

Intervention and assessment phase: Addressing conflict of interest in pluralistic health systems: an interventional study in Pakistan

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Background

Many low and middle income countries (LMIC) health systems are characterised by a failure of the public sector to adequately provide, regulate and monitor health services, resulting in a dominant private health sector (1). There is strong evidence from a range of settings that the profit generating model of private providers can lead to a conflict of interest (COI) resulting in prescription of medication or diagnostic tests that are either unnecessary or more costly than available alternatives (2, 3). In this context, we define COI as a situation whereby the impartiality of a healthcare provider's professional judgment may be influenced by a secondary interest, such as financial gain, leading to a decision that conflicts with their own interpretation of the patient's best interest.

This dominance of private, for-profit providers, combined with a persisting failure to deliver social benefit, makes finding interventions to improve their quality of care essential for health systems strengthening and achieving Universal Health Coverage (1, 4). However, there are two major impediments to progress on this front. First, there is limited evidence from robust assessments of interventions to improve quality of care delivered by private providers in LMIC (5, 6). Second, there has been marked absence of attention by researchers and policymakers to the role of political, social, economic and cultural factors that influence the effectiveness and scalability of interventions (the 'software' of health systems) even through there is now a growing body of evidence highlighting the importance of these elements (7) (8).

Evidence from several studies, including our own empirical work, shows that private doctors are often responsible for driving irrational use of medicines - identified as one the most pressing challenges facing global health by the World Health Organization (WHO) (9) – by prescribing medicines that are inappropriate for the patients' clinical need (10, 11). The limited available evidence on governance interventions in LMIC shows that prohibiting or constraining private doctors through the enforcement of regulations typically fails because of a lack of political and social support and enforcement capacity, as well as insufficient public sector capacity to provide care (5).

Therefore, training interventions focusing on increasing technical knowledge and skills is the most common approach used to improve the quality of care (16, 17). Training interventions assume that poor technical quality of care occurs primarily because of inadequate medical knowledge, and therefore the educational materials do not typically cover norms and values. It is clear, however, from consistent evidence on the 'know-do' gap that COI related to profit generation from medicine sales plays a critical role in prescribing decisions, as do values associated with professional ethics and altruism (18, 19).

We use irrational prescribing of antibiotics (IPA) as an indicator of irrational prescribing of medicines more broadly, since antimicrobial resistance is particularly high on the global policy agenda at present, and has attracted national stakeholders' attention towards the quality of healthcare in some LMIC, including Pakistan (20, 21). We focus on private doctors operating solo practices, by which we mean a single doctor running his or her standalone for-profit clinic receiving out-of-pocket payments from patients. Private doctors in our study will include those with a basic medical qualification and those with specialist training; there are over 200,000 registered in Pakistan, and it is estimated that more than double this number run clinics without registration. Doctors that work exclusively in the private sector and those that work concurrently in the public and private sector will be included to reflect the true composition of private doctors. While we acknowledge the role of patient demand in prescribing decisions, this study will focus on the supply side.

Literature review

In preparing this application we conducted a literature review in PubMed using broad search terms (ethic* AND [doctor OR physician OR medicine] AND Pakistan) to identify existing studies, and searched Google Scholar using similar terms to capture additional peer-reviewed and grey literature. We found only eight studies related in any way to doctors' professional ethics in receiving personal benefits linked to their medical decision making in Pakistan. Repeating the search to find studies conducted in other LMIC, including India, Bangladesh and Cambodia revealed a similar paucity of

research on this topic, with nine papers identified in total. Examining the literature from Pakistan showed that very little had changed since a review in 2001 concluded that ‘there is a dearth of published discourse on healthcare ethics in Pakistan. A lack of effective policy and legislation concerning the ethical practice of medicine is reported to have negative effects on the profession’. The majority of research conducted since 2001 focused on the ethics of organ donation, professional relationships between doctors working together and clinical dilemmas related to patients’ preferences. Of the relevant studies we reviewed, three surveyed medical students or trainee doctors, and another three, focusing on ethics of practising doctors, had strikingly similar policy recommendations: the need for urgent improvements in sensitisation of doctors to medical ethics supported by clear guidelines on ethical practice covering doctors and pharmaceutical companies.

