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LOMWRU.

LOMWRU Annual Report 2023
Lao-Oxford-Mahosot Hospital-Wellcome Trust Research Unit

Annual Report 2023

LOMWRU (Lao PDR)
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Lao-Oxford-Mahosot Hospital-Wellcome Trust Research Unit

LOMWRU.

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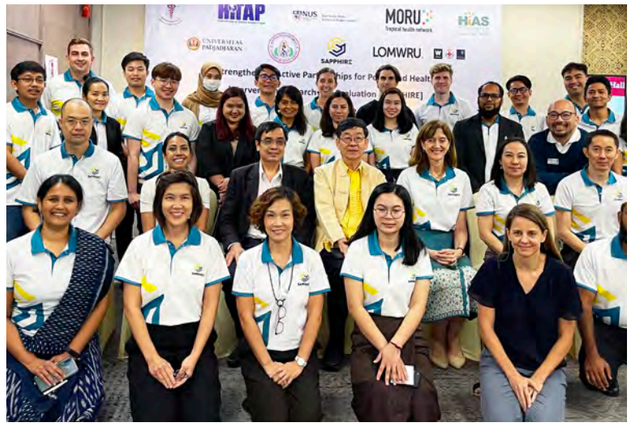
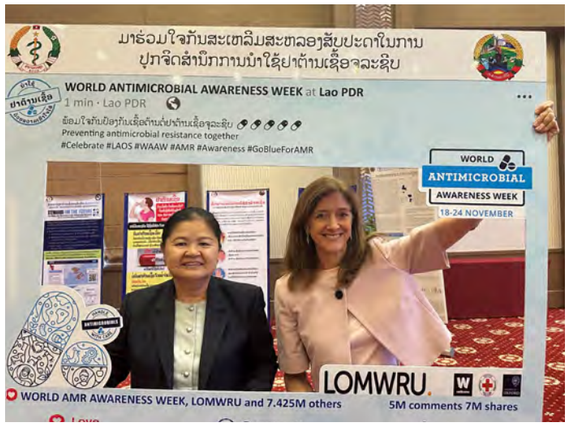
Lao-Oxford-Mahosot Hospital-Wellcome Trust Research Unit (LOMWRU)





ກ່ຽວກັບໜ່ວຍງານຄົ້ນຄວ້າຂອງພວກເຮົາ

ໂຄງການຮ່ວມມືຄົ້ນຄວ້າດ້ານພະຍາດເຂດຮ້ອນລະຫວ່າງໂຮງໝໍມະໂຫສົດ - ມະຫາວິທະຍາໄລອ໋ອກຟອດ-ແວວຄ໋ຳທີ່ຕູ້ສ ຫຼື The Lao-Oxford-Mahosot Hospital-Wellcome Trust Research Unit (LOMWRU) ແມ່ນໜ່ວຍງານທີ່ມີການຮ່ວມມືລະຫວ່າງມະຫາວິທະຍາໄລອ໋ອກຟອດ ແລະ ໂຮງໝໍມະໂຫສົດ, ນະຄອນຫຼວງວຽງຈັນ, ສປປ ລາວ ໂດຍໄດ້ຮັບທຶນຊ່ວຍເຫຼືອຫຼັກ ຈາກແວວຄ໋ຳຕູ້ສ ປະເທດອັງກິດ. ພວກເຮົາຍັງແມ່ນສ່ວນໜຶ່ງຂອງເຄືອຂ່າຍໜ່ວຍງານຄົ້ນຄວ້າພະຍາດເຂດຮ້ອນ (MORU Tropical Health Network) ທີ່ມີສູນຄົ້ນຄວ້າ ຕັ້ງຢູ່ ປະເທດໄທ, ກຳປູເຈຍ, ສປປ ລາວ, ມຽນມາ ແລະ ສາທາລະນະລັດ ປະຊາທິປະໄຕ ຄອງໂກ.

ການຮ່ວມມືລະຫວ່າງ ໂຄງການຄົ້ນຄວ້າພະຍາດເຂດຮ້ອນລະຫວ່າງ ໂຮງໝໍມະໂຫສົດ-ແວວຄ໋ຳຕູ້ສ-ມະຫາວິທະຍາໄລອ໋ອກຟອດ ແລະ ສະຖາບັນຄົ້ນຄ້ວາເພື່ອການພັດທະນາຝຣັ່ງ Institut de Recherche pour le Développement ຫຼື IRD) ແມ່ນ ເລີ້ມມາຕັ້ງແຕ່ປີ 2006. ປະຈຸບັນ ພວກເຮົາມີພະນັກງານທັງໝົດ 73 ຄົນ ຊຶ່ງລວມມີ ພະນັກງານທີ່ເຮັດວຽກປະຈຳຢູ່ນະຄອນຫຼວງວຽງຈັນ ແລະ ຕ່າງແຂວງ ທີ່ເປັນໜຶ່ງໃນວຽກງານການຮ່ວມມືຄົ້ນຄ້ວາ, ແລະ ໃນນັ້ນຍັງມີພະນັກງານພາກລັດຈາກພະແນກຈຸລິນຊີ ວິທະຍາ ຈຳນວນ 24 ຄົນ ໂດຍມີ ດຣ ມະນີວັນ ວົງສຸວັດ ເປັນຫົວໜ້າພະແນກ. ໜ່ວຍງານຄົ້ນຄວ້າ LOMWRU ມີ ຫ້ອງວິເຄາະ ທາງພັນທຸກຳ, ຫ້ອງວິເຄາະເຊໂຣໂລຊີ ແລະ ຫ້ອງວິເຄາະຄວາມປອດໄພ ລະດັບ 3 (BSL3) ສຳລັບປຸກເຊື້ອ rickettsial, *Mycobacterium* spp., *B. pseudomallei* ແລະ ເຊື້ອໄວຣັສ. ສຈ. ປອ. ດຣ ມາຍຟອງ ມາຍຊາຍ, ຮອງອະທິການບໍດີ ມະຫາວິທະຍາໄລ ວິທະຍາສາດ ສຸຂະພາບ ຊ່ວຍຊີ້ນຳວຽກງານຮ່ວມມືຄົ້ນຄວ້າກັບບັນດາ ແຂວງ ແລະ ວຽກງານຄົ້ນຄວ້າ ພາກສະໜາມ. ໜ່ວຍງານຄົ້ນຄວ້າ LOMWRU ໄດ້ສະໜັບສະໜຸນການບົ່ງມະຕິພະຍາດທີ່ເກີດຈາກເຊື້ອຈຸລະຊີບໃນ ສ.ປ.ປ ລາວ, ສະໜັບສະໜຸນການຝຶກອົບຮົມ ບັນດານັກເຕັກນິກ ແລະ ນັກວິທະຍາສາດການແພດລາວ ແລະ ຍັງຈັດຕັ້ງປະຕິບັດການສຶກສາຄົ້ນຄວ້າ ໂດຍສະເພາະຂົງເຂດທີ່ກ່ຽວກັບພະຍາດຊຶມເຊື້ອ.

Who we are

The Lao-Oxford-Mahosot Hospital-Wellcome Trust Research Unit (LOMWRU) is a research collaboration between Oxford University and Mahosot Hospital in Vientiane, Lao PDR, with core funding from the Wellcome Trust in the UK. We are part of the MORU Tropical Health Network (THN), which has research units in Thailand, Cambodia, Laos, Myanmar and Democratic Republic of Congo (DRC). The virology department has been partially supported by the Unité des Virus Émergents (UVE), Marseille, France, funded by the Institut de Recherche pour le Développement (IRD), since 2006. Currently, there is a team of 73 research and support staff in the capital and the provinces, working on projects as part of the collaboration, working alongside 24 Lao Government employees led by Dr Manivanh Vongsouvath, Head of the Mahosot Microbiology Laboratory. In addition, LOMWRU has molecular and serology laboratories and a BSL3 laboratory for rickettsial, *Mycobacterium* spp., *Burkholderia pseudomallei* and virus culture. The Head of Field Research is Professor Mayfong Mayxay, who is Vice President of the University of Health Sciences in Vientiane. LOMWRU supports microbiological diagnosis in Laos, trains Lao medical technologists and scientists, and conducts research on a wide range of infectious diseases.

ຮູບພາບ ໃນເດືອນມິຖຸນາ 2023, ທ່ານ ປອ ດຣ ຊຸຊາດ (ນັ່ງດ້ານຂວາ), ຜູ້ອຳນວຍການໂຮງໝໍມະໂຫສົດ ເປັນປະທານ ແລະໄດ້ລົງນາມ ໃນພິທີມອບ-ຮັບ MOU ລະຫວ່າງໂຮງໝໍມະໂຫສົດ ແລະ ໂຄງການ LOMWRU ຈົນເຖິງປີ 2032.

In June 2023 Dr Susath Vongphachanh (*seated, right*), Director of Mahosot Hospital, hosted a ceremony to mark the signing of our new MOU, which runs until 2032. © LOMWRU.

ຄຳເຫັນຂອງທ່ານ

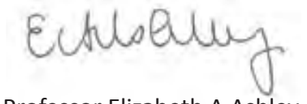
Prof Elizabeth Ashley

ກິດຈະກຳດ້ານການສຶກສາຄົ້ນຄວ້າຂອງພວກເຮົາໄດ້ເລີ່ມຟື້ນຕົວອີກເທື່ອໜຶ່ງໃນປີ 2023 ເນື່ອງຈາກສະຖານະການ ຂອງພະຍາດ COVID-19 ຄ່ອຍໆຫຼຸດລົງຕ່ຳເນື່ອງ. ເຖິງຢ່າງໃດກໍຕາມ ພວກເຮົາຍັງເຫັນຜົນກະທົບຄ້າງຄ້ຳຂອງການຟື້ນໂຕ ທີ່ຜິດປົກກະຕິຂອງເຊື້ອບາງຊະນິດທີ່ກ່ຽວຂ້ອງກັບການການຫຼຸດຜ່ອນມາດຕະການປ້ອງກັນການແຜ່ເຊື້ອໄວຣັສ ລວມທັງ ອັດຕາການສ້າງພູມຄຸ້ມກັນທົ່ວປະເທດທີ່ຫຼຸດລົງໃນໄລຍະການແຜ່ລະບາດ.

ໃນໄລຍະເລີ່ມຕົ້ນແບບກ້າວກະໂດດຂອງການແຜ່ລະບາດພະຍາດ COVID-19 ພວກເຮົາໄດ້ແນໃສ່ການເຮັດການສຶກສາ ຄົ້ນຄວ້າກ່ຽວກັບການຈຳແນກສາຍພັນເຊື້ອ ດ້ວຍຄວາມມຸ່ງຫວັງທີ່ຈະເຫັນນັກຄົ້ນຄວ້າລາວລຸ້ນໃໝ່ໆທີ່ມີຄວາມຊ່ຽວຊານ ໃນດ້ານນີ້. ປີນີ້ໜ່ວຍງານພວກເຮົາມີນັກຄົ້ນຄວ້າສາຍອາຊີບລຸ້ນໃໝ່ທີ່ກຳລັງສຶກສາຕໍ່ໃນລະດັບປະລິນຍາໂທເພີ່ມຫຼາຍຂຶ້ນ ໃນປະເທດໄທ, ປະເທດອັງກິດ ແລະ ປະເທດນິວຊີແລນ. ພວກເຮົາມີຄວາມປິຕິຍິນດີທີ່ໄດ້ຕ້ອນຮັບນັກຄົ້ນຄວ້າອາວຸໂສ ທ່ານ ດຣ Cindy Chu ສູ່ໜ່ວຍງານ LOMWRU ໃນເດືອນສິງຫາ ເພື່ອເຮັດວຽກກ່ຽວກັບການກຳຈັດພະຍາດມາລາເຣຍ ຊະນິດ vivax ແລະ ໂຄງການອື່ນໆ. ທ່ານ ດຣ Cindy ເຄີຍເຮັດວຽກຢູ່ ສປປ ລາວ ກັບໜ່ວຍງານ Health frontiers ຕັ້ງແຕ່ປີ 2006 – 2008 ກ່ອນທີ່ທ່ານຈະຍ້າຍໄປຢູ່ສູນວິໄຈມາຣາເລຍ Shoklo ຢູ່ຊາຍແດນລະຫວ່າງປະເທດໄທ - ມຽນມາ.

ນັບວ່າເປັນເວລາຫຼາຍກວ່າ 2 ປີ ຕັ້ງແຕ່ພວກເຮົາໄດ້ຍ້າຍມາຕຶກພະຍາດຊຶມເຊື້ອໃໝ່ຂອງໂຮງໝໍມະໂຫສົດ ແລະ ການ ກໍ່ສ້າງໄລຍະຖັດມາກໍໄດ້ດຳເນີນໄປຢ່າງໄວວາ. ໜຶ່ງໃນສິ່ງທີ່ພົ້ນເດັ່ນຂອງປີ 2023 ແມ່ນພິທີທີ່ມີຄວາມໝາຍສຳຄັນທີ່ ໂຮງໝໍມະໂຫສົດໄດ້ຮ່ວມແລກປ່ຽນບົດບັນທຶກຄວາມເຂົ້າໃຈທີ່ລົງນາມການຕໍ່ອາຍຸການຮ່ວມມືຄັ້ງລ່າສຸດຈົນເຖິງປີ 2032. ທ່ານ ປອ ດຣ ຊຸຊາດ ວົງພະຈັນ, ຜູ້ອຳນວຍການໂຮງໝໍມະໂຫສົດ ພ້ອມດ້ວຍຄະນະ ທ່ານນາງ ບົວວັນ ປະທຸມ ທອງ, ດຣ ໄຊຊະນະ ສົມບັນດິດ, ດຣ ບຸນໂຮມ ກັນທະວົງ ແລະ ດຣ ໄຄສີ ລາຊະວົງ ທີ່ໄດ້ເຂົ້າຮ່ວມພິທີພ້ອມກັນກັບ ຫົວໜ້າຕາງໜ້າພະແນກຕ່າງໆຂອງໂຮງໝໍມະໂຫສົດ ແລະ ທ່ານ ສຈ Nick Day ແລະ ທ່ານ David Burton ຈາກ MORU Tropical Health Network ແລະ Chief Operating Officer, ຕາມລຳດັບ.

ພວກເຮົາຫວັງວ່າຈະໄດ້ເຮັດວຽກຮ່ວມກັນອີກຫຼາຍໆປີຕໍ່ຈາກນີ້.ຂ້າພະເຈົ້າຂໍກ່າວຄຳຂອບໃຈແກ່ທ່ານ ປອ ດຣ ຊຸຊາດ ວົງ ພະຈັນ, ຜູ້ອຳນວຍການໂຮງໝໍມະໂຫສົດ ແລະ ຄະນະອຳນວຍການພ້ອມທັງພາກສ່ວນກ່ຽວຂ້ອງໃນໂຮງໝໍມະໂຫສົດທີ່ ໃຫ້ການຮ່ວມມື ແລະ ຊ່ວຍເຫຼືອທີ່ດີມາຕະຫຼອດຢ່າງຕໍ່ເນື່ອງ.
ດ້ວຍຄວາມນັບຖື ແລະ ຮັກແພງ,



Professor Elizabeth A Ashley
ຜູ້ອຳນວຍການ LOMWRU

ຮູບພາບ ທີມງານ LOMWRU ໃນການຈັດງານ Pint of Science ທີ່ຮ້ານຄໍເບຍ (Corebeer), ທີ່ນະຄອນຫຼວງວຽງຈັນ ໃນເດືອນພຶດສະພາ 2023. ໃນແຕ່ລະປີ, ງານມະຫະກຳວິທະຍາສາດນີ້ຍັງຈັດຂຶ້ນໃນ 25 ປະເທດທົ່ວໂລກ.

Representatives of the LOMWRU Pint of Science Team outside Corebeer Brewhouse, Vientiane in May 2023. This global science festival takes place in 25 countries worldwide every year. © LOMWRU/MORU. Photographer: Matt Robinson.

Message from the Director

Professor Elizabeth Ashley

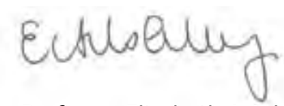
LOMWRU research activities began to ramp up again in 2023 as COVID-19 receded. However, we are still seeing the after-effects in Laos with atypical resurgences of some infections related to relaxation of precautions to prevent virus transmission, and to a drop in immunisation rates in the country during the pandemic.

After a jump-start during COVID, we are taking on more whole-genome sequencing projects and hope to see a new generation of Lao scientists proficient in this method. This year we have more early career scientists studying for master's degrees in Thailand, UK and New Zealand. We were delighted to welcome senior researcher Dr Cindy Chu to LOMWRU in August 2023 to work on vivax malaria elimination, among other projects. Cindy used to work in Laos for Health Frontiers from 2006-2008.

It has been more than two years since we moved into the new Mahosot Hospital Infectious Diseases Building, and the next phase of building works is progressing rapidly. One of the highlights of 2023 was a meaningful ceremony at Mahosot Hospital to exchange our signed Memorandum of Understanding (MoU) following the recent renewal until 2032. Dr Susath Vongphachanh, Director of Mahosot Hospital, and Deputy Directors Mrs Bouavanh Pathoumthong, Dr Xaysana Sombandith, Dr Bounhome Kanthavong and Dr Khaysy Rassavong attended, as did Heads of Department from Mahosot Hospital and MORU THN Director Prof Nick Day and Chief Operating Officer (COO) Mr David Burton. We look forward to continuing to work together for many years to come.

On that note, I would like to thank Dr Susath Vongphachanh, and all the hospital Directors as well as all other colleagues at Mahosot Hospital for their continued collaboration and support.

Best wishes,



Professor Elizabeth A Ashley
Director

ຮູບພາບ (ຊ້າຍຫາຂວາ) Prof Paul Turner (ผู้ถิ่นถอ้าหลัก ของโถงภาม ACORN), Dr Anousone Douangnouvong (ผู้ประสานงาน ของโถงภาม ACORN ประจำ สปป ลาว) ແລະ Dr Miliya Thyl (ผู้ประสานงานของโถงภาม ACORN ประจำประเทดกำปูเจย) ที่ภากประชุม ผู้ถิ่นถอ้าของโถงภาม ACORN ที่บางกอก, ประเทดไท ในอันที่ 14-16 เดือนมินา ปี 2023. © LOMWRU/MORU. Photographer: Elizabeth Ashley.

ผົນການຄົ້ນຄວ້າທີ່ພົ້ນເດັ່ນໃນປີຜ່ານມາ

ການຕ້ານຕໍ່ຢາຕ້ານເຊື້ອຈຸລະຊີບ ແລະ ການນຳໃຊ້ຢາຕ້ານເຊື້ອຈຸລະຊີບ

ການຕ້ານຕໍ່ຢາຕ້ານເຊື້ອຈຸລະຊີບ (AMR) ແລະ ການນຳໃຊ້ຢາຕ້ານເຊື້ອຈຸລະຊີບ (AMU) ຍັງຄົງເປັນຫົວຂໍ້ຫຼັກໃນ ການຄົ້ນຄວ້າວິໄຈ. ໂຮງໝໍມະໂຫສົດ ແລະ ໂຮງໝໍເຊດຖາທິລາດ ເປັນໂຮງໝໍທີ່ໄດ້ເຂົ້າຮ່ວມການຄົ້ນຄວ້າ ACORN (A Clinically Oriented Antimicrobial Resistance Network) ທີ່ມີເຄືອຂ່າຍໃນທົ່ວໂລກ, ໂຮງໝໍທີ່ເຂົ້າຮ່ວມ ການຄົ້ນຄວ້ານີ້ ມີທັງໝົດ 15 ແຫ່ງ ຢູ່ໃນ 9 ປະເທດໃນຂົງເຂດທະວີບອາຊີ ແລະ ທະວີບອາຟຣິກາ, ເຊິ່ງໄດ້ຮັບທຶນ ສະໜັບສະໜູນ ຈາກ Wellcome. ໂຄງການເຝົ້າລະວັງນີ້ໄດ້ເກັບລວບລວມເອົາຂໍ້ມູນຜົນການປິ່ນປົວຂອງຄົນເຈັບ ແລະ ການຊຶມເຊື້ອທີ່ ກ່ຽວຂ້ອງກັບການດູແລຄົນເຈັບໃນໂຮງໝໍ, ເຊິ່ງມີຄວາມແຕກຕ່າງໄປຈາກການເຝົ້າລະວັງທົ່ວໄປທີ່ເນັ້ນໃສ່ເຊື້ອພະຍາດ ເປັນຫຼັກ. ໂຄງການເຝົ້າລະວັງນີ້ ຈະຊ່ວຍໃຫ້ພວກເຮົາເຂົ້າໃຈໄດ້ເຖິງຜົນກະທົບທາງດ້ານຄລີນິກ ແລະ ພາລະແບກຫາບ ທີ່ແທ້ຈິງຂອງການຕ້ານຕໍ່ຢາຕ້ານເຊື້ອຈຸລະຊີບໃນ ສປປ ລາວ. ກ່ອນໜ້ານີ້ ໂຮງໝໍມະໂຫສົດໄດ້ເປັນໜຶ່ງ ໃນສາມ ປະເທດ ເພື່ອທຳການທົດສອບວິທີວິທະຍາຂອງການເຝົ້າລະວັງ ກ່ອນທີ່ຈະຂະຫຍາຍໄປໃນຫຼາຍໆປະເທດ. ຜົນການເຝົ້າ ລະວັງໃນໄລຍະຂອງການທົດສອບວິທີວິທະຍາຂອງການເຝົ້າລະວັງ (Pilot) ຢູ່ໃນ ສປປ ລາວ, ປະເທດ ກຳປູເຈຍ ແລະ ສສ ຫວຽດນາມ, ໃນຊ່ວງເດືອນທັນວາ ປີ 2019 ຈົນເຖິງ ເດືອນຕຸລາ ປີ 2020, ພົບວ່າ ອັດຕາການເສຍຊີວິດໃນມື້ ທີ 28 ນັບຈາກມື້ເຂົ້າຮ່ວມການຄົ້ນຄວ້າແມ່ນ 8.7% ໃນຄົນເຈັບທີ່ເຂົ້າຮ່ວມການເຝົ້າລະວັງ ຈຳນວນທັງໝົດ 2,294 ຄົນ. ການຕ້ານຕໍ່ຢາຕ້ານເຊື້ອ cephalosporins ລຸ້ນທີສາມ (ເຊັ່ນ ceftriaxone) ສູງຢ່າງໜ້າເປັນຫ່ວງ, ເຊິ່ງພົບໄດ້ເຖິງ 54.2% (39/72) ໃນເຊື້ອ *E. coli* ແລະ 38.7% (12/31) ໃນເຊື້ອ *K. pneumoniae* ທີ່ຖືກໄຈ້ແຍກໄດ້. ໝາຍຄວາມ ວ່າສ່ວນໃຫຍ່ແລ້ວ, ຢາທາງເລືອກທຳອິດທີ່ນຳໃຊ້ເຂົ້າໃນການປິ່ນປົວການຊຶມເຊື້ອຮຸນແຮງທີ່ມີສາເຫດມາຈາກການຕິດ ເຊື້ອ Gram negative ແມ່ນບໍ່ມີປະສິດທິຜົນໃນ ສປປ ລາວ.

