2022
ANNUAL REPORT

Lao-Oxford-Mahosot Hospital-Wellcome Trust Research Unit

LOMWRU.

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wellcome

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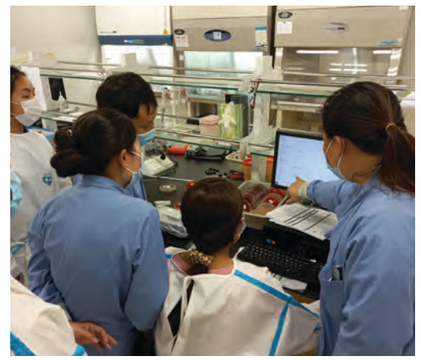
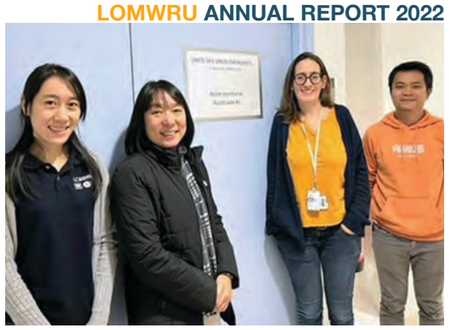
Table of Contents









The Lao-Oxford-Mahosot Hospital-Wellcome Trust Research Unit

ກ່ຽວກັບໜ່ວຍງານຄົ້ນຄວ້າຂອງພວກເຮົາ

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

ການຮ່ວມມືລະຫວ່າງ ໂຄງການຄົ້ນຄວ້າພະຍາດເຂດຮ້ອນລະຫວ່າງ ໂຮງໝໍມະໂຫສົດ-ແວວຄໍາທ໌ຕັ້ສ-ມະຫາວິທະຍາໄລອ໋ອກຟອດ ແລະ ສະຖາບັນຄົ້ນຄ້ວາເພື່ອການພັດທະນາຝຣັ່ງ Institut de Recherche pour le Développement ຫຼື IRD) ແມ່ນ ເລີ້ມມາຕັ້ງແຕ່ປີ 2006. ທີ່ທ່ານ ດຣ Audrey Dubot-Pérès ຫົວໜ້າໜ່ວຍງານ ຈຸລະໂລກວິທະຍາ ປະຈໍາ LOMWRU ເຊິ່ງປະຈຸບັນ ປະຈໍາການຢູ່ ໜ່ວຍງານຈຸລະໂລກ ທີ່ເກີດຂຶ້ນໃໝ່ (UVE), ທີ່ເມືອງ ມາກຊາຍ, ປະເທດຝຣັ່ງ.

ປະຈຸບັນ ພວກເຮົາມີພະນັກງານທັງໝົດ 68 ຄົນ ຊຶ່ງລວມມີ ພະນັກງານທີ່ເຮັດວຽກປະຈໍາຢູ່ນະຄອນຫຼວງວຽງຈັນ ແລະ ຕ່າງແຂວງ ທີ່ເປັນໜຶ່ງໃນວຽກງານການຮ່ວມມືຄົ້ນຄ້ວາ, ແລະ ໃນນັ້ນຍັງມີ ພະນັກງານພາກລັດຈາກພະແນກຈຸລິນຊີວິທະຍາ ຈໍານວນ 20 ຄົນ ໂດຍມີ ດຣ ມະນີວັນ ວົງສຸວັດ ເປັນຫົວໜ້າພະແນກ. ໜ່ວຍງານຄົ້ນຄວ້າ LOMWRU ມີຫ້ອງວິເຄາະ ທາງພັນທຸກໍາ, ຫ້ອງວິເຄາະເຊໂຣໂລຊີ ແລະ ຫ້ອງວິເຄາະຄວາມປອດໄພລະດັບ 3 (BSL3) ສໍາລັບປູກເຊື້ອ Rickettsial, *Mycobacterium* spp., *B. pseudomallei* ແລະ ເຊື້ອໄວຣັສ. ສຈ. ປອ. ດຣ ມາຍຟອງ ມາຍຊາຍ, ຮອງອະທິການບໍດີ ມະຫາວິທະຍາໄລ ວິທະຍາສາດ ສຸຂະພາບ ຊ່ວຍຊີ້ນໍາວຽກງານຮ່ວມມືຄົ້ນຄວ້າກັບບັນດາ ແຂວງ ແລະ ວຽກງານຄົ້ນຄວ້າ ພາກສະໜາມ. ໜ່ວຍງານຄົ້ນຄວ້າ LOMWRU ໄດ້ສະໜັບສະໜູນການບົ່ງມະຕິພະຍາດທີ່ເກີດຈາກເຊື້ອຈຸລະຊີບໃນ ສ.ປ.ປ ລາວ, ສະໜັບສະໜູນການຝຶກອົບຮົມ 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 which has research units in Thailand, Cambodia, Laos, Myanmar and Democratic Republic of Congo.

The collaboration between LOMWRU and Unit for Emerging Viruses in Marseille, funded by the Institut de Recherche pour le Développement (IRD), dates back to 2006. Dr Audrey Dubot-Pérès is the Head of Virology at LOMWRU but is based in the Unité des Virus Emergents (UVE), Marseille, France.

