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NOTES FROM THE FIELD

Lessons learnt conducting minimally invasive autopsies in private mortuaries as part of HIV and tuberculosis research in South Africa

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Current estimates of the burden of tuberculosis (TB) disease and cause-specific mortality in human immunodeficiency virus (HIV) positive people rely heavily on indirect methods that are less reliable for ascertaining individual-level causes of death and on mathematical models. Minimally invasive autopsy (MIA) is useful for diagnosing infectious diseases, provides a reasonable proxy for the gold standard in cause of death ascertainment (complete diagnostic autopsy) and, used routinely, could improve cause-specific mortality estimates. From our experience in performing MIAs in HIV-positive adults in private mortuaries in South Africa (during the *Lesedi Kamoso* Study), we describe the challenges we faced and make recommendations for the conduct of MIA in future studies or surveillance programmes, including strategies for effective communication, approaches to obtaining informed consent, risk management for staff and efficient preparation for the procedure.

Tuberculosis (TB) is likely the leading cause of death (CoD) among human immunodeficiency virus (HIV) positive people and is often under-recognised as a cause of morbidity.[1] Estimating TB mortality is challenging: current estimates depend heavily on death certificates, which are often inaccurate in HIV-positive people;[2] verbal autopsy, which differentiates poorly between TB and other HIV-associated CoD;[3] and mathematical modelling.[4] Complete diagnostic autopsy is the gold standard for determining CoD, but rates are declining worldwide;[5] minimally invasive autopsy (MIA), however, performs well in diagnosing infectious disease,[6] and is faster, technically easier, more portable, probably cheaper and more acceptable to individuals and families.[7] Most autopsy studies have included only individuals dying in health facilities,[1] and are poorly representative of most high TB burden countries, where many deaths occur in the community.

A community-based MIA surveillance programme at sentinel sites would improve quantification of disease burden and mortality estimates, but any such venture would encounter many challenges. From mid-2013 to late 2016, we conducted an MIA study in South Africa (*Lesedi Kamoso* ["light for the future"]) to estimate 1) the autopsy prevalence of TB and other infections,[8] and 2) CoD[9] in HIV-positive adults who died after enrolment into a trial of empirical TB treatment ("TB Fast Track").[10] Based on our experiences in conducting MIAs in private mortuaries and using information collated from field notes and discussions with the research team, we describe how challenges were overcome and provide guidance for those planning similar studies or considering incorporating MIA into surveillance programmes. We do not discuss technicalities of the MIA procedure, as detailed guidance has been published by other groups.[11,12]

The parent and substudy received ethical approval from the research ethics committees of the University of the Witwatersrand (Johannesburg, South Africa), the London School of Hygiene & Tropical Medicine (London, UK) and local health authorities.

ASPECTS OF INTEREST

Preparation

Three to six months before data collection begins, the proposed autopsy activity should be discussed with local stakeholders (Figure), including community, traditional and religious leaders; the police; patient advocates; mortuary owners; managers of local clinics and hospitals; and, ideally, a representative of the Department of Health. We suggest providing a plain-language written summary in local languages, with contact details of key personnel and oversight bodies. Meetings should be held at regular intervals for the duration of the programme, allowing for findings to be shared and for stakeholders to discuss concerns.

This preparation period should ideally also include formative work conducted by social scientists to gain a deeper understanding of the dynamics within the community, burial and cremation practices, and beliefs around death, dying and autopsy. The scope of religious beliefs and practices should also be explored. Information collected during the formative work should inform the design of participant information sheets, the routes by which participants and families are approached, and the training of staff in obtaining consent and counselling individuals and families.

Death notification

We were largely reliant on family members informing clinic-based research staff of the death of a participant. On most occasions (229/289 deaths, 79%), notification occurred after burial and an autopsy could not be completed. We observed that the likelihood of timely notification depended on the trust between the clinic-based researcher and the participant/their family:

