Chapter 4.3 Audio Podcast Script – monologue format

Hello, my name is Matthew Coldiron from Epicentre, in Paris, France, and I am one of the authors of chapter 4.3 in *The WHO Guidance on Research Methods for Health Emergency and Disaster Risk Management* about the design and conduct of cluster randomized trials.

As a physician and an epidemiologist, I've worked in a variety of health emergency settings across the world, and have designed and implemented cluster randomized trials in these settings. In this chapter, we wanted to explain how and why cluster randomized trials can be very well-adapted for performing research in emergencies, and to lay out some of the potential pitfalls to look out for.

Most people are familiar with the concept of an individually randomized trial, where participants receive intervention X or Y, and outcomes are compared; and these are described in chapter 4.1 of the WHO Guidance. But in a cluster randomized trial, the intervention takes place at a larger level, such as a village, school, or different wards of a hospital. Cluster randomized trials can look at the effects of mass vaccination campaigns, or mass prophylaxis campaigns, or different packages of interventions – like hygiene in the hospital, water and sanitation programs in the community, or teaching school students about disaster risks.

In this chapter, we talk about the special considerations necessary for designing a cluster randomized trial such as, on a basic level, things like defining and selecting the clusters; and then how to decide on when the interventions will be delivered, for example in parallel in the different clusters, or in a stepped-wedge fashion, where all clusters eventually receive the intervention, just at different points in time. Two other methodological points we discuss are about minimizing "crossover" between the clusters, and mathematical considerations that need to be taken into account for clustering when the trial is analysed.

Cluster randomized trials are well-suited to Health EDRM settings, where many interventions are directed at larger groups of people. And in some ways, for policymakers, their results can be easier to interpret and understand making them easier to translate directly into policy change. Recent trials have evaluated Ebola vaccines, and the effects of village-wide antibiotic prophylaxis in a meningitis epidemic. Nonetheless, cluster randomized trials don't come without their challenges and disadvantages, which can include the large number of participants, a level of statistical complexity that goes beyond a simpler individually randomized trial, and the fact that they are not generally designed to show individual-level effectiveness of an intervention.

We also discuss the special considerations regarding informed consent in cluster-randomized trials. Most researchers are familiar with obtaining informed consent in an individually randomized trial, when trial procedures, potential harms and benefits are explained to potential participants, who are then able to ask questions and take an independent decision about whether to participate. This is not always practical or even possible in a cluster

randomized design, so researchers have set out a series of guidelines in the Ottawa Statement on the Ethical Design and Conduct of Cluster Randomized Trials. One of the key elements is who can be considered the “gatekeeper” who will provide permission for a group of people to participate (like a village chief or nurse manager of a hospital ward). But remembering that permission does not force participation on individuals, and researchers must still communicate with the larger group or community about the study and its risks and benefits. But in Health EDRM settings, these are particularly important points to consider.

In summary, given that the cluster randomized design can be especially useful and relevant to Health EDRM settings, we hope that this chapter provides useful guidance to readers.

Thank you very much for listening.