

Translating evidence into policy in low-income countries: lessons from co-trimoxazole preventive therapy

Eleanor Hutchinson,^a Benson Droiti,^b Diana Gibb,^c Nathaniel Chishinga,^d Susan Hoskins,^c Sam Phiri^e & Justin Parkhurst^f

Abstract In the April 2010 issue of this journal, Date et al. expressed concern over the slow scale-up in low-income settings of two therapies for the prevention of opportunistic infections in people living with the human immunodeficiency virus: co-trimoxazole prophylaxis and isoniazid preventive therapy. This short paper discusses the important ways in which policy analysis can be of use in understanding and explaining how and why certain evidence makes its way into policy and practice and what local factors influence this process. Key lessons about policy development are drawn from the research evidence on co-trimoxazole prophylaxis, as such lessons may prove helpful to those who seek to influence the development of national policy on isoniazid preventive therapy and other treatments. Researchers are encouraged to disseminate their findings in a manner that is clear, but they must also pay attention to how structural, institutional and political factors shape policy development and implementation. Doing so will help them to understand and address the concerns raised by Date et al. and other experts. Mainstreaming policy analysis approaches that explain how local factors shape the uptake of research evidence can provide an additional tool for researchers who feel frustrated because their research findings have not made their way into policy and practice.

Abstracts in **عربي**, 中文, Français, Русский and Español at the end of each article.

Introduction

In recent years, three separate papers in leading medical journals have raised the question of why co-trimoxazole prophylaxis for opportunistic infections in patients living with the human immunodeficiency virus (HIV) has not been more widely scaled up in low-income countries. Published in *The Lancet Infectious Diseases*,¹ the *BMJ*² and the *Bulletin of the World Health Organization*,³ these papers have all expressed the authors' frustration at knowing that an intervention known to be highly efficacious, cost-effective, amply researched and urgently needed has not become widely available, especially in Africa. In the most recent article, Date et al. combined analyses of the development of policy on co-trimoxazole prophylaxis and on isoniazid preventive therapy to raise concerns about the uptake of both interventions. While operationally the need to rule out active disease before initiating treatment creates problems that make isoniazid preventive therapy especially challenging, Date et al. highlight similarities in the frustration generated by the slow scale-up of both co-trimoxazole prophylaxis and isoniazid preventive therapy. They point out that at the national level both the development of co-trimoxazole prophylaxis and the development and implementation of policy on isoniazid preventive therapy have been sluggish, and they argue that "strong advocacy and dissemination of evidence-based information regarding the benefits of co-trimoxazole prophylaxis and isoniazid preventive therapy are urgently required at the national and international level".

Several efforts have been made internationally to improve the way in which research evidence is conveyed to health policy-

makers and to advocate for the bridging of the gap between evidence and policy. The Evidence Informed Policy Network, launched by the World Health Organization (WHO), is an example of an entity whose purpose is to promote these functions (www.who.int/rpc/evipnet/en/). However, advocacy and dissemination can only go so far in influencing policy change and implementation in practice. As Date et al. explain, evidence-based data on the benefits of both co-trimoxazole prophylaxis and isoniazid preventive therapy has not been lacking internationally. The findings from the first studies conducted on co-trimoxazole prophylaxis were published in the *Lancet* as early as 1999^{4,5} and subsequent studies showed that co-trimoxazole prophylaxis was beneficial in adults and children in areas of high resistance to co-trimoxazole⁶⁻⁸, as well as in adults on anti-retroviral therapy (ART).⁹ Research on the efficacy of isoniazid preventive therapy began even earlier and has already been the subject of three Cochrane reviews.¹⁰⁻¹² Beyond these research findings, the Joint United Nations Programme on HIV/AIDS, WHO and the United Nations Children's Fund have all issued guidelines on the use of co-trimoxazole prophylaxis on three different occasions,¹³⁻¹⁵ while isoniazid preventive therapy was the subject of WHO recommendations first published in 1998 and later reaffirmed by the Stop TB partnership in 2007 and 2011.¹⁶⁻¹⁸

In these examples, research findings were available and in many cases had been clearly disseminated or advocated for by the research and international public health communities. Those who feel frustrated by the lack of uptake of research results and the apparent stalling of policy development must understand the

^a Department of Global Health and Development, London School of Hygiene and Tropical Medicine, 15-17 Tavistock Place, London, WC1H 9SH, England.

