Teaching Notes: “Malaria and DDT in Uganda”

Part A: Introduction to Public Health Issues by Nancy Kane, DBA

Part B: Epidemiology Sessions by Karin Michels, ScD, PhD

There are two sets of notes here designed for two different types of classes that can be taught using the Malaria and DDT in Uganda case. Part A focuses on using the case to introduce a cross-disciplinary approach to public health issues; Part B is designed for a class on epidemiology and assumes some knowledge of epidemiology by the instructor.

Part A: Introduction to Public Health

Synopsis of case

In October 2008, Dr. Richard Mgaga, Head of the Malaria Control Programme in Uganda, reviewed the monthly malaria statistics report for the district of Apac, which in April of 2008 had undergone a pilot indoor residual spraying (IRS) of Dichlorodiphenyltrichloroethane (DDT) in a campaign to prevent mosquitoes from biting and spreading malaria. The campaign was halted by a court injunction requested by organic farmers, exporters, and environmentalists in May 2008, and the injunction was upheld by the High Court in June. In early August, the Uganda Health Ministry began spraying a pyrethroid insecticide in place of DDT. Meanwhile the Ugandan Attorney General was challenging the High Court’s decision.

Apac is a region of very high malaria prevalence (presence in the population at any point in time) and incidence (rate of new infections), with residents being bitten about six times per night, the highest rate in Uganda. The use of bed nets and antimalarial drugs has been inadequate to stem the morbidity, mortality, and economic losses caused by malaria. DDT appears to be the most cost-effective vector-control strategy (in the case of malaria, the mosquito is the “vector” that passes the disease from one human to another). But there is concern that DDT may pose a risk to human health. Dr. Mgaga was under pressure by the Presidential Malaria Initiative (PMI) to undertake a full program of IRS in 300,000 households in the northern districts of Uganda, including Apac. However, he was unsure whether to proceed, given the opposition and apparent problems that surfaced when the Apac pilot was implemented.
Teaching Objectives
This case was written to be multi-disciplinary and illustrative of the range of public health perspectives required to address public health issues. It allows for a discussion of basic concepts of epidemiology (incidence, prevalence, surveillance, study design), environmental health (risk exposure, measuring health outcomes, risk management), social determinants of health (socioeconomic influences on health), health policy (political analysis, health systems structure and function), as well as the biological basis of a major infectious disease. The case can also be used for a more in-depth exploration of concepts from any one or more of these disciplines.

This note addresses the use of the case as a general introduction to the field of public health and its multiple disciplines. It can be used in undergraduate or graduate programs in public health. It can be used on a stand-alone basis (e.g., during an orientation to introduce participants to the field) or as part of a longer course introducing core public health concepts. As such, the key learning objectives are to:

• Provide an introduction to the field of public health
• Experience a multidisciplinary approach to problem-solving
• Critique alternative approaches to malaria control or eradication in Uganda

Assignment Questions
1. How would you define the problem facing Dr. Mgaga, the head of the Malaria Control Program in Uganda?
2. How should Dr. Mgaga go about resolving this issue?

Roadmap for discussion
The discussion can cover three major areas:
1. How might we define the problem facing Dr. Mgaga?
2. Who are the key stakeholders involved? How should Dr. Mgaga engage with them?
3. Should Dr. Mgaga continue with IRS spraying with DDT, or what other alternative(s) should he pursue?

Question 1: “How would you define the problem facing Dr. Mgaga?”
The first assignment question is a good one to start discussion of this case. Responses from the class can be clustered into the various public health perspectives to which they pertain. Below are some likely ways to characterize the problem:

Clinical/Biological Perspective
Thousands of people are dying every year. Malaria is the number one killer in Uganda, targeting children and pregnant women in particular, and Apac Province, the target province for the DDT indoor spraying program, has the highest malaria rates in the country.

Malaria is a parasite that attacks the red blood cells of humans. The health impacts can be severe—the parasite multiplies rapidly in the liver and then in red blood cells, where it can cause symptoms from mild fever and vomiting to convulsions, impaired
Teaching Note:

“Malaria and DDT in Uganda”

consciousness, respiratory distress, spontaneous abortion, or death. Malaria is the leading cause of morbidity and mortality in Uganda, with an estimated 10.6 million cases and 43,000 deaths in 2006.