Formative research and study objective

The formative phase of our research received prior approval by the LSHTM and Aga Khan University ethics committees. In this phase, we conducted semi-structured, in-depth interviews with 28 primary care doctors (GPs), 29 policy actors, and 11 pharmaceutical company sales representatives in Karachi. The policy actors interviewed included regulatory authorities, professional medical associations, and health communication/media consultants. Our formative research has already addressed the research questions below:

1. How is COI and professional ethics conceptualised by Pakistani policy actors and to what extent do governance conflicts influence the priority they give to tackling COI?
2. Which factors shape private doctors’ perceptions of ethically unacceptable and acceptable COI with respect to prescribing antibiotics?
3. How should messages that sensitise private doctors to professional ethics and the role of COI driving irrational prescription of antibiotics be framed, and should sensitisation to COI be combined with any other strategies to encourage behaviour change?

Based on inductive analysis of the interview data, we have found that professional ethics has deteriorated gradually over the past several decades while various incentives structures have been firmly and routinely established in the provision of healthcare. We identified a diverse array of financial and non-financial incentives used to develop longstanding relationships of ‘give and take’ between pharmaceutical companies and GPs (mediated by sales representatives). The growth of the domestic pharmaceutical industry has been supported by government policies, which has led to ‘over-competition’ and more elaborate incentives structures, and the strong political pressure from industry and providers who benefit from the current system feeds COI at higher levels of policymaking. There is an accountability deficit across policymaking actors and institutions whereby no actor or institution is willing to prioritise or take ownership of COI as a health policy issue.

It is within this complex and dynamic context, shaped by our findings and a limited body of existing literature and policy recommendations on COI in healthcare decision-making, that we will develop and test a ‘soft’ governance approach to address COI in private doctors in Pakistan. The objective of our study is to design and assess a multi-faceted intervention to shift the practice and attitudes of private doctors with respect to unethical benefits from pharmaceutical companies for prescribing medicines (focusing on antibiotics).

Intervention outcomes

The primary outcome of our study is the practice change of doctors with respect to accepting incentives linked to prescribing targets from pharmaceutical sales representatives (assessed using a novel methodology, described below)

The secondary outcomes are:

1. Change in knowledge of doctors about professional ethics, conflict of interest and relevant guidelines
2. Change in attitude of doctors about what is appropriate ethical practice with regards to incentivisation for prescribing medicines

Methodology

Our methods bring together different disciplinary perspectives and have been developed jointly by the research team in close consultations with policy actors already engaged in our research. In this intervention phase, we will conduct a randomised controlled study to compare knowledge, attitudes and practice of doctors who receive the intervention package with those who attend placebo seminars with no mention of COI. While there may be a risk of contamination across control and intervention groups, we will take adequate measures to minimise it. For instance, the list of private general physicians (GPs), we obtained from the Sindh Healthcare Commission (SHCC) includes vital information related to administrative districts and clinic addresses. Based on the addresses given, we will tease out towns located in each district of Karachi. A sample design based on administrative towns with diverse socioeconomic and infrastructural conditions may help us to avoid contamination. In addition, we will schedule all four seminars with minimal breaks (i.e., one seminar per week) and this may not allow GPs time, enough to socialise and discuss efforts taken by the research team. We will generate robust evidence on the impact of our intervention on behaviour by using a novel objective assessment of doctors' interaction with Standardised Pharmaceutical Sales Representatives (SPSR) offering incentives for prescribing antibiotics. We describe these elements in more detail in the subsequent paragraphs.