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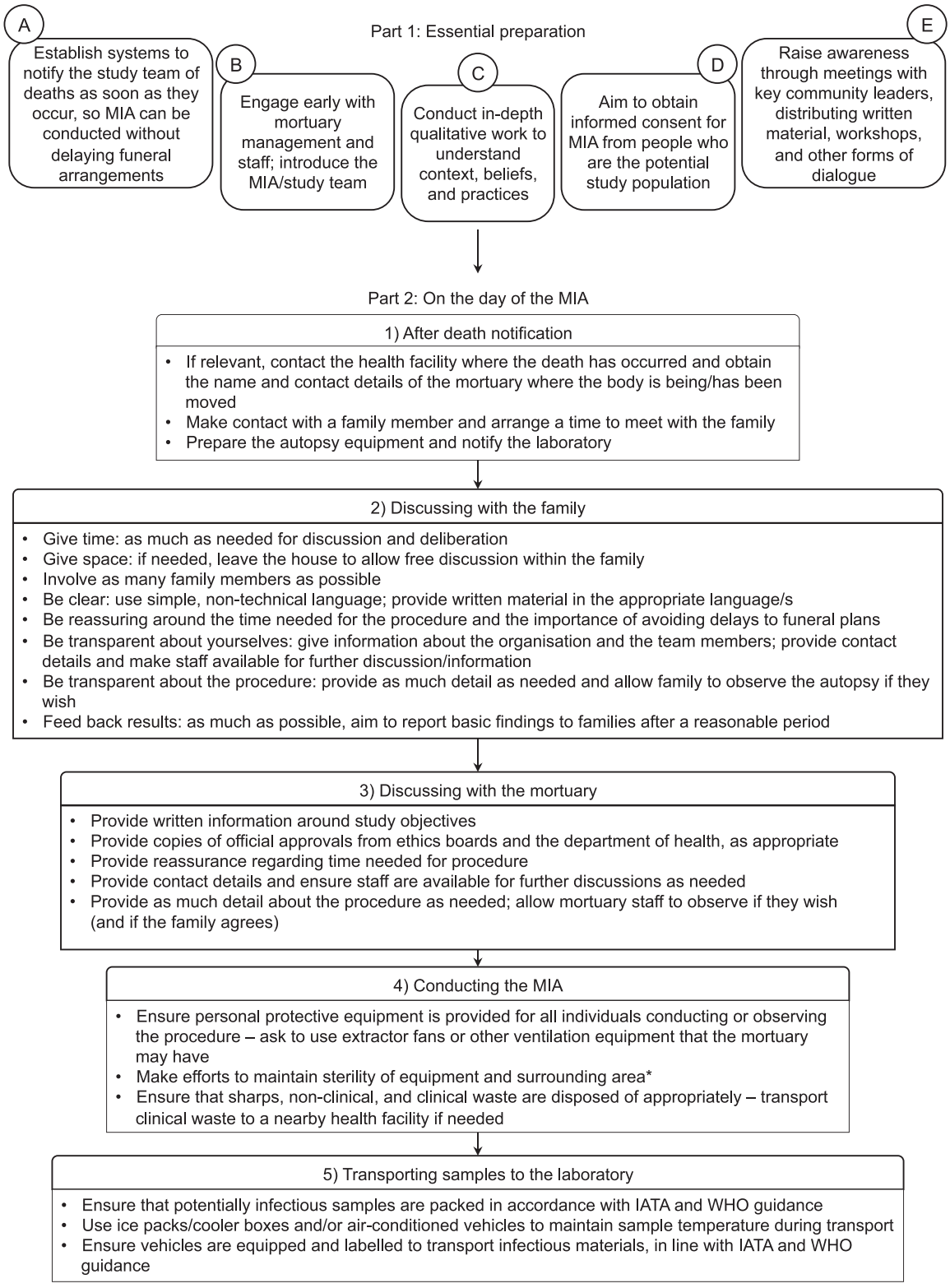

FIGURE Overview of processes and interactions needed to obtain consent for and conduct MIA in a private mortuary or other community location. *Sterile precautions required only if attempting to collect samples for bacteriology (e.g., microscopy or culture). MIA = minimally invasive autopsy; IATA = International Air Travel Association; WHO = World Health Organization.

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KEY WORDS
research design; mortality; public health; methods; TB

researchers were more likely to be informed in time if they were seen as supportive and understanding, and particularly, if they were regularly 'checking in' (sometimes informally) on the health of the participant.

Informed consent

Whenever possible, we requested consent for MIA from participants at enrolment to the parent trial: of 2200 participants asked, 1675 (76%) agreed; participants were not offered a financial incentive for participation. We approached the family for permission to proceed if the decedent had consented to MIA at enrolment or for written consent if the decedent had not been asked (the MIA substudy was initiated some months after the start of the parent study and therefore, some participants were not asked to consent to MIA at enrolment). If a decedent had declined to consent at enrolment, the family was not approached. Of 43 families approached, 36 (84%) gave consent for MIA.

We developed consent procedures after discussion with clinical research experts in South Africa, including those previously involved in autopsy studies. It should be noted that these procedures were considered suitable for a study involving adults only; studies or programmes that involve children will entail different considerations, and consent processes should be formulated after consultation with relevant experts. Investigators must be familiar with local legislation around human tissue research, adhere to informed consent guidelines published by professional and regulatory bodies, and are advised to consult local experts and institutional review boards. The recommendations below are intended to improve communication during the consent-taking process (a common reason for initial refusal of consent in our study was misunderstanding of the purpose of autopsy; for example, we were frequently asked to justify the need for further examination when the person had already died). As in all health research, participants or families giving consent should be allowed to make an informed decision about their own or their relative's participation, and all parties must be made aware that they are free to decline or withdraw consent at any point without risk of immediate or deferred consequences.

