Institution: Imperial College London

Unit of Assessment: 02 Public Health, Health Services and Primary Care

Title of case study: Developing Methods for Monitoring Global HIV Epidemic Trends that have Informed the Worldwide Response to the Pandemic

1. Summary of the impact (indicative maximum 100 words)

The Joint United Nations Programme on HIV/AIDS (UNAIDS) and World Health Organisation (WHO) regularly report estimates for the prevalence of HIV and associated metrics for almost every country in the world. These statistics are essential for tracking the scale and the impact of HIV epidemic and are used routinely in the policy decisions and funding allocation decisions of national governments and international donors and therefore have a major impact on international public health. The methods underlying those estimates were originally developed, and continue to be refined and updated, by an international group of researchers at Imperial College London.

2. Underpinning research (indicative maximum 500 words)

Key Imperial College London researchers:
Professor Geoff Garnett, Professor of Microparasite Epidemiology (2002-2012)
Professor Simon Gregson, Professor in Demography and Behavioural Science (2001-present)
Professor Nicholas Grassly, Professor of Infectious Disease and Vaccine Epidemiology (2001-present)
Dr Peter White, Senior Lecturer (2002-present)
Professor Timothy Hallett, Professor of Global Health (2004-present)

In 2002, the data that were available to generate international estimates for HIV consisted of measurements of HIV prevalence among small samples of pregnant women attending a non-random selection of antenatal-clinics in each country. Methods developed by Professor Grassly and Professor Garnett provided a way to integrate those sparse data points within a unified theory for epidemiological dynamics so that reliable estimates of the time-course of HIV prevalence could be generated (1). In 2005, Professor Grassly and colleagues created a method to estimate the number of orphans generated by the HIV epidemic (a key impact of HIV) (2), and, in 2003, the group also invented a decision-making tool, the 'Modes of Transmission' model (3), and showed that it could be used to analyse surveillance data and identify priority groups for HIV prevention interventions. These estimates were then used in extended models to investigate the impact that expanded responses to the HIV epidemic can generate (4).

The group has since led the continuous evaluation and development of the estimation methods. The methods have been adapted to produce estimates of mother-to-child transmission rates and the numbers in need of antiretroviral therapy. Additional methods developed by the group demonstrated that changes in sexual behaviour had led to a decline in the HIV epidemic in Zimbabwe, at that time the largest epidemic for which such a change had occurred. Methods developed in 2008 by Professor Hallett and Professor Gregson allow for the sex-ratio and age-pattern of new HIV infections to be estimated reliably from available data (5), allowing for substantially refined estimates of demographic impact of HIV and highlighting the burden of HIV among women. New analyses and data collection by Professor's Hallett and Gregson in 2010, also demonstrated that the way in which UN agencies track progress toward *Millennium Development Goal* 5 (child mortality) could lead to significant biases (6), which subsequently led to the official monitoring methods being revised.

This body of work has had a clear and lasting impact on policy and funding in the field of global health at the highest decision-making levels.

3. References to the research (indicative maximum of six references)

(1) Artzrouni, M., Brown, T., Feeney, G., Garnett, G., Ghys, P., Grassly, N., Schneider, D.,

Stanecki, K., Stover, J., Schwartlander, B., Walker, N., Way, P., Yan, P., Zaba, B., Zlotnik, H., Timaeus, I., Walker, N. (2002). UNAIDS Reference Group on Estimates Modelling and Projections. Improved methods and assumptions for estimation of the HIV/AIDS epidemic and its impact: Recommendations of the UNAIDS Reference Group on Estimates, Modelling and Projections. *AIDS*. 16(9), W1 - 14. DOI Times cited: 99 (as at 4th Novemebr 2013 from ISI Web of Science). Journal Impact Factor 6.4

(2) Grassly, N.C., Timaeus, I.M. (2005). Methods to estimate the number of orphans as a result of AIDS and other causes in Sub-Saharan Africa. *Journal of Acquired Immune Deficiency Syndromes*, 39, 365 – 375. Times cited: 8 (as at 4th November 2013 from ISI Web of Science). Journal Impact Factor 4.65

(3) Pisani, E., Garnett, G.P., Grassly, N.C., Brown, T., Stover, J., Hankins, C., Walker, N., & Ghys, P. (2003). Back to basics in HIV prevention: focus on exposure. *BMJ*, 326, 1384-1387. DOI. Times cited: 75 (as at 4th November 2013 from ISI Web of Science). Journal Impact Factor: 17.21

