that has contributed to poor prevention and

insufficient HIV treatment, in particular, may be burdened by the presence of an HIV biomedical trial that incurs, as one example, unwanted adverse effects after the trial is completed (MacQueen et al., 2007). Even during a trial and in the presence of state of the art technologies for testing the intervention, it is well recognized that 'offshore' trials cannot provide the same quality of care as available in the national context of the trial sponsor (Craddock, 2004:241; MacQueen et al., 2007: 554) Hence, it is apparent that the conduct of an RCT poses what are recognized as bioethical concerns. In recognition of these, international normative agencies such as UNAIDS/WHO (2007) provide guidance on issues of participant consent, provision of other forms of prevention (at present, counseling and condoms) and provision of medical care. Indeed, bearing in mind debate within the HIV field as evidenced in reports by UNAIDS/WHO (2007) and UNAIDS/AVAC (2007), it could be argued that HIV biomedical prevention RCTs are considerably more ethical than their counterparts in other areas of biomedical and, specifically, pharmaceutical research. With the exception of HIV vaccine trials, pharmaceutical companies have no direct involvement and arguments about the use of offshore 'experimental populations' and their likely lack of access to a drug intervention resulting from their risky labour contribution (Petryna, 2005; Rajan, 2007: 78,80), can be readily countered. Funding for the trials comes from philanthropic sources or public monies and the research itself is conducted by scientists employed within the academy or by large non-government not-for-profit organizations. Further, such organizations may — as part of their research or, more aptly, as an expected extension of their research — engage in ongoing activities about access to the intervention if it is found effective.^{viii}

Nevertheless, the trials have not been without controversy (as we note below), and given critical engagement from within the HIV social science field is, with few exception (see Kippax, 2010, 2008; Craddock, 2004: MacQueen, 2007), remarkably limited, it is our contention that by relying on the code of practice set out by international bioethics little is done to redress the conditions that provide justification for such trials. Moreover, resort to bioethics with its requirements for participant consent, weighing of benefit over risk and reciprocity in the form of later access to the intervention under trial detract from a more comprehensive account of ethics (see Rosengarten & Michael, 2009; Michael and Rosengarten, forthcoming). Despite the goal of achieving more effective prevention, it is often the case that state of the art science is directed solely toward testing the efficacy of the intervention and not whether it will be effective in practice (Kippax, 2010).^{ix} The following quote exemplifies this while providing insight into how the relations between the global and local are configured in the world of a non-capital driven science. As such, it highlights the need for a critique of RCTs that encompasses the problematic nature of interests that are not only attached to the pursuit of market gain (Petryna, 2005; Rajan, 2007) but also to 'scientific standards'. As one leading (publicly funded) scientist has written, the *ethical problem* is of providing trial participants with the best standard of prevention:

To comply with ethical guidelines, we have reduced our ability to assess new prevention methods by comparing them to the best available prevention standards of care (eg, limitless sexually transmitted infection treatment; frequent, individualised, and *expensive* [our emphasis] condom counselling). Such strategies are not representative of the standard of typical prevention services in the community and are not sustainable after completion of the trial. (Padian et al., 2008: 593).

It is apparent in the above statement that ethics are seen as a potential hindrance to accomplishing a statistically significant outcome through the achievement of a substantial number of HIV infections. It is also apparent that prevention counseling, referred to as expensive, is an obstruction to the gold standard of the trial. But even more startling is the way in which the RCT is dependent on access to a community enacted as not having good prevention services. Here we see that the goal of achieving a biomedical prevention technology may transcend the goal of prevention. Arguably, we are returned to the concerns set out by Petryna and Rajan about accessibility but not, as they discuss, accessibility to the trial engineered intervention. Rather, the need for the intervention has become subordinated to the scientific project of testing. So, both in relation to RCTs and their related ethics, there are putatively universalistic clinical research standards being enacted *which are simultaneously* subject to a range of generic ethical questions – what we might call, an accompanying ‘ethical problematique’.^x