A Clinically Oriented antimicrobial Resistance surveillance Network (ACORN): pilot implementation in three countries in Southeast Asia, 2019-2020. van Doorn HR, Miliya T, Douangnouvong A, Ta Thi Dieu N, Soputhy C, Lem M, Chommanam D, Keoluangkhot V, Soumphonphakdy B, Rassavong K, Thanadabouth K, Sayarath M, Chansamouth V, Vu MD, Dong PK, Dang VD, Tran VB, Do TKY, Ninh TN, Nguyen HL, Kim NH, Prak S, Vongsouvath M, Van DT, Nguyen TKT, Nguyen HK, Hamers RL, Ling C, Roberts T, Waithira N, Wannapinij P, Vu TVD, Celhay O, Ngoun C, Vongphachanh S, Pham NT, Ashley EA, Turner P. *Wellcome Open Res*. 2022 Dec 22;7:309. doi: 10.12688/wellcomeopenres.18317.1. PMID: 37854668; PMCID: PMC10579863.

ນອກຈາກນີ້ ພວກເຮົາຍັງໄດ້ເປັນສ່ວນໜຶ່ງໃນການທົບທວນເອກະສານກ່ຽວກັບຂໍ້ມູນ ການຕ້ານຕໍ່ຢາຕ້ານເຊື້ອຈຸລະຊີບ ໃນກຸ່ມ ປະຊາກອນເດັກນ້ອຍ ໃນຂົງເຂດອາຊີຕາເວັນອອກສຽງໃຕ້. ເຊິ່ງຜົນການສຶກສາ ໄດ້ສະແດງໃຫ້ເຫັນອັດຕາທີ່ ໜ້າຕົກໃຈຂອງການຊຶມເຊື້ອ ທີ່ມີສາເຫດຈາກເຊື້ອຕ້ານຕໍ່ຢາຕ້ານເຊື້ອໃນເດັກອ່ອນ (infants) ແລະ ເດັກນ້ອຍ, ເຊິ່ງ ວ່າຢາຕ້ານເຊື້ອທາງເລືອກທຳອິດຫຼາຍຕົວແມ່ນບໍ່ມີປະສິດທິພາບ ໃນການປິ່ນປົວພະຍາດຊຶມເຊື້ອທົ່ວໄປທີ່ຖືກພົບເຫັນ ເລື້ອຍໆ. Ampicillin ສາມາດຄວບຄຸມແຕ່ 26% ຂອງເຊື້ອພະຍາດທີ່ຖືກໄຈ້ແຍກໄດ້ຈາກການຊຶມເຊື້ອເລືອດ/ ອັກເສບ ເຍື່ອຫຸ້ມສະໝອງໃນເດັກແດງ (neonatal) ເທົ່ານັ້ນ. ໃນຂະນະທີ່ gentamicin ກໍ່ສາມາດຄວບຄຸມໄດ້ພຽງແຕ່ 45% ເທົ່ານັ້ນ.

Coverage gaps in empiric antibiotic regimens used to treat serious bacterial infections in neonates and children in Southeast Asia and the Pacific. Williams PCM, Jones M, Snelling TL, Duguid R, Moore N, Dickson B, Wu Y, Saunders J, Wijeratne P, Douangnouvong A, Ashley EA, Turner P. *Lancet Reg Health Southeast Asia*. 2023 Oct 31;22:100291. doi: 10.1016/j.lansea.2023.100291. PMID: 38482147; PMCID: PMC10934317.

ໃນຂະນະທີ່ຄວາມຊົງຈຳກ່ຽວກັບການລະບາດຂອງພະຍາດ COVID-19 **ກຳລັງຈາງຫາຍໄປ** ແຕ່ເຊື້ອໄວຣັສຍັງບໍ່ທັນ ໄດ້ຫາຍໄປໃສເທື່ອ. ພວກເຮົາເປັນສ່ວນໜຶ່ງຂອງການຄົ້ນຄວ້າທົດລອງທາງຄລີນິກ (**clinical trial**) ທີ່ນຳພາໂດຍ ເພື່ອນຮ່ວມງານຂອງພວກເຮົາທີ່ຢູ່ ໜ່ວຍງານຄົ້ນຄວ້າ ມະຫາວິທະຍາໄລ ມະຫິດົນ-ອ໋ອກຟອດ (MORU) ເພື່ອເບິ່ງ ຄວາມໄວໃນການຕອບສະໜອງຂອງເຊື້ອໄວຣັສ ຕ່ໍການປິ່ນປົວ ໃນຄົນເຈັບທີ່ມີອາການບໍ່ຮ້າຍແຮງ ຈຸດປະສົງແມ່ນເພື່ອ ປະເມີນປະສິດທິພາບໃນການປິ່ນປົວ ຂອງຢາຕ້ານເຊື້ອໄວຣັສຕົວໃໝ່. ວິທີການນີ້ອາດຊ່ວຍໃນການປະເມີນຢາຕ້ານເຊື້ອ ໄວຣັສ ໃນສະຖານະການທີ່ມີການລະບາດອັນໃໝ່ ເນື່ອງຈາກ ການສຶກສາຕ້ອງການຈຳນວນຄົນເຈັບບໍ່ຫຼາຍ ທີ່ສາມາດ ຊ່ວຍໃນການຄັດເລືອກຕົວຢ່າງໄວວາ ເຊິ່ງຢາດັ່ງກ່າວຈະເປັນຕົວຢາບຸລິມະສິດ ເພື່ອໃຊ້ໃນການສຶກສາທົດລອງທາງຄລີນິກຂະໜາດໃຫຍ່. ການສຶກສາ PLATCOV (Platform trial of antiviral pharmacodynamics in early symptomatic COVID-19; NCT05041907) ແມ່ນກຳລັງດຳເນີນການຄົ້ນຄວ້າຢູ່ພະແນກປອດ ແລະ ວັນນະໂລກ ຂອງໂຮງໝໍ ມະໂຫສົດ ຕັ້ງແຕ່ ປີ 2022 ເຊິ່ງນຳພາໂດຍ ດຣ. ສິສຸພັນ ວິດາມາລີ ພ້ອມດ້ວຍທີມງານ. ຜ່ານມາທີມງານກຳໄດ້ຕີພິມຜົນ ຂອງຢາ **ivermectin** (ເຊິ່ງບໍ່ພົບປະສິດທິພາບຂອງຢາໃນການກຳຈັດເຊື້ອໄວຣັສ ໃນຄົນເຈັບທີ່ເປັນ COVID-19), **remdesivir** (ຊ່ວຍເລັ່ງໃນການກຳຈັດເຊື້ອໄວຣັສ), ແລະ **molnupiravir** (ຊ່ວຍເລັ່ງໃນການກຳຈັດເຊື້ອໄວຣັສ). ພວກເຮົາ ຄາດຫວັງວ່າຈະເລີ່ມການຄົ້ນຄວ້າ AD ASTRA (NCT05648448) ໃນເດືອນໜ້າ ເຊິ່ງເປັນການສຶກສາຄ້າຍຄືກັນທີ່ເຮັດ ໃນຄົນເຈັບທີ່ຕິດເຊື້ອ **influenza**.

Antiviral efficacy of molnupiravir versus ritonavir-boosted nirmatrelvir in patients with early symptomatic COVID-19 (PLATCOV): an open-label, phase 2, randomised, controlled, adaptive trial. Schilling WHK, Jittamala P, Watson JA, Boyd S, Luvira V, Siripoon T, Ngamprasertchai T, Batty EM, Cruz C, Callery JJ, Singh S, Saroj M, Kruabkontho V, Ngernseng T, Tanglakmankhong N, Tubprasert J, Abdad MY, Madmanee W, Kouhathong J, Suwannasin K, Pagornrat W, Piaraksa N, Hanboonkunupakarn P, Hanboonkunupakarn B, Poovorawan K, Potaporn M, Srisubat A, Loharjun B, Taylor WRJ, Chotivanich V, Chotivanich K, Imwong M, Pukrittayakamee S, Dondorp AM, Day NPJ, Teixeira MM, Piyaphanee W, Phumratanaprapin W, White NJ; PLATCOV Collaborative Group. *Lancet Infect Dis*. 2024 Jan;24(1):36-45. doi: 10.1016/S1473-3099(23)00493-0. Epub 2023 Sep 28. Erratum in: Lancet Infect Dis. 2023 Dec;23(12):e511. PMID: 37778363; PMCID: PMC7615401.

ເສດຖະສາດສາທາລະນະສຸກ

ບົດລາຍງານການຄົ້ນຄ້ວາຄັ້ງທຳອິດຂອງໜ່ວຍງານໃໝ່ໃນການຢັ້ງຢືນ ແລະ ນະໂຍບາຍດ້ານສຸຂະພາບ (UHEP), ເຊິ່ງຕັ້ງຢູ່ ທີ່ມະຫາວິທະຍາໄລວິທະຍາສາດສຸຂະພາບ ໃນນະຄອນຫຼວງວຽງຈັນ ທີ່ໄດ້ຮັບການຕີພິມໃນປີນີ້. ນີ້ແມ່ນການວິເຄາະຄວາມ ຄຸ້ມຄ່າຂອງຕົ້ນທຶນເພື່ອກວດສອບຜົນກະທົບຂອງການນຳໃຊ້ວັກຊີນ conjugate typhoid (TCV) ໃນປະເທດລາວ.

ກົງກັນຂ້າມກັບຜົນໄດ້ຮັບຂອງການວິເຄາະອື່ນໆທີ່ວິເຄາະໂດຍບໍ່ໄດ້ນຳໃຊ້ຂໍ້ມູນຂອງປະເທດລາວ, ພວກເຮົາພົບວ່າການໂຮມເອົາ TCV ເຂົ້າໃນໂຄງການສັກຢາກັນພະຍາດແຫ່ງຊາດນັ້ນຈະຄຸ້ມຄ່າຖ້າຫາກຈຳນວນການເກີດພະຍາດໄຂ້ທໍລະພິດທີ່ແທ້ຈິງແມ່ນສູງກວ່າທີ່ພວກເຮົາຄາດຄະເນໄວ້ເຖິງ 25 ເທົ່າ. ນີ້ແມ່ນຂໍ້ມູນທີ່ສຳຄັນເພື່ອສະໜອງໃຫ້ແກ່ກຸ່ມທີ່ປຶກສາດ້ານວິຊາການທາງພູມຄຸ້ມກັນແຫ່ງຊາດທີ່ກຳລັງຄຸ້ມຄອງກ່ຽວກັບການຫັນປ່ຽນທີ່ມີຄວາມຍາກລຳບາກຈາກໝ່ວຍງານ Gavi ທີ່ສະໜັບສະໜຸນການສັກຢາວັກຊີນໃນປະເທດລາວ.

Cost-effectiveness analysis of typhoid vaccination in Lao PDR. Soukavong M, Luangasanatip N, Chanthavilay P, Teerawattananon Y, Dabak SV, Pan-Ngum W, Roberts T, Ashley EA, Mayxay M. *BMC Public Health*. 2023 Nov 17;23(1):2270. doi: 10.1186/s12889-023-17221-2. PMID: 37978481.

ໃນຫົວຂໍ້ທີ່ຄ້າຍຄືກັນ, ພວກເຮົາໄດ້ມີການຮ່ວມມືກັບ **PATH** ເພື່ອປະເມີນຄ່າໃຊ້ຈ່າຍຂອງການເຈັບປ່ວຍຂອງພະຍາດສະໝອງອັກເສບຍີ່ປຸ່ນ (**JE**), ທັງໃນໄລຍະທີ່ມີອາການແບບກະທັນຫັນ ແລະ ໄລຍະຍາວ, ທີ່ມາຈາກຜົນສືບເນື່ອງທາງດ້ານລະບົບປະສາດທີ່ຮ້າຍແຮງເຊິ່ງມັກມີຄວາມກ່ຽວຂ້ອງກັບພະຍາດ **JE**. ພວກເຮົາພົບວ່າຄ່າໃຊ້ຈ່າຍສະເລ່ຍຂອງການເຂົ້ານອນປິ່ນປົວໃນໂຮງໝໍຍ້ອນພະຍາດ **JE** ແບບກະທັນຫັນແມ່ນປະມານ 2,000 ດອລລ່າ, ເຊິ່ງສູງກວ່າລາຍຮັບຂອງຄອບຄົວທົ່ວໄປຢ່າງຫຼວງຫຼາຍ, ແລະ ສິ່ງຜົນໃຫ້ບາງຄອບຄົວຕ້ອງມີໜີ້ສິນຫຼາຍປີ. ພະຍາດ **JE** ເປັນພະຍາດທີ່ສາມາດປ້ອງກັນໄດ້ ແລະ ວັກຊີນດັ່ງກ່າວໄດ້ມີການນຳໃຊ້ຢູ່ທົ່ວປະເທດລາວຕັ້ງແຕ່ປີ 2015 ເປັນຕົ້ນມາ ເຖິງແມ່ນວ່າບໍ່ມີຄົນເຈັບໃນການສຶກສາຂອງພວກເຮົາຈື່ໄດ້ວ່າເຄີຍໄດ້ຮັບວັກຊີນແລ້ວກໍ່ຕາມ. ມີພຽງແຕ່ໂຮງໝໍມະໂຫສົດເທົ່ານັ້ນທີ່ສາມາດບົ່ງມະຕິພະຍາດ **JE** ໄດ້ເປັນປະຈຳໂດຍການນຳໃຊ້ເຕັກນິກທາງເຊຣັ່ມ ແລະ ໂມເລກຸນປະສົມກັນ. ການຂາດການເຂົ້າເຖິງການບົ່ງມະຕິການຕິດເຊື້ອໃນລະບົບປະສາດສູນກາງ **CNS**, ແລະ ຄວາມຈິງທີ່ວ່າການບົ່ງມະຕິໃນປະຈຸບັນແມ່ນຍັງບໍ່ໄດ້ດີເທົ່າທີ່ຄວນ, ເຊິ່ງເປັນອຸປະສັກໃນການປະເມີນບັນຫາຂອງພະຍາດທີ່ແທ້ຈິງໃນປະເທດ.

Estimating the cost of illness of acute Japanese encephalitis and sequelae care in Vietnam and Laos: A cross-sectional study. Nguyen ALT, Slavkovsky R, Phan HT, Nguyen HTT, Vannachone S, Le DH, Dubot-Pérès A, Vongsouvath M, Dinh ST, Marfin AA, Letson GW, Vu HM, Tham DC, Mayxay M, Ashley EA, Pham TQ, Pecenka C. *PLOS Glob Public Health*. 2023 Jun 13;3(6):e0001873. doi: 10.1371/journal.pgph.0001873. PMID: 37310946; PMCID: PMC10263309.

Vayouly Vidhamaly (*left*) and Mayulee Thalongsengchanh from LOMWRU's Clinical Trials Support Group checking research data during a visit to Attapeu Provincial Hospital. © LOMWRU/MORU. Photographer: Elizabeth Ashley.

Lao members of the South and Southeast Asian Community Based Trials Network (SEACTN) recruiting patients for the study, which is an ambitious attempt to delineate the incidence, causes and outcomes of febrile illness in the region. © LOMWRU.

Research highlights in 2023

Here we highlight a selection of research outputs of LOMWRU and partner organisations published in 2023. The complete list with abstracts is found in the Publications section of the report.

Antimicrobial resistance (AMR) and antimicrobial use (AMU)

Antimicrobial resistance (AMR) and antimicrobial use (AMU) continue to be a major research theme. Mahosot Hospital and Setthathirath Hospital are sites for the global multicentre ACORN (A Clinically Oriented antimicrobial Resistance Network) project, taking place at 15 hospitals across nine Asian and African countries, funded by Wellcome. This surveillance project is different to conventional pathogen-focused surveillance in that we also collect data on patient outcomes and healthcare-associated infections, which will help us to understand the clinical impact and true burden of AMR in Laos. Mahosot Hospital was a site for the earlier ACORN pilot project which tested the methodology in three countries before scaling up. Results of the pilot, which ran in Laos, Cambodia and Viet Nam, from December 2019 until October 2020, showed that among 2294 patients recruited the 28-day mortality was 8.7%. Resistance to third-generation cephalosporins (eg ceftriaxone) was concerningly high in 54.2% (39/72) of *E. coli* and 38.7% (12/31) of *K. pneumoniae* isolates. This means that the standard first-line empirical treatment for serious infection in Laos is no longer effective in most cases of Gram-negative sepsis.

A Clinically Oriented antimicrobial Resistance surveillance Network (ACORN): pilot implementation in three countries in Southeast Asia, 2019-2020. van Doorn HR, Miliya T, Douangnouvong A, Ta Thi Dieu N, Soputhy C, Lem M, Chommanam D, Keoluangkhot V, Soumphonphakdy B, Rassavong K, Thanadabouth K, Sayarath M, Chansamouth V, Vu MD, Dong PK, Dang VD, Tran VB, Do TKY,

Ninh TN, Nguyen HL, Kim NH, Prak S, Vongsouvath M, Van DT, Nguyen TKT, Nguyen HK, Hamers RL, Ling C, Roberts T, Waithira N, Wannapinij P, Vu TVD, Celhay O, Ngoun C, Vongphachanh S, Pham NT, Ashley EA, Turner P. *Wellcome Open Res*. 2022 Dec 22;7:309. doi: 10.12688/wellcomeopenres.18317.1. PMID: 37854668; PMCID: PMC10579863.

We were also part of a systematic review of AMR data in the paediatric population in Southeast Asia which shows alarming rates of drug-resistant infections in infants and young children rendering many first-line empirical antibiotic regimens ineffective at targeting common causes of infections. Ampicillin only covered 26% of the pathogens isolated in neonatal sepsis/meningitis while gentamicin did not fare much better at 45% coverage.

Coverage gaps in empiric antibiotic regimens used to treat serious bacterial infections in neonates and children in Southeast Asia and the Pacific. Williams PCM, Jones M, Snelling TL, Duguid R, Moore N, Dickson B, Wu Y, Saunders J, Wijeratne P, Douangnouvong A, Ashley EA, Turner P. *Lancet Reg Health Southeast Asia*. 2023 Oct 31;22:100291. doi: 10.1016/j.lansea.2023.100291. PMID: 38482147; PMCID: PMC10934317.

COVID-19

While the memory of the COVID-19 pandemic may be fading the virus has not gone away. We are part of a clinical trial led by our MORU colleagues which uses the early virological response to treatment in patients with non-severe early symptomatic disease to predict the therapeutic efficacy of new antiviral agents. This promising approach could revolutionise assessment of antivirals in another pandemic situation, since it requires a relatively small number of patients, enabling earlier selection of medicines which should be prioritised for evaluation in larger trials with clinical endpoints. The PLATCOV study (Platform trial of antiviral pharmacodynamics in early symptomatic COVID-19; NCT05041907) has been running in Mahosot Hospital with the Lung Ward team, led by Dr Sisouphanh Vidhamaly, since 2022. So far, the group have published the results for ivermectin (no effect on viral clearance in early symptomatic COVID-19), remdesivir (accelerates viral clearance), and molnupiravir (accelerates viral clearance). We plan to start the AD ASTRA study (NCT05648448) soon, which is a similar study in patients with influenza.