(4) Stover, J., Walker, N., Garnett, G.P., Salomon, J.A., Stanecki, K.A., Ghys, P.D., Grassly, N.C., Anderson, R.M., Schwartlander, B. (2002) Can we reverse the HIV/AIDS pandemic with an expanded response? *Lancet*, 360, 73–77. DOI. Times cited: 100 (as at 4th November 2013 on ISI Web of Science). Journal Impact Factor: 39.06

(5) Hallett, T.B., Zaba, B., Todd, J., Lopman, B., Mwita, W., Biraro, S., Gregson, S., Boerma, J.T.; ALPHA Network. (2008). Estimating incidence from prevalence in generalised HIV epidemics: methods and validation. *PLoS Med,* 5 (4), 611 – 622. DOI. Times cited: 38 (as at 4th Novemebr 2013 from ISI Web of Science). Journal Impact Factor: 15.25

(6) Hallett, T.B., Gregson, S., Kurwa, F., Garnett, G.P., Dube, S., Chawira, G., Mason, P.R., Nyamukapa, C.A. (2010). Measuring and correcting biased child mortality statistics in countries with generalized epidemics of HIV infection. *Bull. World Health Organ.*, 88 (10), 761 - 768. DOI. Times cited: 5 (as at 4th November 2013 from ISI Web of Science). Journal Impact Factor: 5.25

Key funding:

- UNAIDS (2001-2003; £49,104), Principal Investigator (PI) G. Garnett, Estimating the present and future impact of HIV – the establishment of a reference group.
- UNAIDS (2003-2010; £576,742), PI G. Garnett, Secretariat for Global Reference Group on HIV.
- UNAIDS (2009-2012; £341,318), PI G. Garnett, Providing Academic Leadership through a Secretariat for the UNAIDS Reference Group on Estimates Modelling and Projections.

4. Details of the impact (indicative maximum 750 words)

Impacts include: health and welfare, public policy and services, international development
Main beneficiaries include: UNAIDS, International Government bodies, international donors

The methods developed at Imperial are used by UNAIDS, the UN agency with responsibility to lead the international response to AIDS (www.unaids.org), to generate AIDS statistics for almost every country in the world (http://www.unaids.org/en/dataanalysis/). These statistics are used by countries and international donors (e.g. the Global Fund to Fight AIDS, Tuberculosis and Malaria) to track the epidemic and determine funding and policy decisions for HIV prevention and treatment interventions. These estimates have been crucial in describing the scale and the nature of the HIV epidemic. Without this basic information, effective and sustained action against the epidemic would not have been possible. Furthermore, it would not be possible to detect reductions in HIV prevalence that may be ascribed to programmes, which are expected to be vital in strengthening the response to epidemics. Without these estimates, neither the numbers in need of treatment nor the potential impact of interventions would have been known, both of which have been crucial in allowing major international and bilateral donors to donate billions of dollars to tackling HIV.

The routine use and impact of these statistics are typified by citations by President George W Bush as he announced the President's Plan for AIDS Relief (PEPFAR, which continued between 2008 and 2013) and more recently by President Barack Obama and Senator Hilary Clinton in public

addresses in 2009, 2011 and 2012. In his keynote speech in 2009, President Obama is quoted as saying: "Globally, there are over 33 million people living with HIV. While millions have died from this disease, the death rate is slowly declining due, in part, to our Nation's global effort through the President's Emergency Plan for AIDS Relief (PEPFAR) program." [1]. In a keynote speech (2012), Hilary Clinton cited the UNAIDS estimates of HIV impact: "Just last week, UNAIDS announced that, over the past decade, the rate of new HIV infections has dropped by more than half in 25 low-and-middle-income countries, most of them in Sub-Saharan Africa. Just listen to these numbers: In Zimbabwe, a 50% reduction; in Namibia, a 68% reduction; and in Malawi, a 73% in the rate of new infections. So as we continue to drive down the number of new infections and drive up the number of people on treatment, eventually we will be able to treat more people than become infected every year. That will be the tipping point. We will then get ahead of the pandemic, and an AIDS-free generation will be in our sight. Now, we don't know how long it will take to do this everywhere..." [2]. The only source for the statistics is the UNAIDS reports that are developed using the Imperial methods.

