

A conversation with Professor Michael Eddleston and Dr. Leah Utyasheva, November 23, 2017

Participants

- Professor Michael Eddleston – Director, Centre for Pesticide Suicide Prevention
- Dr. Leah Utyasheva – Policy Director, Centre for Pesticide Suicide Prevention
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Note: These notes were compiled by GiveWell and give an overview of the major points made by Professor Michael Eddleston and Dr. Leah Utyasheva.

Summary

GiveWell spoke with Professor Eddleston and Dr. Utyasheva of the Centre for Pesticide Suicide Prevention (CPSP) for an update on its work. In August 2017, CPSP received a GiveWell Incubation Grant of \$1,336,409 to start work aimed at reducing deaths from deliberate ingestion of pesticides. Conversation topics included the progress that CPSP has made on its stated plans, its staff and local contacts in India and Nepal, fundraising, and other opportunities for pesticide suicide research.

Progress on stated plans

Delay in receiving grant funding

CPSP received the grant funding two weeks ago (about three months behind schedule); Edinburgh University lent it £50,000 to cover its costs in the interim. This caused CPSP to delay its initial visits to India and Nepal, which were planned for September or October, but did not otherwise affect its timeline. CPSP has been able to begin making contacts and apply for ethics approval without traveling, and is ahead of its initial schedule despite the delay. The delay did not affect recruiting because CPSP cannot begin hiring people without receiving ethics approval, and the approval process takes six months.

Initial timeline and updates

CPSP initially shared with us the following timeline for its planned studies in India and Nepal:

- In the first three months, beginning to meet people in India and Nepal, and ideally visiting both places to do so. As noted above, these visits were delayed due to a delay in receiving the grant funding.
 - **Nepal:** Dr. Utyasheva is going to Nepal in four days to meet with CPSP's collaborators there, including the pesticide registrar and a junior doctor with whom Professor Eddleston has been working for

the last 2-3 years on national guidelines for pesticide poisoning treatment in Nepal. Both of these collaborators have been enthusiastic about working with CPSP.

- **India:** Professor Eddleston and/or Dr. Utyasheva will go to India in January to begin meeting people.
- By six months, having received ethics approval to begin collecting data from across India and Nepal.
 - **Nepal:** In Nepal, ethics approval is granted by a national committee. CPSP staff have almost completed an ethics application with the main hospital it will be working with there, and they hope to submit it after Dr. Utyasheva's visit to Nepal. The approval process is expected to take 3-4 weeks.
 - **India:** In India, ethics approval is granted by local ethics committees. Together with the partners in Nepal, CPSP staff have put together two ethics applications: one for a study in the north through the Emmanuel Hospital Association (EHA) in Delhi and one for a study in the south through Christian Medical College (CMC) in Vellore. The ethics applications for both studies were completed about a month ago, and the EHA application has been submitted. The CMC application will be submitted after each partner hospital submits a letter confirming its interest in participating in the study; so far seven out of 11 letters have been submitted. CPSP staff hope to receive ethics approval for this study in the next few weeks and are aiming to begin employing researchers to collect data in January or February, which would meet this six-month goal. Some of the hospitals CPSP will be working with in India are happy to accept the ethics approval from CMC, and others want to have their own ethics approval.
 - Once the three main ethics applications have been approved, CPSP will be able to begin working with all hospitals that either are happy to accept these ethics approvals or have their own ethics approval in place. This will likely apply to 4-5 hospitals in each of the three locations. CPSP staff expect to begin collecting data in Nepal and India in the second half of January. This may be delayed by about a month; Professor Eddleston would be disappointed if it were delayed until mid-March, although this is possible.
 - The ethics application process is relatively straightforward because CPSP staff will only be looking at medical records rather than intervening in patient care.
- By December 1, 2017, having recruited in-country staff in Nepal and India.
 - Since local staff cannot begin work until CPSP has received ethics approval, the CPSP and its partners have decided to delay hiring until the approval has been received. CPSP discussed with local partners qualifications necessary for the hires. Hiring could be done quickly as

some of the partners have identified potential candidates. These are not the researchers that CPSP hoped to have hired by December 1, however.