Localizing the Globalizing

In both the cases of the AIDS Clock and the PrEP RCTs and their accompanying ethical problematique, a particular sort of spatiotemporality is played out. This is a smooth spatiotemporality where the meanings of Clock and PrEP RCT/ethics can move uninterruptedly. The AIDS Clock and PrEP RCT/ethics remain unchanged any place, any time: the Clock will always and everywhere impress the urgency of the task of preventing HIV; the PrEP RCT/ethics will always and everywhere generate robust clinical knowledge in ethically reflexive, and hopefully, ethically sound, ways. In both cases, external systems of ‘measurement’ are applied: an algorithm that extrapolates a global number of people living with HIV on the basis of epidemiological statistics based on UNAIDS 2006 Report on the Global AIDS Epidemic; a set of clinical research principles and ethical techniques determine what can ‘count’, clinically and ethically, as a valid trial. This is a Euclidian space-time - or rather, more accurately, a Euclidian spatialization-temporalization - where the particular events of deaths and trials can be converted into general values and effects (a click of the digital AIDS Clock and its impact upon a generic viewer; that validity of trial and its implications for the generic implementation of PrEP programmes).

Yet, both clock and trial are profoundly local. In relation to the AIDS Clock, we have a global estimated count that is meant to serve as a constant reminder of the constantly increasing number of HIV infections across the world. While the symbolism is undeniably powerful, such a measure necessarily diffuses the specificity of, and differences amongst, infections. Behind such a number there is huge complexity. Indeed this is conveyed, if only in a very partial way, by those responsible for the AIDS Clock when they state 'Behind each number is a face, a family and a circle of loved ones who are also affected'. The number rests on an abstraction of 'infection' from the 'local' where different rates and qualities of infection take place. Even the additional web links which, for example, show differences in numbers of infections in different countries, do not convey the particularity of local, national and regional differences in the social phenomena that enable or disable HIV transmission to occur (see for example: Hirsch et al., 2009; Kalipeni et al., 2004; Kippax, 2009; Smith & Whiteside, 2010). Nor do they convey the quality of life and life expectancy of those infected, the varying implications for relatives, and so on and so forth (see for example: Biehl, 2007; Fassin, 2007; Kaleeba, 2004; Guest, 2004).

But further, and perhaps more crucially, we must ask who can access the AIDS Clock? Despite being on the web, it seems to be accessible by relatively few, and even fewer who can respond productively to it – who can be inspired by its affective qualities to develop and implement 'viable' clinical responses, for example. Put another way, the AIDS Clock is an assemblage entailing numerical estimations, algorithms, public relations, institutional positioning, website media, design choices and so on and so forth. It is an ordering device for what is ultimately a particular and delimited audience comprised of scientists, policy-makers, clinicians, activists etc.

In relation to the PrEP RCTs/ethics, the initial implementation of these met with considerable resistance — forms of resistance that had not been previously made apparent in relation to other HIV biomedical prevention trials such as those for vaccines or topical microbicides (GCM 2008a; 2008b). In this context, PrEP trials generated a more public community resistance with demonstrations at an international conference that led to widespread international medial coverage. With PrEP, one of the first RCTs and the only one to target injecting drug users was challenged as being unethical because of the lack of provision of clean needles and syringes. Clean needles and syringes provide 100% protection against HIV infection and, therefore, would remove the need for a biomedical prevention technology such as PrEP (Jintarakanon et al., 2005).

Protests against this PrEP trial conducted in Thailand, and others in Cameroon and Cambodia intended to test PrEP against sexual exposure,⁹ suggest that PrEP RCT/ethics are viewed as mediating particular interests.¹⁰ Even where local support for trials is pursued and gained, ethical-seeming RCTs do not address the specificities of localities which might affect trial participation and outcomes. In

the Thai example mentioned above, for instance, it has been said that although the trial organisers provide bleach to enable the 'safe' re-use of needles and that clean needles can be purchased legally in Thailand, a context of fear and poverty affects the everyday livelihood of injecting drug users and others and it is this culture which needs to be addressed in order to achieve safe and effective prevention. In 2001, the Thai government implemented a 'war on drugs' that was represented as targeting drug traffickers. However, a report by Human Rights Watch states that by 2004, over 2000 people, including some with no connection to drug use and certainly no involvement in trafficking, had been killed by sections of the police who were paid accordingly. The same report notes that a culture of terror was created and many people still fear that purchasing needles could lead to them being accused of trafficking with life threatening consequences. At the same time, in some cases, protests against the trial draw on principles that are claimed to have global applicability, notably the bioethical principle set down by the Declaration of Helsinki that a new treatment or technique should only be tested against the best current prophylactic (in this instance, clean needles and syringes), diagnostic or therapeutic methods (The Thai AIDS Treatment Action Group TTATAG, 2004).