^b Medical Research Council Uganda Virus Research Institute, Research Unit on AIDS in Uganda, Entebbe, Uganda.

^c Medical Research Council Clinical Trials Unit, London, England.

^d Zambia AIDS Related TB Project, Lusaka, Zambia.

^e Lighthouse Trust, Lilongwe, Malawi.

^f London School of Hygiene and Tropical Medicine, London, England.

Correspondence to Eleanor Hutchinson (e-mail: eleanor.hutchinson@lshtm.ac.uk).

(Submitted: 31 March 2010 – Revised version received: 31 January 2011 – Accepted: 1 February 2011 – Published online: 28 February 2011)

need to move beyond the assumption that the epidemiological and cost-effectiveness data that are available, once communicated, will be automatically integrated into policy. Broader analyses are needed to support researchers as they seek to get clinically effective interventions into place. Such analyses require established methods and frameworks from the field of policy analysis to improve the understanding of the process of health policy development in a given national and international context. Those who look with consternation on the lack of uptake of available health research evidence for guiding policy and practice need to engage more explicitly with policy analysis approaches. While efforts to bridge the gap between researchers and policy-makers are important, decision-making, by its very nature, calls for many other factors to be considered; communicating the evidence is not enough.

Between September 2008 and March 2010, we conducted a policy analysis in three sub-Saharan African countries (Malawi, Uganda and Zambia) for the purpose of studying the processes involved in the formulation of national policies on co-trimoxazole prophylaxis. By doing so we hoped to explain the factors that hindered or facilitated the translation of clinical and cost effectiveness data into national policy. To expand on this work, members of our research team are currently investigating the implementation of co-trimoxazole prophylaxis by applying a policy implementation lens to better understand the factors that shape the uptake of national policies among service providers in these settings.

Our work has focused on policy structures and process to which differences in the uptake and timing of the translation of research into policy have been attributed in non-health sectors in developing countries. We selected the study countries through purposive sampling. This was done because all countries had hosted high-profile research projects on the efficacy of co-trimoxazole prophylaxis, yet their policy processes had unfolded in different ways. Of the three countries, Malawi had the first national policy on co-trimoxazole prophylaxis (published in 2002) but limited the intervention to HIV-positive (HIV+) patients with tuberculosis. Uganda followed in April 2005 with a policy for all HIV+ patients, while that same year Malawi broadened its policy to include all

HIV+ positive patients (with or without tuberculosis). In Zambia, the need for a co-trimoxazole prophylaxis policy was agreed on at the national level in 2006 and detailed guidelines were issued in 2007. However, in all settings questions remain about the implementation process and our ongoing and future work will address these questions, as there is a lack of rigorous data on the extent to which co-trimoxazole prophylaxis has been implemented in resource-poor settings. This question is being addressed by another study undertaken by the Medical Research Council Clinical Trials Unit of the United Kingdom of Great Britain and Northern Ireland.

In our work on research evidence uptake, we used a framework originally developed by the Overseas Development Institute for resource-poor settings to identify the country-specific elements influencing the uptake of co-trimoxazole prophylaxis and to identify commonalities. The framework conceptualises the uptake of research in policy development as a function of three key elements: (i) the national health care *context* (with due attention to the influence that global policy and development agencies may exercise at the national level in sub-Saharan Africa); (ii) the networks and *links* between the individuals involved in research and policy-making, and (iii) the nature of the *evidence* available (including the different ways in which different actors may interpret it).^{19,20} This framework, focused on the context, the human links and the evidence, guided qualitative inquiry among key individuals involved in the policy development process and enabled us to map the processes by which co-trimoxazole prophylaxis was taken up in different settings. It also allowed us to identify both the stable and the dynamic elements that appeared to either facilitate or hinder that process in each country. Our critical ongoing work on policy implementation will assess current practice, in quantitative and qualitative terms, surrounding the provision of co-trimoxazole prophylaxis for eligible patients. This work will also document the barriers to the implementation of co-trimoxazole prophylaxis faced by facility-level health-care providers.