Process for collecting data

The studies in India and Nepal will involve reading medical records to gather data on which pesticides are used most commonly in pesticide self-poisoning. Research staff will look through one year of past medical records and will do ongoing data collection for the duration of the study.

Since hospital staff may not have an incentive to accurately record which pesticide was used in each case of self-poisoning, existing medical records may only give a rough idea of which pesticides are problematic in a given area. The accuracy of the medical records is expected to improve as CPSP research staff engage with hospital staff, emphasizing the importance of accurately reporting which pesticide was used and providing resources to help identify pesticides. One resource that CPSP may provide is a poster showing photographs of the bottles of all locally common pesticides, so that the families of patients can easily identify which pesticide was used by pointing to the image.

Potential informal partnership with the Food and Agriculture Organization of the United Nations (FAO)

FAO may be interested in either signing a memorandum of understanding (MOU) with CPSP or having a less formal partnership. FAO staff are interested in a couple aspects of CPSP's work:

- They think that every country in which pesticide suicide is a problem should have an understanding of the scale and form of the problem, while acknowledging that this area has not been a focus for FAO. They think that CPSP could serve a useful role in building an understanding of the problem in the countries where it works through research.
- FAO shares CPSP's interest in the policy role of changing pesticide regulations. It has 1-2 staff members working on this in 185 countries, with a focus on Africa; it recently worked on pesticide regulation in Mozambique.

CPSP staff plan to meet with FAO again in January or February to put together a description of how the organizations might work alongside one another. FAO is interested in having Dr. Utyasheva's help working on policy issues and will likely rely on data that CPSP provides to help inform policy decisions.

Goals of CPSP's work

1. Collecting baseline data on pesticide suicide rates, which has only been done in Sri Lanka. These data will be collected through the studies that CPSP is preparing to conduct in India and Nepal.

2. Working with pesticide regulators to influence policy by helping them to ban the most lethal and problematic pesticides. This is Dr. Utyasheva's primary goal.
 - a. **Nepal:** Working with the pesticide regulator in Nepal will be particularly important since pesticide regulation is under-resourced there. This work will be fairly straightforward because Nepal is a small country and pesticide regulation is managed by a single individual, who is interested in working with CPSP. CPSP staff are developing a better understanding of the pesticide regulation process in Nepal and now need to determine what kind of assistance would be most useful for it to provide.
 - b. **India:** Pesticide regulation will be more complex in India due to the role of states in implementing regulation. CPSP is working on gaining a better understanding of how pesticide regulation works in India in order to be better able to influence it. CPSP has made contact with national pesticide regulation officials, but it is not clear whether a national ban on certain pesticides would be sufficient for states to stop using them, or if states act independently. CPSP staff plan to investigate this over the next 3-6 months; they have contacted a staff member of Pesticide Action Network India (PAN India) and plan to look for other people who can advise them on how the pesticide regulation system works.

Staff and local contacts

Staff

In addition to Professor Eddleston and Dr. Utyasheva, CPSP staff and collaborators include:

- Manjula Weerasinghe, a full-time Sri Lankan postdoc who has been working with CPSP since August 2017. His job will involve teaching CPSP's researchers in India and Nepal about the subtleties of his work with pesticides. He is currently doing research on pesticide poisoning and effects of pesticide regulation in Sri Lanka.
- Duleeka Knipe, a postdoc in the United Kingdom who is beginning to compile the data from Sri Lanka and write a paper on it. Dr. Knipe is expected to apply for a post-doctoral post with CPSP that will be advertised soon. The successful applicant for this post will continue her work compiling data on baseline suicide rates in India and Nepal.
- A consultant who works with Edinburgh University but lives in Nepal and works at civil society and public health organizations there.
- Several collaborators who are working with, but not paid by, CPSP. This includes CPSP's advisory board and Melissa Pearson, who will likely be

working on a publication about the regulatory system in India as a collaboration with Dr. Utyasheva.