Further, some practitioners have also queried the validity of HIV biomedical prevention RCTs/ethics, raising concerns about the fact that while contexts where there is HIV vulnerability, high HIV prevalence (existing infections) and poor prevention provide the best research conditions, the research itself can exacerbate these conditions (McQueen et al., 2007:559). In contrast to what is available in the home country of the trial sponsor and lead researchers, a trial participant in a low or middle income country is likely to have significantly less access to health care and medical resources. In turn, their trial-incurred needs may place more pressure on already inadequate familial, local and national resources. On top of this, the very possibility of a new prevention technology against HIV may provide some communities with a diminished sense of transmission risk thereby undermining existing prevention practices and leading to new infections (see Vernazza, 2009; Grant et al., 2005, AVAC 2008). Ironically, then, trials may reinforce the local conditions which make those localities so technically attractive for conducting trials.

In order to address this problem of the potentially negative impacts of RCTs — as framed by international bioethics regulatory bodies — a complex set of procedures are undertaken by those responsible for undertaking RCTs. These include the provision of 'objective' ethical oversight whereby the trial protocol is monitored by an independent group of researchers, the provision of follow-up medical care for adverse events, the obtaining of informed consent from participants prior to their enrolment plus the provision of 'state of the art' methods of protection, for example: male and female condoms, sterile injecting equipment, treatment for other sexually transmitted infections, counseling, possibly access to male circumcision, PEP (post exposure prophylaxis). However, the recognition that 'state of the art' methods must be provided is itself subject to

criticism by scientists (Padian et al., 2008): as such methods are made locally available, so 'partial' protection is likely to increase, and thus it becomes more difficult to assess the statistical significance of efficacy of the particular intervention that is being trialled (in this case PrEP). In other words, the bioethical problematique is itself open to criticism on the basis that it interferes with the science.

In sum, RCTs (eg those in Thailand) are locally problematized, ironically by the sometime recourse to a globalizing discourse (Declaration of Helsinki); similarly, the ethical problematique (which insists on the local provision of 'state of the art' methods of prevention), also faces criticism by scientists fearful that their local trials will be unable to attain statistical significance. Here, we see how the globalizing both the AIDS Clock and RCTs/ethics are localized in various ways, but also how such localization draws on ostensibly globalizing resources (Declarations and statistics).

The Topos of (Our) Critical-Analytic Story

So, the argument here is that the standardizations enacted by the AIDS Clock and PrEP RCT/ethics create a smooth spatiotemporal space where seemingly distant categories, spaces and times – HIV infections, HIV trials, ethical problems - that appear highly divergent can be topologically assembled, brought into contact with one another, shown to share an identity. And yet, we have also seen how the globality of AIDS Clock and PrEP RCT/ethics can be problematized – they do not quite describe a smooth spatiotemporal space where anywhere, anyplace their meaning remains assured. Rather, we find that these are enacted in profoundly localized ways, even if part of that localization might be grounded in the globalizing.

The foregoing comprises our 'first-order' argument, but this is related to another concerning the form of our own argumentation. In key respects, our own account of HIV, ironically, amounts to a *standardized* critical-analytic story about how the performance of standardization is compromised by local variability. That is to say, our arguments in relation to globalizing or standardizing aspirations of PrEP RCTs/ethics and the AIDS Clock are themselves no less globalizing or standardizing. This analytic has long been exercised in sociology which has examined the ways in which technical standardization presupposes a particular, often inappropriate, local social world – that is to say, practices what Brian Wynne (1988) calls 'a naïve sociology' which might nevertheless be highly sophisticated in its productivity, as we find in relation to the standardization wrought by audit.¹¹

Despite all these lay, political and academic critical responses, these global standards nevertheless remain durable insofar as they are constantly reiterated: the Clock will apparently always and everywhere count HIV infections, however inappropriately generic those infections might appear; and standardized RCT/ethics will always and everywhere apply in the production of the best

ethically derived, clinically robust knowledge despite their 'subversion', or at least, problematization, by local contingencies.