The parasite is “endemic” to the region, meaning it is present in the population at an infectious level all year round due to the rural environment, poor housing, rainy weather, and open water/swampland where mosquitos (the “vector” that transmits the malaria parasite from one person to another) thrive. A large percentage of the population is infected, so that mosquitos are very likely to bite an infected person. Also the type of mosquito in Uganda, the Anopheles, is a late-night, indoor “feeder” that bites most aggressively between 1 a.m. and 5 a.m., while people are sleeping. Indoor mosquitos are difficult to control in open-air housing stock where people in poor households are likely to be living.

The most vulnerable populations are children under the age of 5, pregnant women, and travelers from non-endemic areas. Of the 43,000 deaths attributed to malaria in Uganda in 2006, over 90% (39,000) were children under the age of 5. Cerebral malaria, an extremely severe neurological complication of malaria, affects children’s intellectual development and ability to succeed in school, resulting in an enormous waste of societal resources.

The parasite becomes drug-resistant quickly due to its genetic makeup which allows for rapid mutation/adaptation to its human and chemical environment.

Health System Perspective

Inadequate health system infrastructure.

The public sector in Uganda was chronically underfunded, understaffed, and lacked essential supplies and medicines, including diagnostic capabilities. Poor rural populations often had to rely on the private sector of traditional healers and drug shops, most of which was unsupervised and at times unscrupulous. Thus, much of the population could not confirm the presence of malaria when symptoms appeared, nor could they access effective antimalarial drugs. Even so, the poor spent a disproportionate share of household income, up to 34%, on malaria treatments, most of which were not effective because of drug resistance, because the drugs were counterfeit, and/or because the patient failed to take a full dosage of medicine. The same problem occurred with access to the supply of bed nets—nearly two-thirds of those in use (see Exhibit 11b) were purchased in the private for-profit sector; and two-thirds of households had no mosquito nets at all.

Environmental Health Perspective

DDT is effective at eliminating the disease vector (mosquitoes) but poses (uncertain) risks to human health and (more certain) risks to the environment.
DDT, the pesticide used to eradicate malaria in many countries in the developed and less developed world in the first decade after World War II, is a “persistent organic pollutant” (POP), which means that it persists in the environment, travels long distances in the air when sprayed, and then attaches to soil, where it enters the food supply. DDT and its primary metabolite, DDE, exists in the tissues and blood of humans exposed to the chemical for many years. DDE can be transferred to the fetus through the placenta and to the infant through breast milk. DDT was classified as a possible human carcinogen, although the evidence is based primarily on animal studies.

Exhibit 13 of the case describes some of the research on the human health effects of DDT exposure; most studies do not detect a statistically meaningful health effect (i.e., the odds of the exposed population having an adverse health outcome (breast cancer, diabetes) were not significantly different from the odds faced by the unexposed population). As with many environmental health studies, the difficulties of determining level of exposure can create “misclassification” of exposure status. For example, as can be seen in Exhibit 13, the Brody study (2004) identified the “exposed population” as persons living at home addresses in communities where there were records of agricultural DDT use in Cape Cod. Students can discuss the likelihood of misclassification using this approach: e.g., people listed at “exposed” home addresses would have variable levels of exposure depending on whether the person was outdoors often, lived full-time at the address, how many years they spent at that address, their proximity to areas of DDT use; the amount of DDT used, etc. Also the “unexposed” population—people who did not live at addresses proximal to registered DDT use—may have been exposed to DDT elsewhere (through consumption of DDT-contaminated food, for instance). Blood serum measures were available for the other two studies cited, which is less likely to lead to misclassification issues, but blood samples are much harder to obtain from a population.

DDT has been shown to have harmful effects on wildlife (e.g., the shells of eggs laid by birds exposed to DDT were thinner and tended to break before hatching, killing the offspring), and the Stockholm Convention on POP outlawed the use of most POP, allowing for the use of DDT for disease control only if “no safe, effective, affordable alternatives were available” (see p. 10 of the case).