Context, links and evidence in practice

In each of our study countries, the political and economic context was found to

influence how co-trimoxazole prophylaxis evidence was interpreted locally and how useful the results of research were perceived to be from the standpoint of the country's needs. At its most simple, if research is not a priority within a particular government programme, it is unlikely that research findings will make their way into policy. Politicized and highly publicized debates about other health issues, such as the discussions around ART therapy for HIV+ patients that dominated the agenda in Zambia for some time, can also obscure other, less widely known research findings.

But just as some policy contexts can hinder the uptake of research results for policy-making, others can be more conducive to such uptake. For example, while Malawi had very little money for scaling up activities for the treatment of HIV+ individuals at the turn of the century, the National TB Control Programme was actively looking for biomedical approaches to reduce HIV-related deaths among tuberculosis patients. The research on the efficacy of co-trimoxazole prophylaxis for HIV+ patients with tuberculosis was conducted in close collaboration with the national tuberculosis control programme. The findings were quickly translated into policy and implemented within an existing and smoothly functioning national tuberculosis control programme with plentiful resources.

Beyond context, however, the three countries revealed the important role played by key actors – so-called “policy entrepreneurs” – in facilitating the uptake of policy or in moving the policy-making process forward. Research results may well be known about within policy circles; but unless a key actor presents the data, addresses other policy-makers' concerns and makes sure that the item remains a priority on the agenda, efforts can stall early in the policy development phase. In all our study countries, successful policy entrepreneurs were found to be well connected to critical national networks, both in the research and policy-making community. When such actors are well positioned, they can pull networks closer together and forge links by introducing key individuals.

Finally, the type of evidence available and the perception of its significance are central to the ways in which policy-making agendas are developed. While scientists harbour the notion that evidence should speak for itself, it very often

does not. For the evidence to be taken up and converted into policy, it is necessary for someone to convey it in the right way. So, for instance, the case in favour of co-trimoxazole prophylaxis may have simply been framed in a manner that was not conducive to a change of policy in Zambia. Since co-trimoxazole was already a well known and readily used medication, at first the new evidence was perceived as relevant for clinical practice rather than for national policy. A reframing of co-trimoxazole prophylaxis as a policy issue in and of itself was needed in this case to facilitate policy action.

Discussion

To understand how evidence gets taken up and integrated into policy, and how policy, in turn, translates into practice, we need to find ways to move beyond the assumption that policy and practice will directly follow from the dissemination of convincing scientific findings, or that

implementation is straightforward and a simple matter of scaling up a policy decision. Political realities and national contexts influence policy development, but well established policy analysis approaches make it possible to identify and analyse these influences. They further allow the development of context-specific explanations for particular situations. The case of co-trimoxazole prophylaxis provides a clear example of this and affords several lessons that can be applied in dealing with the similar challenges posed by the scale-up of other treatments, such as isoniazid preventive therapy.

After several epidemiological and cost-effectiveness studies and multiple recommendations from international organizations, questions are still raised as to why the uptake of co-trimoxazole prophylaxis and isoniazid preventive therapy in low-income settings was so slow. In the case of co-trimoxazole prophylaxis, evidence uptake was inconsistent. To

explain the individual response of each country would require an analysis of various aspects of the local context, the institutional and human networks in place, the way the evidence was framed and the roles of key policy entrepreneurs. Explaining implementation requires an understanding of local constraints (e.g. lack of funds and resources or the high turnover of health ministry staff) and of the contexts in which the policy was applied. There is no simple formula for improving the uptake of research findings, but a better understanding of these elements can help researchers and advocates in ensuring more rapid uptake of research results favouring interventions such as isoniazid preventive therapy. We hope that our work has succeeded in illustrating the importance of a policy analysis perspective for researchers in similar settings concerned with getting their findings integrated into policy. ■

Competing interests: None declared.

الملخص

ترجمة البيانات إلى سياسات في البلدان المنخفضة الدخل: دروس من المعالجة الوقائية بالكوتريموكسازول

من يسعون إلى إعداد السياسات الوطنية حول المعالجة الوقائية بالأيزونيازيد والعلاجات الأخرى. ويجري تشجيع الباحثين على نشر نتائج بحثهم على نحو واضح، ولكن عليهم أيضاً أن يراعوا كيف تؤثر العوامل البنيوية، والمؤسسية، والسياسية على إعداد وتنفيذ السياسات. وسيساعدتهم ذلك في التفهم والتصدي لمشاعر القلق التي ذكرها دات وشركاه، وسائر الخبراء. وإن تعميم مراعاة أساليب تحليل السياسات، التي تشرح كيف تؤثر العوامل المحلية على اتخاذ بيانات البحوث، يمكن أن يقدم أداة إضافية للباحثين الذين يشعرون بالإحباط نتيجة لعدم وصول نتائج بحثهم إلى السياسات والممارسات.