Currently there is a team of 68 research and support staff in the capital and the provinces working on projects as part of the collaboration, working alongside 20 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 viral 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.

ໜ່ວຍງານຄົ້ນຄວ້າ LOMWRU ທີ່ເດີນຈອດເຮລິຄອບເຕີ້ ຂອງໂຮງໝໍມະໂຫສິດ. © 2023 LOMWRU. ຮູບພາບໂດຍ: Gerhard Jørén.

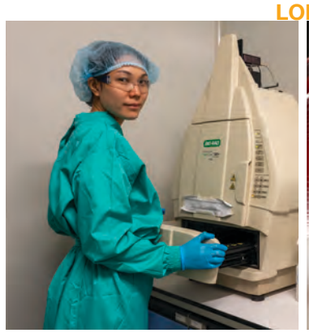
Message from the Director

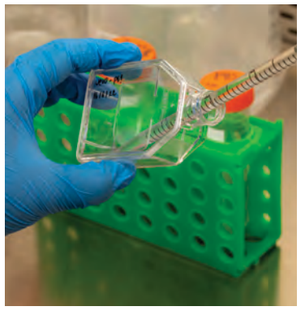
ຄຳເຫັນຂອງທ່ານ Professor Elizabeth Ashley

ໃນປີ 2022, ຊີວິດການເປັນຢູ່ຂອງເຮົາໄດ້ຄ່ອຍໆປັບໂຕສູ່ສະພາບປົກກະຕິ ເມື່ອທົ່ວໂລກໄດ້ຮຽນຮູ້ທີ່ຈະຢູ່ຮ່ວມກັບພະຍາດ COVID-19. ດ່ານສາກົນລະຫວ່າງ ສປປ ລາວ ແລະ ນາໆຊາດກໍໄດ້ກັບມາເປີດຮັບນັກທ່ອງທ່ຽວຢ່າງເປັນທາງການອີກຄັ້ງໃນວັນທີ 09 ພຶດສະພາ 2022 ເຖິງແມ່ນວ່າຈະໃຊ້ເວລາຫຼາຍເດືອນໃນການຈັດການຖ້ຽວການເດີນທາງ. ສິ່ງທີ່ຫຼົງເຫຼືອຈາກພະຍາດ COVID-19 ຍັງຄົງຢູ່ ພ້ອມກັບຄວາມເສຍຫາຍຕໍ່ເສດຖະກິດລາວ ແລະ ຄວາມສ່ຽງທີ່ສຳຄັນດ້ານສຸຂະພາບ ແລະ ການພັດທະນາຕະຫຼອດໄລຍະສອງທົດສະວັດທີ່ຜ່ານມາ ອາດເຮັດໃຫ້ຫັນກັບຄືນໄດ້.

ໃນອີກໜຶ່ງດ້ານທີ່ເປັນດ້ານດີ ພວກເຮົາສາມາດເຮັດການສຶກສາຄົ້ນຄວ້າ ແລະ ການຝຶກອົບຮົມໄດ້ຫຼາຍຂຶ້ນຕະຫຼອດປີ 2022. ການແຜ່ລະບາດນີ້ ເປັນແຮງຊຸກຍູ້ຂອງພວກເຮົາໃນການສຶກສາການຈັດລຳດັບພັນທຸກຳເຊື້ອ ໃນ LOMWRU ໃຫ້ຫຼາຍຂຶ້ນ. ດ້ວຍການສະໜັບສະໜຸນຈາກ Wellcome Trust, ພວກເຮົາໄດ້ຈຳແນກສາຍພັນເຊື້ອໄວຣັສ SARS-CoV-2 ໃນຄົນເຈັບຄົນລາວ ເຊິ່ງເປັນໜຶ່ງໃນວຽກງານການເຝົ້າລະວັງດ້ານພັນທຸກຳແຫ່ງຊາດ ທີ່ນຳພາໂດຍສູນວິເຄາະ ແລະ ລະບາດວິທະຍາ. ພວກເຮົາໄດ້ແບ່ງປັນຂໍ້ມູນການແຍກສາຍພັນຫຼາຍກວ່າ 700 ເຊື້ອໃຫ້ແກ່ GISAID (Global Initiative on Sharing Avian Influenza Data) ແລະ ຖານຂໍ້ມູນຂອງ GenBank. ນອກນີ້ ພະຍາດ COVID-19 ຍັງໄດ້ເປັນໜັກຄວາມສຳຄັນຂອງແນວທາງ One Health ເພື່ອຈັດການກັບພະຍາດຊຶມເຊື້ອ ແລະ ການດື້ຢາ.