- A part-time secretary employed by the university who works on CPSP for four hours per week.

In the future, CPSP expects to hire:

- Full-time staff in both India and Nepal.
- A part-time consultant to help understand the policy situation in India and Nepal. This person may be a policy, civil society, environmental, or public health expert.

Local contacts

- **India:** Professor Eddleston has two long-established contacts in the CMC hospital network, which includes hospitals in the rural, underserved areas where pesticide suicide is most common. These connections have made it possible for CPSP to work with EHA and a network of 20-25 hospitals across the country and have made it easier to begin work in India remotely.
- **Nepal:** Neither Professor Eddleston nor Dr. Utyasheva has worked in Nepal. Dr. Utyasheva is going there to make initial contacts and determine what the needs are and how CPSP can best help to fill them. CPSP has three contacts in Nepal: 1) a junior doctor with whom Professor Eddleston has worked for the past three years over email, 2) a senior civil servant in the agricultural department interested in working on improving pesticide regulation, and 3) the consultant for Edinburgh University mentioned above. The consultant will help CPSP to organize initial meetings and understand the situation in Nepal.

Fundraising

CPSP staff plan to reach out to major funders who may be interested in funding work on non-communicable diseases, though they do not plan to do any fundraising in the next six months because they will be focusing on getting programs up and running in India and Nepal. Before beginning to fundraise, CPSP staff would like to create a clearer picture of what the organization will be doing over the next few years. This will put them in a better position to request funding for specific activities and to have a better idea of how much funding they will need.

Other opportunities for pesticide regulation work

Over the next year, CPSP would like to begin exploring opportunities to work on pesticide regulation from different angles. It has identified several such opportunities.

Collecting data on consequences of paraquat ban and regulatory processes in Taiwan

Taiwan recently banned paraquat, a highly lethal pesticide, and there are ongoing discussions there about the agricultural health consequences of the ban. Shu-Sen Chang, an epidemiologist in Taiwan, is on CPSP's board of advisers and is interested in working with CPSP to understand the consequences of the ban and how the pesticide regulation process works. Gaining a better understanding of regulatory processes and the outcomes of pesticide bans will enable CPSP to make more confident recommendations to pesticide regulators in other countries. CPSP is considering giving this epidemiologist between £10,000-£40,000 to fund a researcher to collect pilot data for 6-12 months.

Documenting regulation processes in Tanzania

Pesticide self-poisoning is a problem in Africa, but it is often downplayed and ignored because suicide is generally not discussed. Professor Eddleston met with someone who runs a poison center in Tanzania and is on the government's pesticide regulatory board; she has been involved in multiple pesticide regulatory decisions. To date, no one has recorded how these processes occur, how decisions are made, who influences the decisions, and what the outcomes of the decisions are; CPSP would be interested in working with this person to document these processes. This would not cost additional money, but would cost the time of a postdoc to work with her.

An advantage of working with the government of Tanzania is that it is a large country that is important in Africa and can serve as a good example for the rest of the continent. CPSP has contacts in healthcare, pesticide regulation, and government in Tanzania who understand how the pesticide regulation system works. It would not cost very much to pursue the possibility of working there and may be a good opportunity.

Working with a network of pesticide regulators in Africa and the Caribbean

For the past 3-4 years, Professor Eddleston has worked with Professor Andrea Rother, who is based in Cape Town, South Africa and runs a course for pesticide regulators across the Caribbean and Africa. This is an online distance course that includes two weeks per year in Cape Town. It is the only such course that Professor Eddleston is aware of. She has now trained about 200 people across Africa.

Pesticide self-poisoning is a problem in Africa, but suicide is often not discussed. CPSP is beginning discussions with Professor Rother and FAO about the possibility of working with this network of trainees to influence the regulatory process they use, thereby helping 20-40 countries with their pesticide regulation simultaneously. FAO is interested in working with CPSP on this, though it may be difficult to measure the impact on suicide rates.