The experiences of staff and our field notes suggest that individuals enrolled into the parent study were more likely to consent to MIA if a researcher could discuss MIA in an open and transparent manner; had a good understanding of the purpose of autopsy in a research context; and was willing to discuss broader topics, such as life after death. An individual consenting to MIA for themselves was also made more likely by the involvement of a family member in the consent process, availability of additional plain-language written information, and availability of a staff member for follow-up conversations (some individuals came back to give consent for MIA at a later date, or simply wanted to continue the conversation with the researcher).

The process of getting consent or permission from the family of a deceased individual may be complicated by pre-existing tensions within the family; we found it helpful to make our discussions as inclusive as possible and took particular care to communicate with senior family members. On some occasions, we had to make two or three visits to a household before a final decision was made. Families were not offered a financial incentive for participation, although they were often (informally) assisted with transport to and from the mortuary on the day of the MIA. Among families who gave permission, we made sure that decision-making family members understood the MIA procedure and the purpose of the study—that the discussion took place some days before the funeral, with reassurance that MIA would not delay proceedings, and, most importantly, that the researcher(s) had a good understanding of the relevant cultural norms and were able to listen, empathise and give families space and time for discussion.

To our surprise, on more than one occasion a family member requested to observe the autopsy and reported afterwards that they found it a positive experience; however, this was not the norm, and acceptability of this practice may be very different in other settings, depending on local expectations and beliefs, which highlights the need for a robust understanding of the context in which MIAs are to be conducted. In addition, almost all individuals enrolled into our study were from a Christian background, and the funeral often did not take place for a week or more after death, giving us time to obtain permission and complete the MIA. This too may be very different in other settings, which may give researchers a smaller window in which to conduct the MIA; the success of an MIA programme in such settings is likely to depend on the existence of a strong death notification system, ideally one that is integrated into hospitals.

INTERACTIONS WITH HOSPITALS AND MORTUARIES

Many private mortuaries in South Africa have informal agreements with hospital staff to facilitate the rapid transfer of the deceased from hospital to mortuary; these are often well-established networks with financial implications for those involved. Our experiences suggest that attempts to conduct MIAs in hospitals are unlikely to succeed unless clear instructions are issued and enforced by senior hospital management or unless the MIA programme is integrated into hospital procedures.

In our study, all MIAs were conducted in private mortuaries; most mortuary staff were helpful and welcoming, although we did encounter some opposition: on two occasions, we were unable to complete the MIA. As described above and in the Figure, early engagement with mortuary managers, with opportunities for questions and clarification, would have made these interactions considerably easier; however, our study was conducted over a wide geographical area that included several hundred mortuaries, and we were not able to do this. We advise that, if possible, researchers travel to the mortuary accompanied by a senior family member on the day of the MIA to facilitate direct communication between the family and mortuary staff. Providing mortuaries with written information and contact details of study personnel helped establish trust and made future interactions considerably easier; over the course of the study, we developed relationships with some mortuary managers, and would visit mortuaries on days when autopsies were not being conducted to update them on the study's progress.

OTHER CONSIDERATIONS

Sterile instruments and procedures are not needed if conducting only histological examination of samples; however, we wished to perform aerobic and mycobacterial culture on samples, but had no access to an autoclave and encountered difficulties when trying to establish and maintain sterile fields. Useful items of equipment, including those used to maintain asepsis in the field, are listed in the Table. All waste generated during MIA should be considered potentially infectious: as many private mortuaries do not have procedures for clinical waste disposal, we transported waste to a nearby health facility where this could be done safely. The

TABLE Suggested essential equipment for conducting a minimally invasive autopsy in the field