Sample size

As our literature review identified no relevant surveys of private doctors in Pakistan, we have used data from two studies on medical students and trainee doctors, and our formative qualitative research data, to estimate the proportion of private doctors that will be classified as 'yes' in the SPSR assessment for our sample size calculations. One survey of medical students found that 81% favoured pharmaceutical sponsorship of events at medical colleges and the other study on trainee doctors in public hospitals reported that 57% had no knowledge of any code of medical ethics. Our qualitative research with private doctors also showed that receiving benefits for prescribing was very common. We therefore estimate that 80% of private doctors in the control group will be classified as 'yes' and assume that our intervention shifts this to 65% (in line with changes observed in the few interventional studies addressing COI in medical professionals (48, 49)). Using these assumptions, a sample size of 138 per group gives a power of 80% to detect a difference owing to the intervention. We will include 320 private doctors in our sample to account for drop-outs.

Process for sampling and randomisation

For the purpose of this study, doctors with a formal training in medicine (MBBS), who are registered with Pakistan Medical Council (PMC) and work as primary care general practitioners (GPs) in Karachi will be eligible to participate in the study. Doctors who only work in tertiary care facilities will be excluded. In line with our eligibility criteria, we will begin by creating a sampling frame consisting of all private (GP) clinics in Karachi working with project partner and regulator the Sindh Healthcare Commission (SHCC), which routinely maintains a list of registered medical facilities. We will randomly select 320 private doctors meeting our eligibility criteria from the sampling frame, which we expect will consist of over 600 private doctors, to form our study population and seek consent to include them in the study. We anticipate a 20% refusal rate, resulting in approximately 280 doctors being willing to participate. As soon as a private doctor consents, he or she will be randomly allocated to the intervention or control group (140 in each group).

To avoid contamination of the information regarding seminars for control and intervention groups, we will design generic information sheets containing information about doctors' knowledge, attitudes, and practices regarding health and medical practice. As part of the formative phase of the study, we will conduct a baseline survey to assess doctors and knowledge and attitude about professional ethics and medical practice, and we will use this opportunity to invite doctors to the seminars and take their consents. The randomisation process will be completed once consents are taken from the sampled doctors during the baseline survey.

Participants can withdraw participation in the study at any point and we will include data already collected, as outlined to participants in the information sheet.

Intervention

We will take a sample of 400 GPs, representing all the districts of Karachi, including East, West, South, Central, Korangi, and Malir. We aim to conduct a randomised control trial (RCT), where 200 GPs from the control group will receive seminars on Anemia, while the other 200 GPs from the intervention group will receive seminars on ethical medical practice. After compiling a list of eligible and consenting GPs, which we have already initiated, we will request the Clinical Trial Unit (CTU), the Aga Khan University (AKU) to help us will randomising GPs. Based on CTU's randomisation, the GPs will be included in to control and intervention groups. The plan is for each seminar to last between 1.5 – 2.00 hours. The seminars will be delivered in three steps: first, GPs will receive lectures from presenters on medical ethics (for intervention group and anaemia (for the control group). Second, following the lectures, the seminars will include a video/film on medical ethics (for the intervention group) and anaemia (for the control group). Third, the GPs will be organised in small groups to enable discussions on key messages from lectures and videos.

We will engage GPs in the intervention group using the specially designed emotive messages that will aim to shift GPs perspectives on COI and unethical incentivisation, focusing on unnecessary prescribing of medicine. The framing of these messages has been informed by the interviews we have conducted, and we will work with communication experts, educators and ethicists to develop powerful messages and message delivery strategies, and to design the seminar for GPs. Seminars are planned to include the following:

- A 10-15-minute film (or other media format) showing doctors the impact of unnecessary prescribing on patients and highlighting doctors' responsibilities and role in society.
- Short talks from ethical opinion leaders (religious leaders with medical training have also been suggested).
- A presentation from the provincial regulator, SHCC, on actions they will be taking against unethical prescribing or 'quackery' (by doctors or untrained providers) to indicate that there will be consequences for continued unethical practice.
- Small group discussions between doctors (with or without facilitators).

Seminars may be conducted in educational establishments, or other locations that will support high attendance. GPs in the control group will attend a seminar on anaemia or mental health in Pakistan (depending on existing medical education content and material that AKU have at-hand) without mention of COI.