Antiviral efficacy of molnupiravir versus ritonavir-boosted nirmatrelvir in patients with early symptomatic COVID-19 (PLATCOV): an open-label, phase 2, randomised, controlled, adaptive trial. Schilling WHK, Jittamala P, Watson JA, Boyd S, Luvira V, Siripoon T, Ngamprasertchai T, Batty EM, Cruz C, Callery JJ, Singh S, Saroj M, Kruabkontho V, Ngernseng T, Tanglakmankhong N, Tubprasert J, Abdad MY, Madmanee W, Kouhathong J, Suwannasin K, Pagornrat W, Piaraksa N, Hanboonkunupakarn P, Hanboonkunupakarn B, Poovorawan K, Potaporn M, Srisubat A, Loharjun B, Taylor WRJ, Chotivanich V, Chotivanich K, Imwong M, Pukrittayakamee S, Dondorp AM, Day NPJ, Teixeira MM, Piyaphanee W, Phumratanaprapin W, White NJ; PLATCOV Collaborative Group. Lancet Infect Dis. 2024 Jan;24(1):36-45. doi: 10.1016/S1473-3099(23)00493-0. Epub 2023 Sep 28. Erratum in: Lancet Infect Dis. 2023 Dec;23(12):e511. PMID: 37778363; PMCID: PMC7615401.

Health economics

The first research output of the new Unit for Health Evidence and Policy (UHEP), based at the University of Health Sciences in Vientiane was published this year. This was a cost-effectiveness analysis examining the impact of introducing typhoid conjugate vaccine (TCV) in Laos. Contrary to the results of another analysis conducted without using Lao data, we found that inclusion of TCV in the national immunization program would only be cost-effective if the true typhoid incidence is 25 times higher than our estimate. This is important information to provide to the National Immunisation Technical Advisory Group who are managing the difficult transition from Gavi support of vaccination in Laos.

Cost-effectiveness analysis of typhoid vaccination in Lao PDR. Soukavong M, Luangasanatip N, Chanthavilay P, Teerawattananon Y, Dabak SV, Pan-Ngum W, Roberts T, Ashley EA, Mayxay M. *BMC Public Health*. 2023 Nov 17;23(1):2270. doi: 10.1186/s12889-023-17221-2. PMID: 37978481; PMCID: PMC10656839.

On a similar theme, we collaborated with PATH to estimate the cost of illness of Japanese encephalitis (JE), both during the acute episode and longer term, given the severe neurological sequelae often associated with JE. We found that the average cost of hospitalization with acute JE was around 2,000 USD, well above the typical household income, and leading to years of debt for some families. JE is a preventable disease and the vaccine has been available nationwide in Laos since 2015, although no patients in our study remembered being vaccinated. Only Mahosot Hospital can routinely make the diagnosis of JE using a combination of serological and molecular techniques. Lack of access to diagnosis of CNS infections, and the fact current diagnostics are not very sensitive, are barriers to estimating the true burden of disease in the country.

Estimating the cost of illness of acute Japanese encephalitis and sequelae care in Vietnam and Laos: A cross-sectional study. Nguyen ALT, Slavkovsky R, Phan HT, Nguyen HTT, Vannachone S, Le DH, Dubot-Pérès A, Vongsouvath M, Dinh ST, Marfin AA, Letson GW, Vu HM, Tham DC, Mayxay M, Ashley EA, Pham TQ, Pecenka C. *PLOS Glob Public Health*. 2023 Jun 13;3(6):e0001873. doi: 10.1371/journal.pgph.0001873. PMID: 37310946; PMCID: PMC10263309.

Pi Mai Lao party games in the Mahosot Microbiology Laboratory in April 2023. © LOMWRU/MORU. Photographer: Elizabeth Ashley.

Training highlights in 2023

Tehmina Bharucha on her graduation day with her daughter Annabel. © LOMWRU/MORU. Photo: Tehmina Bharucha.

Training scientists and technicians is one of our key activities and we have seen an increase in the number of early career researchers entering Master's programmes recently.

Postgraduate Training

Doctoral students

Congratulations to **Dr Tehmina Bharucha** who had her DPhil graduation ceremony on 5 Aug 2023 at the University of Oxford. Tehmina's thesis was titled 'Protein promise? Application of mass spectrometry-based proteomics techniques to identify cerebrospinal fluid biomarkers for diagnosing suspected central nervous system infections - a focus on Japanese encephalitis virus infection' and her supervisors were Nicole Zitzmann, Paul Newton and Audrey Dubot-Pérès. Tehmi was a previous research physician at LOMWRU and we would all like to congratulate her on this huge achievement.

Dr Vilada Chansamouth is in the final year of her DPhil with the University of Oxford as part of her Wellcome Trust International Training Fellowship. She is studying the implementation of national antimicrobial treatment guidelines, delivered in paper-based format and on a smartphone application, on prescribing in a stepped-wedge cluster-randomised trial.

Pharmacist Konnie Bellingham, previously with MORU's Medicine Quality Research Group (MQRG), started her PhD through The Open University UK mid-2023. Konnie aims to provide evidence that economic analysis is a necessary and achievable criterion that should be included in the antimicrobial selection process for the National Essential Medicines Listing of Lao PDR.

Master's students

Dr Manophab Luangraj, LOMWRU Research Physician, passed his MSc in epidemiology from the London School of Hygiene & Tropical Medicine (LSHTM) in 2023. He put his newly acquired skills to good use for his project on The Epidemiology and Risk Factors of Severe Melioidosis in the Lao PDR: An 18-Year Prospective Hospital-Based Study.

Dr Tim Venkatesan, an MSc student in Tropical Medicine & International Health from the London School of Hygiene & Tropical Medicine, came to Vientiane May-July 2023 to conduct his MSc project, supervised by Prof David Dance, former Senior Clinical Fellow at LOMWRU, and by LOMWRU's Tamalee Roberts and Matthew Robinson here in Laos. Tim was able to demonstrate the presence of *B. pseudomallei* in Vientiane aquaria, with implications for the international trade in Southeast Asian ornamental fish.

Mr Vanheuang Phommadeechack, Rickettsia technician and BSL3 Laboratory Manager, continued his two-year Master's degree course in Tropical Medicine at Mahidol University, Bangkok. This year, Vanheuang focused on his thesis: looking at the risk of vector-borne diseases being transmitted between household pets and their owners in Vientiane, in particular spotted fever rickettsia. This builds on previous work by IFMT/Lao TPH Master's student Manh Hung Nguyen (2018) by looking for serological evidence of infections in both pets and their owners. In addition, Vanheuang trialled the use of MALDI-TOF for the identification of arthropod vectors collected from pets. Vanheuang was awarded the 2023 Sylvia Meek Scholarship for Entomology, which supports students to study entomology at universities in Nigeria, South Africa and Thailand. Vanheuang was the only student awarded the scholarship in Thailand in 2023.

Dr Inthaphavanh Kitignavong (*left*) and **Dr Laddaphone Bounvilay** (*right*) finally made the journey to New Zealand in February 2023 after long COVID-related delays. They are both studying for an MSc in Public Health at the University of Auckland.

Ms Amphone Sengduangphachanh, Senior Mahosot Laboratory technician, is studying for an MSc in Clinical Microbiology and Laboratory Management, a hybrid course organized by Siriraj Hospital in Bangkok.

Ms Manilung Nalongsack, LOMWRU Research Pharmacist, has been awarded a prestigious Chevening Scholarship by the UK government. Manilung recently completed a one-year internship at the Health Intervention and Technology Assessment Program (HITAP) in Bangkok, and is currently studying for a Master's in Health Policy, Planning and Financing at LSHTM and the London School of Economics (LSE).

Veterinarian **Dr Vilaiphone Phomsisavath** joined LOMWRU in 2022 when she was awarded a Fellowship by the Southeast Asia One Health University Network (SEAOHUN) to investigate *Escherichia coli* isolates from pigs and humans in Lao PDR for colistin resistance. In 2023, after completing her fellowship successfully, she applied for and was awarded a scholarship by the Institute of Tropical Medicine (Antwerp) and the Belgian Development Cooperation to study for an MSc in Global One Health: diseases at the human-animal interface. This is a part-time course over two years, starting in January 2024, which includes periods of study in Belgium and South Africa.

Other training

UK Fleming Fund Lao country grant

LOMWRU and the Mahosot Hospital microbiology laboratory continued to support Fleming Fund activities in Laos in 2023 in collaboration with Fondation Mérieux and the National Centre for Laboratory and Epidemiology (NCLE). The Fleming Fund is a UK Aid programme that aims to support the strengthening of national AMR surveillance systems and laboratories, and improve public awareness of AMR and global data use. LOMWRU/Mahosot Hospital support five provincial hospital laboratory sites within Laos (Xieng Khuang, Salavan, Luang Namtha, Savannakhet and Vientiane Province) with NCLE/Fondation Mérieux supporting another five. This year once again saw a lot of activities. There were two weeks' onsite training at the five provincial laboratories in July. Provincial laboratory staff came for intensive two-week training sessions at Mahosot Hospital four times in 2023 with a focus on specimen processing, organism identification processes and antimicrobial susceptibility testing techniques and interpretation. In October, 10 infectious diseases clinicians came for a week of training at LOMWRU/Mahosot Hospital with daily board and lab rounds and afternoon training sessions and case presentations. October also saw 10 nurses from provincial hospitals come for training in the Infectious Diseases Ward at Mahosot Hospital with sessions on aseptic techniques for taking blood cultures and other samples, and correctly filling out request forms. The highlight of 2023 was a June workshop where staff from the five provincial hospitals (hospital directors, infectious diseases doctors, nurses and lab staff), and representatives from Fondation Mérieux, NCLE and WHO attended. The meeting included updates on the activities of LOMWRU-supported Fleming Fund sites, an AMR update, challenges to treatment in Laos, diagnostic stewardship, including a case study from Xieng Khuang Hospital, and concluded with lively breakout group discussions focusing on lab training and diagnostic stewardship. The Lao country grant will be extended for another 2 years with a focus on quality data and laboratory quality management systems.

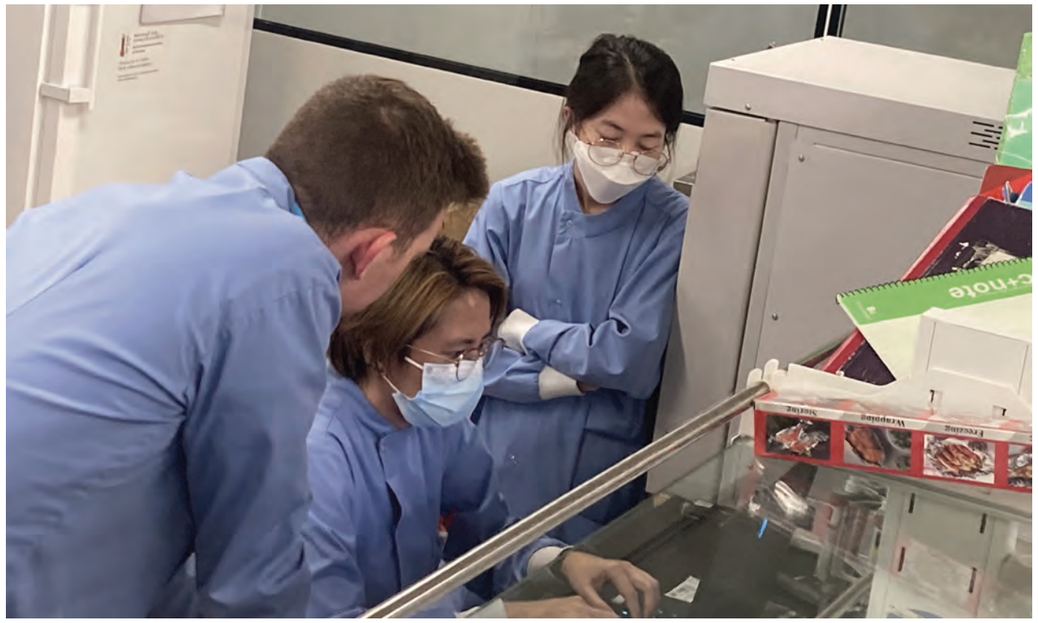
Site Initiation Visit (SIV) training at LOMWRU for the MEL-OB1 study, a clinical observational study of melioidosis taking place in Thailand and Laos. © LOMWRU. Photo: Vayouly Vidhamaly.

International Master's course in Tropical Medicine and International Health at the Lao Tropical Medicine and Public Health Institute

Staff from LOMWRU/Mahosot Hospital Microbiology Department participated in teaching 12 Master's students studying Tropical Medicine and International Health at the Lao Tropical Medicine and Public Health Institute. Staff delivered lectures on infectious diseases, clinical microbiology, and antimicrobial resistance. There was also a two-day practical session at the Mahosot Hospital microbiology laboratory with training in microbiology and molecular biology techniques.

Whole-genome sequencing

COVID-19 gave us a kick-start to do more whole-genome sequencing (WGS). LOMWRU is increasing the number of projects incorporating Oxford Nanopore WGS. Starting end May 2023, Dr Mike Wiley and Mr Ryan Chapman from the University of Nebraska, USA gave a two-week training on hybrid-capture sequencing and Bioinformatics to Siribun Panapruksachat, Manila Souksavanh, Malavanh Vongsouvath and Vilaiphone Phomsisavath. This was part of our surveillance of acute respiratory infection and febrile illness work in collaboration with NAMRU-IP.



From left, Ryan Chapman, Siribun Panapruksachat and Manila Souksavanh during a hybrid-capture sequencing training. © LOMWRU/MORU.

Leadership skills training

In December 2023 Dr Koukeo Phommasone, Deputy Head of Mahosot Microbiology Laboratory, completed 21 months of training and coaching sessions focusing on leadership, communication, and skills of personal effectiveness as part of MORU's Make a Difference (MaD) programme, created by Rob Hale, an executive coach. MaD brought together members of staff from every unit and department of the MORU Tropical Health Network, with participants coming from all grades and disciplines (scientists and administrators). The key to MORU's continued success is establishing strong teamwork and leadership across the organisation.

The 2023 Make a Difference graduates in Bangkok including the coach Rob Hale (*5th from left),* MORU Director Prof Nick Day, and Koukeo Phommasone (*2rd from right*). © LOMWRU/MORU. Photographer: Gerhard Jørén.

LOMWRU publications in 2023

In 2023 LOMWRU published 35 articles, book chapters or letters in peer-reviewed journals and gave eight presentations at scientific conferences. Abstracts are reproduced below with articles grouped by theme.

Microbiology, including antimicrobial resistance (AMR)

Evolutionary and functional history of the *Escherichia coli* K1 capsule. Arredondo-Alonso S, Blundell-Hunter G, Fu Z, Gladstone RA, Fillol-Salom A, Loraine J, Cloutman-Green E, Johnsen PJ, Samuelsen Ø, Pöntinen AK, Cléon F, Chavez-Bueno S, De la Cruz MA, Ares MA, Vongsouvath M, Chmielarczyk A, Horner C, Klein N, McNally A, Reis JN, Penadés JR, Thomson NR, Corander J, Taylor PW, McCarthy AJ. *Nat Commun*. 2023 **14**(1): 3294. DOI: 10.1038/s41467-023-39052-w. PMID: 37322051. PMCID: PMC10272209.

The K1 capsule was detected in 25% of E. coli *bloodstream infections and is associated with extra-intestinal infection. The K1 genetic locus is usually associated with an additional pathogenicity island. The capsule protects against complement deposition. Enzymatic removal of the capsule is a potential novel therapeutic approach and resulted in increased complement binding and reduced bacterial survival in human serum.*

E. coli is a leading cause of invasive bacterial infections in humans. Capsule polysaccharide has an important role in bacterial pathogenesis, and the K1 capsule has been firmly established as one of the most potent capsule types in *E. coli* through its association with severe infections. However, little is known about its distribution, evolution and functions across the *E. coli* phylogeny, which is fundamental to elucidating its role in the expansion of successful lineages. Using systematic surveys of invasive *E. coli* isolates, we show that the K1-*cps* locus is present in a quarter of bloodstream infection isolates and has emerged in at least four different extraintestinal pathogenic *E. coli* (ExPEC) phylogroups independently in the last 500 years. Phenotypic assessment demonstrates that K1 capsule synthesis enhances *E. coli* survival in human serum independent of genetic background, and that therapeutic targeting of the K1 capsule re-sensitizes *E. coli* from distinct genetic backgrounds to human serum. Our study highlights that assessing the evolutionary and functional properties of bacterial virulence factors at population levels is important to better monitor and predict the emergence of virulent clones, and to inform therapies and preventive medicine to effectively control bacterial infections while significantly lowering antibiotic usage.

Global diversity and antimicrobial resistance of typhoid fever pathogens: Insights from a meta-analysis of 13,000 *Salmonella* Typhi genomes. Carey ME, Dyson AZ, Ingle DJ, Amir A, Aworh MK, Chattaway MA, et al. *Elife*. 2023 **12**: e85867. DOI: 10.7554/eLife.85867. PMID: 37697804. PMCID: PMC10506625.

The newly established Global Typhoid Genomics Consortium conducted a meta-analysis of 13,000 S. *Typhi genomes. The geographic and temporal changes in antimicrobial susceptibility profiles that are identified are important for devising treatment guidelines and in guiding vaccination strategies. Travel-related cases provide additional data for source countries with scarce sequencing capacity. The Consortium supports ongoing data sharing and collaboration.*

BACKGROUND:

The Global Typhoid Genomics Consortium was established to bring together the typhoid research community to aggregate and analyse *Salmonella enterica* serovar Typhi (Typhi) genomic data to inform public health action. This analysis, which marks 22 years since the publication of the first Typhi genome, represents the largest Typhi genome sequence collection to date (n=13,000).

METHODS:

This is a meta-analysis of global genotype and AMR determinants extracted from previously sequenced genome data and analysed using consistent methods implemented in open analysis platforms GenoTyphi and Pathogenwatch.

RESULTS:

Compared with previous global snapshots, the data highlight that genotype 4.3.1 (H58) has not spread beyond Asia and Eastern/Southern Africa; in other regions, distinct genotypes dominate and have independently evolved AMR. Data gaps remain in many parts of the world, and we show the potential of travel-associated sequences to provide informal 'sentinel' surveillance for such locations. The data indicate that ciprofloxacin non-susceptibility (>1 resistance determinant) is widespread across geographies and genotypes, with high-level ciprofloxacin resistance (≥3 determinants) reaching 20% prevalence in South Asia. Extensively drug-resistant (XDR) typhoid has become dominant in Pakistan (70% in 2020) but has not yet become established elsewhere. Ceftriaxone resistance has emerged in eight non-XDR genotypes, including a ciprofloxacin-resistant lineage (4.3.1.2.1) in India. Azithromycin resistance mutations were detected at low prevalence in South Asia, including in two common ciprofloxacin-resistant genotypes.

CONCLUSIONS:

The consortium's aim is to encourage continued data sharing and collaboration to monitor the emergence and global spread of antimicrobial resistant Typhi, and to inform decision-making around the introduction of typhoid conjugate vaccines (TCVs) and other prevention and control strategies.

ACORN (A Clinically-Oriented Antimicrobial Resistance Surveillance Network) II: protocol for case based antimicrobial resistance surveillance. Mo Y, Ding Y, Cao Y, Hopkins J, Ashley EA, Waithira N, et al. *Wellcome Open Res*. 2023 **8**: 179. DOI: 10.12688/wellcomeopenres.19210.2. PMID: 37854055. PMCID: PMC10579854.

The ACORN II and ACORN-HAI protocols described here build upon the ACORN study, extending much needed clinical-based antimicrobial surveillance in multiple countries in Africa and Asia, and including all bacterial infection admissions. This study will address the data void linking AMR and outcomes from LMICs while prioritising antibiotic and diagnostic stewardship activities.

BACKGROUND:

AMR surveillance is essential for empiric antibiotic prescribing, infection prevention and control policies and to drive novel antibiotic discovery. However, most existing surveillance systems are isolate-based without supporting patient-based clinical data, and not widely implemented especially in low- and middle-income countries (LMICs).

METHODS:

A Clinically-Oriented Antimicrobial Resistance Surveillance Network (ACORN) II is a large-scale multicentre protocol which builds on the WHO Global Antimicrobial Resistance and Use Surveillance System to estimate syndromic and pathogen outcomes along with associated health economic costs. ACORN-healthcare associated infection (ACORN-HAI) is an extension study which focuses on healthcare-associated bloodstream infections and ventilator-associated pneumonia. Our main aim is to implement an efficient clinically-oriented AMR surveillance system, which can be incorporated as part of routine workflow in hospitals in LMICs. These surveillance systems include hospitalised patients of any age with clinically compatible acute community-acquired or healthcare-associated bacterial infection syndromes, and who were prescribed parenteral antibiotics. Diagnostic stewardship activities will be implemented to optimise microbiology culture specimen collection practices. Basic patient characteristics, clinician diagnosis, empiric treatment, infection severity and risk factors for HAI are recorded on enrolment and during 28-day follow-up. An R Shiny application can be used offline and online for merging clinical and microbiology data, and generating collated reports to inform local antibiotic stewardship and infection control policies.

DISCUSSION:

ACORN II is a comprehensive AMR surveillance activity which advocates pragmatic implementation and prioritises improving local diagnostic and antibiotic prescribing practices through patient-centred data collection. These data can be rapidly communicated to local physicians and infection prevention and control teams. Relative ease of data collection promotes sustainability and maximises participation and scalability. With ACORN-HAI as an example, ACORN II has the capacity to accommodate extensions to investigate further specific questions of interest.

Diagnostics for Typhoid Fever: Current Perspectives and Future Outlooks for Product Development and Access. Sapkota J, Roberts T, Basnyat B, Baker S, Hampton LM, Dittrich S. *Open Forum Infectious Diseases* 2023 **10**(Suppl 1): S17–S20. DOI: 10.1093/ofid/ofad120. PMID: 37274534. PMCID: PMC10236505.

The performance of existing diagnostic tests for typhoid fever is inadequate, and there are no assays optimised for use in rural or low-resource settings. Therefore, there is an unknown prevalence of this disease in many areas, and this prevents appropriate roll-out and efficacy assessment of vaccination campaigns.