عبر دات وشركاه، في العدد الصادر في نيسان/أبريل 2010 من المجلة، عن قلقهم من بطء تعميم علاجات وقائين للعداوى الانتهازية للمعاشين لفبروس العوز المناعي البشري في الأماكن المنخفضة الدخل وهما: التوقية بالكوتريموكسازول، والمعالجة الوقائية بالأيزونيازيد. وتناقش هذه المقالة القصيرة الطرق الهامة التي يمكن عن طريقها الاستفادة من تحليل السياسات لتفهم وشرح كيفية إيجاد السبيل لتطبيق البيانات المحددة في السياسات والممارسات، وأي العوامل المحلية التي تؤثر على هذه العملية. وتستقي الدروس الرئيسية عن إعداد السياسات من بيانات البحوث حول التوقية بالكوتريموكسازول، لأن هذه الدروس يمكن أن تثبت جدواها في مساعدة

摘要

低收入国家证据转化为政策：复方新诺明预防疗法的教训

在本杂志2010年4月份的期刊上，Date等人曾针对在人类免疫缺陷病毒（HIV）携带者中利用复方新诺明预防疗法和异烟肼预防疗法进行机会性感染预防的措施在低收入地区进展缓慢的情况表示过担忧。本文讨论了用于理解和解释某些证据转化为政策制定和实践的实现方法和原因及其地方因素对这一进程影响的重要政策分析方法。基于复方新诺明预防疗法研究证据的政策制定的主要经验教训，

将对寻找影响异烟肼预防疗法和其他疗法的国家政策制定者有用。尽管研究人员应以清楚明确的方式传播其研究成果，但他们还应注意决定政策制定和实施的体制、体制和政治因素。这样做将有助于他们了解并解决Date等人以及其他专家提出的担忧。解释当地因素如何决定研究证据摄取的主流政策分析方法为那些因其研究结果未能用于政策和实践的研究者提供了另外一种工具。

Résumé

Traduire les preuves en politique dans les pays à faible revenu: leçons tirées de la thérapie préventive au cotrimoxazole

Dans l'édition d'avril 2010 de cette revue, Date et al. ont exprimé leur inquiétude quant à la lenteur de la généralisation, dans les pays à faible revenu, de deux thérapies de prévention des infections opportunistes chez les personnes vivant avec le virus de l'immunodéficience humaine:

la prophylaxie par le cotrimoxazole et la thérapie préventive à l'isoniazide. Ce court article décrit de quelles façons importantes l'analyse de la politique peut s'avérer utile pour comprendre et expliquer comment et pourquoi certaines preuves s'intègrent à la politique et à la pratique,

et quels facteurs locaux influencent ce processus. Les leçons clés de l'élaboration des politiques sont tirées des preuves des recherches réalisées sur la prophylaxie au cotrimoxazole car ces leçons peuvent servir aux personnes qui souhaitent influencer le développement de la politique nationale en matière de thérapie préventive à l'isoniazide et d'autres traitements. Les chercheurs sont encouragés à diffuser leurs découvertes d'une manière claire, mais ils doivent également rester attentifs à la façon dont les facteurs structurels, institutionnels et politiques façonnent

le développement et l'application des politiques. Ce faisant, ils pourront comprendre et résoudre les problèmes soulevés par Date et al., mais aussi par d'autres experts. L'intégration des approches d'analyse des politiques, qui expliquent comment les facteurs locaux modèlent la compréhension des preuves des recherches, peut fournir un outil supplémentaire aux chercheurs frustrés par le fait que les résultats de leurs recherches ne trouvent pas leur aboutissement dans la politique et la pratique.