Post intervention re-enforcement:

For 1-2 months after the seminars, we will use the following ways to remind participants about the seminar content before assessing practice change:

- Short videos sent via WhatsApp or SMS containing key messages from the seminars
- An online quiz on the content of the seminars. Here, to avoid contamination

We will organise two separate lists of GPs designated for control and intervention groups. Only GPs in intervention groups will receive short videos via WhatsApp or SMS. Because we aim to complete the seminars within tight timelines (4 weeks), and this can allow avoiding contamination across control and intervention groups. Additionally, the video messages are a part of the intervention package, and hence, messages delivered during the seminars as well as COI messages document sent by SHCC to intervention group GPs will potentially have a major impact on GP's knowledge, attitudes, and behaviour related to COI in medical practice. From this perspective the risk of contamination may be limited in case the video is somehow shared across GPs from both groups because the video is not a major source of information on medical ethics, rather something that supplements the broader intervention.

- Pledge on ethical practice to display in GPs' clinics, or educational posters, or a graphic recording of the seminars.

- Reminder letters from SHCC (and/or the Pakistan Medical Commission) summarising key messages about incentivisation rules.

Intervention assessment

During the seminars, we will inform the GPs that as part of the study, the impact of the seminars will be assessed. Assessment will be as follows:

1. We will develop a tool to collect individual level information about private doctors': sociodemographic characteristics, medical knowledge, reported level of training on clinical medicine and medical ethics, and attitudes towards incentivisation for prescribing. This tool will be used to compare doctors' knowledge and attitudes towards COI before and after the intervention seminars, and between the control and intervention arms.
2. Conduct interviews with 20-25 doctors in the intervention group to better understand how effective the COI seminar was

Additionally, the standardised pharmaceutical sales representatives SPSR will be visiting their clinics unannounced to assess impact of the seminars. This is an innovative extension of the well-established approach of using Standardised Patients to collect data on the behaviour of medical professionals that we will design based on data from our formative research interviews.

In addition to the research team (with LSHTM members who are experienced in similar methods) and our Pakistani and international advisors, we will seek help from a former pharmaceutical sales representative (who is also currently helping us with a baseline survey with general practitioners (GPs) in Karachi) to provide standardized pharmaceutical sales representatives, with training.

The practice of private doctors in control and intervention groups in relation to incentives for prescribing antibiotics, will be assessed after the seminars using the Standardised Pharmaceutical Sales Representative (SPSR) methodology between 2-4 months after the participants attended the seminar. This is an innovative extension of the well-established approach of using Standardised Patients to collect data on the behaviour of medical professionals that we will design based on data from our formative research interviews.

The SPSR assessment can potentially be carried out by two methods:

1. We can collaborate with a local registered pharma company that can allow us to induct SPSRs who, while marketing their products, will assess doctors' interest in taking unethical incentives.

OR

2. We can train some qualified (i.e., former sales representatives, medical doctors/students, or pharmacologists) as SPSRs who will present themselves as representatives from a new domestic company looking to expand market share of their third line generic antibiotic.

The SPSRs will assess the behaviour of private doctors by interacting with them in their clinics in the typical way that a pharmaceutical sales representative would. To initiate the interaction, the SPSR will approach the doctor's office when called in and recite a script meant for the products of the partner pharma company. The script will be simultaneously piloted with GPs in Karachi and translated into Urdu. The script will introduce the SPSR in character, provide brief information on the medicines, and engage the GP on a discussion regarding incentives that they are able to offer or that the GP would like to request. The SPSR will also carry with them the company's brochure with information regarding the medicines they are promoting, and a business card with their company name on it. Based on our formative research detailing how sales representatives develop a relationship with GPs, we anticipate SPSRs might need 1-2 'familiarisation visits' before they are able to discuss and assess the GPs practice regarding incentives. We will factor in these visits into the SPSR training and implementation planning.