Typhoid is an enteric disease caused by *Salmonella* Typhi. Like many febrile illnesses, typhoid presents with nonspecific symptoms. In routine healthcare settings in low- and middle-income settings, typhoid fever is suspected and treated empirically. Though many diagnostic tests are available for typhoid diagnosis, there are currently no diagnostic tests that meet ideal requirements for sensitivity, specificity, speed, and cost-effectiveness. With introduction of typhoid conjugate vaccine, it is essential to explore the current and future typhoid approach in the context of use case and access to ensure their utilization for disease control.

The highly diverse plasmid population found in *Escherichia coli* colonizing travellers to Laos and its role in antimicrobial resistance gene carriage. Snaith AE, Dunn SJ, Moran RA, Newton PN, Dance DAB, Davong V, Kuenzli E, Kantele A, Corander J, McNally A. *Microb Genom* 2023 **9**(5): mgen001000. DOI: 10.1099/mgen.0.001000. PMID: 37171860. PMCID: PMC10272864.

Long-read sequencing was used to sequence plasmids from 48 E. coli *isolates from stool. 105 distinct, diverse plasmids were identified. 38% carried resistance genes, including ESBL- and colistin-resistance genes, with evidence of stable accumulation of resistance genes on individual plasmids. Some of these plasmids are probably maintained as they also confer resistance to heavy metals.*

Increased colonization by antimicrobial-resistant organisms is closely associated with international travel. This study investigated the diversity of mobile genetic elements involved with AMR gene carriage in extended-spectrum beta-lactamase (ESBL)-producing *E. coli* that colonized travellers to Laos. Long-read sequencing was used to reconstruct complete plasmid sequences from 48

isolates obtained from the daily stool samples of 23 travellers over a 3-week period. This method revealed a collection of 105 distinct plasmids, 38.1% (*n*=40) of which carried AMR genes. The plasmids in this population were diverse, mostly unreported and included 38 replicon types, with F-type plasmids (*n*=23) the most prevalent amongst those carrying AMR genes. Fine-scale analysis of all plasmids identified numerous AMR gene contexts and emphasized the importance of IS elements, specifically members of the IS*6*/IS*26* family, in the evolution of complex multidrug resistance regions. We found a concerning convergence of ESBL and colistin resistance determinants, with three plasmids from two different F-type lineages carrying $bla_{(CTX\text{-}M)}$ and *mcr* genes. The extensive diversity seen here highlights the worrying probability that stable new vehicles for AMR will evolve in *E. coli* populations that can disseminate internationally through travel networks.

A Clinically Oriented antimicrobial Resistance surveillance Network (ACORN): pilot implementation in three countries in Southeast Asia, 2019-2020. van Doorn HR, Miliya T, Douangnouvong A, Ta Thi Dieu N, Soputhy C, Lem M, Chommanam D, Keoluangkhot V, Soumphonphakdy B, Rassavong K, Thanadabouth K, Sayarath M, Chansamouth V, Vu MD, Dong PK, Dang VD, Tran VB, Do TKY, Ninh TN, Nguyen HL, Kim NH, Prak S, Vongsouvath M, Van DT, Nguyen TKT, Nguyen HK, Hamers RL, Ling C, Roberts T, Waithira N, Wannapinij P, Vu TVD, Celhay O, Ngoun C, Vongphachanh S, Pham NT, Ashley EA, Turner P. *Wellcome Open Res* 2022 **7**: 309. DOI: 10.12688/wellcomeopenres.18317.1. PMID: 37854668. PMCID: PMC10579863.

2294 patients were enrolled in this case-based AMR surveillance study, which is a blueprint for larger-scale studies. Addition of clinical data in real time is valuable to clinicians and policy makers, and the data remains compatible with AMR networks. Overall mortality was 8.7%, though markedly higher in adults (21.7%). ESBL E. coli *rates were 54% across the 3 countries. A plausible pathogen was identified in 11.7% of cases.*

BACKGROUND:

Case-based surveillance of AMR provides more actionable data than isolate- or sample-based surveillance. We developed A Clinically Oriented antimicrobial Resistance surveillance Network (ACORN) as a lightweight but comprehensive platform, in which we combine clinical data collection with diagnostic stewardship, microbiological data collection and visualisation of the linked clinical-microbiology dataset. Data are compatible with WHO GLASS surveillance and can be stratified by syndrome and other metadata. Summary metrics can be visualised and fed back directly for clinical decision-making and to inform local treatment guidelines and national policy.

METHODS:

An ACORN pilot was implemented in three hospitals in Southeast Asia (1 paediatric, 2 general) to collect clinical and microbiological data from patients with community- or hospital-acquired pneumonia, sepsis, or meningitis. The implementation package included tools to capture site and laboratory capacity information, guidelines on diagnostic stewardship, and a web-based data visualisation and analysis platform.

RESULTS:

Between December 2019 and October 2020, 2294 patients were enrolled with 2464 discrete infection episodes (1786 community-acquired, 518 healthcare-associated and 160 hospital-acquired). Overall, 28-day mortality was 8.7%. Third generation cephalosporin resistance was identified in 54.2% (39/72) of *E. coli* and 38.7% (12/31) of *K. pneumoniae* isolates . Almost a quarter of *S. aureus* isolates were methicillin resistant (23.0%, 14/61). 290/2464 episodes could be linked to a pathogen, highlighting the level of enrolment required to achieve an acceptable volume of isolate data. However, the combination with clinical metadata allowed for more nuanced interpretation and immediate feedback of results.

CONCLUSIONS:

ACORN was technically feasible to implement and acceptable at site level. With minor changes from lessons learned during the pilot ACORN is now being scaled up and implemented in 15 hospitals in 9 low- and middle-income countries (LMICs) to generate sufficient case-based data to determine incidence, outcomes, and susceptibility of target pathogens among patients with infectious syndromes.

Coverage gaps in empiric antibiotic regimens used to treat serious bacterial infections in neonates and children in Southeast Asia and the Pacific. Williams PCM, Jones M, Snelling TL, Duguid R, Moore N, Dickson B, Wu Y, Saunders J, Wijeratne P, Douangnouvong A, Ashley EA, Turner P. *Lancet Reg Health Southeast Asia*. 2023 Oct 31;22:100291. doi: 10.1016/j.lansea.2023.100291. PMID: 38482147; PMCID: PMC10934317.

Pathogens and their antibiotic susceptibility rates for neonatal and paediatric infections were systematically drawn for the literature. Modelling these data demonstrates that WHO-recommended empiric antibiotic regimens are ineffective for a significant number of cases of sepsis and meningitis. Urgent review of empiric regimens is required, particularly in regions where antibiotic resistance rates are high and laboratory infrastructure is poor.

BACKGROUND:

High levels of AMR are propagating deaths due to neonatal and paediatric infections globally. This is of particular concern in Southeast Asia and the Pacific, where healthcare resources are constrained and access to newer agents to treat multidrug-resistant pathogens is limited.

METHOD:

To assess the coverage provided by commonly prescribed empiric antibiotic regimens for children in Southeast Asia and the Pacific, we built a weighted incidence syndromic combination antibiogram (WISCA), parameterised using data obtained from a systematic review of published literature incorporating WHO-defined SEARO and WPRO regions in Ovid MEDLINE, EMBASE, Global Health and PubMed. Susceptibility data for bacterial pathogens were extracted to provide coverage estimates for pre-specified antibiotics (aminopenicillins, gentamicin, third-generation cephalosporins and carbapenems), reported at the regional level.

FINDINGS:

6648 bacterial isolates from 11 countries across 86 papers were included in the Bayesian WISCA model, which weighted bacterial incidence and antimicrobial susceptibility of relevant isolates. Coverage provided by aminopenicillins in neonatal sepsis/meningitis was 26% (80% credible interval: 16–49) whilst gentamicin coverage was 45% (29–62). Third-generation cephalosporin coverage was only 29% (16–49) in neonatal sepsis/meningitis, 51% (38–64) in paediatric sepsis and 65% (51–77) in paediatric meningitis. Carbapenems were estimated to provide the highest coverage: 81% (65–90) in neonatal sepsis/meningitis, 83% (72–90) in paediatric sepsis and 79% (62–91) in paediatric meningitis.

INTERPRETATION:

These findings reveal alarmingly high rates of resistance to commonly prescribed empirical therapies for neonatal and paediatric sepsis and meningitis in the Asia–Pacific region.

Meliodosis

Melioidosis in Global Perspective and Challenges for Surveillance. Chapter 1 in *Clinical Melioidosis: A Practical Guide to Diagnosis and Management*. Dance DA. Ed. Mohapatra PR. *CRC Press* 2023. DOI 10.1201/9781003324010.

Over the past 40 years, it has become apparent that melioidosis is not only highly endemic in Southeast Asia and northern Australia but is also widespread elsewhere in the tropics. Modelling suggests that there could be as many as 165,000 cases in 79 countries around the world each year, leading to some 89,000 deaths, with some 44% of these occurring in South Asia. In reality, far fewer cases than this are being diagnosed. There are numerous obstacles to accurate surveillance, especially since this is an infection that predominantly affects the rural poor, who are the last people to have access to good diagnostics. The potential for *Burkholderia pseudomallei* to be used as a bioweapon has had beneficial spin-offs, no matter how unlikely it is ever to be used in this way. Nonetheless, melioidosis deserves to be formally recognized as a neglected tropical disease (NTD) in the hope that this will help to raise awareness, improve management, and reduce the avoidable death toll from this silent killer.

Glanders & Melioidosis. In *Zoonoses: Infections affecting humans and animals*. Virk HS, Nic Fhogartaigh C, Dance DA. Ed Sing A. *Springer Cham* 2023. DOI https://doi.org/10.1007/978-3-030-85877-3_35-1.

This fascinating book chapter encompasses the history, epidemiology, pathogenesis, and treatment of glanders and melioidosis with an additional focus on their zoonotic characteristics. It is highly readable and will deepen all readers' understanding of these neglected diseases.

Malaria

Pf7: an open dataset of *Plasmodium falciparum* genome variation in 20,000 worldwide samples. Abdel Hamid MM, Abdelraheem MH, Acheampong DO, Ahouidi A, Ali M, Almagro-Garcia J, et al. *Wellcome Open Res* 2023 **8**: 22. DOI: 10.12688/wellcomeopenres.18681.1. PMID: 36864926. PMCID: PMC9971654.

Pf7 is a brand-new dataset of 20,000 Plasmodium falciparum *whole genome sequences from across the globe. Significant advances in sequencing methods allowed dried blood spot samples to be used. The open-access dataset is extensively annotated, with particular attention given to mutations impacting on drug susceptibility and vaccine efficacy.*

We describe the MalariaGEN Pf7 data resource, the seventh release of *P. falciparum* genome variation data from the MalariaGEN network. It comprises over 20,000 samples from 82 partner studies in 33 countries, including several malaria endemic regions that were previously underrepresented. For the first time we include dried blood spot samples that were sequenced after selective whole genome amplification, necessitating new methods to genotype copy number variations. We identify many newly emerging *crt* mutations in parts of Southeast Asia, and show examples of heterogeneities in patterns of drug resistance within Africa and within the Indian subcontinent. We describe the profile of variations in the C-terminal of the csp gene and relate this to the sequence used in the RTS,S and R21 malaria vaccines. Pf7 provides high-quality data on genotype calls for 6 million SNPs and short indels, analysis of large deletions that cause failure of rapid diagnostic tests, and systematic characterisation of six major drug resistance loci, all of which can be freely downloaded from the MalariaGEN website.

Virology

Deep proteomics network and machine learning analysis of human cerebrospinal fluid in Japanese encephalitis virus infection. Bharucha T, Gangadharan B, Kumar A, Myall AC, Ayhan N, Pastorino B, Chanthongthip A, Vongsouvath M, Mayxay M, Sengvilaipaseuth O, Phonemixay O, Rattanavong S, O'Brien DP, Vendrell I, Fischer R, Kessler B, Turtle L, de Lamballerie X, Dubot-Pérès A, Newton PN, Zitzmann N, SEAe Consortium. *J Proteome Res* 2023 **22**(6): 1614–1629. PMID: 37219084. PMCID: PMC10246887. DOI: 10.1021/acs.jproteome.2c00563.

The proteome of CSF samples from patients with Japanese encephalitis (JE) was compared to patients with other central nervous system infections. Proteins with altered regulation were identified, and 9 were selected as a signature of JE infection. These may have a role in the development of a rapid diagnostic test, and allow a deeper understanding of the biology of JE infection.

Japanese encephalitis (JE) virus is a leading cause of neurological infection in the Asia-Pacific region with no means of detection in more remote areas. We aimed to test the hypothesis of a JE protein signature in human cerebrospinal fluid (CSF) that could be harnessed in a rapid diagnostic test (RDT), contribute to understanding the host response and predict outcome during infection. Liquid chromatography and tandem mass spectrometry (LC-MS/MS), using extensive offline fractionation and tandem mass tag labelling (TMT), enabled comparison of the deep CSF proteome in JE vs other confirmed neurological infections (non-JE). Verification was performed using data-independent acquisition (DIA) LC-MS/MS. 5,070 proteins were identified, including 4,805 human proteins and 265 pathogen proteins. Feature selection and predictive modeling using TMT analysis of 147 patient samples enabled the development of a nine-protein JE diagnostic signature. This was tested using DIA analysis of an independent group of 16 patient samples, demonstrating 82% accuracy. Ultimately, validation in a larger group of patients and different locations could help refine the list to 2-3 proteins for an RDT. The mass spectrometry proteomics data have been deposited to the ProteomeXchange Consortium via the PRIDE partner repository with the dataset identifier PXD034789 and 10.6019/PXD034789.

Implementation of recommendations on the use of corticosteroids in severe COVID-19. Camirand-Lemyre F, Merson L, Tirupakuzhi Vijayaraghavan BK, Burrell AJC, Citarella BW, Domingue MP, Lévesque S, Usuf E, Wils EJ, Ohshimo S, Martin-Loeches I, Sandulescu O, Laake JH, Lamontagne F; ISARIC Clinical Characterisation Group. *JAMA Netw Open* 2023 **6**(12): e2346502. DOI: 10.1001/jamanetworkopen.2023.46502. PMID: 38147336. PMCID: PMC10751594.

Increased use of life-saving corticosteroids in severe COVID was seen globally following publication of the landmark RECOVERY trial and WHO guidelines. However, adoption of guidelines was poorest in Africa. Implementation of the guidelines was poorest in countries that contributed least to the clinical trials, and emphasizes the need for all countries to contribute to, and be represented in, clinical research.

IMPORTANCE:

Research diversity and representativeness are paramount in building trust, generating valid biomedical knowledge, and possibly in implementing clinical guidelines.

OBJECTIVES:

To compare variations over time and across World Health Organization (WHO) geographic regions of corticosteroid use for treatment of severe COVID-19; secondary objectives were to evaluate the association between the timing of publication of the RECOVERY (Randomised Evaluation of COVID-19 Therapy) trial (June 2020) and the WHO guidelines for corticosteroids (September 2020) and the temporal trends observed in corticosteroid use by region and to describe the geographic distribution of the recruitment in clinical trials that informed the WHO recommendation.

DESIGN, SETTING, AND PARTICIPANTS:

This prospective cohort study of 434 851 patients was conducted between January 31, 2020, and September 2, 2022, in 63 countries worldwide. The data were collected under the auspices of the International Severe Acute Respiratory and Emerging Infections Consortium (ISARIC)-WHO Clinical Characterisation Protocol for Severe Emerging Infections. Analyses were restricted to patients hospitalized for severe COVID-19 (a subset of the ISARIC data set).

EXPOSURE:

Corticosteroid use as reported to the ISARIC-WHO Clinical Characterisation Protocol for Severe Emerging Infections.

MAIN OUTCOMES AND MEASURES:

Number and percentage of patients hospitalized with severe COVID-19 who received corticosteroids by time period and by WHO geographic region.

RESULTS:

Among 434 851 patients with confirmed severe or critical COVID-19 for whom receipt of corticosteroids could be ascertained (median [IQR] age, 61.0 [48.0-74.0] years; 53.0% male), 174 307 (40.1%) received corticosteroids during the study period. Of the participants in clinical trials that informed the guideline, 91.6% were recruited from the United Kingdom. In all regions, corticosteroid use for severe COVID-19 increased, but this increase corresponded to the timing of the RECOVERY trial (time-interruption coefficient 1.0 [95% CI, 0.9-1.2]) and WHO guideline (time-interruption coefficient 1.9 [95% CI, 1.7-2.0]) publications only in Europe. At the end of the study period, corticosteroid use for treatment of severe COVID-19 was highest in the Americas (5421 of 6095 [88.9%]; 95% CI, 87.7-90.2) and lowest in Africa (31 588 of 185 191 [17.1%]; 95% CI, 16.8-17.3).

CONCLUSIONS AND RELEVANCE:

The results of this cohort study showed that implementation of the guidelines for use of corticosteroids in the treatment of severe COVID-19 varied geographically. Uptake of corticosteroid treatment was lower in regions with limited clinical trial involvement. Improving research diversity and representativeness may facilitate timely knowledge uptake and guideline implementation.

A multi-country analysis of COVID-19 hospitalizations by vaccination status. Gonçalves BP, Jassat W, Baruch J, Hashmi M, Rojek A, Dasgupta A, Martin-Loeches I, Reyes LF, Piubelli C, Citarella BW, Kartsonaki C, Lefèvre B, López Revilla JW, Lunn M, Harrison EM, Kraemer MUG, Shrapnel S, Horby P, Bisoffi Z, Olliaro PL, Merson L; ISARIC Clinical Characterisation Group. *Med* 2023 **4**(11): 797–812. DOI: 10.1016/j.medj.2023.08.005. PMID: 37738979.

The clinical features and outcomes of >83,000 patients hospitalised with SARS-CoV-2 infection in 38 countries were compared, stratified by vaccination status. Countries varied by vaccine coverage, presenting symptoms, predominant circulating variant, and patient cohorts included. Noting that patients with co-morbidities were more likely to be vaccinated early in the pandemic, in this analysis, mortality rates were higher in unvaccinated patient groups.

BACKGROUND:

Individuals vaccinated against severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), when infected, can still develop disease that requires hospitalisation. It remains unclear whether these patients differ from hospitalized unvaccinated patients with regard to presentation, coexisting comorbidities, and outcomes.

METHODS:

Here, we use data from an international consortium to study this question and assess whether differences between these groups are context specific. Data from 83,163 hospitalized COVID-19 patients (34,843 vaccinated, 48,320 unvaccinated) from 38 countries were analysed.

FINDINGS:

While typical symptoms were more often reported in unvaccinated patients, comorbidities, including some associated with worse prognosis in previous studies, were more common in vaccinated patients. Considerable between-country variation in both in-hospital fatality risk and vaccinated-versus-unvaccinated difference in this outcome was observed.

CONCLUSIONS:

These findings will inform allocation of healthcare resources in future surges as well as design of longer-term international studies to characterise changes in clinical profile of hospitalized COVID-19 patients related to vaccination history.

Estimating the cost of illness of acute Japanese encephalitis and sequelae care in Vietnam and Laos: A cross-sectional study. Nguyen ALT, Slavkovsky R, Phan HT, Nguyen HTT, Vannachone S, Le DH, Dubot-Pérès A, Vongsouvath M, Dinh ST, Marfin AA, Letson GW, Vu HM, Tham DC, Mayxay M, Ashley EA, Pham TQ, Pecenka C. *PLOS Global Public Health* 2023 **3**(6): e0001873. DOI: 10.1371/journal.pgph.0001873. PMID: 37310946. PMCID: PMC10263309.

Detailed, holistic analysis of acute, short-term and long-term costs associated with JE in Viet Nam and Laos showed that these are frequently catastrophic, and often involved expensive loans. Other intangible losses include school and work absence. The WHO has pre-qualified several vaccines, which are cost-effective or highly cost-saving, but most patients had not been vaccinated.

BACKGROUND:

JE is a leading cause of acute encephalitis syndrome and resulting neurological disability in Asia and the Western Pacific. This study aims to estimate the cost of acute care, initial rehabilitation and sequelae care, in Viet Nam and Laos.

METHODOLOGY:

We conducted a cross-sectional retrospective study using a micro-costing approach from the health system and household perspectives. Out-of-pocket direct medical and non-medical costs, indirect costs, and family impact were reported by patients and/or caregivers. Hospitalization costs were extracted from hospital charts. Acute costs covered expenditures from pre-hospital to follow-up visits while sequelae care costs were estimated from expenditures in the last 90 days. All costs are in 2021 US dollars.

PRINCIPAL FINDINGS:

242 patients in two major sentinel sites in the North and South of Viet Nam and 65 patients in a central hospital in Vientiane, Laos, with laboratory-confirmed JE were recruited regardless of age, sex, and ethnicity. In Viet Nam, the mean total cost was $3,371 per acute JE episode (median $2,071, standard error [SE] $464) while annual costs were $404 for initial sequelae care (median $0, SE $220) and $320 for long-term sequelae care (median $0, SE $108). In Laos, the mean hospitalization costs in acute stage were $2,005 (median $1,698, SE $279) and the mean annual costs were $2,317 (median $0, SE $2,233) for initial sequelae care and $89 (median $0, SE $57) for long-term sequelae care. In both countries, most patients did not seek care for their sequelae. Families perceived extreme impact from JE and 20% to 30% of households still had sustained debts years after acute JE.