**Economic Perspective**

*Agriculture, including organic farming, is the largest source of Uganda’s economic wealth. Organic farming in particular is threatened by the use of DDT.*

Uganda’s economy is highly dependent on agriculture-related activities which employ 85% of the population and generate 42% of the country’s Gross Domestic Product. It ranked first in Africa for its organic produce, which it exports, and is thus subject to international standards for organic farming. Organic farmers in Apac use their homes to store their harvested produce, so indoor residential spraying with DDT exposes the harvest to prohibited pesticides. The farmers in Apac are facing a significant economic
loss in terms of prices and access to distribution channels due to the use of DDT in their province.

**Behavioral and Social Determinants of Health Perspective**

*Behavioral and socioeconomic factors undermine the effective use of DDT and other antimalarial interventions.*

Several behavioral and socioeconomic factors influence the impact of malaria interventions.

- The use of DDT for Indoor Residual Spraying (IRS) requires careful adherence to logistics and spraying protocols (in the storing, use, and clean-up of DDT for IRS). The case suggests that in Apac Province these protocols were not adhered to—that sprayers poured the pesticide into ant hills, or sprayed without resident education or permission, did not mix DDT with alcohol properly, and did not provide containers for households to sweep the waste. Due to resident resistance, they only sprayed 40% of the households targeted in the pilot area, which did not provide enough coverage to reduce malaria’s infection rates.

- The use of bed nets, either plain or insecticide-treated (ITN), was well below the 80% of households needed to control the spread of malaria. Both ownership and use were well below the needed levels. Exhibit 11a shows that only 34% of the country’s population owned any bed nets, and that ownership was more likely in urban areas and by households with higher incomes. Even fewer households owned ITN’s. The distribution of bed nets (Exhibit 11b) appeared to be largely through the private sector, suggesting that affordability might be inhibiting population access to bed nets. Even worse than the lack of ownership of bed nets was the lack of use of bed nets, particularly by the most vulnerable populations: children under 5 and pregnant women. Exhibit 11c indicates that only 21.5% of children slept under any bed net; children in urban, high-income households were more likely than others, but still less than half of children even in these more privileged households slept under a bed net. Pregnant women were only slightly more likely than children (24.4%) to have slept under any net in the previous night.

- Prophylactic use of antimalarial drugs by pregnant women was also well below half of potential users (Exhibit 10); wealthier and more highly educated urban women with a live birth in the prior two years were more likely to have taken any antimalarial drug, but relatively few (16–17%) took even two doses, despite the guidelines that four doses be taken during pregnancy.

- Prompt treatment of children within 24 hours of fever onset was also recommended, but social and health system barriers to this guideline existed:
  - the need for the husband/father’s permission could delay prompt medical attention.
  - the most effective antimalarial drugs were not available for home-based treatment, and the home-based drug packets available to households were more likely to be resisted by malaria parasites.
Study Design and Program Evaluation Perspective

The monthly statistics indicated that the controversial IRS intervention in Apac province during the pilot had no impact on the reported number of malaria cases—although the quantitative data itself was inadequate.

The monthly statistics before and after the April-May 2008 IRS intervention showed no reduction in reported cases—the July 2008 statistics showed 2,403 cases in the last week of July, while the February statistics indicated 2,422 cases in the first week of February. Reported cases had been rising since August.

Some students are likely to appropriately question whether these numbers are indicative of anything, due to a number of flaws in the malaria surveillance system in Uganda:

• The reported cases may or may not be malarial infections—given the frequent reliance on clinical symptoms rather than lab-confirmed results. In epidemiological terms, this could lead to a misclassification of the “outcome”—a case of malaria.
• Malaria has a peak season 4–6 weeks after the rainy season, which in Apac means the peak would be January–March. A more appropriate comparison, then, might be January–March 2008 compared to January–March 2009, to adjust for the seasonality of malaria transmission.
• Other factors can also influence the number of cases, including population migration in and out of Apac, the clearing of land, actual weather patterns at the time, and possible other interventions underway at the same time (e.g., bed net distribution, drug access).
• It would be preferable to compare the number of cases coming from the households that underwent spraying to those coming from “similar” households that did not undergo spraying; the statistics cited are province-wide, which may mask meaningful differences in sprayed households.

These kinds of issues of “study design,” “exposure” (to DDT) and “outcome” (malaria infection) are central to the work of epidemiologists. Appendix 1 provides an in-depth teaching note for those who would want to teach key epidemiology concepts in greater depth with this case.