Drawing on SPSRs, each doctor from the control as well as the intervention groups will be paid at least one visit to evaluate the extent to which the doctors accept incentives from pharmaceutical companies. SPSRs will assess the behaviour of private doctors by interacting with them in their clinics in the typical way that a pharmaceutical sales representative would. Following the interaction, the SPSR will immediately fill out a questionnaire to record details of the interaction in terms of how the GP

responded/reacted to the scripted questions. The questionnaire will be analysed by research team members (blinded to the allocation of private doctors to control or intervention groups) who will assign a binary outcome for each private doctors e.g., 'yes' or 'no' for unethical benefit for prescribing the SPSR's antibiotic, using a checklist based on the PMC and SHCC endorsed codes of ethical conduct. Doctors will be aware, through the consent procedure, that their behaviour will be assessed covertly at some stage over a 6-month period but will not know details of the assessment to avoid the Hawthorne effect.

We considered this novel experimental design based on SPSR to be superior to a revealed preferences approach (i.e., based on medical records) because records of prescribing by private doctors usually do not exist or are of poor quality in Pakistan, and to a stated preference design as it would rely on honest reporting of behaviour that is highlighted as unethical in the COI presentation. This methodology will be piloted with some GPs from the SHCC list, who will not be part of our sample. This pilot will help us to determine the validity of our assessment methodology and improve it for the actual use.

Statistical analysis

The primary outcome will be assessed by comparing the proportion of doctors classified as 'yes' to accepting an unethical benefit (according to the regulator's guidelines) for prescribing the SPSR's antibiotic between the control and intervention groups. The proportions will be compared using a two-proportion z-test.

Secondary outcomes such as knowledge and attitude shifts will be assessed by comparing mean scores in survey responses of control and intervention groups using unpaired t-test and proportions scores in survey responses using the z-test.

Confidentiality

We will ensure to protect the study participants by making the information we receive confidential – allocating GPs with IDs and removing all the information that can help identify them (i.e., name, registration number, clinic name/address). The collaboration with the SHCC also means that the SHCC will help the research team to undertake the intervention (inviting GPs to participate, issuing a key ethical messages document to intervention group GPs), rather than taking actions against certain practices. To clarify, and as mentioned in the consent form, we will not provide any agency with information about the attitudes or practices of individual GPs. We will only share aggregated data of the control and intervention groups collectively to allow an assessment of the impacts, which will have important implications regarding policymaking.

Personal information will be used for introductory and familiarity purposes alone and will not be used in a publication or presentation. All research data will be anonymised and coded at the earliest opportunity. Any data placed in a database or shared with other members of the research team will only contain anonymised information.

Research Project Team

The project has been developed by a multidisciplinary group of researchers bringing together expertise in Health Policy and Systems Research (HPSR), epidemiology, governance, infectious diseases, political economy and anthropology. The Dr Mishal Khan, a Pakistani Associate Professor of HPSR, acts as a PI from the London School of Hygiene and Tropical Medicine (LSHTM). A specialist in applying epidemiological methods to health systems research, she has over a decade of experience in leading qualitative and quantitative studies in Pakistan, Cambodia, Myanmar and China, with a focus on private healthcare providers. Khan is uniquely positioned to manage the study, benefiting from internationally recognised academic credentials combined with deep-rooted local knowledge. Since she is fluent in Urdu and has lived in Karachi for several years, Khan has the advantage of being able to conduct critical qualitative interviews herself, check accuracy of translations, train data collection staff in the local language, and lead on designing locally relevant

dissemination materials (working closely with well-established collaborators at AKU). She will work with Miss Rahman-Shepherd from the LSHTM side, who is a Research Fellow experienced in health governance and policy research.

Professor Hasan and Dr Shakoor are two of Pakistan's most prominent researchers on drug resistance. They have worked with Khan and Associate Professor Hanefeld on two HPSR grants in Pakistan and are excellent at facilitating access to relevant interviewees. Shakoor (AKU PI) will manage day to day AKU research activities with Dr Noor and Miss Sharif. Noor is an Assistant Professor at AKU and trained social scientist with extensive experience in health policy and systems theory and research. Sharif is a senior project staff member at AKU with significant experience in health policy research and qualitative methodology. They will work with Associate Professor R Siddiqui (an epidemiologist) who has an extensive experience in assessing health systems interventions, to develop the study sampling frame and lead on the intervention design and evaluation from AKU (with Khan leading from LSHTM, supported by Associate Professor Wiseman, a health economist specialising in evaluation of complex interventions). Hasan is one of AKU's most experienced medical education faculty members and will guide development of the continuing medical education intervention. Prof S Siddiqui brings outstanding academic and practical expertise on health system governance and quality of care, having joined AKU after serving as the director of Health Systems Development in WHO's Eastern Mediterranean Region Office and working in the World Bank and the Pakistan Ministry of Health. Hanefeld and Associate Professor Legido-Quigley are experts in political economy analysis in LMIC, focusing on the role of actor power and networks.