CONCLUSIONS:

JE patients and families in Viet Nam and Laos suffer extreme medical, economic, and social hardship. This has policy implications for improving JE prevention in these two JE-endemic countries.

Antiviral efficacy of molnupiravir versus ritonavir-boosted nirmatrelvir in patients with early symptomatic COVID-19 (PLATCOV): an open-label, phase 2, randomised, controlled, adaptive trial. Schilling WHK, Jittamala P, Watson JA, Boyd S, Luvira V, … Day NPJ, Teixeira MM, Piyaphanee W, Phumratanaprapin W, White NJ; PLATCOV Collaborative Group. *Lancet Infect Dis*. 2024Jan;**24**(1):36-45. doi: 10.1016/S1473-3099(23)00493-0. Epub 2023 Sep 28.

The rate of SARS-CoV-2 viral clearance (a surrogate for clinical efficacy) in mild COVID-19 infections was faster if patients were receiving molnupiravir (37% faster) or ritonavir/nirmatrelvir (84% faster). Treatment with molnupiravir was not non-inferior. Viral and symptom rebound was commoner in the ritonavir/nirmatrelvir arm, and viral mutations were more common when treated with molnupiravir.

BACKGROUND:

Molnupiravir and ritonavir-boosted nirmatrelvir are the two leading oral COVID-19 antiviral treatments, but their antiviral activities in patients have not been compared directly. The aim of this ongoing platform trial is to compare different antiviral treatments using the rate of viral clearance as the measure of antiviral effect.

METHODS:

PLATCOV is an open-label, multicentre, phase 2, randomised, controlled, adaptive pharmacometric platform trial running in Thailand, Brazil, Pakistan, and Laos. The component of the trial reported here was conducted in the Hospital for Tropical Diseases, Faculty of Tropical Medicine, Mahidol University, Bangkok, Thailand. We recruited low-risk adult patients aged 18-50 years with early symptomatic COVID-19 (<4 days of symptoms). Eligible patients were randomly assigned using block randomisation via a centralised web app to one of seven treatment groups: molnupiravir, ritonavir-boosted nirmatrelvir, casirivimab-imdevimab, tixagevimab-cilgavimab, favipiravir, fluoxetine, or no study drug. The no study drug group always comprised a minimum proportion of 20% of patients, with uniform randomisation ratios applied across the active treatment groups. Results for the concurrently randomised molnupiravir, ritonavir-boosted nirmatrelvir, and no study drug groups are reported here. The primary endpoint was the rate of oropharyngeal viral clearance assessed in a modified intention-to-treat population, defined as patients with more than 2 days of follow-up. Safety was assessed in all participants who took at least one dose of the medication. The viral clearance rate was derived under a Bayesian hierarchical linear model fitted to the log(10) viral densities in standardised duplicate oropharyngeal swab eluates taken daily over 1 week (18 measurements). Treatment groups with a probability of more than 0.9 that viral clearance was accelerated by more than 20% compared with no drug entered a non-inferiority comparison (with a 10% non-inferiority margin) compared with the platform's current most effective drug. This ongoing trial is registered at ClinicalTrials.gov, NCT05041907.

FINDINGS:

From 6 June 2022-23 Feb 2023, 209 patients in Thailand were enrolled and concurrently randomly assigned to molnupiravir (n=65), ritonavir-boosted nirmatrelvir (n=59), or no study drug (n=85). 129 (62%) of the patients were female and 80 (38%) were male. Relative to the no study drug group, the rates of viral clearance were 37% (95% credible interval 16-65) faster with molnupiravir and 84% (54-119) faster with ritonavir-boosted nirmatrelvir. In the non-inferiority comparison, viral clearance was 25% (10-38) slower with molnupiravir than ritonavir-boosted nirmatrelvir. Molnupiravir was removed from the study platform when it reached the prespecified inferiority margin of 10% compared with ritonavir-boosted nirmatrelvir. Median estimated viral clearance half-lives were 8.5 h (IQR 6.7-10.1) with ritonavir-boosted nirmatrelvir, 11.6 h (8.6-15.4) with molnupiravir, and 15.5 h (11.9-21.2) with no study drug. Viral rebound occurred more frequently following nirmatrelvir (six [10%] of 58) compared with the no study drug (one [1%] of 84; p=0.018) or the molnupiravir (one [2%] of 65; p=0.051) groups. Persistent infections following molnupiravir had more viral mutations (three of nine patients had an increased number of single nucleotide polymorphisms in samples collected at 7 or more days compared with those at baseline) than after nirmatrelvir (zero of three) or no study drug (zero of 18). There were no adverse events of grade 3 or worse, or serious adverse events in any of the reported treatment groups.

INTERPRETATION:

Both molnupiravir and ritonavir-boosted nirmatrelvir accelerate oropharyngeal SARS-CoV-2 viral clearance in patients with COVID-19, but the antiviral effect of ritonavir-boosted nirmatrelvir was substantially greater. Measurement of oropharyngeal viral clearance rates provides a rapid and well tolerated approach to the assessment and comparison of antiviral drugs in patients with COVID-19. It should be evaluated in other acute viral respiratory infections.

Epidemiological profile of dengue in Champasak and Savannakhet provinces, Lao People's Democratic Republic, 2003-2020. Zafar S, Overgaard HJ, Pongvongsa T, Vannavong N, Phommachanh S, Shipin O, Rocklov J, Paul RE, Rahman MS, Mayxay M. *Western Pac Surveill Response J*. 2022;13(4): 1-13. Epub 20221123. doi: 10.5365/wpsar.2022.13.4.932. PMID: 36817500; PMCID: PMC9912291.

Surveillance data for dengue was collected in Champasak and Savannakhet between 2003 and 2019. These two provinces account for 33% of all cases nationally. High-transmission seasons occurred in 2013 and 2019. Children and young adults remain the most at risk. Cases are increasingly being reported away from densely populated districts, likely due to extensive development in these areas.

Dengue is a public health issue in tropical Southeast Asia responsible for significant morbidity and mortality. Information on dengue epidemiology is necessary to develop strategies to control infections effectively. In Lao PDR, Champasak and Savannakhet provinces account for around 30% of the national dengue burden. In this study, the dengue epidemiological profile in these two southern Lao provinces was described by analysing seasonal and spatial dengue notification data from 2003–2020 using the long-term mean (LTM) method. Savannakhet had a higher LTM (132.0 cases/month, 95% confidence interval [CI]: 92.2–171.7) than Champasak (113.3 cases/month, 95% CI: 86.0–140.5), with peaks in dengue notifications following the rainy season in both provinces. The highest notification rates were observed July to September; these months were also when the LTM was most frequently exceeded. Previously, dengue notifications were largely confined to the western districts of Savannakhet and the northern districts of Champasak, but more recently, notifications have increased in the eastern districts of Savannakhet and southern districts of Champasak. While the notification rate remained high in children and young adults (5–30 years), especially among students and farmers, a shift in the age structure of dengue cases was observed, with a greater proportion of notifications now occurring in those aged over 30 years. Community-based vector control and prevention programmes are needed to restrict the spread of dengue into new geographical areas in the southern provinces of Lao PDR.

Other infectious diseases

Chronic pulmonary aspergillosis: clinical presentation and management. Evans TJ, Lawal A, Kosmidis C, Denning DW. *Semin Respir Crit Care Med*. 2024 Feb;45(1):88-101. doi: 10.1055/s-0043-1776914. Epub 2023 Dec 28. PMID: 38154471

Chronic pulmonary aspergillosis is massively under-diagnosed, despite significant attributable morbidity and mortality. It has a variety of clinical subtypes which are reviewed here, along with diagnosis, differential diagnosis, treatment and questions for further research.

Chronic pulmonary aspergillosis (CPA) refers to several clinical syndromes resulting from the presence and local proliferation of *Aspergillus* organisms in the lungs of patients with chronic lung disease. CPA is more common than was realised two decades ago. Recognition remains poor, despite recent studies from many countries highlighting the high prevalence in at-risk populations. CPA may be misdiagnosed and treated as tuberculosis (TB). In addition, CPA may develop following successful TB treatment. The coronavirus disease pandemic has resulted in significant disruption to provision of TB care, likely leading to more extensive lung damage, which could increase the risk for CPA. Although CPA refers to various syndromes, the classic presentation is that of chronic cavitary pulmonary aspergillosis, which manifests as one or more progressive cavities with or without a fungal ball, accompanied by systemic and respiratory symptoms for at least 3 months. Diagnosis relies on *Aspergillus* immunoglobulin G in serum, as sputum culture lacks sensitivity. Differential diagnosis includes mycobacterial infection, bacterial lung abscess or necrotizing pneumonia, lung cancer, and endemic fungi. The aim of antifungal treatment in CPA is to improve symptoms and quality of life, and to halt progression, and possibly reverse radiological changes. Current recommendations suggest treatment for 6 months, although in practice many patients remain on long-term treatment. Improvement may manifest as weight gain and improvement of symptoms such as productive cough, haemoptysis, and fatigue. Surgical management should be considered in cases of diagnostic uncertainty, in significant haemoptysis, and when there is concern for lack of response to therapy. Itraconazole and voriconazole are the first-line azoles, with more experience now accumulating with posaconazole and isavuconazole. Side effects are frequent and careful monitoring including therapeutic drug monitoring is essential. Intravenous antifungals such as echinocandins and amphotericin B are used in cases of azole intolerance or resistance, which often develop on treatment. Relapse is seen after completion of antifungal therapy in around 20% of cases, mostly in bilateral, high-burden disease. Several research priorities have been identified, including characterization of immune defects and genetic variants linked to CPA, pathogenetic mechanisms of *Aspergillus* adaptation in the lung environment, the contribution of non-*fumigatus Aspergillus* species, and the role of new antifungal agents, immunotherapy, and combination therapy.

Global, regional, and national burden of meningitis and its aetiologies, 1990-2019: a systematic analysis for the Global Burden of Disease Study 2019. GBD 2019 Meningitis Antimicrobial Resistance Collaborators. *Lancet Neurol*. 2023 Aug;**22**(8):685-711. doi: 10.1016/S1474-4422(23)00195-3. PMID: 37479374; PMCID: PMC10356620.

This detailed description of the incidence, mortality and aetiology of meningitis stratified by location and age charts progress towards the WHO's goals to reduce meningitis mortality by 2030. An estimated 2.51 million cases of meningitis occurred in 2019, causing 236,000 deaths. Since 1990, age-standardised mortality has fallen from 7.5 per 100,000 to 3.3 per 100,000 population.

BACKGROUND:

Although meningitis is largely preventable, it still causes hundreds of thousands of deaths globally each year. WHO set ambitious goals to reduce meningitis cases by 2030, and assessing trends in the global meningitis burden can help track progress and identify gaps in achieving these goals. Using data from the Global Burden of Diseases, Injuries, and Risk Factors Study (GBD) 2019, we aimed to assess incident cases and deaths due to acute infectious meningitis by aetiology and age from 1990 to 2019, for 204 countries and territories.

METHODS:

We modelled meningitis mortality using vital registration, verbal autopsy, sample-based vital registration, and mortality surveillance data. Meningitis morbidity was modelled with a Bayesian compartmental model, using data from the published literature identified by a systematic review, as well as surveillance data, inpatient hospital admissions, health insurance claims, and cause-specific meningitis mortality estimates. For aetiology estimation, data from multiple causes of death, vital registration, hospital discharge, microbial laboratory, and literature studies were analysed by use of a network analysis model to estimate the proportion of meningitis deaths and cases attributable to the following aetiologies: *Neisseria meningitidis*, *Streptococcus pneumoniae*, *Haemophilus influenzae*, group B *Streptococcus*, *Escherichia coli*, *Klebsiella pneumoniae*, *Listeria monocytogenes*, *Staphylococcus aureus*, viruses, and a residual other pathogen category.

FINDINGS:

In 2019, there were an estimated 236,000 deaths (95% uncertainty interval [UI] 204,000-277,000) and 2.51m (2.11-2.99) incident cases due to meningitis globally. The burden was greatest in children younger than 5 years, with 112,000 deaths (87,400-145,000) and 1.28 million incident cases (0.947-1.71) in 2019. Age-standardised mortality rates decreased from 7.5 (6.6-8.4) per 100,000 population in 1990 to 3.3 (2.8-3.9) per 100,000 population in 2019. The highest proportion of total all-age meningitis deaths in 2019 was attributable to *S. pneumoniae* (18.1% [17.1-19.2]), followed by *N. meningitidis* (13.6% [12.7-14.4]) and *K. pneumoniae* (12.2% [10.2-14.3]). Between 1990 and 2019, *H. influenzae* showed the largest reduction in the number of deaths among children younger than 5 years (76.5% [69.5-81.8]), followed by *N. meningitidis* (72.3% [64.4-78.5]) and viruses (58.2% [47.1-67.3]).

INTERPRETATION:

Substantial progress has been made in reducing meningitis mortality over the past three decades. However, more meningitis-related deaths might be prevented by quickly scaling up immunisation and expanding access to health services. Further reduction in the global meningitis burden should be possible through low-cost multivalent vaccines, increased access to accurate and rapid diagnostic assays, enhanced surveillance, and early treatment.

Accuracy of the direct agglutination test for diagnosis of visceral leishmaniasis: a systematic review and meta-analysis. Roberts T, Keddie SH, Rattanavong S, Gomez SR, Bradley J, Keogh RH, Barenbold O, Falconer J, Mens PF, Hopkins H, Ashley EA. *BMC Infect Dis*. 2023;**23**(1):782. Epub 20231109. doi: 10.1186/s12879-023-08772-1. PMID: 37946107; PMCID: PMC10636880.

This meta-analysis compared sensitivity and specificity of the Direct Agglutination Test for diagnosis of visceral leishmaniasis to all other tests performed; values were 95% for both metrics. Test performance varied slightly depending on HIV status and symptoms of the patients, geography, and the DAT test format.

BACKGROUND:

Parasitological investigation of bone marrow, splenic or lymph node aspirations is the gold standard for the diagnosis of visceral leishmaniasis (VL). However, this invasive test requires skilled clinical

and laboratory staff and adequate facilities, and sensitivity varies depending on the tissue used. The direct agglutination test (DAT) is a serological test that does not need specialised staff, with just minimal training required. While previous meta-analysis has shown DAT to have high sensitivity and specificity when using parasitology as the reference test for diagnosis, meta-analysis of DAT compared to other diagnostic techniques, such as PCR and ELISA that are increasingly used in clinical and research settings, has not been done.

METHODS:

We conducted a systematic review to determine the diagnostic performance of DAT compared to all available tests for the laboratory diagnosis of human VL. We searched electronic databases including Medline, Embase, Global Health, Scopus, WoS Science Citation Index, Wiley Cochrane Central Register of Controlled Trials, Africa-Wide Information, LILACS and WHO Global Index. Three independent reviewers screened reports and extracted data from eligible studies. A meta-analysis estimated the diagnostic sensitivity and specificity of DAT.

RESULTS:

Of 987 titles screened, 358 were selected for full data extraction and 78 were included in the analysis, reporting on 32,822 participants from 19 countries. Studies included were conducted between 1987-2020. Meta-analysis of studies using serum and DAT compared to any other test showed pooled sensitivity of 95% (95%CrI 90-98%) and pooled specificity of 95% (95%CrI 88-98%). Results were similar for freeze-dried DAT and liquid DAT when analysed separately. Sensitivity was lower for HIV-positive patients (90%, CrI 59-98%) and specificity was lower for symptomatic patients (70%, CrI 43-89%). When comparing different geographical regions, the lowest median sensitivity (89%, CrI 67-97%) was in Western Asia (five studies).

CONCLUSIONS:

This systematic review and meta-analysis demonstrates high estimated pooled sensitivity and specificity of DAT for diagnosis of VL, although sensitivity and specificity were lower for different patient groups and geographical locations. This review highlights the lack of standardisation of DAT methods and preparations, and the lack of data from some important geographical locations. Future well-reported studies could provide better evidence to inform test implementation for different patient populations and use cases.

A systematic review of neglected tropical diseases (NTDs) in Myanmar. Swe MMM, Phyo AP, Cooper BS, White NJ, Smithuis F, Ashley EA. *PLoS Negl Trop Dis* 2023 **17**(11): e0011706. DOI: 10.1371/journal.pntd.0011706. PMID: 37910592. PMCID: PMC10619876.

This systematic review of neglected tropical diseases in Myanmar reveals a hidden burden of infectious disease underpinned by poor sanitation, lack of clean drinking water, and over-crowded urban areas. Despite significant gaps in the available data, this study emphasises the need for public health measures, improved treatment strategies, and more thorough monitoring of disease.

BACKGROUND:

Neglected tropical diseases (NTDs) affect most impoverished communities in developing countries like Myanmar in Southeast Asia. NTDs have been understudied and underreported in Myanmar.

METHODS:

A systematic review of published and grey literature (1900-2023) on NTDs in Myanmar was conducted. The literature search included five international databases: PubMed, EMBASE, Ovid Global Health, and Web of Science Core Collection, and one national database, the Myanmar Central Biomedical Library (locally published papers and grey literature). The selection criteria included articles with all types of study designs of current or previous infections conducted in humans, that reported NTDs, recognised by WHO, US CDC, and listed in PLoS NTDs. We included melioidosis and rickettsioses which we consider also meet the definition of an NTD.

RESULTS:

A total of 5,941 records were retrieved and screened, of which, 672 (11%) met the selection criteria and were included in this review. Of the included articles, 449 (65%) were published after 2000 and 369 (55%) were from two regions (Yangon and Mandalay) of Myanmar. Of the included articles, 238 (35%) reported bacterial NTDs, 212 (32%) viral NTDs, 153 (23%) helminth NTDs, 25 (4%) protozoal NTDs, and 39 (6%) reported more than one aetiology. Based on reported frequency in descending order, the bacterial NTDs were leprosy, *E. coli* enteritis, salmonellosis, cholera, shigellosis, melioidosis, leptospirosis and rickettsioses; the viral NTDs were dengue, chikungunya and Japanese encephalitis virus (JEV) infection; the protozoal NTDs were amoebiasis, giardiasis and leishmaniasis, and the helminth NTDs were ascariasis, trichuriasis, hookworm disease, filariasis, and strongyloidiasis.

CONCLUSIONS:

This review summarises NTDs reported in Myanmar over the past 100 years. The findings suggest that most NTDs are likely to be underreported, especially from parts of the country far from academic centres. Research capacity building together with strengthening of laboratory systems would lead to better understanding of the true burden of NTDs in Myanmar.

Zoonoses and animal health

A review of coxiellosis (Q fever) and brucellosis in goats and humans: Implications for disease control in smallholder farming systems in Southeast Asia. Burns RJL, Le KK, Siengsanun-Lamont J, Blacksell SD. *One Health* 2023 **16**: 100568. DOI: https://doi.org/10.1016/j.onehit.2023.100568. PMID: 37363211. PMCID: PMC10288130.

This review of Coxiella burnetii *and* Brucella *spp. in Southeast Asia discusses the risk factors for seropositivity of these pathogens in goats. These intracellular zoonotic pathogens are likely underdiagnosed in livestock and humans, and are potential bio-terrorism agents. They likely have a significant economic impact on smallholders, though improved animal management and food hygiene will reduce human infections.*

Coxiella burnetii and *Brucella* spp. are pathogenic bacteria that can cause large-scale outbreaks in livestock. These infectious agents can cause zoonotic infections and therefore pose a risk to the close relationship between farm households and their livestock, especially goats. A review of seroprevalence studies of *Coxiella burnetii* and *Brucella* spp. in domestic goats demonstrated large differences in the total number of samples tested in different regions and countries. This review aims to provide information on coxiellosis (Q fever in humans) and brucellosis in goats concerning the characteristics of the causative agent, surveillance, and available prevention and control measures at a global level. Implications for *Coxiella burnetii* and *Brucella* spp. infections in domesticated goats in Southeast Asia are discussed.

Retrospective investigation of the 2019 African swine fever epidemic within smallholder pig farms in Oudomxay province, Lao PDR. Matsumoto N, Siengsanan-Lamont J, Halasa T, Young JR, Ward MP, Douangngeun B, Theppangna W, Khounsy S, Toribio J, Bush RD, Blacksell SD. *Front Vet Sci*. 2023;**10**:1277660. Epub 20230929. doi: 10.3389/fvets.2023.1277660. PMID: 37841473; PMCID: PMC10576527.

This investigation of the 2019 African swine fever outbreak in northern Laos showed distinct differences compared to southern Laos, such as increased financial losses per household. Farming practices were identified that contribute to disease transmission, such as swill-feeding, free-ranging, and poor biosecurity protocols. Since pig farming practices vary across Laos, context-specific interventions are needed to prevent and contain outbreaks.

The 2019 African swine fever (ASF) outbreak in Lao PDR represented a major epidemiologic event where a transitioning LMIC experienced a viral epidemic in a naïve pig population. The diversity of pig management styles creates challenges for local and regional policymakers when formulating recommendations to control an ASF outbreak. The aim of this study was to investigate the management of pigs in villages of Oudomxay province that were affected by ASF in 2019, as a case study in a smallholder pig-raising system in northern Laos. The frequencies of well-known risk factors were measured in the affected villages and timelines and household level stock losses due to the outbreak were investigated. These findings were compared to data available from a similar outbreak in the southern province of Savannakhet. Disease control implications of these findings are discussed. Mean losses were 3.0-23.3 pigs per household, with a mean lost herd value of $349, 95% CI (294-415). These pig losses reflect those estimated in Savannakhet (6.7 pigs per household). However, the financial loss estimated per household was higher, $349 versus $215, possibly due to higher pig values and a higher input/output management approach in Oudomxay. The investigation revealed the presence of numerous ASF risk factors, such as swill-feeding and free-ranging. In addition, poor biosecurity practices that could contaminate the environment, such as inappropriate garbage disposal and slaughtering, were present. ASF cases occurred across all villages from June-December 2019, with outbreak periods ranging from 22-103 days. These values are consistent with the outbreak in Savannakhet; however, notable differences in management styles were observed. These findings demonstrate the need for more disease control resources from the village to the Governmental level. Villages need support to enact context appropriate biosecurity measures, while the ongoing surveillance and investigation of ASF require investment in logistical and veterinary resources at the Governmental level.