But notice, arguably the counter-examples and counter-arguments seem to be following these standardizations, always and everywhere. It would seem that critique (including our analysis) fits into the same formal globalizing categories enacted in the AIDS Clock and PrEP RCTs/ethics themselves. And this present reflection is itself a re-localization as we point to the local peculiarities of this standardizing critique: does it always apply (given the durability of some of these standardizations, perhaps something else is needed?) or apply equally across the two cases of the AIDS Clock and and PrEP RCTs/ethics?

This is our 'second-order' argument: that a topological analysis of this form does not escape the topological patterns of globalizing and localizing practices, indeed, it exemplifies them. Moreover, just as these map onto patterns of ordering and disordering for the AIDS Clock and and PrEP RCTs/ethics (eg standardized trials are implemented locally but resisted locally by using standardized principles), so too our standardized analytic argument is undermined by its localization which, ironically, reinforces the self-same globalizing argument.

Topology, Prepositions and Propositions.

In this section we attempt to theorise further this topological analytic, drawing especially on the work of Michel Serres, Bruno Latour and Alfred North Whitehead. Arguably Michel Serres is a topological thinker. Very simply put, Serres (eg 1982a, b, 1995; Serres and Latour, 1995) has always been fundamentally interested in heterogeneous relations—between science and art, subject and object, and the material and the semiotic. Serres is concerned with how such connections take place to render patterns of order and disorder. In the process he has developed various figures that might enable us to grasp the mediation of these exchanges between humans and nonhumans, arts and sciences: the north-west passage; the parasite; Hermes; angels. In all this, he is pursuing a 'philosophy of prepositions'. Instead of such commonplace prepositions (such as between, above, inside) that typically denote physical relations, Serres' vocabulary is one of prepositional figures (Hermes,, parasite etc) that attempts to capture heterogeneous relations and exchanges. Things that are seemingly distant – the semiotic and the material, the arts and the sciences, pasts and futures - turn out to be far more promiscuous and can be shown to be in far closer proximity than one might initially imagine. This perspective is particularly well-expressed in his topological model of time. As he puts it¹²:

(Time is) is not laminar (flowing smoothly). The usual theory supposes time to be always and everywhere laminar. With geometrically rigid and measurable distances – at least constant....No, time flows in a turbulent

and chaotic manner; it percolates....this time can be schematized by a kind of crumpling, a multiple, foldable diversity (Serres and Latour, 1995: 59)

He continues:

If you take a handkerchief and spread it out in order to iron it, you can see certain fixed distances and proximities. If you sketch a circle in one area, you can mark out nearby points and far-off distances. Then take the same handkerchief and crumple it by putting it in your pocket. Two distant points suddenly are close, even superimposed. If, further, you tear it in certain places, two points that were close can become very distant. The science of nearness and rifts is called topology, and the science of stable and well-defined distances is called metrical geometry..... Admittedly, we need the latter for measurements, but why extrapolate from it a general theory of time. People usually confuse time and the measurement of time which is a metrical reading on a straight line (Serres and Latour, 1995: 60).

So, here we have a topological world of promiscuous, rhizomic (eg Deleuze and Guattari, 1988), mixing. The measure of relationalities that make up those mixings is not an external one, but topologically internal to the process of mixing.¹³ Serres' call for a philosophy of prepositions is thus a simultaneous call for a topological sensibility, and in what follows, we will draw especially on the concept of a preposition in order to trace the relations enacted in the topologies of both our two cases study examples and our analysis of them.

Before we do this, we supplement the notion of preposition. Here, we draw on the work of Bruno Latour whose work, especially in relation to Actor-Network Theory (ANT), and his later ironic reformulation of this as 'actant-rhizome ontology' (Latour, 2005, p.9), certainly points to a topological sensibility not least insofar as seemingly 'distant' actors are very 'close' by virtue of the circulation of intermediaries or the translations of mediators (also see, for example, Mol and Law, 1994; Blok, 2010). However, in the present paper, we make use of another aspect of his work – his thinking on 'proposition' - which reflects a different topological feature, namely, that the relations between points, or entities, unfold in ways that are open, immanent, emergent. For Latour, 'Propositions are not statements, or things, or any sort of intermediary between the two. They are, first of all, actants... What distinguishes propositions from one another is not a single vertical abyss between words and the world but the many differences between them, without anyone knowing in advance if these differences are big or small, provisional or definitive, reducible or irreducible' (Latour, 1999: 141). If propositions emphasize the divergent hybridities of actants, prepositions address the 'how' of this hybridity – how 'this' has gone with 'that' in this or that event. However, additionally, propositions are dynamic insofar as they are not stable but are "occasions given to different entities to enter into contact. These occasions for interaction allow the entities to modify their definitions over the course of an event" (Latour 1999, 141). On this score, Latour reflects Whitehead's (1978) own

