CHAPTER 14

Misoprostol Use and Its Impact on Measuring Abortion Incidence and Morbidity

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Abstract

Misoprostol is an effective and increasingly popular medication abortion option, especially in developing countries where abortion remains legally restricted. Taking a pill is noninvasive and the method does not require sophisticated storage. In settings where abortion is legally restricted, women can purchase the drug at pharmacies, often without a prescription, and self-administer it. Yet measuring misoprostol use remains a methodological challenge, especially where women and providers are hesitant to report use and/or accurate hospital records of women presenting with complications are unavailable. The research community is interested in developing sound methodologies to quantify self-use of misoprostol to induce abortion, since its use can impact the measurement of abortion incidence and morbidity in complex ways. Substantial self-use of misoprostol to induce abortion can potentially both temporarily increase and/or ultimately decrease overall induced abortion estimates. To address this research challenge, we present three types of data methodologies—national pharmacy sales data sets; face-to-face interviews; and pharmacy-based "mystery client" studies. We explain each method with its corresponding advantages and limitations, and how to incorporate the resulting data into abortion estimates. Finally, we highlight challenges in disseminating findings about misoprostol in settings where abortion is legally restricted.

Introduction

Misoprostol (marketed as Cytotec) is a synthetic analogue of the prostaglandin E1 that entered the global market in the late 1980s and was originally produced for the prevention of gastrointestinal ulcers. It is now registered for this indication in more than 80 countries in the Americas, Europe and South Asia (Shannon and Winikoff 2004). But misoprostol also has gained widespread recognition for its off-label use as an effective abortifacient when used alone or with other drugs (e.g., mifepristone or methotrexate), particularly within the first nine weeks of pregnancy (Bracken et al. 2007; Grapsas et al. 2008, Middleton et al. 2005). Numerous studies over the past two decades demonstrate misoprostol's potential for use in other obstetric indications, including the prevention and treatment of postpartum hemorrhage and induction of labor (Blanchard et al. 2002; Prata et al. 2009; Harper et al. 2007).

Misoprostol has the potential to help reduce pregnancy-related morbidity and mortality, especially in low-resource settings where abortion remains legally restricted (Miller et al. 2005). A modeling exercise conducted in Latin America, Africa and Asia demonstrated that increasing the use of misoprostol for elective abortions could have a notable impact on abortion-related maternal mortality (Harper et al. 2007). In the Latin American region, which has lower maternal mortality than Asia or Africa, the study estimated that there would be a 26% reduction in maternal mortality if 40% of abortions were misoprostol induced. Furthermore, the extent to which misoprostol is used to induce abortions affects the accuracy of estimates of abortion incidence and related morbidity (Singh 2006). Since sound research on abortion incidence and morbidity is critical for effecting policy changes to further women's reproductive rights, we must recognize and try to account for misoprostol's impact on these data.

This chapter describes methodologies that rely on three information sources to estimate misoprostol use in settings where abortion is legally restricted: data on national pharmaceutical sales; face-to-face surveys of women and providers; and individual pharmacy-based studies that use fictitious clients. Drawing on recent examples of work conducted in Mexico and other Latin American countries where abortion is legally restricted, we discuss how to obtain and interpret data from different sources to estimate misoprostol use. We consider advantages and limitations of these techniques within the broader context of abortion research.

Few studies address how women's self-use of misoprostol can affect abortion estimates, especially in legally restricted settings. Existing studies that explore misoprostol use in several countries show that the drug is readily available and widely used to induce abortion. Most of these studies document its use in convenience samples

of women and/or providers in clinics, pharmacies and community samples. A hospital-based study conducted by Clark (2004) among obstetrician-gynecologists in Brazil, Jamaica and the United States found that 27% of providers used misoprostol to induce first-trimester abortions and 23%, second-trimester procedures. Most providers also used misoprostol for uterine evacuation after pregnancy loss (61%) and a minority used it for labor induction (46%). In a survey of women hospitalized for pregnancy loss in Fortaleza, Brazil, 48% were women who reported having tried to terminate their pregnancies; of these, 66% said they had self-administered misoprostol (Misago et al. 1998).

Given misoprostol's sale through pharmacies in many countries, pharmacy-based studies are useful in estimating the drug's availability and use, as well as in assessing pharmacists' knowledge and opinions of the drug. One such study used surveys of pharmacy staff and "mystery client scenarios" in a large Latin American city. It reported that 74% of staff spontaneously recommended an abortifacient drug when a client inquired about ways to self-induce abortion; almost 40% of these staff members recommended misoprostol (Lara et al. 2006a). Another study with a similar methodology was conducted among private pharmacies in Mexico and Bolivia. That study found higher levels of information about and availability of misoprostol in Mexico than in Bolivia, though a greater percentage of pharmacists spontaneously recommended it in Bolivia than in Mexico (52% vs. 35%) (del Paso et al. 2007).

An accurate assessment of the degree to which misoprostol affects estimates of abortion incidence and morbidity in a given geographic and sociocultural context is challenging and requires inputs from several perspectives. Several studies use data triangulation, or reliance on more than one methodology, to increase the validity of the measures of abortion incidence and morbidity (see Chapter 9). One noteworthy example is a study that used multiple data sources to estimate the impact of misoprostol use on the incidence of abortion complications in 2005 in two states in Mexico, Chiapas and Guanajuato (Lara et al. 2007).