Category/sub-category/item(s)			Comments
Documentation	Approvals from research ethics committee/s and national, provincial and district departments of health Plain-language summary of study aims and activities for families Plain-language summary of study aims and activities for mortuary owners and staff Formal information sheets and consent forms Laboratory request forms		All documentation that is handed to families or mortuary staff should be approved by monitoring bodies and should include study team contact details
Personal protective equipment	N95 mask Goggles, visor or other eye protection Gown/apron Non-sterile latex gloves Alcohol gel Hair net and shoe covers (or rubber boots)		Suggested as a minimum set per person. Appropriate training around universal precautions and disposal of sharps should be conducted
Autopsy kit	Preparatory	Headtorch Folding work surface/s For cleaning: Povidone iodine; cold sterilant (min 150 ml)* For samples: formalin; sterile saline	Medium for transportation of samples should be tailored to laboratory requirements.
	Sharps	Sharps bin Scalpel (small) Tissue biopsy needles 18G hypodermic needles Spinal needle/s Skin sutures (nylon, 4-0) Surgical scissors	Suggest use of disposable equipment unless able to access sterilising facilities (cold sterilant* can be used to disinfect)
	BAL/CSF/blood/urine	Catheter/s (male and female)† Nasogastric tube/s‡ Syringes (20 ml) Sterile lubricating gel (sachets) Sterile saline pack/s (200 ml)‡	
	Other	Sterile gauze; alcohol swabs; surgical forceps; needle holder; plasters Sterile gloves and sterile procedure kits (if needed)	
Miscellaneous	Waste and transport	Waste bags (one for clinical waste, one for general waste) Paper towels and cleaning fluid Bio-bottles Ice packs Styrofoam insulation container	See WHO/IATA guidelines for requirements around transportation and labelling of potentially infectious specimens
	Other	Clipboard, pens, and permanent marker Scissors and adhesive tape Spare batteries (for head torch)	

*Can be used to disinfect (in ~5–10 min) or sterilise (in ~15–20 minimum, depending on manufacturer) steel instruments.
†Required only if collecting urine.
‡Required only if conducting modified BAL.
BAL = bronchoalveolar lavage; CSF = cerebrospinal fluid; WHO = World Health Organization IATA = International Air Transport Association.

World Health Organization provides guidance for transporting potentially infectious materials.[13]

To minimise risk during MIA, staff (four research assistants and a driver in our study) should be trained in safe practices, educated about potential risks and advised of the importance of knowing their own HIV status. These procedures should ideally be embedded within an occupational health programme: all staff should undergo regular screening for active TB, and staff who are HIV-positive should be made aware of their increased risk of TB and encouraged to take antiretroviral therapy. In addition, we organised regular debriefing sessions led by a psychologist to discuss issues arising from conducting autopsies and dealing with bereaved families, and to provide team members with tools to manage stress and avoid burnout.

CONCLUSIONS

When used in routine surveillance, MIA could improve estimates of disease burden and cause-specific mortality, but the barriers to effective deployment should not be underestimated. If autopsies

are to be more widely conducted outside of hospitals, health professionals and research organisations will need to engage wholeheartedly with the communities in which they work and strive to understand local beliefs and practices around death. Thorough preparation, education, transparency, respect, trust and partnership with communities will be central to this process.

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Les estimations actuelles du poids de la tuberculose (TB) maladie et de la mortalité qui lui est due parmi les patients positifs à l'infection par le virus de l'immunodéficience humaine (VIH) dépendent beaucoup de méthodes indirectes, qui sont moins fiables pour vérifier les causes de décès au niveau individuel et de modèles mathématiques. Une autopsie peu invasive (MIA) est utile au diagnostic de maladies infectieuses, fournit une approximation raisonnable de l'étalon or de la vérification de la cause du décès c'est-à-dire une autopsie diagnostique complète. Si elle est utilisée en routine, elle pourrait améliorer les estimations de mortalité spécifique d'une cause. A partir de nos expériences de MIA sur des adultes positifs au VIH dans des morgues privées d'Afrique du Sud (au cours de l'étude *Lesedi Kamoso*), nous décrivons les défis rencontrés et faisons des recommandations pour la réalisation de MIA dans des études futures ou des programmes de surveillance, incluant des stratégies de communication efficaces, des approches visant à obtenir un consentement éclairé, une prise en charge du risque pour le personnel et une préparation efficace de la procédure.

Las estimaciones actuales de morbilidad por tuberculosis (TB) y de mortalidad por causas específicas en las personas positivas frente al virus de la inmunodeficiencia humana (VIH) se fundamentan en su mayor parte en métodos indirectos que son menos fiables para determinar las causas de muerte individuales y en modelizaciones matemáticas. La autopsia mínimamente invasiva (MIA) es útil en el diagnóstico de las enfermedades infecciosas, ofrece un sustituto aceptable al método de referencia para determinar la causa de muerte (que es la autopsia diagnóstica completa), y cuando se usa de manera sistemática, mejora las estimaciones de la mortalidad por causas específicas. A partir de su experiencia con la MIA en adultos con infección por el VIH en empresas fúnebres privadas en Suráfrica (durante el estudio *Lesedi Kamoso*), los autores describen las dificultades que encontraron y formulan recomendaciones que se pueden aplicar en el futuro al realizar la autopsia mínimamente invasiva en estudios de investigación o en programas de vigilancia; se preconizan estrategias de comunicación efectivas, métodos de obtención del consentimiento informado, la gestión de riesgos para el personal y la preparación eficiente del procedimiento.

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