characterization of a proposition as ‘a hybrid between pure potentialities and actualities’ (1978: 185-6). Propositions thus are ontologically heterogeneous both in their admixtures of the human and the nonhuman, but also in their embodiment of the actual and the potential (see Halewood and Michael, 2008). Put simply, the term ‘proposition’ indicates that an emerging entity propositions particular relations with other entities, that is, proposes a particular future for ‘itself’.

In sum, pre-positions and pro-positions together reflect the ‘how’ and the ‘what’ that goes into the emergence, content and potentiality of an event (or entity).¹⁴ Crucially, what neither concepts does is specify externally, or at outset, the ‘what’ and ‘how’ that comprises an event and its potentiality.

PrEP RCTs/Ethics and the AIDS clock both entail the particular bringing together of a series of entities: risks, drugs, measures of effectivity, ethical issues, HIV infected people. But the ‘how’ of this bringing together involves, as we have seen, particular forms of standardization. The result is a potentiality for both PrEP RCTs/Ethics and the AIDS Clock that can be distilled as ‘more of the same’: both will remain durable through a continuing ‘deformation’ of ‘what’ it is that can enter into the process of their emergence.

To detail these pre/pro-positional processes we can draw on the two topological categories that can serve, albeit tentatively, as pre/propositional figures.¹⁵ These are forms of classification or equivalence: the stricter or narrower homeomorphic criteria of similarity in which belonging to the same set means having the same general features (in the case of classifying capital letters of the English alphabet, this might involve criteria such as numbers of holes and tails, thus $A=R$); and the more liberal or broader homotopic categorization (in which criteria of similarity allow for some forms of deformation, such as ‘squishing’ features such as tails out of view, thus $A=R=P=O$).

Thus we might see the durability of the AIDS Clock and PrEP RCT/ethics as a homotopic mediation: forms of deformation of infections that allow for particular forms of equivalence. In the case of the clock, the local details of infections are stripped away to produce a ‘generic infection’. The ‘generic infection’ is, it might be argued, a major ‘deformation’ that is linked to a particular reformation – that of the AIDS Clock and international research, policy, programmes and so on generated with the production of a generic number that globally instils a sense of urgency. The preposition that classifies together – genericizes - a vast diversity of infections and their conditions of emergence propositions the prospect of global urgency and global action. In the case of PrEP RCT/ethics — its formation as globally relevant goes hand in hand with prepositional deformation into generic at-risk bodies, drug effectiveness and ethical problematique that propositionally opens out onto its own continuing universal relevance. This suggests, though we cannot pursue it here, that one implication is that the

pre/propositions entailed in both the AIDS Clock and PrEP RCT/ethics are as much concerned with the 'continuation of research' as with the prevention of HIV.

In contrast, a homeomorphic equivalence might be seen to apply in the classification of the two key local-global enactments that we have described above. There is a basic similarity between, on the one hand, the deformations of local specificity enacted by the globalizing AIDS Clock and PrEP RCTs/ethics, and, on the other, the deformation of that local specificity into the form of a 'principle' (everything is local) to resource a globalizing or standardizing critique of the globalizing or standardizing aspirations of the AIDS Clock and PrEP RCTs/ethics. As noted immediately above, homotopic equivalences between infections are drawn in order to enact the AIDS Clock and PrEP RCTs/ethics. However, in parallel, homotopic equivalences are rendered in our critical-analytic account whereby different specific locals which might, as we saw, lay claim to universalist principles such as those promoted through say the Declaration of Helsinki, are genericized for the purpose of establishing a critique of global reach. The preposition that classifies together – genericizes - a vast diversity of local cases 'propositions' the prospect of globalizing critique on the ironic basis that *everything* is local, globally. As such, there seem to be two parallel, homeomorphically equivalent types of homotopy enacted here which share prepositional and propositional forms. However, where the AIDS Clock and PrEP RCTs/ethics deform the local to accentuate the global, our critical-analytic account accentuates the local to critique the global thereby globalizing this form of critique.