Research Impact

We will plan the seminars to be consistent with typical continuing medical education activities that doctors attend, in order to facilitate scale-up and delivery in the future by healthcare commissions or PMC as part of relicensing or licensing requirements. The messaging and emotive media on professional ethics and COI in relation to incentivisation for prescribing medicines and tests, that will be used in the intervention arm seminar, will form a major output of the research. In addition to the core research team, we have been seeking advice from a group of relevant advisors from AKU, and organisations like Pakistan Medical Commission (PMC), and SHCC to receive their view on the messages we have developed on COI. After incorporating their feedback, we will send the finalised version of the messages to PMC and SHCC for endorsement. Similarly, for video, we have been approaching to various media agencies to obtain pitch/proposals from them. In consonance with our messages, we will advise media agencies to share scripts/video ideas with us. The video content then will be finalised by the wider AKU-LSHTM teams, along with by our advisors from the AKU media and communications. These processes will ensure the content of the messages and the video are in alignment with our objective – reducing COI in medical practice – and is valid to be delivered to GPs in the intervention group. These outputs have been designed with the intention of becoming part of mandatory continuing medical education run by the SHCC. They will also be made available for other organisations in Pakistan and LMIC to adapt for medical education purposes. Moreover, the key messages that will be developed will contribute to an updated code of conduct on ethical practice and COI for doctors, endorsed by the SHCC and other relevant national/international stakeholders (e.g., PMC, WHO).

Our study will generate qualitative and quantitative data on the current status of GPs' knowledge, attitudes and behaviour with respect to professional ethics, COI, and incentivisation, and evidence of change post-intervention, which will help guide policymaking to improve and enhance doctors' professionalism in Pakistan and inform similar policy initiatives in LMIC more widely. This study will also generate new HPSR research methods and new knowledge on the role of professional ethics and COI—an understudied aspect of the software of health systems.

Ethics

We will work to ensure no hazards to participants. Owing to the potentially sensitive nature of our research, we will ensure participants' confidentiality, and will remain mindful of the potential consequences of this work on study participants and private doctors more widely. We do not anticipate distress as our data collection questions and messages presented during the intervention will be carefully designed with input from doctors, ethics experts and communication

experts. However, participants may experience challenging emotions when reflecting on ethical practice or their behaviours, and may have complex feelings about the topic. The data collectors will be trained via the 'good clinical practice' course under AKU core team and this will help them to recognise if, at any point, participants feel uncomfortable. We will give them an opportunity to ask questions about the study purpose, to share their thoughts with research team members, and to consider taking a break to be able to further think about their participation while reassuring them of their right to withdraw from the study. We will also provide access to written materials with guidelines on ethical practice. We will ensure that the SPSR assessment in no way borders on entrapment, by: simulating a scenario which doctors frequently encounter during interactions with sales representatives and preventing any legal or social consequences on doctors by restricting access to information about individual private doctors to the study team for the purpose of this analysis only. In addition to oversight from our Advisory Committee, who will review project updates twice per year, we will seek input on ethical considerations from a working group on Standardised Patients that the PI is part of. Members of this group are drafting guidelines for ethics committees on how to assess studies using Standardised Patients. Ethical approval will be sought through the AKU and LSHTM institutional ethics committees; the research team has experience of multiple successful applications both, and CI R Siddiqui is highly experienced in conducting interventional studies in Pakistan. Furthermore, AKU is one of the only LMIC institutions to have a 'Standardised Patients Bank' since they use Standardised Patients routinely as part of medical teaching.

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