Briefly, the data sources were hospital records of women treated for abortion complications; a survey of health care providers (who estimated the proportion of women who had had a misoprostol-induced abortion and were treated in public hospitals for complications); a pharmacy component; and national drug sales data. According to preliminary results, the percentage of hospitalized abortion cases that corresponded to misoprostol use was much higher in Chiapas than in Guanajuato (15.9% vs. 4.5%) (Lara et al. 2007). A related study mentioned earlier measured misoprostol's potential to reduce maternal mortality by modeling its impact in Africa, Asia and Latin America using prevailing mortality rates in the three regions. The exercise yielded different scenarios of low and high estimates of misoprostol's impact, depending on assumptions used in the models (Harper et al. 2007).

The Challenge of Measuring Misoprostol's Contribution

Now to the primary question of this chapter: How does misoprostol use affect the measurement of abortion incidence and morbidity? The short answer is that misoprostol can affect both measures significantly and in complex ways. In many settings where abortion is legally restricted, accurate data on misoprostol use are scarce and all we have is anecdotal evidence. We can, however, expect misoprostol use to affect abortion incidence estimates in one of two ways. First, if the true portion of all induced abortions that are self-induced with misoprostol goes undocumented, the result is an underestimate of all induced abortions in a given setting. In fact, in a study to estimate incidence by Juarez and colleagues in Mexico that took misoprostol into account, increased use of the drug actually was associated with increased abortion incidence (Juarez et al. 2008).

On the other hand, because hospital-treated complications are an important data source for indirectly calculating abortion, the measurement of abortion incidence may be affected by a temporary increase in such admissions resulting from three potential situations: women may not yet know how the drug works and thus seek hospital care believing that the normal symptoms of pregnancy termination are true complications; women may have bleeding and a complete abortion but decide to go for care to confirm that the pregnancy has ended; and women may have limited bleeding and go to the hospital assuming that they need treatment for an incomplete abortion. For example, a woman who is not well informed that the drug can take up to two weeks to work may seek hospital attention well before then and be registered in hospital records incorrectly as having had an "abortion-related complication."

In addition, the drug has some known side effects, even though they occur very rarely, as well as a small failure rate. Both could lead to real abortion-related complications and hospital admissions. It is logical that as more women self-administer misoprostol, the incidence of known drug-related side effects, such as excessive bleeding and cramping, will increase proportionately. Therefore, we may see a slight increase in hospital admissions for real misoprostol-related complications as well.

Misoprostol use also affects estimates of abortion-related morbidity by reducing the rate of serious complications that women otherwise would suffer from an unsafe

abortion (self-induced or obtained from a nonmedical provider), which is different from the temporary increase in spurious hospital complications in the above scenario where women seek care for what they believe are complications but are actually the normal effects of the drug. A retrospective study in Brazil with 1,840 women who obtained hospital-based postabortion treatment found the incidence of infection among women who had used misoprostol to be almost one-twelfth that of women who had used other methods (4.2% vs., 49.4%) (Faundes et al. 1996). In addition, given women's limited knowledge of misoprostol, they may experience real complications associated with taking the drug inappropriately, especially after the first nine weeks of pregnancy. For example, a study conducted in Rio de Janeiro among women who experienced abortion complications reported that 57% had self-administered misoprostol at a median dosage of 800 mcg (Costa and Vessey 1993). The most common reported reasons for seeking hospital care, which could have been normal side effects of the drug, included vaginal bleeding and cramping.

These studies illustrate how misoprostol can affect overall abortion incidence estimates and related data on morbidity. They highlight the importance of using sound methods to calculate misoprostol use. The next section describes three methodologies for measuring misoprostol use in legally restricted settings, as well as the pros and cons associated with each.

Data from National Pharmacy Sales

Type of Data and How They Are Obtained

Pharmaceutical companies in many countries maintain databases of national pharmacy sales to monitor sales trends of their products, including commercial drugs containing misoprostol. These databases offer a "big-picture" perspective on misoprostol sales volume, market share, types of sales (e.g., prescription or over the counter), types of units sold and other product characteristics that can be helpful in measuring use in a single year or over time. It is important to keep in mind that these databases are not universally available to researchers and also can vary in quality and level of detail, depending on the product and country. To understand the broader legal and political context in which the drug is being prescribed and dispensed, it is important to first confirm whether misoprostol is registered in the country and/or on a list of essential drugs.

In many countries, commercial research firms work with pharmaceutical companies and can access these databases. Researchers can contract these private firms to analyze national- and state-level information on misoprostol sales. This approach can be expensive; however, it is a good option especially when used in conjunction with misoprostol use data from other sources, such as surveys (detailed below).

What We Can Infer from These Data About Misoprostol Use

In settings where abortion is legally restricted, we can use national pharmacy sales data to infer several pieces of information critical to our understanding of misoprostol use. Key indicators include how sales trends vary over time at the national level in relation to trends in abortion incidence and treated complications (to make general observations about the relationship, not infer causality); where misoprostol is sold (e.g., pharmacies or clinics); and average cost per pill by state or region (if available). In some cases, commercial research firms may also collect independent information from physicians regarding prescribing practices, including indications for use. Data on the primary reason for prescribing misoprostol will tell us whether the drug was prescribed for gastrointestinal problems or for obstetric reasons (although in legally restricted settings, physicians are unlikely to explicitly admit to prescribing misoprostol to induce abortion).

How to Conduct a Study Using These Data: An Example from Mexico

Using a real-life example from an unpublished study in Mexico, a country where abortion is legally restricted (except in Mexico City), we outline how pharmacy sales data can be used to answer research questions related to the market share of misoprostol products and trends in sales and prices over time. This information is indicative of the extent to which these products are used for induced abortion and other indications.