In essence, then, topology might serve as a source of pre/pro-positional figures for (social scientifically) grasping the complex circuits of identification and differentiation, or emergence and prospect, that characterize cases such as the AIDS Clock and PrEP RCTs/ethics, and their critique. And yet, this move itself raises topological issues about the pre/pro-positional relations amongst disciplines, especially in relation to the migration of concepts from topology and sociology.

Complexifying the Conclusion

Thus far we have treated the AIDS Clock and the PrEP RCTs/ethics as separate (topological) events, yet, of course, there are links between – they are pre/pro-positionally related to one another. As we have documented, the AIDS Clock serves as a symbol to motivate efforts to decrease numbers of infections, and in this respect we might say that it is part of the affective mechanisms behind such efforts. Yet, PrEP can best be clinically trialled in situations where the incidence of HIV is relatively high, and where there are 'sufficiently' impoverished prevention mechanisms in place to enable the effects of PrEP to be clinically detectable and generalisable. Put another way, the cumulative sum displayed on the AIDS Clock is what the PrEP RCT/ethics partially affectively 'depends' upon as a spur to action, a call to arms. While the AIDS Clock standardizes infections, its impact through specific interventions such as treatment and prevention

programmes but also RCTs is highly localized – affectively impacting on those in a position to react (most relevant in the present case, researchers and ethicists).¹⁶ Simultaneously, PrEP RCT/ethics partially technically depends on non-generic infections in the most deprived areas, namely impoverished conditions which elevate the risk of infection and thus facilitate the capacity of RCTs - because of their standardized RCT/ethics procedures - to generate ‘useful’ data. But a trial’s very presence, by virtue of its particular instantiation of RCT/ethics procedures, may both reduce participant risk of infection (through prevention counselling) *and* precipitate behavioural disinhibition (eg lead to more infections say through increased non-use of condoms).¹⁷ The increased infections, born out of the specificities of a situated implementation of standardized RCT/ethics procedures, eventually become translated back into the generic infections of the AIDS Clock. The AIDS Clock serves as a symbol to motivate efforts to decrease numbers of infections....

In sum, we move from the globalization enacted by the AIDS Clock, through the localization of its impacts on medical researchers and their ethics fellow-travellers, who apply the globalized standards of RCTs and the accompanying ethical problematique which requires and therefore does not act to prevent local infections which translate into the generic infections of the globalizing AIDS Clock. What seems to be happening here is a switching of generic and non-generic status, globalization and localization, the standardizing and the situating. The AIDS Clock propositions a particular constituency (researchers) that is prepositioned with an ethical problematique to proposition itself in terms of universal scientifico-ethical technique which generates local infections that are generically prepositioned in the ongoing emergence of the AIDS Clock. Or to draw on that topological cliché, the Moebius strip, if one’s thumb is on the globalizing, genericizing ‘side’, and forefinger on the localizing, diversifying ‘side’, a little travel soon reverses these contacts.

At the practical level, the topological forms traced here suggest there is no simple way to ‘turn back the AIDS clock’. For example, if RCTs (that have been facilitated by the AIDS Clock) show that PrEP works, this could affect the development of a vaccine which becomes more difficult to test if risk of HIV infection is statistically reduced by PrEP.¹⁸ Any turning back of the clock is unlikely to be an unalloyed good, and any triumphalism is likely to generate its own topological challenges.

However, as the paragraph above hints, the topological accounting presented in this paper is inevitably partial. The pre/pro-positions we have explored are very particular ones, and certainly other topological trajectories could have been followed (say, in relation to interactions between vaccine and prophylactic research programmes, or to the pattern of local protests and movements). What the foregoing has illustrated, hopefully, is an outline of a means – or a sensibility - for exploring, analysing and narrating forms of complex and sometimes

surprising connection, emergence and prospect, that also addresses those very processes of exploration, analysis and narration.