Political Perspective

Political history of Uganda generated a lack of trust in government among populations that supported opposition party leaders.

Uganda’s political history since independence from Great Britain in 1961 was marked by instability, civil war, and atrocities visited upon the civilian population. The political parties were geographically and tribally based. The current president of Uganda, Yoweri Museveni, came from a western province and was also closely politically allied with southern Ugandans; prior Ugandan leadership, the murderous Idi Amin and Milton Obote—also a serious abuser of human rights—had been from the north. Apac is a
northern province. Thus the IRS program, which had been successfully implemented in the southeast just months before, was viewed with suspicion by the Apac residents, who did not support Museveni and who may have felt that the spraying with DDT was political retribution.

Summary of Question 1 Discussion

All of these “problem definitions” are part of the “problem” faced by Dr. Mgaga in October 2008. They also represent a good overview of the field of public health. After a 20–25 minute discussion of these problems, the instructor can summarize the breadth of the problem, and point out that the set of skills and concepts involved in addressing these problems—clinical, political, environmental, quantitative, cultural—are broad and interdependent. Approaching the problem from any one of these perspectives without appreciating the other perspectives is likely to lead to a less than optimal result—one that allows more damage to health and economy—than approaches that are multidisciplinary. This is the essence of the field of public health.

Question 2: How should Dr. Mgaga approach the various stakeholders involved to try to come to a politically acceptable resolution of the situation?

A brief “stakeholder” analysis of the groups likely to be for or against IRS can be undertaken using some of the characters/organizations in the case. This can be helpful to Dr. Mgaga as he tries to resolve the situation in a way that minimizes political resistance, whether he decides to proceed with DDT spraying or pursue an alternative.

The following table offers one of the typical frameworks used for such an analysis.

- “Players” are the stakeholders who are directly involved in determining the use or abandonment of IRS to fight malaria in Apac Province, or who are indirectly involved because their interests might be affected by the use of IRS.
- “Power” can be assessed as high, medium, or low with respect to the ability to influence the decision to use/not use IRS, and is based on a source of power such as control over financial or other material resources, political power, regulatory or judicial power, reputational power, etc.
- “Position” is the stakeholder's stated position for or against the use of IRS.
- “Urgency” is an assessment of the relative importance of the issue to the stakeholder, which in turn affects the stakeholder’s likelihood of taking action to protect his/her interests. This analysis can be used to help Dr. Mgaga prioritize who needs to get on board and with what type of persuasion.