In 2007, the Population Council contracted a research firm to assess national- and state-level sales trends in all drugs containing misoprostol over the past five years, as well as trends in price, prescription requirements and drug marketing from 2003 to 2007. The data sources included monthly reports from wholesale distributors; monthly audits of national- and state-level sales; a profile of vendors and providers who received the drugs; and lists of recipients of promotional material for each product. The analysis focused on six products that contained misoprostol (Cytotec and other brand names) at dosages that could be used to induce abortion.

We present preliminary (unpublished) results to illustrate the wealth of information we can gain from pharmacy sales data. Over the past five years and in 2007, Cytotec was the dominant brand by grams sold—though by units sold, each brand has a similar percentage of the market. Earlier data show that while national-level Cytotec sales increased from 1989 to 2000, they declined slightly

from 2000 to 2007. Fifty percent of all Cytotec sales were concentrated in six of the 31 states in the Republic, with Mexico City having the highest sales volume of the drug.

Interestingly, price data suggest that Cytotec sold as bottles of 28 pills doubled in cost from 640 pesos (US$64) in 2003 to 1,232 pesos (US$120) in 2007, but sales did not increase. As of July 2009, the price quoted by a major pharmacy chain was $1,322 pesos per bottle (US$99). Given the devaluation of the peso since the beginning of 2009 (as of this writing in mid-2009, the peso is at 13.3 to the dollar instead of 10.5 in 2007), the price has remained stable over the past two years.

The prescription data revealed that only 3% of Cytotec sales required a prescription, confirming the belief that the drug is easily available over the counter. Moreover, misoprostol sales increased slightly in Mexico City, but not in other states, just after the Legislative Assembly legalized first-trimester abortions in that state in May of 2007. The principle reason for prescribing Cytotec was for abortion, but the main reason for prescribing other misoprostol drugs (i.e., Artrene, Artrenac and Artrotec) was for inflammation and pain relief. Furthermore, obstetrician-gynecologists most often prescribed Cytotec (79%) compared with other drugs containing misoprostol, again suggesting that Cytotec is used almost exclusively for abortion and obstetric complications (e.g., labor induction and postpartum hemorrhage) and not for gastrointestinal problems.

We also requested that the firm review the promotional literature about Cytotec in Mexico dating back to 1998, to assess how it was being marketed. We found virtually no mention of Cytotec's use as an abortifacient, suggesting that word has spread about its off-label use through other channels.

The other products containing misoprostol on the market in Mexico, such as Artrene, Artrenac and Artrotec, are approved (and mainly used) for inflammation and pain relief, since they contain a combination of diclofenac and misoprostol. These drugs have high annual sales volumes and some have increased in sales in the last five years. For example, sales of Artrene, which contains 100 mcg of misoprostol per tablet, increased from 54,000 units in 2003 to around 200,000 units in 2007. Even though some of this increase could be related to use to induce abortion, it is difficult to quantify.

From these sales data, we can make the following preliminary conclusions: Cytotec is the most popular misoprostol product on the Mexican market used to induce abortion and it is sold primarily without a prescription. Although total sales of Cytotec decreased slightly over the past five years, we have no evidence to conclude that its use as an abortifacient is declining as well. On the contrary, the data suggest that there are new ways of packaging and purchasing the product, such as unit sales in pharmacies, herbal markets and over the Internet.

Limitations of National Pharmacy Sales Data

While these data can provide important insight into misoprostol sales, their use has some limitations. National pharmacy sales data usually are not exhaustive or captured in a way that is nationally representative of all misoprostol sales, though some databases are more comprehensive than others. For example, if pharmacy sales data capture sales at the national level only, we cannot generalize to the state or local level. It is important to understand the extent to which this data source can be representative of larger sales trends up-front. In addition, though it is tempting to link trends in misoprostol sales to trends in abortion and related morbidity, we cannot infer any causal relationship between these phenomena (or else we commit "ecological inference fallacy" by not accounting for individual-level confounders). Additionally, we do not know what proportion of misoprostol sales correspond to induced abortions, since some providers or clients can also buy the product for other obstetric indications, such as labor induction or postpartum hemorrhage.

We also do not know what proportion of Cytotec bottles are sold in pharmacies only to be resold as single pills or repackaged in some other way. Evidence based on informal conversations suggests that physicians, obstetrician-gynecologists and clients purchase misoprostol in pharmacies for other indications, such as labor induction, postpartum hemorrhage and incomplete abortion. More research is needed to estimate the proportion of sales used to induce abortion to understand the influence of the drug on abortion incidence. Finally, there are cost and data quality considerations we must explore before trying this method to estimate misoprostol's contribution to abortion incidence. In sum, national pharmacy sales data provide information on only one way abortions are induced in a particular setting, and this information can be incomplete. However, we can use these data to enhance our understanding, formulate new hypotheses and cross-validate other data sources to arrive at more accurate estimates of induced abortion.

Surveys and In-Depth Interviews with Women and Providers

Type of Data and How They Are Obtained

Surveys with women, providers and pharmacists are popular and effective ways to gauge knowledge about misoprostol and its use and complications (Miller et al. 2005; Ganatra et al. 2005; Garcia et al. 2004; Misago et al. 1998; Lisker et al. 2006). The survey format depends on the study objectives and sample population. Such surveys

can follow the format of surveys to assess knowledge, attitudes and practices (or "KAP") or focus specifically on one of those components. They can include closed or open-ended questions (or a combination of the two) and use convenience or random samples at the national, state or local level. Qualitative studies are particularly useful for understanding more complex research questions that we cannot answer with quantitative methods, such as attitudes about misoprostol, experiences using the drug to induce abortion and barriers to access. Because of the sensitive nature of questions on abortion, anonymous or self-administered surveys or the use of indirect questioning (described below) can be feasible alternatives and increase the veracity of self-reporting.