Резюме

Воплощение научных данных в политические мероприятия в странах с низким доходом: уроки превентивной терапии котримоксазолом

В статье Dale et al., опубликованной в апрельском номере нашего журнала за 2010 год, была выражена озабоченность в связи с медленным распространением в странах и районах с низким доходом двух методов лечения, направленных на профилактику оппортунистических инфекций у больных, живущих с вирусом иммунодефицита человека: профилактического приема котримоксазола и превентивной терапии исониазидом. В нашей небольшой статье обсуждаются важные способы применения прикладного политического анализа для понимания и объяснения того, как и почему конкретные результаты научных исследований воплощаются в политику и практику, и какие местные факторы влияют на этот процесс. На основе результатов научных исследований, посвященных профилактическому приему котримоксазола, формулируются ключевые выводы, касающиеся разработки политических мероприятий. Они могут оказаться полезными для тех, кто стремится повлиять

на формирование национальной стратегии в области превентивной терапии исониазидом и других методов лечения. Необходимо, чтобы ученые распространяли результаты своих исследований в понятной форме, однако они также обязаны обращать внимание на то, каким образом структурные, институциональные и политические факторы оказывают определяющее воздействие на разработку и внедрение политических мероприятий. Это поможет им понять и решить проблемы, поднятые Date et al. и другими экспертами. Широкое применение концепций прикладного политического анализа, объясняющих, как местные факторы формируют отклик на результаты научных исследований, может расширить инструментарий ученых, которые чувствуют себя разочарованными тем, что выводы их исследований не нашли применения в политике и на практике.

Resumen

Conversión de datos en planes de acción en los países de ingresos bajos: el tratamiento preventivo con la asociación de trimetoprim y sulfametoxazol como ejemplo

En la edición de abril de 2010 de esta publicación, Date *et al.* expresaron su preocupación por el lento progreso, en los países de ingresos bajos, de dos tratamientos preventivos de las infecciones oportunistas en personas con el virus de la inmunodeficiencia humana: la profilaxis con la asociación de trimetoprim y sulfametoxazol y el tratamiento preventivo con isoniazida. Este breve artículo aborda la importancia de la utilización del análisis de los planes de acción para entender y explicar cómo y por qué determinadas evidencias se introducen en las políticas y se llevan a la práctica y qué factores locales influyen en este proceso. Las lecciones principales de la elaboración de políticas se extraen de las investigaciones basadas en la evidencia de la profilaxis con la asociación de trimetoprim y sulfametoxazol, y dichas lecciones pueden resultar muy útiles a quienes

deseen influir en el desarrollo de políticas nacionales sobre el tratamiento preventivo con isoniazida y otros tratamientos. Se insta a los investigadores a divulgar sus hallazgos de una manera clara, pero también deben prestar atención a la manera en que los factores estructurales, institucionales y políticos perfilan el diseño y la puesta en marcha de dichas políticas. De esta manera les resultará más fácil entender y abordar las inquietudes manifestadas por Date *et al.* y otros expertos. Aquellos investigadores que puedan sentirse frustrados porque los hallazgos de sus investigaciones no se hayan materializado en un plan de acción ni se hayan puesto en práctica, pueden valerse de una herramienta adicional: los métodos establecidos para el análisis político que explican cómo los factores locales moldean la aplicación de los datos científicos.

References

1. Zachariah R, Harries AD, Luo C, Bachman G, Graham SM. Scaling-up co-trimoxazole prophylaxis in HIV-exposed and HIV-infected children in high HIV-prevalence countries. *Lancet Infect Dis* 2007;7:686–93. doi:10.1016/S1473-3099(07)70239-6 PMID:17897611
2. Anglaret X, Eholie S. Cotrimoxazole for HIV infected adults reduces mortality even where bacterial resistance is high. *BMJ* 2008;337:184.
3. Date AA, Vitoria M, Granich R, Banda M, Fox MY, Gilks C. Implementation of co-trimoxazole prophylaxis and isoniazid preventive therapy for people living with HIV. *Bull World Health Organ* 2010;88:253–9. doi:10.2471/BLT.09.066522 PMID:20431788
4. Anglaret X, Chêne G, Attia A, Toure S, Lafont S, Combe P et al.; Cotrimo-CI Study Group. Early chemoprophylaxis with trimethoprim-sulphamethoxazole for HIV-1-infected adults in Abidjan, Côte d'Ivoire: a randomised trial. *Lancet* 1999;353:1463–8. doi:10.1016/S0140-6736(98)07399-1 PMID:10232311
5. Wiktor SZ, Sassin-Morokro M, Grant AD, Abouya L, Karon JM, Maurice C et al. Efficacy of trimethoprim-sulphamethoxazole prophylaxis to decrease morbidity and mortality in HIV-1-infected patients with tuberculosis in Abidjan, Côte d'Ivoire: a randomised controlled trial. *Lancet* 1999;353:1469–75. doi:10.1016/S0140-6736(99)03465-0 PMID:10232312