<table>
<thead>
<tr>
<th>Player</th>
<th>Power</th>
<th>Position for/against IRS with DDT</th>
<th>Urgency</th>
</tr>
</thead>
<tbody>
<tr>
<td>Presidential Malaria Initiative (US Government)</td>
<td>High: Very influential through the distribution of financial and material resources to combat malaria</td>
<td>Supportive of IRS in endemic areas—but also of alternative approaches</td>
<td>Medium: as an outsider, would probably accede to local authorities on the best course of action in any specific situation; but they may be under some pressure from Congress to show short-term results for their investment—most likely to come from IRS with DDT than other alternatives</td>
</tr>
<tr>
<td>Player</td>
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<td>Urgency</td>
</tr>
<tr>
<td>-------------------------------------------------------</td>
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<td>--------------------------------------------------------------------------------------------------</td>
<td>-------------------------------------------------------------------------</td>
</tr>
<tr>
<td>Private sector drug shops (4,000 unlicensed)</td>
<td>Medium to Low: drug sales provide employment, which helps with the local economy—but not clear that this group is organized into an effective advocacy force or has the resources to hire effective representation</td>
<td>Likely not to be supportive as IRS is a substitute for drug treatment</td>
<td>Medium to high: if IRS is as successful in Apac as in other parts of Uganda, a substantial portion of their sales/profits would disappear</td>
</tr>
<tr>
<td>Traditional healers</td>
<td>Medium to low: similar to drug shops. But they may have local population’s trust, so can influence popular movement/opinion.</td>
<td>Not supportive/ substitute for their services</td>
<td>Similar to private sector drug vendors</td>
</tr>
<tr>
<td>Organic Farmers and Food Exporters</td>
<td>High: contribute significant share of national economy; they have some financial resources and are organized to protest and to back legal action (as members of UNETMAC)</td>
<td>Not supportive: ruins their organic status</td>
<td>High: their livelihood is at stake</td>
</tr>
<tr>
<td>Government health providers</td>
<td>Not clear how well organized they are or how willing to speak up; they have the power of knowledge of the damage that malaria causes, but they may not be organized/ mobilized to help educate the population about the problem</td>
<td>Supportive: they see the impact of malaria on health directly</td>
<td>Medium: they deal with the high levels of morbidity and mortality in an underfunded health system</td>
</tr>
<tr>
<td>Poor rural populations in Apac</td>
<td>Medium: not organized to have influence at this level of decision-making; but they can refuse IRS in their homes as individuals</td>
<td>Mixed: some are supportive, especially those with children who may understand the health impact of malaria, but they may not be well-educated on the benefits of IRS</td>
<td>High: they are infected with malaria on average 4 x/year; treatment costs 1/3 of their household income</td>
</tr>
<tr>
<td>Opposition politician (Ken Lukyamuzi)</td>
<td>High: able to organize protests in Kampala, the capital of Uganda, and to get a message out through the media</td>
<td>Against: possibly because IRS presents an opportunity to exploit the political distrust that is a by-product of a violent political history</td>
<td>High: exploit every opportunity to get a seat in Parliament (only had one seat in last election in 2006)</td>
</tr>
<tr>
<td>Museveni, President of Uganda</td>
<td>High: has been the country’s president since 1986 and is the head of the dominant political party</td>
<td>Unclear but suspect he would like international donors like PMI to keep giving money to Uganda. On the other hand, he wants to keep the political support of the affluent middle class—including organic farmers.</td>
<td>High: could become an election issue that might affect his party’s success in next election.</td>
</tr>
</tbody>
</table>
Students can determine which stakeholders are the highest priorities for Dr. Mgaga, and suggest what he should do to persuade them to be supportive of whichever policy he finally decides to implement. This analysis suggests that the stakeholders who are against IRS with DDT are well-organized and are likely to be motivated to exert their influence to stop any further spraying with DDT. The Malaria Control Programme is a part of the Museveni government, which is likely to prefer to avoid a head-on clash with some of its most powerful constituents.

**Question 3:** “Should Dr. Mgaga continue with the IRS intervention in Apac, if the Ugandan Attorney General is successful in overturning the High Court’s injunction? Why/why not?”

The final question the instructor can ask is for a recommendation or vote: to continue spraying with DDT or stop spraying with DDT:

**Some arguments for continued spraying:**

1. The logistical shortfalls of IRS could be overcome by using a trained workforce and/or training local residents, who are more likely to be trusted by local homeowners.
2. The organic produce problem cannot be remedied quickly, so they might as well finish the job and eliminate the scourge of malaria from Apac Province as quickly as possible. Perhaps the government should compensate the organic farmers for their economic loss—which is less than the economic loss suffered by the province that is caused by endemic malaria.
3. The human impact of DDT spraying is not confirmed, may be long-term in nature, but the loss of children and a productive workforce is immediate—the Province would gain productive years of life even if DDT shortens the life of a small subset of the population over the long run.
4. The international community/PMI supports this approach and may not be as supportive if the country cannot implement it in the province with the highest prevalence and incidence of malaria.

**Arguments against:**

1. The stakeholders who are against IRS are important and influential parties who could destabilize the political power enjoyed by the Museveni government.
2. Environmental damage of DDT is long-lasting; the risk should not be taken when there are other viable alternatives (this argument can be expanded to ask students which alternative they favored and why—pros and cons)
   a. Bed nets:
      On the plus side, they are cheap, can be paid for by international donors, and are conceptually simple to use; the distribution challenges can be overcome by a concerted effort—through government agencies, NGO’s, donor-supported initiatives—to get them to every home, and to instruct households as to their use. On the negative side, they are very uncomfortable to sleep under—hot and claustrophobic. When a person using them has to get up in the middle of the night to use the bathroom, for instance, they are no longer protected. Finally, the most effective bed nets are the ITN—which must be retreated periodically,
adding to the logistical challenge. At least 80% of households must be using them effectively to generate the kind of protection needed to stop the spread of malaria in a population. That said, bed nets have been very effective at reducing malarial infections in some African countries.