What We Can Infer from These Data About Misoprostol Use

These surveys provide individual-level data on misoprostol knowledge and use. They are essential for understanding the extent to which misoprostol can affect abortion incidence and morbidity. Surveys among women offer a wealth of information on actual use. Key indicators include knowledge about the drug, specifically how and where women obtain it; whether a prescription is needed; and women's levels of knowledge about misoprostol's function, side effects and complications. In addition, we can measure use, specifically, how extensively women (or people they know) use misoprostol, whether they use the correct dosage and whether they experience side effects or complications.

Provider and pharmacist surveys can complement these findings. Specifically, we can measure these professionals' awareness of medication abortion drugs; their knowledge of the correct dosage and administration of misoprostol; their understanding of the drug's side effects and warning signs; their attitudes about the drug as an abortifacient and toward women who use it to induce abortion; how often they prescribe or dispense it as an abortifacient; and how often they dispense it for its licensed health indications (e.g., gastric ulcers).

How to Address Potential Underreporting

Abortion, like intimate partner violence and HIV, is a sensitive and stigmatized topic in many countries. Both women and providers may be hesitant to discuss it during face-to-face interviews. Therefore, we should anticipate some underreporting, especially among women. However, there are ways to overcome this potential obstacle, such as through indirect questioning. Instead of asking very personal questions, such as "have you ever used misoprostol to induce abortion?" it is better to ask more general questions that generate less anxiety, such as "do you know of anyone who has used misoprostol to induce abortion?" or "would you recommend misoprostol to a friend/family member who needs an abortion?"

Investigators have used this approach to survey providers in countries where abortion is legally restricted, such as in Mexico and Brazil (Garcia et al. 2004; Faundes et al. 1996; Costa and Vessey 1993). Although indirect questions do not tell us whether the respondent has ever used misoprostol, we can get a sense of the drug's prevalence in a given sample without making respondents feel uncomfortable or judged. Another drawback of indirect questioning is that respondents may not have much information about their friends' or acquaintances' misoprostol use if the latter groups are hesitant to disclose personal information.

In legally restricted settings, indirect questions also may be appropriate for providers who fear backlash or criminal persecution. Some providers who offer misoprostol to patients who seek an abortion may feel uncomfortable responding to direct questions about their experiences with the drug. To address this problem, we can ask about providers' perceptions of misoprostol use. Researchers have employed this technique with health care providers in surveys that gauged knowledge, perceptions and use of misoprostol in Mexico (Garcia et al. 2004; Juarez et al. 2008; Lara et al. 2007; please see Chapter 9 of this volume).

With indirect questioning, we can ask providers to estimate the prevalence of misoprostol use to induce abortion and its associated complications in their patients and geographic setting; the resulting data can be useful in further calculations of the drug's potential effect on abortion incidence and morbidity. Briefly, as part of an application of the Abortion Incidence Complications Method in Mexico (AICM, Chapter 6), Juarez and colleagues (2008) modified the AICM's usual survey of health professionals who are knowledgeable about abortion to ask providers how frequently women had requested an abortion from them. The questionnaire also asked all health professionals to assess the the proportion of abortions professionals believe to be induced by misoprostol; the proportion of abortions induced with misoprostol that require follow-up treatment in a hospital; the number of years that misoprostol has been used in Mexico to induce abortions; and the most common providers of the drug in Mexico. The investigators then used this self-reported information to estimate the incidence of medication abortion with misoprostol—and then of all induced abortions—in Mexico.

Anonymous, self-administered surveys are another option. Some providers and pharmacists may feel more comfortable answering sensitive questions when they know that confidentiality is assured. Doing so can include assuring providers that responses or study materials can-

not be linked to any individual provider. In addition, some providers may prefer a self-administered questionnaire simply because they can complete it on their own time. The primary limitation of this type of survey is its potential to yield a low response rate and incomplete data.

Although other chapters of this volume discuss anonymous abortion survey techniques in detail, we briefly mention two here. The "sealed envelope technique," developed for a study on abortion incidence in the Philippines, is used when it may not be feasible to ask sensitive questions about women's abortion history through face-to-face interviews (Juarez et al. 2007). Briefly, this technique consists of giving women a separate short survey with the most sensitive questions about abortion, which they fill out anonymously and place in a sealed envelope after completing the larger survey.

The randomized response technique is another indirect survey method to measure highly sensitive and underreported behaviors. For this technique, participants are assigned to one sensitive yes-or-no question or one non-sensitive yes-or-no question with a known probability (such as "what color are your eyes?"). The interviewer does not know which question was asked and only records the participants' response. This technique can be used to estimate the proportion of respondents who answered "yes" to the sensitive question (Lara et al. 2004, Lara et al. 2006a). In fact, investigators who compared four methods of collecting information on induced abortion in Mexico found this technique to be the most accurate (Lara et al. 2004, see Chapter 9) and successfully applied it to a national-level study that estimated induced abortion in Mexico (Lara et al. 2006a).

When indirect questioning is not feasible, we can use a method of direct questioning called the "value-free technique." This method has been shown to increase reporting of abortion in legally restricted settings and is described in greater detail elsewhere (Okonofua et al. 2003). With this method, respondents are asked a series of closed-ended questions about unwanted pregnancy outcomes. If the respondent has had an unwanted pregnancy, she is asked how she resolved it with predetermined response options (e.g., continued the pregnancy, unsuccessfully tried to abort, successfully had an induced abortion, etc.). Women who respond affirmatively to having tried to abort, regardless of outcome, can be asked which method they used to elicit information on possible use of misoprostol or another abortifacient.