For each country, UNAIDS also recommends application of the 'Modes of Transmission' model (research reference 4) as part of a UNAIDS-GAMET (Global AIDS Monitoring and Evaluation Team) supported synthesis process, a component of the UNAIDS 'know your epidemic, know your response' strategy, and the World Bank's Epidemic, Response and Policy Syntheses [3]. Over 30 countries have completed, or are currently conducting, analyses with the model [4, 5]. The results from these applications have been used for the design of prevention programmes, for resource allocation and prioritisation and to inform the development of national strategic planning for HIV. In many cases, the findings have led to realignment of funding, sometimes increasing the focus of intervention in key populations that had been previously neglected. For example, in Morocco strategic information has been used to optimize the allocation of resources [6]. The distribution of the people newly infected with HIV according to the Imperial-developed model was compared with recent spending patterns to focus future prevention planning. As a result, the 2012–2016 National Strategic Plan for Morocco proposed to allocate 63% of AIDS resources towards prevention among key populations at higher risk, up from about 25% according to the 2008 spending assessment, which the model indicated would generate a far greater health impact in that setting.

Estimates of Mother-To-Child Transmission events and numbers in need of Antiretroviral Therapy in every country in the world are used by WHO to track progress toward their goals of eliminating mother-to-child transmission and universal access to antiretroviral therapy [7]. The UN methods of estimating child mortality were updated to correct for the bias effects that our research demonstrated, and these estimates are now used to measure progress against a key Millennium Development Goal [8]. Without a demonstration of that effect, it is possible that child mortality could have been substantially under-estimated which could have resulted in an inappropriate reduction in focus on child mortality in post-2015 targets.

5. Sources to corroborate the impact (indicative maximum of 10 references)

[1] In his keynote speech, President Obama, cites the UNAIDS statistics, which are taken from the UNAIDS Global Reports November 25th, 2009 (paragraph 3): http://www.whitehouse.gov/the-press-office/presidential-proclamation-world-aids-day Archived on 26th November 2013.

[2] In her keynote speech in November 29th 2012, the Secretary Clinton cites the UNAIDS estimates of HIV impact: http://www.state.gov/secretary/rm/2012/11/201198.htm (refer to paragraph 12). Archived on 26th November 2013.

[3] UNAIDS recommends the use of the 'Modes of Transmission model' is setting a country's priorities for spending: Modelling the expected Short-term Distribution of new HIV Infections by Modes of transmission. https://www.unaids.org/en/media/unaids/contentassets/documents/document/2012/guidelines/JC2427_ModelingNewHIVInfectionsbyModesofTransmission_en.pdf (refer to p.2). Archived on 4th November 2013.

[4] The estimates produced by UNAIDS/WHO are based on methods and parameters that are

informed by the UNAIDS Reference Group on HIV/AIDS Estimates (2010) Global Report http://www.unaids.org/globalreport/documents/20101123_GlobalReport_full_en.pdf (refer to page 8). Archived on 4th November 2013.

[5] UNAIDS. New HIV infections by mode of transmission in West Africa: A multi-country   analysis. Dakar, Senegal: UNAIDS Regional Support Team for West and Central Africa; 2010. http://www.unaids.org/en/media/unaids/contentassets/documents/countryreport/2010/201003_ MOT_West_Africa_en.pdf. Archived on 4th November 2013.

[6] HIV modes of transmission in Morocco and reallocation of resources: http://www.unaids.org/en/media/unaids/contentassets/documents/epidemiology/2012/gr2012/20 121120_UNAIDS_Global_Report_2012_en.pdf (see page 68). Archived on 4th November 2013.

[7] Tracking Numbers on Antiretroviral Therapy. A key report provides the statistics: UNAIDS/WHO. Monitoring the Declaration of Commitment on HIV/AIDS: Guidelines on construction of core indicators: 2010 Reporting. Geneva, WHO. http://data.unaids.org/pub/manual/2009/jc1676_core_indicators_2009_en.pdf Archived on 4th November 2013.

[8] UN methods for estimating Child Mortality Updated. A paper describing the updates to the methods (Walker, N., Hill, K., Zhao, F. (2012). Child Mortality Estimation: Methods Used to Adjust for Bias due to AIDS in Estimating Trends in Under-Five Mortality. *PLoS Med* 9(8): e1001298. DOI. Provides a direct citation to our article 6 on page 2 as providing the evidence for the need to change in the UN methods and guidance on the correction. The following quotes are taken from that paper: *"To our knowledge, only one analysis of the magnitude of bias in direct child mortality estimates due to AIDS mortality has been carried out using real data rather than simulations. Hallett et al. [8] used data from a prospective open cohort in Manicaland, Zimbabwe, to measure the bias introduced by deaths of HIV-positive mothers.… Based on the findings of **Hallett** et al., UN IGME [United Nations Inter-agency Group for Child Mortality Estimation] recently implemented an adjustment approach for use in countries where prevalence of HIV/AIDS has reached 5% or above in the adult population (ages 15–49 years)."*