Utilising abattoir sero-surveillance for high-impact and zoonotic pig diseases in Lao PDR. Matsumoto N, Douangngeun B, Theppangna W, Khounsy S, Phommachanh P, Toribio JA, Bush RD, Selleck PW, Gleeson LJ, Siengsanan-Lamont J, Blacksell SD. *Epidemiol Infect*. 2023;**151**:e40. Epub 20230208. doi: 10.1017/S095026882300016X. PMID: 36750223; PMCID: PMC10028928.

Abattoir-based sero-surveillance is feasible in Lao PDR, with positivity rates of 68.7% for Classic Swine Fever and 39.5% for Porcine Respiratory and Reproductive Syndrome. Risk factors for infection include mass movement of pigs during outbreaks and lack of traceability of animals, including their vaccination records. This approach is important for food security.

National disease surveillance systems are essential to a healthy pig industry but can be costly and logistically complex. In 2019, Lao PDR piloted an abattoir disease surveillance system to assess the presence of high impact pig diseases (HIPDs) using serological methods. The Lao Department of Livestock and Fisheries (DLF) identified Classical Swine Fever (CSF), Porcine Respiratory and Reproductive Syndrome (PRRS) and *Brucella suis* as HIPDs of interest for sero-surveillance purposes. Porcine serum samples (n = 597) were collected from six Lao abattoirs in March to December of 2019. Serological enzyme-linked immunosorbent assay (ELISA) methods were chosen for their high-throughput and relatively low-costs. The true seroprevalence for CSF and PRRS seropositivity were 68.7%, 95% CI (64.8-72.3) and 39.5%, 95% CI (35.7-43.5), respectively. The results demonstrated no evidence of *Brucella* spp. seroconversion. Lao breed pigs were less likely to be CSF seropositive ($P < 0.05$), while pigs slaughtered at <1 year of age were less likely to be PRRS seropositive ($P < 0.01$). The testing methods could not differentiate between seropositivity gained from vaccine or natural infection, and investigators were unable to obtain the vaccine status of slaughtered pigs from abattoirs. These results demonstrate that adequate sample sizes are possible from abattoir sero-surveillance and that lifetime health traceability is necessary to understand HIPDs in Lao PDR.

***Bartonella* species in Cambodia, Ghana, Laos, and Peru: results from vector and serosurveys.** Mullins K, Canal E, Ouch P, Prasetyo D, Tagoe J, Attram N, Yeboah C, Kumordjie S, Fox A, Letizia AG, Rachlin A, Nguyen HM, Robinson MT, Vongsouvath M, Davong V, Maxay M, Simons MP, Caranci A, Newton PN, Richards AL, Farris CM. *Vector Borne Zoonotic Dis*. 2023;23(1):9-17. doi: 10.1089/vbz.2021.0090. PMID: 36633562; PMCID: PMC7614129.

Significant seropositivity to Bartonella *spp. is seen in patients with undifferentiated fever in various countries – suggesting that* B. henselae *and* B. quintana *are important causes of febrile presentations. Cross-reactivity with other* Bartonella *species, such as* B. bacilliformis*, is demonstrated, and may suggest that unidentified* Bartonella *species are also relevant. Vectors had notably low rates of* Bartonella *detection.*

BACKGROUND:

Bartonella species are fastidious gram-negative vector-borne bacteria with a wide range of mammalian reservoirs. While it is understood that some species of *Bartonella* are human pathogens, the extent of human exposure to *Bartonella* species (both pathogenic and non-pathogenic) is yet to be fully understood.

MATERIALS AND METHODS:

To this end, residual sera from participants enrolled in undifferentiated fever studies in Cambodia, Ghana, Laos, and Peru were screened for the presence of IgG antibodies against *Bartonella quintana* and *Bartonella henselae*, using the FOCUS diagnostics Dual Spot-*Bartonella* IgG Immunofluorescence assay. 48 patients with suspected or confirmed *Bartonella bacilliformis* exposure or infection in Peru were screened to assess cross-reactivity of the FOCUS assay for IgG against other *Bartonella* species.

RESULTS:

10 of 13 patients with confirmed *B. bacilliformis* infection were *Bartonella*-specific IgG positive, and overall, 36/48 of the samples were positive. In addition, 79/206, 44/200, 101/180, and 57/100 of the samples from Peru, Laos, Cambodia, and Ghana, respectively, were *Bartonella*-specific IgG positive. Furthermore, ectoparasite pools from Cambodia, Laos, and Peru were tested using quantitative real-time PCR (qPCR) for the presence of *Bartonella* DNA. Of the sand fly pools collected in Peru, 0/196 were qPCR positive; 15/140 flea pools collected in Cambodia were qPCR positive; while 0/105 ticks, 0/22 fleas, and 0/3 louse pools collected in Laos tested positive for *Bartonella* DNA.

CONCLUSIONS:

Evidence of *Bartonella* in fleas from Cambodia supports the possibility that humans are exposed to *Bartonella* through this traditional vector. However, *Bartonella* species were not found in fleas, ticks, or lice from Laos, or sand flies from Peru. This could account for the lower positive serology among the population in Laos and the strictly localized nature of *B. bacilliformis* infections in Peru. Human exposure to the *Bartonell*a species and *Bartonella* as a human pathogen warrants further investigation.

Longitudinal comparison of bacterial pathogen seropositivity among wet market vendors in the Lao People's Democratic Republic. Senvanpan N, Phimolsarnnousith V, Rattanavong S, Mayxay M, Reinharz D, Fine AE, Horwood PF, Dussart P, Blacksell SD, Pruvot M, Newton PN, Robinson MT. *One Health*. 2023;**17**:100618. Epub 20230825. doi: 10.1016/j.onehlt.2023.100618. PMID: 37811399; PMCID: PMC7615163.

Zoonoses are a major type of both established and emerging infections. 150 market traders in 3 provinces were assessed for seropositivity for scrub typhus, murine typhus and leptospirosis. 32.7% were seropositive for at least 1 pathogen, and 13.3% seroconverted during the study. This important role of exposure to pathogens in wild meat, domestic meat and vegetable traders requires further investigation.

Wild animal trade for human consumption is a global issue, involving complex interactions between economics, culture, food security, and conservation. While being a biodiversity issue, it is also a major public health concern, with recent epidemics and pandemics of zoonotic pathogens linked to interactions with wildlife. At three time points, between March 2017 and June 2018, a longitudinal sero-survey of 150 market vendors from 3 wet markets in Laos (selling vegetables, domestic animal meat and/or wildlife meat) was conducted to determine if vendors had been differentially exposed to three endemic bacterial pathogens – *Orientia tsutsugamushi*, *Rickettsia typhi*, and *Leptospira* spp. A total of 367 serum samples were tested by IgG enzyme-linked immunosorbent assay (ELISA) and immunofluorescence assay (IFA, for scrub typhus group (STG) and typhus group (TG) only). Among vendors, 32.7% were IgG-positive for at least one pathogen, 13.3% sero-converted during the study. Multi-season occupancy modelling for STG indicated a significantly higher prevalence of STG IgG in vegetable vendors (27.3%) and wildlife vendors (28.4%) than in domestic animal meat vendors (6.9%, p = 0.05), and higher in Phonesavanh market (OR = 9.6, p = 0.03) compared to Lak Sao and Salavan markets. Estimated mean incidence was 57 cases per 10,000 per 7.5-month period. For TG, vendor age had a significant effect on prevalence (OR = 1.04, p = 0.006), estimated mean incidence was 64 cases per 10,000 per season (7.5-month period). Despite individuals selling domestic meat having a higher prevalence of *Leptospira* infections than those that did not (11.6% versus 4.5%), the difference was not significant. While this study has several limitations, including vendors changing what food types they sold and no investigation of exposure outside of markets, the finding that the risk of exposure of vendors to zoonotic pathogens may be associated with types of food sold for human consumption warrants further investigation.

Medicine quality

The quality of antiretroviral medicines: an uncertain problem. Do NT, Boupha P, Newton PN, Caillet C. *BMJ Global Health* 2023 **8**(3): e011423. DOI: 10.1136/bmjgh-2022-011423. PMID: 36921990. PMCID: PMC10030546.

This systematic review of substandard and falsified (SF) anti-retroviral drugs incorporated over 200 publications. Of 3,713 samples of anti-retroviral drugs, 1.4% failed at least one test of quality. This has the potential to seriously impact the Sustainable Development Goal to end AIDS.

OBJECTIVES:

Substandard and falsified (SF) antiretrovirals (ARVs) risk poor outcomes and drug resistance, potentially affecting millions of people in need of treatment and prevention. We assessed the available evidence on SF ARV and related medical devices to discuss their potential public health impact.

METHODS:

Searches were conducted in Embase, PubMed, Google, Google Scholar, Web of Science and websites with interest in ARV quality in English and French up to 30 November 2021. Publications reporting on the prevalence of SF ARV were assessed in a quantitative analysis using the Medicine Quality Assessment Reporting Guidelines (MEDQUARG).

RESULTS:

We included 205 publications on SF ARV and 11 on SF medical devices. 19 prevalence surveys of SF ARV published 2003-2021 were included, with no surveys relevant to SF medical devices. The prevalence survey sample size ranged from 3 to 2,630 samples (median (Q1–Q3): 16.0 (10.5–44.5); 3 (15.8%) used random outlet sampling methods. Of the 3,713 samples included in the prevalence surveys, 1.4% (n=51) failed at least one test. Efavirenz, nevirapine and lamivudine-nevirapine-stavudine combination were the most surveyed ARV with failure frequencies of 3.6% (7/193), 2.6% (5/192) and 2.8% (5/177), respectively. The median (Q1%–Q3%) concordance with the MEDQUARG criteria was 42.3% (34.6%–55.8%).

CONCLUSIONS:

These results suggest that there are few data in the public domain of the quality of ARV in supply chains; the proportion of SF ARV is relatively low in comparison to other classes of essential medicines. Even a low proportion of the ARV supply chain being poor quality could make a large difference in the HIV/AIDS international landscape. The 95-95-95 target for 2026 and other international targets could be greatly hampered if even 1% of the millions of people taking ARV (for both prevention and prophylaxis) receive medicines that do not meet quality standards. More surveillance of SF ARV is needed to ensure issues are detected. All data relevant to the study are included in the article or uploaded as online supplemental information. All data are mapped and can be downloaded on the Infectious Diseases Data Observatory (IDDO) Medicine Quality Surveyor system (https://www.iddo.org/mqsurveyor/%23antiretrovirals).

Medical Products Quality and Public Health. Chapter 6 in *Manson's Tropical Diseases 24th Edition*. Newton PN, Caillet C. Eds Farrar J, Hotez PJ, Junghanss T, Kang G, Lalloo D, White NJ, Garcia PJ. Elsevier 2023.

Estimating the prevalence of poor-quality anti-TB medicines: a neglected risk for global TB control and resistance. Tabernero P, Newton PN. *BMJ Glob Health* 2023 **8**(7): e012039. DOI: 10.1136/bmjgh-2023-012039. PMID: 37433693. PMCID: PMC10347509.

The extent of substandard and falsified (SF) TB medications is unknown, and the impact on patient outcomes and drug resistance has not been explored. This systematic review includes 7,682 medicine samples from 22 countries; >15% samples failed at least one quality test. Data are too scarce to be globally generalisable, and quality analyses should be part of treatment programmes.

OBJECTIVES:

Tuberculosis (TB) remains a major global public health problem, especially with the recent emergence of multidrug-resistant TB and extensively drug-resistant TB. There has been little consideration of the extent of substandard and falsified (SF) TB medicines as drivers of resistance. We assessed the evidence on the prevalence of SF anti-TB medicines and discussed their public health impact.

MATERIALS/METHODS:

We searched Web of Science, Medline, PubMed, Google Scholar, WHO, US Pharmacopeia and Medicines Regulatory Agencies websites for publications on anti-TB medicines quality up to 31 October 2021. Publications reporting on the prevalence of SF anti-TB drugs were evaluated for quantitative analysis.

RESULTS:

Of the 530 screened publications, 162 (30.6%) were relevant to anti-TB medicines quality; of those, 65 (40.1%) described one or more TB quality surveys in a specific location or region with enough information to yield an estimate of the local prevalence of poor-quality TB medicines. 7,682 samples were collected in 22 countries and of those, 1170 (15.2%) failed at least one quality test. 14.1% (879/6255) of samples failed in quality surveys, 12.5% (136/1086) in bioequivalence studies, and 36.9% (87/236) in accelerated biostability studies. The most frequently assessed were rifampicin monotherapy (45 studies, 19.5%) and isoniazid monotherapy (33, 14.3%), rifampicin-isoniazid-pyrazinamide-ethambutol fixed dose combinations (28, 12.1%) and rifampicin-isoniazid (20, 8.6%). The median (IQR) number of samples collected per study was 12 (1-478).

CONCLUSIONS:

SF, especially substandard, anti-TB medicines are present worldwide. However, TB medicine quality data are few, and therefore it is not generalisable that 15.2% of global anti-TB medicine supply is SF. The evidence available suggests that surveillance of TB medicines quality needs to be an integral part of treatment programmes. More research is needed on the development and evaluation of rapid, affordable and accurate portable devices to empower pharmacy inspectors to screen anti-TB medicines.

Other topics

Exploring the views of infection consultants in England on a novel delinked funding model for antimicrobials: the SMASH study. Baltas I, Gilchrist M, Koutoumanou E, Gibani MM, Meiring JE, Otu A, et al. *JAC-Antimicrobial Resistance* 2023 **5**(4): dlad091. DOI: 10.1093/jacamr/dlad091. PMID: 37533762. PMCID: PMC10391702.

Infection doctors in England were surveyed on the new subscription model used to purchase cefiderocol and ceftazidime/avibactam. Fewer than 60% of consultants had heard of the model, but felt it would lead to improvements in patient treatment and research; however, they did not believe it would reduce carbapenem use.

A novel 'subscription-type' funding model was launched in England in July 2022 for ceftazidime/avibactam and cefiderocol. We explored the views of infection consultants on important aspects of the delinked antimicrobial funding model. An online survey was sent to all infection consultants in NHS acute hospitals in England. The response rate was 31.2% (235/753). Most consultants agreed the model is a welcome development (69.8%, 164/235), will improve treatment of drug-resistant infections (68.5%, 161/235), and will stimulate research and development of new antimicrobials (57.9%, 136/235). Consultants disagreed that the model would lead to reduced carbapenem use and reported increased use of cefiderocol post-implementation. The presence of an antimicrobial pharmacy team, requirement for preauthorization by infection specialists, antimicrobial stewardship ward rounds, and education of infection specialists were considered the most effective antimicrobial stewardship interventions. Under the new model, 42.1% (99/235) of consultants would use these antimicrobials empirically, if risk factors for AMR were present (previous infection, colonization, treatment failure with carbapenems, ward outbreak, recent admission to a high-prevalence setting). Significantly higher insurance and diversity values were given to model antimicrobials compared with established treatments for carbapenem-resistant infections, while meropenem recorded the highest enablement value. Use of both 'subscription-type' model drugs for a wide range of infection sites was reported. Respondents prioritised ceftazidime/avibactam for infections by bacteria producing OXA-48 and KPC and cefiderocol for those producing MBLs and infections with *Stenotrophomonas maltophilia*, *Acinetobacter* spp. and *Burkholderia cepacia*. The 'subscription-type' model was viewed favourably by infection consultants in England.

Ethical and cultural implications for conducting verbal autopsies in South and Southeast Asia: a qualitative study. Htun NSN, Perrone C, Phyo AP, Sen A, Phommasone K, Vanna M, et al. *BMJ Glob Health* 2023 **8**(12): e013462. DOI: 10.1136/bmjgh-2023-013462. PMID: 38081771. PMCID: PMC10729118.

This insightful article describes the thematic analysis of conversations with focus groups in 5 countries. It identifies important considerations when undertaking verbal autopsies in rural communities. Due regard for the varied practices and customs of communities allows appropriate and ethical study conduct, and ensures acceptability of verbal autopsies as important research methodology.

INTRODUCTION:

Causes of deaths often go unrecorded in lower income countries, yet this information is critical. Verbal autopsy is a questionnaire interview with a family member or caregiver to elicit the symptoms and circumstances preceding a death and assign a probable cause. The social and cultural aspects of verbal autopsy have gotten less attention than the technical aspects and have not been widely explored in South and Southeast Asia settings.

METHODS:

From October 2021 to March 2023, prior to implementing a verbal autopsy study at rural sites in Bangladesh, Cambodia, Laos, Myanmar and Thailand, focus group discussions were conducted with village heads, religious leaders, and community members from varied demographic backgrounds. Thematic analysis elucidated customs and traditional views surrounding death to understand local ethnocultural sensitivities.

RESULTS:

We found that death rituals varied greatly among religions, ethnicities and by socioeconomic status. Mourning periods were reported to last 3-100 days, and related to the cause of death, age, and how close the deceased person was to the family. Participants advised that interviews should happen after mourning periods to avoid emotional distress, but not long after to avoid recall bias. Interviewers should be introduced to respondents by a trusted local person. To provide reassurance and confidentiality, a family's residence is the preferred interview location. Interview questions require careful local language translation, and community sensitisation is important before data collection.

CONCLUSION:

Verbal autopsy is acceptable across a wide range of cultural settings in Southeast Asia, provided that local norms are preidentified and followed.

Scaling up One Health: a network analysis in Lao PDR. Larkins A, Vannamahaxay S, Puttana V, Chittavong M, Southammavong F, Mayxay M, Boyd D, Bruce M, Ash A. *One Health*. 2024;18:100661. Epub 20231212. doi: 10.1016/j.onehlt.2023.100661. PMID: 38179311; PMCID: PMC10761780.

A variety of successful One Health projects have been conducted in Laos, but interaction between participating organisations – especially international organisations – could be improved. Key contributors to scaling up collaborations include strong interpersonal relationships, a focus on national (rather than donor) priorities, setting goals that are practical, and ensuring adequate resources to realise these ambitions.

BACKGROUND:

One Health focuses on sustainable health for humans, animals, and ecosystems. The approach has been well demonstrated, yet most efforts have not been scaled up. Understanding the organisations involved in scaling up processes is critical to translating research into practice. The Lao People's Democratic Republic has successfully implemented One Health projects for multiple decades; however, the organisational network has not been described, and scaling up efforts have been limited.

METHODS:

Data from organisations involved in One Health projects over the past five years were collected by key-informant interview or workshop. The network was investigated using a mixture of quantitative network analysis and qualitative thematic analysis.

RESULTS:

The organisational network was quantitatively described as sparse and centralised. Organisations were required to harness pre-existing relationships to maximise scarce resources and make coordination and alignment of priorities more efficient. A lack of international organisations in the top 10% of resource-sharing metrics suggests a potential disconnect between donors. This was reflected in the challenges faced by national organisations and a feeling of being stretched thin over numerous externally funded projects with donor-driven priorities.

CONCLUSION:

It appears that high-level political support for country ownership of development and aid priorities remains unrealised. Developing network capacity and capability may assist scaling up efforts and build resilience in the network and its core organisations. This may allow for the inclusion of more development, education, environment, and water, sanitation and hygiene organisations that were perceived to be lacking. Future One Health programmes should focus on practical activities that do not overload staff capacity. There is much for One Health to learn about the art of scaling up and organisations are encouraged to include implementation science in their research to inform future scaling up efforts.

Is this pill an antibiotic or a painkiller? Improving the identification of oral antibiotics for better use. Monnier AA, Do NTT, Asante KP, Afari-Asiedu S, Khan WA, Munguambe K, Sevene E, Tran TK, Nguyen CTK, Punpuing S, Gomez-Olive FX, van Doorn HR, Caillet C, Newton PN, Ariana P, Wertheim HFL, consortium AI. *Lancet Glob Health*. 2023;11(8):e1308-e13. doi: 10.1016/S2214-109X(23)00258-9. PMID: 37474237.

There is no standardisation of antibiotic appearance, and this causes far-reaching confusion among health professionals and patients. This compromises appropriate antibiotic use, patient care and antimicrobial stewardship. A wide range of stakeholders discussed the need to regulate antibiotic appearance, along with barriers and potential approaches.

In this Viewpoint, we discuss how the identification of oral antibiotics and their distinction from other commonly used medicines can be challenging for consumers, suppliers, and health-care professionals. There is a large variation in the names that people use to refer to antibiotics and these often relate to their physical appearance, although antibiotics come in many different physical presentations. We also reflect on how the physical appearance of medicine influences health care and public health by affecting communication between patients and health-care professionals, dispensing, medicine use, and the public understanding of health campaigns. Furthermore, we report expert and stakeholder consultations on improving the identification of oral antibiotics and discuss next steps towards a new identification system for antibiotics. We propose to use physical appearance as a tool to support and nudge awareness about antibiotics and their responsible use.