Limitations of Surveys with Women and Providers

Face-to-face surveys or the self-administered alternative are invaluable for measuring misoprostol use and for subsequent analysis of the extent of the drug's effect on abortion estimates in legally restricted settings. This approach has the same limitations as any survey, specifically, those resulting from poorly designed questionnaires and from sampling bias. The main limitation with respect to abortion research is underreporting, which we can resolve, in part, through the techniques described here and by combining multiple methodologies. For example, a study conducted in Mexico City combined a survey and mystery client methodology (see next section) to gather information about misoprostol provision practices in a random sample of 97 pharmacies (Lara et al. 2006b). The two methodologies yielded very different results. According to the survey responses, 47% of pharmacy staff reported that they required a prescription to sell misoprostol; the mystery client encounters, however, demonstrated that only 11% required a woman to present a prescription (Lara et al. 2006b).

This method can yield representative, and therefore generalizable, results when a random sample is used. For example, random samples were used in public opinion surveys on abortion conducted in Mexico at the national and city levels as well as in a pharmacy-based study (traditional and chain pharmacies) (Garcia et al. 2004; Wilson et al. 2008, Lara et al. submitted for publication). However, in some legally restricted settings, cost, logistics and uneven access to potential participants may make a convenience sample the more feasible option. Strategies for obtaining representative samples of women, providers and pharmacists should be explored in greater depth. When proceeding with surveys of women and providers on such a sensitive topic, we must be particularly mindful of the study sample, the types of questions asked and how we ask them.

Pharmacy-Based Mystery Client Studies

Type of Data and How They Are Obtained

A relatively new methodology in abortion research is the mystery client scenario, which is used primarily in pharmacy-based studies, though it can be applied to any client-provider interaction (Lara et al. 2006b; Billings et al. 2009; del Paso et al. 2007). The premise of this methodology is that the interviewee (i.e., pharmacy staff, physician, etc.) will give a more truthful response about the sensitive issue of misoprostol if asked by a supposed client instead of an interviewer.

The methodology uses fieldworkers who are trained to pose as clients who fit a specific profile at a sample of pharmacies (e.g., chains, franchises, etc.) in different geographic settings. To assess how pharmacy staff respond in different scenarios, researchers can use a variety of mystery client profiles in a single study, such as teenager, middle-aged married woman or male partner of a woman

seeking medication abortion. The clients explain their preassigned situation and inquire about options for medication abortion. For example, a fictitious client may ask for general information about a drug to terminate pregnancy or explain her situation and see whether the provider spontaneously recommends a specific drug. Both of these assigned situations have been tested and shown to be effective in obtaining information on misoprostol (Billings et al. 2009; Lara et al. submitted for publication).

After their interaction with a provider, the mystery clients record any specific information they received about misoprostol and their qualitative observations/comments on a form designed for this purpose. These data can be qualitative, quantitative or a combination. Mystery clients also are trained to stop the interview at any time a pharmacist becomes suspicious or demonstrates any hostility.

What We Can Infer from These Data about Misoprostol Use

Important indicators we can measure using this data collection approach include misoprostol availability at pharmacies; whether pharmacy staff spontaneously recommend the drug during client encounters; the specific recommended dosage; whether providers inform women about complications and side effects and where to go if a complication occurs; pharmacy staff's willingness to sell the drug; whether a prescription is required; and cost per pill/bottle. In addition, the qualitative observations provide further information about the pharmacy location and setting; the number, type and availability of pharmacy staff; the store's hours of operation, etc. We can also explore how pharmacists' responses vary by client profile, pharmacy type and location, and other factors of interest.

In one noteworthy example of a mystery client study conducted in eight cities in Mexico (Lara et al. submitted for publication), investigators used a simple random sample of 192 pharmacies (24 in each of the eight study cities) from a database of 2,994 registered pharmacies maintained by the Mexican government. They then stratified the sample into 12 independent pharmacies and 12 chain pharmacies per city. The sample was stratified again by socioeconomic level of the area to yield equal representation in low and very low socioeconomic status areas and in middle socioeconomic status areas. Sites with incorrect contact information were removed or substituted.

The investigators sent three types of trained mystery clients to every pharmacy in the sample—a young woman (aged 18–25); a slightly older woman (aged 26–35); and a man posing as the partner of a pregnant woman. A total of 576 mystery client–provider interactions were held. If the vendor did not mention Cytotec spontaneously, the client was trained to ask directly about it. For example, the female mystery clients were trained to say that a friend had recommended the drug and to ask if the provider knew about its availability in the pharmacy and if it works. They were trained to use the following prepared text: *"My menstrual period is two weeks late. My last period was six weeks ago. I had a positive pregnancy test. Could you tell me what drug I could take to induce an abortion?"*

The male mystery client was trained to say that his girlfriend was pregnant and he was requesting the drug for her. Mystery clients solicited information only and stopped short of requesting a prescription or otherwise obtaining the drug. Investigators then conducted bivariate analyses to assess how type of pharmacy, type of client and sex of the provider affected the following outcome variables—the provider's spontaneous offer of Cytotec; the recommendation of Cytotec once the client requested it; the recommendation of an effective dose; requiring that the woman have a prescription to receive Cytotec; and the availability of the drug by individual pill in the pharmacy.