But lest we finish on too comfortable a note, it should also be pointed out that this very accounting has its own topological dynamics, this time between disciplines (broadly, social science and topology). In keeping with the sensibility outlined above, and as a part of our 'third-order' argument, we might ask what are the pre/pro-positions that best capture the relation between topology and social science? Is there perhaps too much of a one-way traffic – from topology (homeomorphism, homotopy, Moebius strip) to social science? Ironically, thinking topologically might mean de-privileging topology as a discipline (or multi-discipline). As noted elsewhere (Michael, 2009), we might discover topologically interesting pre/pro-positional figures within the social sciences (and social theory): Simmel's 'stranger', de Certeau's idle walker, Benjamin's angel of history are three intriguing candidates. Conversely, armed with an ontology of a 'multiple, foldable diversity', and following the by-ways of Serres' North-West passage, we might find that topology itself echoes social scientific analytics. Thus, for example, might it be the case that the concepts of the homeomorphic and homotopic resonate with 'membership categorization devices' in conversation analysis or the Protagorean dilemmatic thinking of rhetorical social psychology?

In any case, a topological analytic sensibility needs to be flexibly iterative, in which amongst its giddy folds we find that the topologizing of topology pre/pro-positions its partiality, while topologizing topology reasserts its centrality, or global reach.

The preceding topological convolution points the way to our last twist. The paper has been structured around three 'ordered' arguments. We have placed inverted commas around these because we wanted to connote neither hierarchy nor, indeed, an easy distinction between them. Rather we would argue that our arguments about the topologies of HIV, critique and interdisciplinarity can themselves be regarded as topologically entwined. Thus, the three 'orders' should be regarded not in terms of external parameters (for example, a spatialization in which the empirical, analytic, and interdisciplinary are nested one inside the other) but as immanent in, and emergent from, the complex topological conjunctions entailed in this empirical-analytic-disciplinary space.

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NOTES

ⁱ URL (Consulted last accessed 12 May 2011)

<http://mathworld.wolfram.com/Topology.html>.

ⁱⁱ URL (consulted 9 April 2010) http://www.unfpa.org/aids_clock/.

ⁱⁱⁱ Our particular topological account of RCTs differs from Szerszynski's (this issue).. He illustrates his Agambian topology of inclusive exclusion with reference to Cooper's (2011) analysis of how the mainstream usefulness (inclusiveness) of RCTs has rested on the exposure of marginal (excluded) groups to incalculable risk. Of course, this topology partially applies to our case study: the 'excluded' are the subjects based in the offshore sites of India or East Asia or southern Africa, However, these 'marginal subjects' are included not only through their role in the production of biomedical knowledge, but also through complex topologies of ethics (through which they are afforded a degree of protection) and the ethical and political challenges that they (or their representatives, at least) launch. Over and above this, this paper is mainly concerned with the topologies entailed in particular globalizations of HIV, but also with the topologies of topological analysis.

^{iv} URL (consulted 2 June 2010)

<http://www.unescap.org/ESID/psis/population/popheadline/312/art8.asp>.

^v URL (consulted 9 April 2010) <http://www.opendoorcli.nic.org/>.

^{vi} This does not mean that there are no criticisms of RCT, not least amongst certain practitioners (see Will and Moreira, 2010).

^{vii} The randomised clinical trial is regarded as a fully scientific objective form of evaluating drugs. It involves comparing two groups, one subject to the intervention while the other is not but using a method where those directly involved—the researchers and the trial participants—do not know who is receiving the drug and who is receiving a placebo.

^{viii} According to reporting from CDC, responsible for some of the PrEP trials, discussions have been conducted with the public health authority in Botswana to determine how PrEP might be delivered if found effective. The author Rosengarten has attended discussions on the design of social research to facilitate effective use of PrEP, held by the iPrEX trialists. Its also worth noting that a more nuanced understanding of the role of the HIV pharmaceutical industry may be in order in contrast to a more overt set of operations carried out by the pharmaceutical industry described by Kaushick Sundar Rajan (2007) and Adriana Petryna (2005), Gilead Sciences Inc, manufacturer of the drugs used in PrEP has stated that it will provide no profit pricing access to PrEP by 97 low and middle income countries (see Gilead Sciences Inc, 2011).