Good participatory practice for coronavirus disease 2019 (COVID-19) research: the case of a COVID-19 prevention study. Perrone C, Schilling W, Callery JJ, Ashley EA, Chambers M, Chase H, Dahal P, Kanthawang N, Nedsuwan S, Hanboonkunupakarn B, Intralawan D, Karkey A, Mayxay M, Souvong V, Tran Minh H, Udas Shakya S, Sharma SK, Uranw S, Vannachione S, Woodrow C, White NJ, Cheah PY. *Wellcome Open Res*. 2021;**6**:216. Epub 20221201. doi: 10.12688/wellcomeoperes.16880.3. PMID: 36866279; PMCID: PMC9971639. .

Good participatory practice (GPP) was embedded into the protocol for the COPCOV trial for COVID prophylaxis. Engagement exercises in 5 countries were carried out and led to improved study materials and conduct of the trial. GPP offer multiple benefits to stakeholders and is a valuable component of clinical trials.

BACKGROUND:

The COPCOV study (chloroquine/ hydroxychloroquine prevention of coronavirus disease), which began recruitment in April 2020, is a multi-country double-blind, randomised, placebo-controlled trial conducted in healthcare facilities involved in COVID-19 case management. Participants were staff employed in facilities managing people with proven or suspected COVID-19. As part of the study, we conducted a series of engagement sessions. The aims were to assess the feasibility of the study, identify context-specific ethical issues, understand possible concerns, fine tune research procedures and refine COPCOV information materials.

METHODS:

The COPCOV study was approved by relevant institutional review boards. The sessions described in this paper were part of the study. We conducted a series of engagement sessions, each involving a short presentation of the study, a section where attendees were asked to express their willingness to participate in such a study, which information they would need to change their view, and an open Q&A section. Answers were transcribed and coded into themes by two independent investigators. Themes were derived from the data. They complemented other site-specific engagement, communication, and public relation activities such as press releases and websites.

RESULTS AND CONCLUSIONS:

From 16 March 2020 to 20 January 2021, 12 engagement sessions were conducted in Thailand, Laos, Viet Nam, Nepal and the UK involving 213 attendees in total. Issues raised revolved around the social value and study rationale, safety of trial medications and risk-benefit balance, study design, and commitments. These sessions helped us identify concerns people had, which helped us refine information materials as well as complement site feasibility assessments. Our experience strongly supports the use of participatory practices prior to conducting clinical trials.

A case report of *Ovophis monitcola* (Mountain pit-viper) envenoming in northeastern India resulting in prolonged coagulopathy. Ralph R, Garg D, Balachandran A, Ganesh SR, Lamb T. *Toxicon* 2023 229: 107147. DOI: 10.1016/j.toxicon.2023.107147. PMID: 37127123.

This case report describes a snakebite in northeastern India. Multiple doses of poly-specific venom were given. However, there was no improvement in the patient's coagulopathy because the snake species was initially misidentified. Cross-reactivity of anti-venom occurs in some cases, but should be balanced against the risk of anaphylaxis associated with this treatment.

India is home to a diverse spectrum of medically-significant snakes, accounting for one of the world's largest burdens of envenoming, morbidity and mortality. Indian polyspecific antivenom is derived from the venom of four snake species (*Daboia russelii*, *Echis carinatus*, *Naja naja* and *Bungarus caeruleus*) considered to be responsible for most of the snakebite morbidity and mortality in India. The treatment of envenoming from other less-commonly encountered venomous snake species can be challenging. In this report, we describe the case of a 32-year-old male who presented with local swelling and coagulopathy following a bite from *Ovophis monitcola* (mountain pit-viper) in Nagaland, Northeast India. Local and systemic envenoming, failure to respond to Indian polyspecific antivenom, and venom-induced consumption coagulopathy, confirmed by bedside and laboratory-based clotting assays, persisted for more than three weeks. Remote consultation with a national-level Poison Control Centre helped establish the responsible snake species and guide appropriate medical management.

Cost-effectiveness analysis of typhoid vaccination in Lao PDR. Soukavong M, Luangasanatip N, Chanthavilay P, Teerawattananon Y, Dabak SV, Pan-Ngum W, Roberts T, Ashley EA, Mayxay M. *BMC Public Health*. 2023 Nov 17;**23**(1):2270. doi: 10.1186/s12889-023-17221-2. PMID: 37978481; PMCID: PMC10656839.

Vaccination with typhoid conjugate vaccine (TCV) is not cost-effective in Laos. This contradicts other predictions because the prevalence of enteric fever is much lower than previously estimated (2.17 cases per 100,000 per year). While detailed healthcare economic analyses necessarily rely on many assumptions, accurate figures are particularly important as Laos transitions away from Gavi support for vaccinations.

BACKGROUND:

Typhoid vaccination has been shown to be an effective intervention to prevent enteric fever and is under consideration for inclusion in the national immunization program in Lao PDR.

METHODS:

A cost-utility analysis was performed using an age-structured static decision tree model to estimate the costs and health outcomes of introducing TCV. Vaccination strategies combined with five delivery approaches in different age groups compared to no vaccination were considered from the societal perspective, using the Gavi price of $1.50 per dose. The vaccination program was considered cost-effective if the incremental cost-effectiveness ratio was less than a threshold of 1 GDP per capita for Lao PDR, equivalent to $2,535 in 2020.

RESULTS:

In the model, we estimated 172.2 cases of enteric fever, with 1.3 deaths and a total treatment cost of $7,244, based on a birth cohort of 164,662 births without TCV vaccination that was followed over their lifetime. To implement a TCV vaccination program over the lifetime horizon, the estimated cost of the vaccine and administration costs would be between $470,934 and 919,186. Implementation of the TCV vaccination program would prevent between 14 and 106 cases and 0.1 to 0.8 deaths. None of the vaccination programs appeared to be cost-effective.

CONCLUSIONS:

Inclusion of TCV in the national vaccination program in Lao PDR would only be cost-effective if the true typhoid incidence were 25-times higher than our current estimate.

Conference and meeting abstracts

33rd European Congress on Clinical Microbiology and Infectious Diseases (ECCMID) 2023,
15-19 April 2023, Copenhagen, Denmark.
AmpC β-lactamase producing *Escherichia coli* and *Klebsiella pneumoniae* in Southeast Asia. Roberts T, Ling C, Watthanaworawit W, Cheav C, Sengduangphachanh A, Silisouk J, Hopkins J, Turner P, Ashley EA. Flash E-poster presentation.

BACKGROUND:

AmpC β-lactamase producing *E. coli* and *Klebsiella pneumoniae* can hydrolyse third generation cephalosporins (3GC). AmpC β-lactamases are neglected compared to extended spectrum β-lactamases (ESBLs) as a cause of 3GC resistance in *E. coli* and *K. pneumoniae* in LMICs and the burden is unknown. Therefore, the aim of this study was to investigate the presence of AmpC β-lactamase producing *E. coli* and *K. pneumoniae* from clinical specimens from three clinical research laboratories in Thailand, Cambodia and Lao PDR.

METHODS:

Clinical isolates of *E. coli* and *K. pneumoniae* that were resistant to either ceftriaxone, ceftazidime or cefpodoxime by disc diffusion and ESBL confirmation test (double- disc diffusion test) negative were screened for AmpC using the MASTDISCS AmpC, ESBL and Carbapenemase Detection Set according to the manufacturer's guidelines (D72C, Mast Group Ltd). A subset of isolates that gave a result of AmpC or Inducible AmpC from all sites were sequenced on an Illumina iSEQ100 (yielding 150bp paired-end reads).

RESULTS:

A total of 135 clinical isolates (115 *E. coli* and 20 *K. pneumoniae*) collected between 2012-2020 were included in the study. Phenotypically there were 33/135 (24.4%) AmpC positive, 17/135 (12.6%) inducible AmpC and 4/135 (3%) AmpC and ESBL positive. 31/37 (84%) AmpC positive isolates were ceftriaxone resistant and all inducible AmpC isolates were ceftriaxone sensitive. For the isolates that were sequenced, 20/32 (62.5%) phenotypic AmpC positive isolates were $bla_{\text{CMY-2}}$, 5/32 (15.6%) were $bla_{\text{CMY-42}}$ and 3/32 (9.4%) were $bla_{\text{DHA-1}}$. Sequence results from the phenotypically inducible AmpC isolates showed all were $bla_{\text{DHA-1}}$ (17/17). Other genes detected from the combined phenotypic AmpC positive and inducible AmpC isolates included 2/49 (4.1%) $bla_{\text{CTX-M-15}}$, 27/49 (55.1%) $bla_{\text{TEM-1}}$, 4/49 (8.2%) $bla_{\text{TEM-150}}$, 1/49 (2%) $bla_{\text{NDM-5}}$ and 6/49 (12.2%) $bla_{\text{OXA-48}}$.

CONCLUSIONS:

These results show that AmpC β-lactamases are present in Southeast Asia. As routine screening for AmpC β-lactamases is not common in many laboratories, inducible AmpC β-lactamases may be going undetected with current antimicrobial susceptibility testing. This study supports screening for AmpC β-lactamases when cefoxitin resistant isolates are ESBL negative. There is ongoing work to determine the genetic basis and context for the phenotypic findings.

Lao Women's Union and Mahosot Hospital held a special event on 19 July 2023. *From left*: Lanoi Silichack, Dr Manivanh Vongsouvath, Bountoy Sibounheuang , Viengmon Davong and Phonelavanh Phouminh. The Lao Women's Union (LWU) was established on 20 July 1955 to promote the role of women under the National Constitution. © LOMWRU 2023. Photo: Manivanh Vongsouvath.

American Society of Tropical Medicine and Hygiene (ASTMH) 2023 Annual Meeting,
18-22 October 2023, Hyatt Regency Chicago, Chicago, USA.
What causes febrile illness in Africa and Asia? Results from FIEBRE: infections causing fever among child and adult outpatients and inpatients at sites in Lao PDR, Malawi, Mozambique, and Zimbabwe. FIEBRE consortium.

Fever commonly leads to healthcare seeking and hospital admission in sub-Saharan Africa and Asia. There is only limited guidance for clinicians managing non-malarial fevers, which often results in inappropriate treatment for patients. Furthermore, there is little evidence for estimates of disease burden, or to guide empirical therapy, control measures, resource allocation, prioritization of clinical diagnostics or antimicrobial stewardship. The Febrile Illness Evaluation in a Broad Range of Endemicities (FIEBRE) study seeks to address these information gaps. FIEBRE investigated febrile illness in paediatric and adult outpatients and inpatients using standardised clinical, laboratory and social science protocols over a minimum 24-month period at four sites in Lao PDR, Malawi, Mozambique and Zimbabwe. Patients presenting with fever were enrolled and provided clinical data, pharyngeal swabs and a venous blood sample; selected participants also provided a urine sample. Laboratory assessments targeted treatable and/or preventable infections. Selected point-of-care tests, as well as blood and urine cultures, and antimicrobial susceptibility testing, were performed on site. On day 28, patients provided a second venous blood sample for serology and information on clinical outcome. Further diagnostic assays were performed at international reference laboratories. Blood and pharyngeal samples from matched community controls enabled calculation of attributable fractions, and surveys of treatment seeking allowed estimation of the incidence of common infections. Residual samples from participants were stored for future use. All reference laboratory testing recently has been completed. Preliminary analysis shows that dengue, malaria and typhoid are important causes of fever in specific sites, while respiratory viruses, leptospirosis, and rickettsial and other infections cause a smaller proportion of fevers across all sites. Full results were presented at the ASTMH conference, with commentary on implications for fever case management and diagnostic and antimicrobial stewardship.

Countering the Wicked Problem of Bad Quality Medicines
American Society of Tropical Medicine and Hygiene (ASTMH) 2023 Annual Meeting,
18-22 October 2023, Hyatt Regency Chicago, Chicago, USA
Participants: Marya Lieberman, Paul Newton, Sachiko Ozawa, Céline Caillet, Noudy Sengxeu, Ayenew Ashenef.

This symposium brought together researchers who study the recalcitrant problem of bad quality medicines. The quality of medicines and medical products is a key determinant of clinical care outcomes, yet in 2017, the World Health Organization estimated [WHO 2017] that about 1 in 10 pharmaceuticals sold in low- and middle-income countries (LMICs) failed to meet quality standards. These problems impact every therapeutic category of pharmaceuticals and extend to medical products such as vaccines and rapid diagnostic tests. Regulatory agencies, medical practitioners, donors, and principled manufacturers share a common interest in detecting bad quality products and removing them from markets in LMICs. Six years and a global pandemic later, how many bad quality products are still present in LMIC markets, what is their impact on health, and how can they be discovered and removed? Because the problem of bad quality medicines is concentrated in LMICs and global enforcement activities are relatively weak, regulatory agencies in LMICs are the front-line organizations responsible for exposing and controlling bad quality medical products, and LMIC researchers play vital roles in testing medicines and medical products. A series of talks will introduce methods for modeling the impacts of substandard and falsified (SF) medicines, recent data about the prevalence of poor-quality antimicrobials and chemotherapy products, and new tools for facilitating medicine quality surveys and testing the quality of vaccines. Field screening technologies are an important part of the post-market surveillance strategy in many LMICs. Regulatory agency respondents in 9 out of 10 countries surveyed by Roth et al. [Roth 2018] agreed with the cost-saving arguments for field screening of pharmaceuticals. However, most of the respondents misunderstood the capabilities of current chemical and spectroscopic screening technologies. These technologies are developing rapidly and have great potential as weapons against substandard and falsified pharmaceuticals (SFPs), but there are still many evidence gaps and it is difficult for regulators to compare the effectiveness, usability, and costs of different technologies. The Chairs will sponsor a booth at the Exhibit Hall for participants to try out a variety of field screening instruments, such as portable spectrophotometers, that are used to detect low-quality pharmaceuticals in field settings. This booth was not sponsored or supported by instrument manufacturers. CHAIR: Marya Lieberman University of Notre Dame, Notre Dame, IN, USA and Paul Newton, Medicine Quality Research Group (MQRG), Centre for Tropical Medicine & Global Health (CTMGH), University of Oxford, UK, Oxford, UK.

Joint International Tropical Medicine Meeting (JITMM) 2023,
13-15 December 2023, Eastin Grand Hotel Phayathai, Bangkok, Thailand.
Trends in respiratory virus infections in relation to the COVID-19 pandemic in Lao PDR: a hospital-based surveillance study. Phommasone K, Chommanam D, Christy NC, Yiaye T, Phoutthavong S, Keomoukda P, Thammavong S, Bounphiengsy T, Lathsachack T, Boutthasavong L, Sibounheuang B, Phonemixay O, Panapruksachat S, Praphasiri V, Keomany S, Chaleunphon B, Douangdala P, Robinson MT, Batty E, Vongsouvath M, Letizia AG, Mayxay M, Dubot-Pérès A, Ashley EA.

BACKGROUND:

Circulation of influenza and other seasonal respiratory viruses changed dramatically during the COVID-19 pandemic, thought due to control measures put in place to reduce transmission of SARS-CoV-2. This study aimed to determine the trends of SARS-CoV-2, influenza A, influenza B and respiratory syncytial viruses (RSV) in patients presenting with acute respiratory infections (ARI).

METHODS:

This prospective study was conducted in four provincial hospitals across Lao PDR. Participants of all ages who met our case definition for an ARI (axillary temperature ≥ 37.5°C or history of fever, AND cough or other respiratory symptoms/signs OR loss of smell and/or taste) presenting to the hospital less than 10 days after symptom onset were eligible to be enrolled. Nasopharyngeal (NP) and throat swabs were taken for SARS-CoV-2 E-gene, influenza A, influenza B and human respiratory syncytial virus probe based real-time RT PCR assay.

FINDINGS:

A total of 4,334 patients were recruited between March 2021 and July 2023, of whom 928 (22%) were children less than 5 years old. 7% of patients (302) had a qSOFA score ≥ 2. SARS-CoV 2 was detected in 19.2% patients, followed by influenza A, influenza B and RSV (9.2%, 7.7% and 5.4%, respectively). There were 167 patients with at least two viruses detected. Influenza viruses and RSV were not detected while COVID-19 control measures were implemented.

CONCLUSIONS:

COVID-19 control measures had an added benefit to prevent other respiratory virus infections in Laos. Lifting the restrictions led to a resurgence of influenza A, influenza B and RSV.

Third Asia-Pacific Rickettsia Conference (APRC3),
23-24 September 2023, Radisson Blu Resort Temple Bay, Mahabalipuram, Chennai, India.
Rickettsia, and the human-animal interface. Robinson MT.

Many rickettsial pathogens are zoonotic organisms: They can be transmitted between both animals and humans. While most are not recognised as pathogens of clinical importance, there are several species relevant to both animal and human health: *Orientia tsutsugamushi*, *Rickettsia typhi*, *R. prowazekii*, to name the most recognisable. Transmission of these organisms between individual animals and from animals to humans is usually via an arthropod vector (such as ticks, fleas or lice), either from a direct bite or indirectly via crushing the vector or its excrement into a wound or mucus membrane. There are also occurrences of lab-acquired infections via direct exposure (ie aerosolisation) to high concentrations of pathogen. Understanding how transmission occurs on a day-to-day basis, identifying the interactions between animal hosts and humans, and recognising the risks that increase exposure is vitally important in a One Health approach to understanding the epidemiology, and controlling and preventing infection.

Investigating Antimicrobial Susceptibility of *Rickettsia typhi* Clinical Isolates from Laos using qPCR and Plaque assay. Phuklia W, Padith K, Farris CM, Richards AL, Phommasone K, Robinson MT, Newton PN, Day NPJ, Ashley EA.

BACKGROUND:

Murine typhus is a flea-borne disease caused by *Rickettsia typhi* which is distributed worldwide, including in Laos. Although the disease is treatable, a previous study observed higher rates of clinical failure following treatment with azithromycin compared to doxycycline. The gold standard assay for antibiotic susceptibility testing (AST) for *R. typhi* is the time-consuming plaque assay, taking up to 14 days to perform. AST using qPCR has been applied as a more rapid method to determine minimal inhibitory concentration (MIC). However, there is little published data comparing both methods with clinical and laboratory strains of *R. typhi*. In this study, we aimed to compare antibiotic susceptibility testing for *R. typhi* using qPCR and plaque assays.

METHODS:

24 *R. typhi* isolates (8 laboratory strains and 16 Lao clinical isolates) were cultured in Vero cells to determine *in vitro* antibiotic susceptibility. MIC determination for azithromycin, doxycycline and amoxicillin using qPCR targeting *ompB* and the plaque assay were performed simultaneously. Heat inactivation of *R. typhi* at 56°C for 30 min was used as a control to determine MIC for both methods. MIC using the plaque assay was determined as the lowest concentration without plaque formation, whereas for qPCR we used the concentration corresponding to the Ct value that was equal to or higher than the Ct value obtained for the heated inactivated sample to estimate the MIC. Agreement between two methods was calculated by the Spearman coefficient.

RESULTS:

Median MIC results using qPCR for azithromycin, doxycycline and amoxicillin were 0.0625 mg/l (95%CI, 0.0313-0.1250) 0.0625 mg/l (95%CI, 0.0625-0.1250) and 256 mg/l (95% CI, 128-256), respectively, whereas the median MIC data from the plaque assays were 0.5 mg/l (95%CI, 0.0625-1), 0.0313 mg/l (95%CI, 0.0313-0.0313) and 64 mg/l (95%CI, 64-128), respectively. Spearman coefficients were 0.1045, 0.0636 and 0.0562 for azithromycin (p = 0.6272), doxycycline (p = 0.7680) and amoxicillin (p = 0.7941), respectively.

CONCLUSIONS:

MIC determination using the plaque assay for azithromycin was about 8-fold higher than using qPCR, whereas the MIC for doxycycline and amoxicillin using plaque assay were 2-fold and 4-fold lower, respectively, than MIC based on qPCR. Therefore, antimicrobial susceptibility testing for various *R. typhi* clinical isolates using qPCR was not comparable with the plaque assay to detect viable rickettsiae. Viable qPCR (v-qPCR) may be a promising avenue for further investigation.

Lao Infectious Diseases Society 4th Annual Scientific Conference,
12 January 2023, Mittaphab Hospital, Vientiane.
AMR in Laos: update and treatment challenges. Ashley EA. No abstract available.

Lao Infectious Diseases Society 5th Annual Scientific Conference,
21 December 2023, Mittaphab Hospital, Vientiane.
Unexpected Fever in Laos. Chansamouth V. No abstract available.

When it's not TB. Evans J, Phaxayaseng S. No abstract available.

Other Activities in 2023

Public engagement & advocacy

Pint of Science Laos

LOMWRU hosted Pint of Science Laos 2023 on Monday 22-Tuesday 23 May 2023 at Corebeer, a local Vientiane brewery. Over 90 attendees joined in the festivities, talks and quizzes each night. On 22 May, Phoutmany Thammavong (Save the Children) introduced a *New method for dengue control: Fight fire with fire*, Weerawat Phuklia (LOMWRU) spoke about *Rickettsia: the food thief*, and Vilaysone Khounvisith (Institut Pasteur du Laos) discussed sanitation and infectious diseases with *WASH away diseases*. Tuesday night kicked off with Erik Delaquis (Alliance of Biodiversity International and CIAT) talking about *Seeds: the genetic exchanges enabling Lao agriculture*, followed by Chanthasone Phommachanh (Saola Foundation for Annamit Mountains Conservation) talking about the *Mysterious saola: ecology and conservation of the Lao unicorn*, finishing off with Rica Zomora Duchateau (Clinton Health Access Initiative) and *The special thing about spatial: applying maps to public health in Laos*. The event was an amazing success, and a big thank you goes out to the Pint of Science Laos team: Matt Robinson, Tamalee Roberts, Latsaniphone Boutthasavong, Bountoy Sibounheuang, Kaisone Padith, Vanheuang Phommadeechack, Padthana Kiedsathid, Ooyanong Phonemeexay, Vilaiphone Phomsisavath, Johnny Evans, Aphaphone Adsamouth, Malavanh Vongsouvath & Vayouly Vidhamaly.