We highlight some important findings here. Only 23% (n=132) of providers spontaneously recommended a drug to induce abortion and among those, 81% (n=107) recommended a drug with abortifacient properties (Lara et al. submitted for publication). Within that group, 75% (n=99) specifically recommended Cytotec. In 67% of the cases where the drug was not spontaneously recommended, the provider nonetheless reported knowing about Cytotec when asked directly by the mystery client. However, among the providers who recommended Cytotec, only 16% (n=66) mentioned an effective misoprostol dose (600 mcg) to induce abortion. The findings suggest that despite the supposedly widespread knowledge about and frequent recommendation of misoprostol to induce abortion in Mexican pharmacies, few pharmacy providers were informed about the drug's correct dose. As one of the first studies to use the mystery client methodology to gather data from a random sample of pharmacies, the study shows how the technique can elicit important information that may otherwise be impossible to obtain through traditional research methods.

Another important study used the mystery client technique in a random sample of independent and chain pharmacies in one state in Mexico (n=177 pharmacies) and three cities in Bolivia (n=100 pharmacies) (del Paso et al. 2007). Trained fictitious clients (all women) visited each pharmacy where they were trained to ask for a medication to induce menstruation and clearly state that they were "pregnant." If the medication was offered, the clients proceeded to ask questions about dosing, side effects and efficacy. If it was not spontaneously offered, the fictitious clients were to indicate that someone had told them that misoprostol might work and to ask the pharmacist/staff member for more information.

Results revealed wide variation in misoprostol availability, knowledge and cost by site and country (del Paso et al. 2007). For example, misoprostol was more widely available in Mexico than in Bolivia, even though it was nearly 10 times as expensive (per pill price of US$4 vs. US$0.69). Moreover, a greater percentage of Mexican than Bolivian pharmacy staff provided information about dosing and side effects. In both countries, approximately 80% of pharmacies offered misoprostol without a prescription (del Paso et al. 2007).

Limitations of Mystery Client Pharmacy-Based Data

The major limitation of the methodology is that mystery clients may be unable to obtain sufficient in-depth information about misoprostol because they can only inquire about the drug, not purchase it. This limitation is justified, however, because otherwise the mystery client would act unethically by intentionally deceiving the pharmacist or provider. Another limitation is the potential recall bias of the mystery clients themselves: Information on dosage, side effects and/or complications is particularly susceptible to recall bias. Since fictitious clients cannot take notes during the provider-client interaction, they may forget some of the information exchanged or include information that was not said (e.g., when fictitious clients mix up specific conversations).

In addition, because mystery client studies are relatively new in abortion research, some ethical review boards and even researchers may raise ethical concerns simply because they are not yet well versed in the methodology. The main ethical question that may arise is around informed consent of the pharmacists, pharmacy staff or physicians being interviewed who unknowingly engage in dialogue with a fictitious client and whose responses are used for research purposes. However, we can allay those concerns by keeping in mind the following three arguments.

First, it would be virtually impossible to get reliable and accurate information from providers about misoprostol using any other method because of the sensitivity and stigma around abortifacients in legally restricted settings. Second, mystery clients solicit information only, not the medication itself; they are not asking the provider to do anything that would put him/her at risk for legal action or censure. In addition, the mystery clients are trained to handle several scenarios and know when to stop the conversation from progressing to the point where they get a prescription or physical exam. Third, all of the data that mystery clients collect are completely anonymous and cannot be linked to any individual provider.

Another related limitation of the methodology is that the information collected can vary and be incomplete, since the data stem from a conversation rather than a formal interview. Among the factors beyond the researchers' control that can influence the accuracy of the data are the providers' knowledge and attitudes about abortion; the time they have available for the conversation; and the clients' ability to act out their scenario, ask the appropriate questions, memorize the information given by the provider and correctly fill out the form. To increase the likelihood that the method yields high quality data, we recommend that intensive training be conducted with mystery clients and that the fieldwork be closely supervised.

Using this technique does not preclude the study from being representative. In fact, both studies we describe used random samples of pharmacies. Because the training and oversight for this technique are expensive, conducting a mystery client study that is representative beyond the city/state level may be prohibitively expensive. On the other hand, since this is a new technique in a research area with significant unknowns, it may be more feasible to simply use a large convenience sample of pharmacies, especially in settings where it is impossible to get accurate data on the number of pharmacies needed to generate a random sample.

Another issue with the representativeness of the sampling method is that mystery clients obtain information from only one on-site provider per pharmacy (rather than from everyone on staff). While conducting more than one client-provider conversation per pharmacy would increase representativeness, it would also significantly increase the study cost and put the anonymity of the fictitious client at risk if she/he visits a single pharmacy multiple times. On balance, to assure the integrity of the method, quality of the data and personal safety of the mystery clients, it is more important to maintain anonymity than to achieve a randomized sample at the individual provider level. Therefore, the recommended approach is to randomize by site, but not within site.

Data from mystery clients, like the data from other sources described in this chapter, help strengthen estimates of abortion incidence and morbidity, which, in turn, are critical for developing effective programs to combat maternal mortality. The technique may allow investigators access to accurate data they otherwise could not get through standard face-to-face or self-administered surveys.

Incorporating Estimates of Misoprostol Use into Estimates of Abortion Incidence

Each method we present in this chapter provides a perspective on misoprostol availability, knowledge or use in legally restricted settings and each approach can be used alone or in combination. To develop a more complete picture of the potential effects of misoprostol use on abortion

incidence and morbidity estimates, whenever possible, complementary studies may be analyzed side by side using data triangulation. For example, in typical incidence studies that indirectly measure the incidence of all abortions by assessing the proportion of the total that hospitalized complications represent, the basis for that proportion, the Health Professionals Survey (HPS) questionnaire, can be modified to include questions about professionals' perceptions of misoprostol use, as was done in a recent study from Mexico (Juarez et al. 2008).