^{ix} In general, these trials are ethically justified in light of international bioethics principles and guidelines established within the HIV field on the grounds that those recruited to the trials are in urgent need of the intervention and that sufficient safety monitoring is undertaken through an independent Safety Monitoring Board. The World Medical Association Declaration of Helsinki 'Ethical Principles for Medical Research Involving Human Subjects' includes the following

in its statement on ethical medical research. 'Populations that are underrepresented in medical research should be provided appropriate access to participation in research.' However, this argument also results in what has been identified as a paradox for HIV biomedical research and resulting in debate within the HIV field on what provision of care should be provided alongside the trial for adverse events. The debate turns on the question of whether the level of care should be equivalent to that provided in the trial sponsor's home country (for instance, in the United States or United Kingdom) or be equivalent to the best standard of care available within the country location of the trial although not necessarily within the actual locale of the trial (see MacQueen et al., 2007).

^x We use the term 'problematique' because it connotes the framing of a problem, not simply the problem itself. Thus when we refer to an ethical problematique we are signalling that a particular biomedical intervention is not merely associated with a particular set of ethical problems, but with a specific way of formulating issues as ethical problems of a particular sort.

⁹ In 2004, Cambodian and Cameroon groups representing female sex workers targeted for the first round of PrEP trials claimed that the trials were unethical because they did not provide sufficient information, they did not guarantee medical care for adverse events, and there was no provision of anti-HIV drugs for those who became infected during the trial. These claims have been disputed by those responsible for the design and implementation of the trials (Mills et al 2005). Nevertheless, these claims can be said to reflect the lack of trust that arises in response to 'standardist' claims - whether these be around clinical trials, instructions for the use of pesticides, or innumerable forms of audit. In any case, the two trials were closed.

¹⁰ Trial sponsors and scientists now invest considerable effort in gaining community support for RCTs. The achievement of support is taken as an endorsement of the trial as ethical. But it is also something of a guarantee against further trial closures, costly in terms of dollars and for scientific research (UNAIDS, 2006; UNAIDS & AVAC, 2007).

¹¹ On this score our analysis falls in line with a standard constructionist critical analytic which shows how claims for standardization, universality or globality are undermined by the contingencies of the local. Ironically, it is though the flexibility and adaptability of the local, that these standards are rendered workable (see, for example, Bowker and Star, 1999, and Power, 1999). On another level, our analysis might be said to suffer from a lack of symmetry: we claim that the global is 'constructed' while the local is real (eg Ashmore, 1989, and Woolgar, 1988). Of course, we see both these registers as heterogeneously emergent.

¹² While Serres is here specifically developing a topological model of time, the points he makes apply more generally.

¹³ For an example of prepositional analysis where 'roadkill' is understood in terms of the divergent relational patterns – perpendicularity and frottage - between of cars and animals, or rather automobility and animobility, see Michael (2004).

¹⁴ Or in Whitehead's (1978) terms, we might put it thus: prepositions address how an actual entity or occasion is concresced from prehensions, while propositions

address how an actual entity or occasion becomes a prehension that concretes with other prehensions to generate novel actual entity or occasions.

¹⁵ See, for example, URL (Consulted last accessed 12 May 2011)

<http://mathworld.wolfram.com/Topology.html>.

¹⁶ As a prehension, the AIDS Clock is affective in so far as the actual occasion or entity of a potential trial can accommodate it. For some events, it is an irrelevance. In any case, there is always an element of local teleology in the process of affecting, or, more generally, becoming (Whitehead, 1978).

¹⁷ Padian et al. (2010) frame the concern about the capacity for HIV RCTs to demonstrate efficacy in terms of providing 'enhanced' prevention packages in excess of what is already provided within a community. They state: 'The ethical issues of offering enhanced HIV prevention services in the comparison arm must be weighed against the ethical issues of lengthy and expensive prevention trials that provide the control group with an unsustainable level of prevention services that does not reflect community standards.' (631).

¹⁸ In detail, should PrEP be found to be sufficiently efficacious, what should be given to placebo group participants in other ongoing and future prevention trials? Could PrEP trials continue to be 'ethical' with a placebo arm if PrEP is found to reduce the likelihood of infection? Moreover, would trials for other prevention technologies such as vaccines be required to offer PrEP to all participants? (AVAC, 2008: 9). If so, potentially more efficacious vaccines might be delayed because the effects of the vaccines would be masked, and because, with reduced risk of infection and therefore to compensate statistically, higher numbers of participants will be required. In other words, the HIV toll may be slowed but the specific dynamics comprising it are likely to become more complex. The chances of better interventions for dealing with the virus may, as a consequence, become increasingly more encumbered by the affects of the Clock, PrEP and RCT/ethics currently in existence.