Pint of Science is a global science festival with talks from researchers open to the public. From 22-24 May 2023, there are over 3,000 Pint of Science events in over 400 cities across 26 countries.

World AMR Awareness Week 2023

Themed *Preventing antimicrobial resistance together* and held 18-24 November, World AMR Awareness Week (WAAW) 2023 was marked with several events in the Lao PDR and around the world. On Friday 24 November, the Department of Healthcare and Rehabilitation, Ministry of Health, hosted a half-day meeting sponsored by LOMWRU at the Muong Thanh Luxury Hotel in Vientiane to roll out the Lao antimicrobial prescribing guidelines nationally. Around 80 representatives from all provinces in Lao PDR attended and participated in lively discussions about challenges to prescribing antimicrobials appropriately, especially in provinces with no diagnostic microbiology. Dr Vilada Chansamouth, who led the development of the guidelines and piloted their implementation in six hospitals as part of her DPhil, gave a talk on the current situation of AMR in Lao PDR, and explained how to use the Lao language guidelines, which are available as

a mobile phone application and in pocketbook format. Vilada then facilitated a panel discussion with experts including Assoc Prof Valy Keoluangkhot (former head of the Adult Infectious Diseases Ward, Mahosot Hospital), Dr Sengchanh Kounnavong (former Director-General of the Lao Tropical and Public Health Institute), Dr Khamla Choumlivong (former head of the Adult Infectious Diseases Ward, Setthathirath Hospital), and Dr Bounxou Keohavong (Director General of the Food & Drugs Department, Ministry of Health).

Konnie Bellingham, Vilaiphone Phomsisavath and Tamalee Roberts at the WAAW event. © LOMWRU/MORU. Photographer: Elizabeth Ashley.

Health technology assessment (HTA)

***5th SAPPHIRE Advisory Committee Meeting,* Vientiane**

On behalf of the Lao Unit for Health Evidence and Policy (UHEP), LOMWRU and the University of Health Sciences (UHS) hosted from 9-11 October in Vientiane the *Strengthening Active Partnerships for Policy and Health Intervention Research and Evaluation (SAPPHIRE) 5th Advisory Committee Meeting*. Other member organisations included: the Thailand National Health Foundation (NHF); the Health Intervention and Technology Assessment Program (HITAP); the Saw Swee Hock School of Public Health (SSHSPH), National University of Singapore (NUS); Mahidol Oxford Tropical Medicine Research Unit (MORU), Padjadjaran University in Indonesia; and Hitotsubashi Institute for Advanced Study (HIAS), Hitotsubashi University (HU) in Japan. HTA is a focus of the Asia-based SAPPHIRE network which works on a variety of topics, particularly with a health economics, health systems or strong policy element. The partners also exchange staff and share educational and training opportunities. *(Photo credit Sirithorn Khositchaiwat)*

Participants to the 5th SAPPHIRE Advisory Committee Meeting in Vientiane, October 2023. Photo from HITAP.

Mahosot Microbiology Department wins award for their service

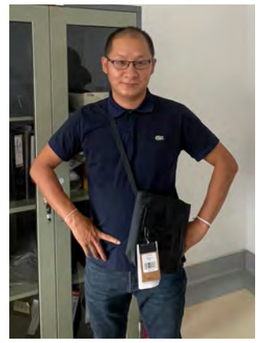
Congratulations to our close colleagues in the Microbiology Department of Mahosot Hospital who won Silver Prize at the annual review of Mahosot Hospital. This was based on feedback from patients and their relatives as part of 'Five Goods One Satisfaction' - a national policy to improve the quality of care for our patients. The Minister of Health, Dr Bounfeng Phoummalaysith, presented members of the microbiology team with their certificates, and LOMWRU's Dr Manivanh Vongsouvath, Director of Microbiology and Deputy Head of Virology, made the front page of a national newspaper.

LAO MEDICAL JOURNAL

LOMWRU continues to support publication of the *Lao Medical Journal*.

FAREWELLS

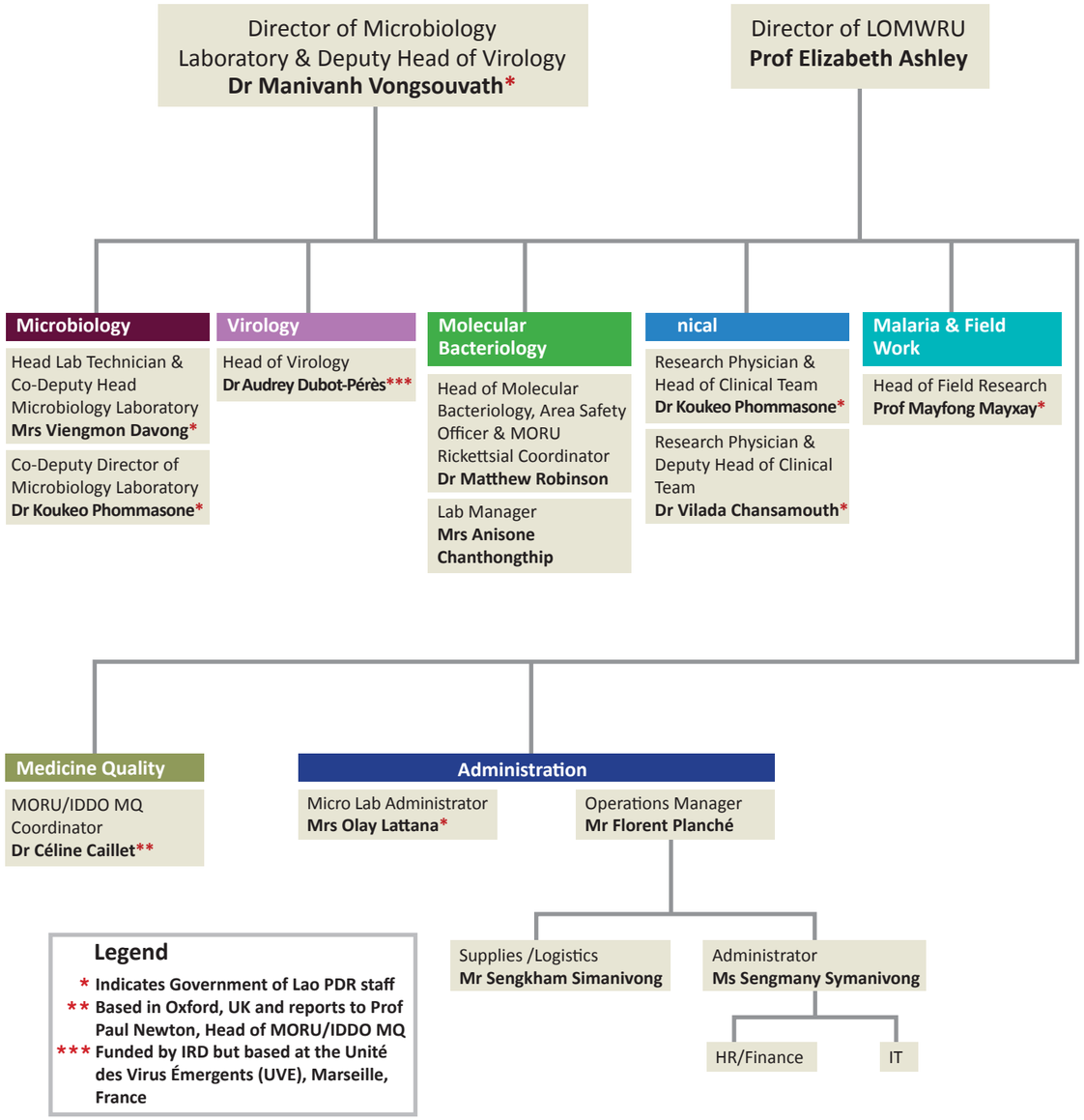
In August 2023, we bid *Bon Voyage!* to Kay (Athirat) Black as she moved back to the UK after 6 years of working in Laos. Kay worked diligently to improve LOMWRU's administrative processes and operations and will be sorely missed by everyone. © LOMWRU 2023. Photographer: Gerhard Joren.



Pao Yang, our IT support manager since 2018, also moved on to bigger and better things with a new position in Laos. We wish him all the best in his new job. Our new IT support manager is Mr Kikhamsen Singvonsa. © LOMWRU 2023. Photographer: Sompany Thepbandith.

Annex A – LOMWRU organisational chart for 2023

Lao-Oxford-Mahosot Hospital-Wellcome Trust Research Unit (LOMWRU)



Annex B – LOMWRU collaborators in 2023

NAMRU-IP visit (LCDR Nate Christy in red) to the Plain of Jars, Xieng Khuang Province with the LOMWRU study team. © LOMWRU 2023. Photographer: Elizabeth Ashley.

1. Department of Communicable Disease Control (DCDC), Ministry of Health, Lao PDR
2. Department of Health Care and Rehabilitation, Ministry of Health, Lao PDR
3. Centre of Malariology, Parasitology & Entomology, Ministry of Health, Lao PDR
4. National Centre for Laboratory & Epidemiology, Ministry of Health, Lao PDR
5. Food and Drug Department, Ministry of Health, Lao PDR
6. University of Health Sciences, Ministry of Health, Lao PDR
7. Provincial Hospitals of Luang Namtha, Xieng Khouang, Salavan, Savannakhet, Attapeu and Vientiane, Lao PDR
8. Central Hospitals in Vientiane Capital: Mittaphab, Setthathirath, National Children's, Mother & Child, Police and Army Hospitals, Lao PDR
9. National Institute of Public Health, Vientiane, Lao PDR
10. Food & Drug Quality Control Laboratory, Ministry of Health, Lao PDR
11. National Animal Health Laboratory, Lao PDR
12. Bureau of Food and Drug Inspection, Ministry of Health, Lao PDR
13. Savannakhet Provincial Health Office, Lao PDR
14. WHO Lao Country Office, Vientiane, Lao PDR
15. Institut de Recherche pour le Développement (IRD), Lao PDR
16. Centre d'Infectiologie Christophe Mérieux du Laos, Lao PDR

17. Institut Pasteur du Laos, Lao PDR
18. Health Frontiers, Vientiane, Lao PDR
19. Dr Mathieu Picardeau, Unité de Biologie des Spirochètes, Institut Pasteur, Paris, France
20. Dr Alain Pierret and Dr Anne Pando, Institut de Recherche pour le Développement, Lao PDR
21. Dr Olivier Ribolzi, Géosciences Environnement Toulouse, Université de Toulouse, France
22. Dr Lee Smythe and Dr Scott Craig, Leptospiral Reference Laboratory, Coopers Plains, Australia
23. London School of Hygiene and Tropical Medicine, London, UK
24. Prof Bart Currie, Menzies School of Health Research, Australia
25. Prof Al Richards, Rickettsial Diseases Research Program, Naval Medical Research Center, USA
26. Naval Medical Research Center Asia Pacific, Singapore
27. Prof David Relman and Dr Stephen Popper, Department of Microbiology and Immunology, Stanford University, California, USA
28. Swiss Tropical and Public Health Institute, Basel/University of Basel, Switzerland
29. Dr Tim Barkham, Tan Tock Seng Hospital, Singapore
30. Dr Kate Bond, Dr Souly Phanouvong, Dr Jude Nwokike, Dr Victor Pribluda and Dr Mustapha Hajjou, United States Pharmacopeia, Rockville, Maryland, USA
31. Dr Todd French and Philip Bulterys, University of California - Los Angeles, USA
32. Dr Daniel Parker, University of California - Irvine, USA
33. Prof Fiona Russell, Murdoch Children's Research Institute (MCRI), University of Melbourne, Victoria, Australia
34. Prof John Crump, University of Otago, New Zealand
35. Prof Nicole Zitzmann and Dr Bevin Gangadharan, Department of Biochemistry, University of Oxford, UK
36. Infectious Diseases Data Observatory (IDDO), Centre for Tropical Medicine & Global Health, University of Oxford, UK
37. Dr Anders Omsland, Paul G Allen School for Global Animal Health, Washington State University, WA, USA
38. Dr John Pettersson, University of Uppsala, Sweden
39. PATH, Seattle, USA
40. Prof Sabine Dittrich, Deggendorf Institute of Technology, Germany
41. Foundation for Innovative New Diagnostics (FIND), Geneva, Switzerland
42. Mathieu Pruvot and Amanda Fine, Wildlife Conservation Society, Wildlife Health Program, Bronx, New York, USA
43. Wildlife Conservation Society, Lao PDR Program, Vientiane, Lao PDR
44. Philippe Dussart and Paul Horwood, Institut Pasteur du Cambodge, Phnom Penh, Cambodia (now at Institut Pasteur du Madagascar, Antananarivo, Madagascar, and Australian Institute of Tropical Health and Medicine, James Cook University, Cairns, Australia, respectively)
45. Prof Xavier de Lamballerie, Unité des Virus Émergents, Aix-Marseille Université, Institut National de la Santé Et de la Recherche Médicale (INSERM), Institut de Recherche pour le Développement (IRD), France
46. Institute of Medical Microbiology, University of Zurich, Switzerland
47. Institute for Health Metrics and Evaluation, USA
48. Médecins sans Frontières, France
49. Ecohealth Alliance, USA
50. Duke-NUS Medical School, Singapore
51. Clinton Health Access Initiative, Lao PDR
52. Dr Martine Barons, University of Warwick, UK
53. Health Intervention and Technology Assessment Program, Bangkok, Thailand
54. InBios International Inc. Innovative Diagnostics, USA
55. Global Access Diagnostics, UK, USA
56. Dr Chanthala Souksakhone, National Blood Transfusion Centre, Lao Red Cross, Vientiane, Lao PDR
57. Foundation Mérieux, Lao PDR
58. Prof David Denning, Manchester Fungal Infections Group, UK
59. Prof David Modrý and Dr Vojtech Baláž, University of Veterinary Sciences Brno, Czech Republic
60. Prof Mike Wiley, University of Nebraska, USA
61. Shoklo Malaria Research Unit (SMRU), Thailand
62. Mahidol Vivax Research Unit (MVRU), Thailand
63. Oxford University Clinical Research Unit (OUCRU), Viet Nam
64. Olivier Celhay, freelance consultant, USA

Dr Alicia Quach from the Murdoch Children's Research Institute, Melbourne, Australia was in Laos the week of 12 June to check on the progress of the LOOP (Laos-Out-Of-Pocket costs) study which is recruiting families in the National Children's Hospital in Vientiane and Salavan Provincial Hospital in southern Laos. The study aims to document the costs to families when a child is acutely unwell requiring hospitalization in different contexts in Laos. Pictured from left, the Vientiane-based LOOP (and Acute Respiratory Infections in Vientiane (ARIVI) team: Amphaivanh Thammavong, Nar Kingkeoooudom, Alicia Quach, Valin Chanthaluanglath and Toukta Bounkhoun. © LOMWRU 2023.

Annex C – LOMWRU staff in 2023

© LOMWRU. Photographer: Elizabeth Ashley.

Lao-Oxford-Mahosot Hospital-Wellcome Trust Research Unit (LOMWRU)

Elizabeth Ashley – Unit Director

Atsamouth, Aphaphone	Laboratory Technician
Bellingham, Khonsavath	Research Scientist
Boutthasavong, Latsaniphone	Senior Laboratory Technician/ Deputy IDC lab Manager
Bounkhoun, Toukta	Research Physician
Bounmanivong, Noy*	Cleaner
Bounvilay, Laddaphone	Research Physician
Caillet, Céline	Medicine Quality Research Group Coordinator/ Research Scientist
Chu, Cindy	Research Physician
Chansamouth, Vilada*	Senior Research Physician/ PhD Student
Chanthaluanglath, Valin	Nurse, Patient Follow up
Chanthongthip, Anisone	Laboratory Manager
Chindavong, Touny	Data Entry Officer
Chommanam, Danoy	Research Physician
Davong, Viengmon*	Deputy Head of Microbiology Laboratory / Lab Manager
Duangmala, Souksavanh	Laboratory Technician - Follow up
Duangmala, Khuanta*	Laboratory Technician
Duangnouvong, Anousone	Research Physician
Dubot-Pérès, Audrey	Virology Group Head
Evans, Terry John	Clinical Fellow in Microbiology
Hanthongsay, Nilamith*	Specimens Storage Manager
Jaksuwan, Risara	Laboratory Management Advisor
Kaech, Chloé	Research Physician
Keokhamhoung, Dala	Patient Follow Up/ Lab Technician
Keomoukda, Phatsalin	Laboratory Technician-Field
Khamsy, Chanthachone	Stock Officer
Khounpaseuth, Khamxeng	Laboratory Technician, Field
Kouaykesone, Phoudthasone	Data Quality Manager
Kiedsathid, Padthana	Laboratory Technician
Kingkeoudom, Nar	Data Entry Officer
Kitignavong, Inthaphavanh	Research Physician
Lathsachak, Thongsavanh	Laboratory Technician - Field
Lattana, Olay*	Head of Micro Lab Admin/ Senior Laboratory Technician
Luangraj, Manophab	Research Physician
Mayxay, Mayfong*	Head of Field Research/ Deputy Dean of University of Health Sciences
Nalongsack, Manilung	Health Technology Assessment Researcher
Opphalavong, Somphone	Security Guard
Panapruksachat, Siribun	Molecular Bacteriologist
Panyanouvong, Phonepasith*	Senior Laboratory Technician
Pimxaythong, Viengsavanh	Research Scientist
Phalivong, Sonexay	Project Coordinator (CMPE)
Phianthanom, Bountherng*	Laboratory Technician
Phimolsannousith, Vilayouth	Research Physician
Phommadichak, Vanheuang	Research Scientist
Phommahasay, Bounkhong*	Laboratory Technician
Phommasone, Koukeo*	Deputy Head of Microbiology Laboratory/ Research Physician
Phonemixay, Ooyanong	Laboratory Technician
Phouminh, Phonelavanh*	Deputy Head of Micro Lab Administration & Senior Lab Technician
Padith, Kaisone	Laboratory Technician
Phuklia, Weerawat	Postdoctoral Scientist
Phakhounthong, Khanxayaphone	Research Physician, Field
Phommavanh, Xaykhamphet	Research Physician, Field
Phommavong, Touy	Research Physician- Field
Phomsisavath, Vilaiphone	Research Veterinarian
Phoutthavong, Soulichanya	Research Physician, Field
Planché, Florent	Operations Manager
Roberts, Tamalee	Research Scientist
Robinson, Matthew	Group Head Molecular Bacteriology & Area Safety Advisor
Seevanhthong, Khambang	Research Physician - Field

* Indicates Government of Lao PDR staff

Sengdatka, Davanh*	Laboratory Technician
Sengduangphachanh, Amphonesavanh*	Quality Control/ Senior Laboratory Technician
Seubsanith, Amphaivanh*	Laboratory Technician
Sibounheuang, Bountoy*	Senior Laboratory Technician
Silichack, Lanoi*	Laboratory Technician
Silisouk, Joy*	Senior Laboratory Technician
Simanivong, Sengkham	Purchase & Supply Administrator
Simanivong, Souksavanh	Field Administrator/Logistician, Field
Simmalavong, Manivone*	Deputy Head of Micro Lab Administration / Laboratory Technician
Siratana, Vannavong	Research Physician
Singvongsa, Kikhamsen	IT Manager
Sihabout, Mongkhounthong	Facilities Officer
Souksavanh, Manila	Laboratory Technician
Solathtanavong, Tadam	Administrative and HR Officer
Soulivong, Ailatda	Research Physician, Field
Soukhammala, Sompasong	Finance and Admin assistant
Souvannasen, Vilason	Laboratory Technician
Syhalath, Somsavanh*	Technician
Symanivong, Sengmany	Finance and HR Administrator
Sydalay, Sengdavanh	Research Physician
Thamavong, Sompong	Laboratory Technician, Field
Thammavongsa, Peeyanout	Research Physician
Thalongsengcha, Mayulee	Clinical research assistant
Thepbandith, Sompany	Finance Officer
Thongpaseuth, Souliyasack	Senior Laboratory Technician
Vang, Sao*	Laboratory Technician
Vannachone, Souphaphone	Research Physician
Vidhamaly, Vayouly	Head of Clinical Trials Support Group
Vilivong, Keoudomphone	Research Physician
Volavong, Souksakhone	Specimens Storage Assistant
Vongsouvath, Manivanh*	Director of Microbiology Laboratory / Deputy Virology Group Head
Vongsouvath, Viengsavanh	Administration Assistant
Vongsouvath, Malavanh*	Laboratory Technician
Xaithilath, Parnthong	Data Entry Officer
Xayaphet, Xaipasong	Research Physician, Field
Xayalath, Somdy	Laboratory Technician, Field
Xongmalaythong, Khamthasone	Data Entry Officer
Xayvanghang, Saiamphone	Project Coordinator
Xayasit, Buasy*	Cleaner
Yang, Pao	IT Helpdesk Support Manager
Yiaye, Touxiong	Research Physician - Field

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