6. Zachariah R, Spielmann MP, Chinji C, Gomani P, Arendt V, Hargreaves NJ et al. Voluntary counselling, HIV testing and adjunctive cotrimoxazole reduces mortality in tuberculosis patients in Thyolo, Malawi. *AIDS* 2003;17:1053–61. doi:10.1097/00002030-200305020-00015 PMID:12700456
7. Mwaungulu FBD, Floyd S, Crampin AC, Kasimba S, Malema S, Kanyongoloka H et al. Cotrimoxazole prophylaxis reduces mortality in human immunodeficiency virus-positive tuberculosis patients in Karonga District, Malawi. *Bull World Health Organ* 2004;82:354–63. PMID:15298226
8. Mermin J, Lule J, Ekwaru JP, Malamba S, Downing R, Ransom R et al. Effect of co-trimoxazole prophylaxis on morbidity, mortality, CD4-cell count, and viral load in HIV infection in rural Uganda. *Lancet* 2004;364:1428–34. doi:10.1016/S0140-6736(04)17225-5 PMID:15488218
9. Walker AS, Ford D, Gilks CF, Munderi P, Ssali F, Reid A et al. Daily co-trimoxazole prophylaxis in severely immunosuppressed HIV-infected adults in Africa started on combination antiretroviral therapy: an observational analysis of the DART cohort. *Lancet* 2010;375:1278–86. doi:10.1016/S0140-6736(10)60057-8 PMID:20347483
10. Wilkinson D. Drugs for preventing tuberculosis in HIV infected persons. *Cochrane Database Syst Rev* 2000;4:CD000171. PMID:11034676
11. Woldehanna S, Volmink J. Treatment of latent tuberculosis infection in HIV infected persons. *Cochrane Database Syst Rev* 2004;1:CD000171. PMID:14973947
12. Akolo C, Adetifa I, Shepperd S, Volmink J. Treatment of latent tuberculosis infection in HIV infected persons. *Cochrane Database Syst Rev* 2010;1:CD000171. PMID:20091503
13. Joint WHO/UNAIDS/UNICEF statement on the use of cotrimoxazole as prophylaxis in HIV exposed and HIV infected children. Geneva: World Health Organization & United Nations Children's Fund; 2004. Available from: <http://www.who.int/3by5/mediacentre/en/Cotrimstatement.pdf> [accessed 17 February 2011].
14. World Health Organization; UNAIDS. Provisional WHO/UNAIDS recommendations on the use of cotrimoxazole prophylaxis in adults and children living with HIV/AIDS in Africa. *Afr Health Sci* 2001;1:30–1. PMID:12833907
15. *Guidelines on co-trimoxazole prophylaxis for HIV-related infections among children, adolescents and adults in resource-limited settings: recommendations for a public health approach*. Geneva: World Health Organization; 2006.
16. *Policy statement on preventive therapy against tuberculosis in people living with HIV*. Geneva: World Health Organization; 1998. Available from: http://whqlibdoc.who.int/hq/1998/WHO_TB_98.255.pdf [accessed 17 February 2011].
17. *Isoniazid preventive therapy (IPT) for people living with HIV: consensus statement of the core group of TB/HIV Working Group of STOP TB partnership*. Geneva: Stop TB partnership; 2007. Available from: http://www.stoptb.org/wg/tb_hiv/assets/documents/IPT%20Consensus%20Statement%20TB%20HIV%20Core%20Group.pdf [accessed 17 February 2011].
18. *Guidelines for intensified tuberculosis case-finding and isoniazid preventive therapy for people living with HIV in resource constrained settings*. Geneva: World Health Organization; 2011. Available from: http://whqlibdoc.who.int/publications/2011/9789241500708_eng.pdf [accessed 17 February 2011].
19. Crewe E, Young J. *Bridging research and policy: context, evidence and links* (Working Paper 173). London: Overseas Development Institute; 2002.
20. Court J, Young J. *Bridging research and policy: insights from 50 case studies* (Working Paper 213). London: Overseas Development Institute; 2003.