If concurrent data from other studies are available, these data can be compared with and "combined with" data from the modified HPS questionnaire. Data triangulation attempts of this sort have been reported (Lara et al. 2007; and see Chapter 9), but are still conceptually new and as with any modeling exercise, they require many assumptions. For example, investigators used the adapted HPS questionnaire from the Mexico incidence study (Juarez et al. 2008) and complementary information from a mystery client study of misoprostol sales in pharmacies (and state-level misoprostol sales data) to estimate the proportion of induced abortions accounted for by misoprostol self-use, and the proportion of all induced abortions complications attributed to misoprostol (Lara et al. 2007). While still a work in progress, a working paper on preliminary results was presented at a 2007 seminar of the International Union on the Study of Population (IUSSP) and is available on the IUSSP Web site.

Dissemination of Findings in Legally Restricted Settings: Proceed with Caution!

Developing an effective and culturally relevant dissemination strategy about misoprostol use is the final step in abortion incidence research. We must consider our key audiences as well as the cultural, political and legal context surrounding abortion in a given setting. Despite abortion being legally restricted in most countries in Latin America and the Caribbean, misoprostol's off-label use is likely widespread in the region. In these settings, we must proceed with caution when disseminating findings about misoprostol to avoid potential political backlash against the drug and the women who use it. While a cautious approach to disseminating data about misoprostol may seem insufficient at first given the public health problem caused by unsafe abortion, it ultimately can be an effective strategy in mainstreaming medication abortion in legally restricted settings. This section provides points to consider when designing effective dissemination strategies in developing countries, using contrasting examples from Brazil and Nigeria.

The Brazilian government's withdrawal of Cytotec from the market in 1991 after its use as an abortifacient was widely publicized is a telling example of the negative consequences of moving too quickly. The "Cytotec controversy" in Brazil, detailed elsewhere (Costa 1998; Guedes 2000; Coelho et al. 1994; Arilha and Barbosa 1993), illustrates how too much publicity about misoprostol's off-label use can lead to the drug's further restriction and ultimately limit women's options. Induced abortion in Brazil is legal only in cases of rape or to save the pregnant woman's life. Even when legal criteria are met, however, women face significant access barriers, including prolonged judicial process, negative provider attitudes and cost (Costa 1998).

Brazil licensed misoprostol for the treatment of gastric ulcers in 1986 and allowed it to be sold over the counter without a prescription. Not surprisingly, the drug became popular as an abortifacient. As information about the drug spread rapidly through networks of providers, pharmacists and women themselves, so did misoprostol's sales and use. A survey of hospital records conducted in Fortaleza, Northeast Brazil, showed that by 1990, misoprostol had been used in 70% of all hospitalized induced abortion cases, compared with only 12% in 1988 (Costa 1998). The Brazilian press's widespread coverage of this increase sparked a heated debate about the drug. While women's groups and some doctors argued that misoprostol use had helped reduce unsafe abortion and abortion-related maternal mortality, other groups, including some medical professionals, began a campaign against the drug. They demanded the withdrawal of misoprostol from the market because of its widespread off-label use.

By 1991, the Brazilian Ministry of Health bowed to political pressure and issued new regulations in an effort to restrict use of the drug. The regulations limited misoprostol sales to pharmacies only, with the additional requirement that a copy of a doctor's prescription remain on file. Some states banned misoprostol sales entirely. While these restrictions made it somewhat harder for women to buy the drug, they had little effect on its use. Instead, clandestine abortions (both surgical and medication) continued to be common. Black market sales of misoprostol increased as did costs of the drug and the numbers of abortions induced with traditional and potentially harmful methods (e.g., herbs and intentional injury) (Costa 1998). Today, advocates favor incremental change in legislation and health services to overcome ambivalence in the medical profession and improve women's reproductive health options (Guedes 2000).

An effective strategy used in Nigeria, another legally restricted setting, is the promotion of misoprostol to prevent maternal mortality through its use to treat postpartum hemorrhage. Since the Nigerian government is committed to addressing maternal mortality, it has approved

misoprostol for this indication. Public health advocates used this approval as a window of opportunity to raise awareness about the drug and also push for its use for other women's health indications.

We can learn from these cases how best to proceed with evidence-based findings on misoprostol in other countries. Our ultimate goal is to ensure that providers and women have accurate information without provoking new controversy about medication abortion. Clearly, to develop an effective dissemination strategy, it is important to gauge the existing political climate and identify key opinion leaders, as well as the major formal and informal channels of communication. Timing is also critical. In a highly volatile political situation, the smartest strategy may be to share findings with only limited select academic and prochoice women's health providers until a more favorable environment arises. Once it does, we can use evidence from misoprostol studies to build advocacy arguments that serve to consolidate favorable public opinion and encourage reform of policies regulating medication abortion.

Conclusion

While data on women's self-use of misoprostol to induce abortion are challenging to collect, and even to interpret, research on this issue is greatly needed to understand women's experiences with the product as well as the medication's potential impact on abortion incidence and morbidity. Clearly, certain research methodologies are more commonly used than others, and all of the methodologies described above have their limitations. Yet readers should feel heartened that, barring cost constraints, these data are not impossible to collect.

In attempting to quantify the potential impact of widespread misoprostol self-use on abortion incidence and morbidity, more rigorous studies are required and are likely to rely on data triangulation techniques in tandem with incidence studies. Still, we caution the reader that further conceptualization and method-testing is needed to validate the underlying assumptions of triangulation techniques. Once they are verified, triangulation efforts could yield valid estimates of misoprostol-related abortion incidence and complications, which can, in turn, be used to estimate the all-important overall incidence of induced abortion.