b. Improved distribution of antimalarial drugs:
On the plus side, international donors and NGO’s are willing to pay for the drugs. On the negative side, the distribution channels for antimalarial drugs are inadequate and frequently corrupt; the private sector may resist a public sector effort to distribute drugs that the private sector is making money from; and too often, drugs are not taken at full dosage, speeding the ability of the malaria parasite to develop drug resistance. Whether used prophylactically or to treat symptoms, drug accessibility, affordability, and susceptibility to generating parasite resistance are huge problems.

c. Students may come up with other alternatives such as draining wetlands, moving populations out of highly endemic areas, building housing that includes windows with screens and materials that can shut out mosquito entry.

This question will force students to acknowledge the pros and cons inherent in either decision. It should generate a lively discussion of the tradeoffs involved. Despite the tradeoffs, a decision must be made—reinforcing a fundamental skill of public health professionals—making decisions in light of the scientific evidence as well as the uncertainties and complexities inherent in all public health problems.

**Related Readings**

**Environmental Health**


**Behavioral and Social Determinants of Health**


Epidemiology

• Aschengrau A and Seage GR. Essentials in Epidemiology in Public Health. Sudbury, Massachusetts: Jones and Bartlett Publishers, 2008; Chapter 2: Measures of Disease Frequency, and Chapter 6: Overview of Epidemiologic Study Designs; 139-142.

Policy


Part B: Epidemiology Sessions on “Malaria and DDT in Uganda”

Required Readings

   Chapter 10, pp 177-194
   Chapter 11, pp 205-212
   Chapter 7, pp 131-146

Synopsis of the Case

In October 2008, Dr. Richard Mgaga, Head of the Malaria Control Programme in Uganda, reviewed the monthly malaria statistics report for the district of Apac, which in April of 2008 had undergone a pilot indoor residual spraying (IRS) of Dichlorodiphenyltrichloroethane (DDT) in a campaign to prevent mosquitoes from biting and spreading malaria. The campaign was halted by a court injunction requested by organic farmers, exporters, and environmentalists in May 2008, and the injunction was upheld by the High Court in June. In early August, the Uganda Health Ministry began spraying a pyrethroid insecticide in place of DDT. Meanwhile the Ugandan Attorney General was challenging the High Court’s decision.

Apac is a high malaria region with residents being bitten about six times per night, the highest rate in Uganda. The use of bed nets has been unsuccessful and DDT appears to be the most cost-effective vector control strategy. But there is concern that DDT may pose a risk to human health. Dr. Mgaga was under pressure by the Presidential Malaria Initiative (PMI) to undertake a full program of IRS in 300,000 households in the northern districts of Uganda, including Apac. However, he was unsure whether to proceed, given the opposition and apparent problems that surfaced when the Apac pilot was implemented.

Learning Objectives

These two class sessions will focus on the following principles of epidemiology as they can be applied to this case:
   1. Incidence and prevalence
   2. Exposure and disease misclassification
   3. Case-control study; selection bias; recall bias
   4. Intervention studies
   5. Randomized clinical trial, randomization

Preparation Questions

1. Based on the data presented in the case, can we decide whether DDT spraying is an effective measure in preventing malaria in the Apac region of Uganda?
2. Can you extract any incidence or prevalence numbers on malaria provided in the case that may be helpful in evaluating the effectiveness of DDT spraying?
3. What are the limitations of the data provided in this case?
4. Using the available data, can you construct an epidemiologic study to answer the case question?
5. What are the strengths and limitations of this study?
6. How would you design a new study to address the question of DDT and malaria?
7. What are the strengths and limitations of this study design?

Session 1: Roadmap for Discussion

10 minutes: Introduction and Warm-up. Define task.
5 minutes: Define main question in this case
15 minutes: Incidence and prevalence
20 minutes: Challenges of case
45 minutes: Study design: case-control study; non-randomized intervention
15 minutes: Wrap-up. Review of concepts covered.

Detailed Class Discussion Plan

Warm-up: Outline of task facing Dr. Mgaga [10 min]
- Question: What is our task in this case?
  - Discussion: We are asked to assist Dr. Mgaga in assessing the effectiveness of DDT spraying in Apac, Uganda, to prevent malaria.
- Briefly discuss the DDT spraying in Uganda in 1959 (page 9) and the Presidential Malaria Initiative (PMI) (pages 9-10).