Since suicide is not discussed seriously in Africa, the main reasons for regulating pesticides are environmental concerns and acute occupational poisoning. Professor Eddleston has an annual two-hour webinar with the pesticide regulators in this network, and they do acknowledge suicide as a problem, but it is not measured or reported at a very high rate.

Getting a more accurate estimate of the suicide rates in African countries

There is little available data on the suicide rates in African countries, in part because suicide is typically not acknowledged. According to United Nations (UN) statistics, which are based on government-reported data, Tanzania has an annual suicide rate of 16.5 people per 100,000. The UN reports high rates of suicide for several other African countries: 29/100,000 people in Sierra Leone, 27/100,000 in Swaziland, and 25/100,000 in Burkina Faso. Suicide rates are also reportedly high in Lesotho, Mozambique, Angola, and Zimbabwe. It is assumed that these numbers are under-reported, which means that some of these countries may have the highest suicide rates in the world.

If we roughly estimate that the annual suicide rate is 10 people per 100,000 across Africa and that there are 1 billion people in Africa, this would mean that there are roughly 100,000 suicides per year in Africa. Conservatively, Professor Eddleston estimates that this number is at least in the tens of thousands. A recent World Health Organization (WHO) systematic review (of which Professor Eddleston is an author) suggests that there are about 34,000 suicides per year in Africa, of which about 2,000 are due to pesticide poisoning. Professor Eddleston thinks that the numbers reported in the review are too low and are based on poor-quality data.

Gathering verbal autopsy data

CPSP has been offered funding to support a student for eight weeks over the summer to set up a system for collecting data from District Surveillance Schemes (DSSs) across Africa. DSSs conduct verbal autopsies to determine the causes of death of people who die outside of hospitals. The student would work on gathering verbal autopsy data from about 20 DSSs to get a more reliable estimate of the rate of suicide from pesticide poisoning in rural areas of Africa.

Randomized controlled trial in Sri Lanka

Recent pesticide suicide data

Professor Eddleston met with the new pesticide registrar in Sri Lanka two weeks ago to talk about pesticide regulation. The new pesticide registrar has been active about regulation and asked Professor Eddleston to share suicide data from the field. Manjula Weerasinghe, a CPSP Research Associate, has been collecting suicide data in Sri Lanka.

Recent pesticide suicide data from a community in Sri Lanka indicate that carbosulfan (a carbamate) was responsible for the most pesticide deaths in 2014-15, followed by profenofos (an organophosphate). Some of the deaths were attributed to unknown pesticides, because people either had unlabeled bottles or arrived at a hospital too sick to report what they had taken; Professor Eddleston estimates that half of these were either carbosulfan or profenofos.

Sri Lankan death records up to May 2016 include a total of 152 pesticide suicides of which 45 (34%) were due to Marshal 20 (the brand name for carbosulfan); 10% were due to profenofos; and 52 deaths were due to an unknown poison, about half of which were likely Marshal 20. Professor Eddleston conservatively estimates that 35-40% of deaths are due to Marshal 20 (which has a case fatality rate of about 12%). This kind of data can be used to make a strong case to the pesticide regulator for banning this compound.

Organophosphates are metabolized into an active form after they are ingested, and people who ingest WHO Class II toxicity organophosphates such as profenofos usually die in 2-3 hours. Carbamates (such as carbosulfan) are already in an active form and people who ingest them may die in about an hour. This means that people who ingest carbosulfan are more likely to die before they reach a hospital, and therefore that hospital data on the most commonly used pesticides is not necessarily representative. Over the next few weeks, CPSP plans to analyze data from the household pesticide storage study (available here: <https://www.ncbi.nlm.nih.gov/pubmed/28807536>) to determine how many people die in hospitals and how many die before presentation to hospitals in the North Central Province of Sri Lanka.