REFERENCES

Arilha M and Barbosa RM, Cytotec in Brazil: "At least it doesn't kill," *Reproductive Health Matters,* 1993, 2:41–52.

Billings D et al., Pharmacy worker practices related to misoprostol for abortion in one Mexican state, *Contraception*, 2009, 79(6):445–451.

Blanchard K et al., Misoprostol for women's health: a review, *Obstetrics & Gynecology*, 2002, 99(2):316–332.

Bracken H et al., Mifepristone followed in 24 hours to 48 hours by misoprostol for late first-trimester abortion, *Obstetrics and Gynecology,* 2007, 109(4):895–901.

Clark S, The use of misoprostol to improve gynecologic and obstetric health in Brazil, Jamaica, and the United States, in: Shannon CS and Winikoff B, eds., *Misoprostol: An Emerging Technology for Women's Health (Report of a Seminar),* New York: Population Council, 2004.

Coelho HL et al., Misoprostol: the experience of women in Fortaleza, Brazil, *Contraception*, 1994, 49(2):101–110.

Costa SH and Vessey MP, Misoprostol and illegal abortion in Rio de Janeiro, Brazil, *Lancet*, 1993, 15(341):1258–1261.

Costa SH, Commercial availability of misoprostol and induced abortion in Brazil, *International Journal of Gynecology & Obstetrics*, 1998, 63(1 Suppl.):S131–S139.

Del Paso G, Walker D and Billings D, Misoprostol in private pharmacies in Mexico and Bolivia, paper presented at Global Safe Abortion Conference, London, Oct. 23–24, 2007.

Faundes A et al., Post-abortion complications after interruption of pregnancy with misoprostol, 1996, *Advances in Contraception,* 12 (1):1–9.

Ganatra B, Manning V and Pallipamulla SP, Availability of medical abortion pills and the role of chemists: a study from Bihar and Jharkhand, India, *Reproductive Health Matters*, 2005, 13(26):65–74.

Garcia S et al., Policy implications of a national public opinion survey on abortion in Mexico, *Reproductive Health Matters*, 2004, 12(24S):65–74.

Grapsas X et al., Misoprostol and first trimester pregnancy termination, *Clinical & Experimental Obstetrics & Gynecology*, 2008, 35(1):32–34.

Guedes A, Abortion in Brazil: legislation, reality, options, *Reproductive Health Matters*, 2000, 8(16):66–76.

Harper CC et al., Reducing maternal mortality due to elective abortion: potential impact of misoprostol in low-resource settings, *International Journal of Gynecology & Obstetrics*, 2007, 98(1): 66–69.

Juarez F, Cabigon J and Singh S, Unwanted pregnancies in the Philippines: the route to induced abortion and health consequences, paper presented at the IUSSP International seminar on measurement of abortion incidence, abortion-related morbidity and mortality, Paris, Nov. 7–9, 2007.

Juarez F et al., Estimates of induced abortion in Mexico: what's changed between 1990 and 2006? *International Family Planning Perspectives*, 2008, 34(4):158–168.

Lara D et al., Measuring induced abortion in Mexico: a comparison of four methodologies, *Sociological Methods and Research*, 2004, 32(4):529–558.

Lara D et al., The measure of induced abortion levels with random response technique in Mexico, *Sociological Methods and Research*, 2006a, 35(2):279–301.

Lara D et al., Pharmacy provision of medical abortifacients in a Latin American city, *Contraception*, 2006b, 74(5):394–399.

Lara D et al., Using multiple data sources to understand the impact of misoprostol on reports of abortion complications in Mexican hospitals, paper presented at the IUSSP International seminar on measurement of abortion incidence, abortion-related morbidity and mortality, Paris, Nov. 7–9, 2007.

Lara D, Garcia SG and Paz F, How often and under which circumstances do Mexican pharmacy workers recommend misoprostol? (submitted for publication).

Lisker R, Carnevale A and Villa AR, Acceptance of induced abortion amongst medical students and physicians in Mexico, *Revista de Investigación Clínica*, 2006, 58(4):305–312.

Middleton T et al., Randomized trial of mifepristone and buccal or vaginal misoprostol for abortion through 56 days of last menstrual period, *Contraception*, 2005, 72(5):328–332.

Miller S et al., Misoprostol and declining abortion-related morbidity in Santo Domingo, Dominican Republic: a temporal association, *International Journal of Gynecology & Obstetrics*, 2005, 112:1291–1296.

Misago C et al., Determinants of abortion among women admitted to hospitals in Fortaleza, North Eastern Brazil, *International Journal of Epidemiology*, 1998, 27(5):833–839.

Okonofua FE et al., Assessing the prevalence and determinants of unwanted pregnancy and induced abortion in Nigeria, *Studies in Family Planning*, 2003, 30(1):67–77.

Prata N et al., Saving maternal lives in resource-poor settings: facing reality, *Health Policy*, 2009, 89(2):131–148.

Shannon CS and Winikoff B, eds., *Misoprostol: An Emerging Technology for Women's Health (Report of a Seminar),* New York: Population Council, 2004.

Singh S, Hospital admissions resulting from unsafe abortion: estimates from 13 developing countries, *Lancet*, 2006, 368(9550):1887–1892.

Wilson K et al., Assessing Mexican public opinion on abortion one year after the passage of the groundbreaking law in Mexico City, paper presented at the Third Research Meeting on Unwanted Pregnancy and Unsafe Abortion: Public Health Challenges in Latin America and the Caribbean, Mexico City, Oct. 7–10, 2008.