Theme: Main question in case [5 min]
- Question: What is the main unanswered question in the case?
  - Discussion: The main question is whether DDT spraying prevents the incidence of malaria.
    “Does DDT spraying prevent malaria?”
 [Write this question on the board—see Board Plan #1 below]

Prevalence and Incidence [15 min]
- Question: Which numbers can we extract from the case that may be helpful in evaluating our case question?
  - Discussion: [Write incidences on the board—see Board Plan #2 below]
  - Discuss impact of rainy and dry season.
- Question: Do these data imply that DDT spraying was successful in preventing malaria?
  - Discussion: No. But difficult to interpret. Should have collected at same months of following (or prior) year because of seasonal variation in malaria incidence.
- Question: Are these prevalence or incidence figures?
  - Discussion: Incidence.
- Question: Are there any prevalence figures provided in the case?
  - Discussion: Exhibit 7 discusses malaria prevalence in Uganda.
Challenges for Dr. Mgaga [20 min]

- **Question:** What are the challenges Dr. Mgaga faces in evaluating the success of DDT spraying?
  - **Discussion:** [List these challenges on the board—see Board Plan #3 below]

Study Design: Case-control Study; Non-randomized Intervention [45 min]

- **Question:** Let’s refocus on the case question: Does DDT spraying reduce the incidence of malaria? Based on the data provided in the case can we construct an epidemiologic study to answer the case question?
  - **Discussion:** There will be discussion on how to set up a study. Where do we start—with exposure or outcome? All data have already been collected. Are we going to use all data? Will we dismiss some of the data?
- **Question:** Let’s define the study population on the disease. Which study design would this be?
  - **Discussion:** Case-control study.
- **Question:** How would we define our cases?
  - **Discussion:** There will be discussion on using all diagnosed malaria cases or only verified malaria cases. Discuss pros and cons. Discuss incidence cases. First onset cases. Malaria comes and goes.
- **Question:** How do we obtain our controls?
  - **Discussion:** Discuss challenges of control selection and selection bias.
    - Individuals free of malaria living in Apac. Controls must be drawn from the same catchment area and drawn from the same source population as the cases.
    - Define reference population, source population, and study population. There will be discussion on whether we have to verify that controls are free of malaria. Discuss pros and cons.
- **Question:** How would we use available exposure information in our case-control study?
  - **Discussion:** Exposure could be defined in various ways:
    - Homes sprayed
    - Homes sprayed appropriately
    - Self-reports => explain concept of recall bias
- **Question:** How would we evaluate the results of our study?
  - **Discussion:** Set up a 2x2 table.
- **Question:** Can we calculate a relative risk or risk ratio?
  - **Discussion:** Review the relative risk being a ratio of two incidences. Cannot calculate incidence of malaria because we fixed case-control ratio.
- **Question:** How do we calculate a measure of association?
  - **Discussion:** Need to retreat to a substitute measure, namely odds ratio. Discuss calculation of odds and odds ratio.
- **Question:** Can we use the data differently to evaluate the data provided in the case?
Discussion: The data lend themselves to use as a non-randomized intervention. Homes were sprayed or not sprayed with DDT. We can now assess malaria cases in sprayed and in non-sprayed homes.

• Question: How was it determined whether a home was sprayed?
  o Discussion: Depended on whether residents refused spraying. Discuss whether this might create a bias in the RR.

• Question: How should we classify homes that were ineffectively sprayed? Or should we exclude them?
  o Discussion: Discuss pros and cons of excluding them.

Wrap-up [15 min]
• Slides with summary points of concepts covered (see accompanying slides)
• Ask for remaining questions and discuss

Board Plans for Session 1

Board Plan #1: Main Question

Main Question: Does DDT spraying prevent malaria?