Sri Lanka has banned many highly lethal pesticides; carbosulfan and profenofos appear to be the only two remaining. There are many pesticides available to farmers, and it is likely that every 2-3 years another highly lethal pesticide will become available and will need to be banned, though the newly common pesticides are consistently less toxic than their predecessors. The pesticide suicide rate is continuing to fall in Sri Lanka; Professor Eddleston expects that in the next 2-3 years it will stabilize, but that if carbosulfan and profenofos are banned, it will fall again. CPSP aims to reduce the suicide rate to below 10 people per 100,000, which would be comparable to the rate in the UK.

Randomized controlled trial on removal of carbosulfan and profenofos

CPSP proposes running a large three-year randomized controlled trial (RCT) in Sri Lanka to measure the change in suicide rates, agricultural yields, and healthcare costs resulting from banning carbosulfan and profenofos and replacing them with safer compounds. A large-scale study would give definitive evidence of the impact of banning these pesticides. The study could either cover the whole, or part of the country as a cluster RCT or a step-wedge cluster RCT.

It remains to be decided whether to use a cluster RCT or step-wedge cluster RCT study design. A step-wedge cluster RCT would implement the ban across the whole island in stages and measure the differences in effects between areas where the ban started at different times. A cluster RCT would include a control group and only implement the ban on part of the island, which would have the advantage of three years of follow-up data.

It would cost about \$1.5 million to run a cluster RCT at a local level and \$2-3 million for a national-level study.

Local vs. national study

A local cluster RCT might look similar to the step-wedge cluster RCT that Professor Eddleston and colleagues are currently planning in Sri Lanka's North Central Province, which is measuring the impact of changing the behavior of shopkeepers. This intervention trains vendors to recognize customers at high risk of self-harm with the purchased pesticide and to not sell to such people. North Central Province has 1.2 million inhabitants and 29 divisions. Over three years, the intervention is gradually being phased into all 29 divisions. The step-wedge study design is useful for interventions that are expected to have a positive effect because it means that systems are set up in all areas studied, which increases the likelihood that the intervention will be sustained in these areas in the future.

There are a few disadvantages of local cluster RCTs as compared with national-scale RCTs:

- **Increased likelihood of contamination:** If the clusters are small, people may travel from one cluster to another to purchase a pesticide that is not available in their own cluster. In the case of the study in North Central Province, each division is only about 20-30 kilometers across, which makes contamination fairly likely since someone who prefers a certain pesticide may be willing to walk several kilometers to get it. A national study could use larger clusters and therefore be less vulnerable to contamination.
- **Reduced study power:** A local cluster RCT the size of the North Central Province study (which has a sample size of 1.2 million people) would be adequately powered to detect changes in the rate of pesticide self-poisoning but not to detect changes in the pesticide suicide rate. In order to detect the latter, a study would need to have a sample size of about 6-10 million people, which would be possible in a national study in Sri Lanka.
- **Increased cost of gathering data from rural hospitals:** Collecting follow-up data from many small rural hospitals is fairly resource-intensive in terms of staff and transportation costs. Professor Eddleston and colleagues are currently running a sensitivity study measuring all forms of self-harm (e.g. drowning and burning); since milder cases do not reach the central hospitals, they must gather data from smaller peripheral hospitals as well. Out of a total

cost of \$1.1 million, about \$1 million is to cover staff and motorbikes to visit all of the hospitals. By contrast, a national study looking just at the change in the pesticide suicide rate (as opposed to pesticide poisoning) would have a large enough sample size that data could be collected just from the central hospitals and coroners, which are easier and cheaper to access. An RCT on this scale measuring deaths from pesticide suicide has not been done before, but would be possible in this case.

Other organizational updates

CPSP has been working on its organizational documentation. It has a communications plan in place and has begun engaging with a search engine optimization expert to work on its website.

All GiveWell conversations are available at <http://www.givewell.org/conversations>