Board Plan #2: Malaria Incidence Data in Apac provided in case

Malaria cases in Apac:
First week of February 2008 (prior to spraying): 2,422 reported cases (page 1)
Spraying: April 2008
Last week of July 2008 (after spraying): 2,403 incident cases (page 1)

Jan–April 2008: 600–800 clinical cases per 100,000 population (page 1)
May–July 2008: 600–800 clinical cases per 100,000 population (page 1)

Rainy season: May–Nov
Malaria peak 4-6 weeks after rainy season => June/July–Dec

Board Plan #3: Challenges for Dr. Mgaga

Challenges for Dr. Mgaga
• Seasonal variation in malaria
• Malaria diagnosis: only 40–50% have blood slide done to confirm diagnosis => disease misclassification
• Clinical diagnosis mostly based on symptoms: miscarriages, fever, vomiting, convulsions, respiratory symptoms, or death => disease misclassification
• Elevated risk in children, pregnant women, foreign travelers, HIV infected
• DDT pilot inadequate trained sprayers, didn’t stick to walls, not mixed with alcohol, covered 40% not 95% of houses sprayed => exposure misclassification
• Population not informed, refused to spray houses => exposure misclassification

Session 2: Roadmap for Discussion
Detailed Class Discussion Plan

Warm-up [10 min]
- **Question:** Let’s remind ourselves what the question is we are trying to address
  - “Does DDT spraying prevent Malaria?”
  - **[Write this question on the board—see Board Plan #1 below]**
- Briefly review discussion from Session 1 and the two study designs discussed.

Misclassification [35 min]
- Briefly review challenges of defining exposure (who was exposed to DDT?) and of defining outcome (who has malaria?).
- **Question:** What implication would misclassification of exposure have on our odds ratio in a case-control study?
  - **[Draw 2x2 tables on board—see Board Plan #2 below]**
- **Question:** How would misclassification of the outcome affect our RR in a non-randomized intervention?
  - **[Draw 2x2 tables on board—see Board Plan #3 below]**

Study Design: RCT [45 min]
- **Question:** Are the data we have good enough to answer the case question and to advise Dr. Mgaga or should we collect additional information? Should we conduct our own study? If we decided to collect new data and design a new study, how would we design such a study?
  - **Discussion:** Design A: Randomized clinical trial.
- **Question:** What does randomization mean?
  - **Discussion:** Every person has the same chance to be in either group.
    - Discuss purpose of randomization.
    - Discuss randomization schemes.
- **Question:** How would we define our intervention?
  - **Discussion:**
    - Spray some houses well. Mix DDT appropriately and spray appropriately. Randomize intervention to spray ½ of the houses well.
    - Requires willingness to participate by all residents. Need to have pre-randomization information sessions.
    - Incentives to participate? E.g., free bed-nets for all? Discuss whether this would compromise our study design.
- **Question:** Do we provide anything to the non-sprayed houses?
  - **Discussion:** Discuss spraying them with water for blinding.
    - Discuss purpose of blinding.
• Students may suggest providing bed nets only to the non-sprayed houses. Discuss how this may affect results.

  • **Question:** How would we define our outcome?
    - **Discussion:** Measure incidence with blood tests.
    - If we don’t have the funds, we have to go by clinical symptoms.
    - Discuss how detection bias could arise if we tested only those residents whose houses were sprayed. [*Refer back to Board Plan #3]*

  • **Question:** Some residents may refuse to have their houses sprayed after randomization. What do we do with these study participants in our analysis?
    - **Discussion:** Discuss intention-to-treat analysis.

**Conclusions [5 min]**

• **Question:** How do you think the question on DDT spraying and malaria should be resolved?
  - **Discussion:** Students will offer their opinions. Restrict to 5 minutes to leave time for wrap-up.

**Wrap up [15 min]**

• Slides with summary points of concepts covered
• Ask for remaining questions and discuss

**Board Plans for Session 2**

**Board Plan #1: Main Question**

**Main Question:** Does DDT spraying prevent malaria?

**Board Plan #2: Misclassification of Exposure—Effect on RR**

<table>
<thead>
<tr>
<th>Misclassification of Exposure</th>
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<tr>
<td><strong>Non-differential</strong></td>
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<tr>
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</tr>
<tr>
<td>DDT</td>
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<tr>
<td>No DDT</td>
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</tbody>
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**Board Plan #3: Misclassification of Outcome—Effect on RR**
Misclassification of Disease

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<thead>
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<tbody>
<tr>
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<td>No DDT</td>
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Non-differential

<table>
<thead>
<tr>
<th></th>
<th>Malaria</th>
<th>No Malaria</th>
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<td>No DDT</td>
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Differential