ຈາກຊ້າຍມື: ຮອງຜູ້ອຳນວຍການໂຮງໝໍ ມະໂຫສິດ ດຣ ໄຄສີ ລາຊະວົງ, ຜູ້ອຳນວຍການ ດຣ ຊຸຊາດ ວົງພະຈັນ, ແລະ ຄະນະຮອງຜູ້ອຳນວຍການ ດຣ ໄຊຊະນະ ສົມບັນດິດ, ທ່ານ ນາງ ບົວລັນ ປະທຸມທອງ ແລະ ດຣ ບຸນໂອມ ກັນທະວົງ. © LOMWRU 2023. ຮູບພາບໂດຍ: Gerhard Jørén (ຮູບຊ້າຍມື) ແລະ ທ່ານ ບຸນໂອມ ກັນທະວົງ. (ຮູບຂວາມື).


ພວກເຮົາຍັງມີຄວາມປິຕິຍິນດີທີ່ໄດ້ຈັດງານ *Pint of Science* ເຊິ່ງຈັດຂຶ້ນເປັນຄັ້ງທຳອິດໃນລາວ ປີ 2022 ນຳພາໂດຍ ທ່ານ Matt Robinson. ງານດັ່ງກ່າວ ເປັນງານເທດສະການວິທະຍາສາດລະດັບໂລກ ທີ່ໄດ້ເຕົ້າໂຮມບັນດານັກຄົ້ນຄວ້າວິທະຍາສາດ ເພື່ອມາແບ່ງປັນຜົນງານຂອງຕົນກັບທຸກໆຄົນທີ່ສົນໃຈໃນສະຖານທີ່ ແລະ ບັນຍາກາດທີ່ສະບາຍໆເຊັ່ນຮ້ານກາເຟ.

ທ່ານນາງ Amanda Milling ລັດຖະມົນຕີກະຊວງການຕ່າງປະເທດ ແຫ່ງເຄືອຈັກກະພົບ ແລະ ການພັດທະນາ ແຫ່ງສະຫະລາຊະອານາຈັກປະຈຳເຂດອາຊີ, ໄດ້ມາຢ້ຽມຢາມ ສປປ ລາວ ໃນວັນທີ 30 ມິນາ ເຖິງ 2 ເມສາ 2022 ເພື່ອສົ່ງເສີມການຮ່ວມມືດ້ານສຸຂະພາບທົ່ວໂລກ, ການປ່ຽນແປງສະພາບອາກາດ ແລະ ການຄ້າ ແລະ ເພີ່ມຍັງໄດ້ຖືໂອກາດເຂົ້າມາຢ້ຽມຢາມພວກເຮົາຢູ່ໂຮງໝໍມະໂຫສິດອີກດ້ວຍ. ເພີ່ນໄດ້ໃຫ້ຄວາມສົນໃຈຮັບຟັງກ່ຽວກັບກອງທຶນ UK Fleming Fund ປະຈຳລາວ ເພື່ອສົ່ງເສີມການເຝົ້າລະວັງ AMR ໃນລາວ ທີ່ລາວເຮົາເປັນສ່ວນໜຶ່ງໃນກອງທຶນດັ່ງກ່າວ.

ສຸດທ້າຍນີ້ ຂ້າພະເຈົ້າຂໍກ່າວຄຳຂອບໃຈແກ່ທ່ານ ປອ ດຣ ຊຸຊາດ ວົງພະຈັນ, ຜູ້ອຳນວຍການໂຮງໝໍມະໂຫສິດ ແລະ ຄະນະອຳນວຍການ ທ່ານນາງ ບົວລັນ ປະທຸມທອງ, ດຣ ໄຊຊະນະ ສົມບັນດິດ, ດຣ ບຸນໂອມ ກັນທະວົງ ແລະ ດຣ ໄຄສີ ລາຊະວົງ, ພ້ອມສະແດງຄວາມຂອບໃຈໄປຍັງທຸກໆພະແນກທີ່ໃຫ້ການຮ່ວມມື ແລະ ຊ່ວຍເຫຼືອທີ່ດີຕະຫຼອດມາຢ່າງຕໍ່ເນື່ອງ.

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ລາຍເຊັນຂອງທ່ານ Professor Elizabeth Ashley

Professor Elizabeth A Ashley
ຜູ້ອຳນວຍການ LOMWRU

The LOMWRU team on the Mahosot Hospital helipad. © 2023 LOMWRU. Photographer: Gerhard Jørén.

Message from the Director

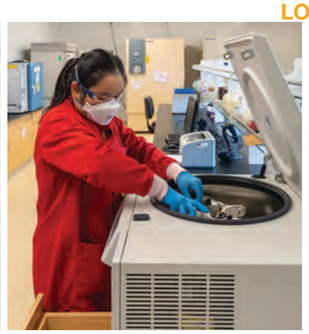
Professor Elizabeth Ashley

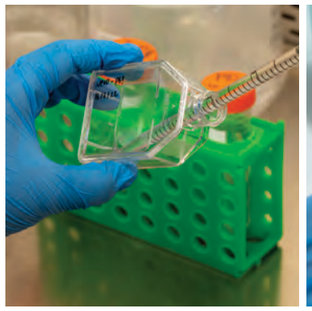
In 2022 life gradually got back to normal as the world learnt to live with COVID-19. The Lao borders re-opened to tourists in May 2022, although it took some months for flight schedules to resume. The legacy of COVID-19 remains with damage to the Lao national economy and the risk that important gains in health and development made over the last two decades may be reversed.

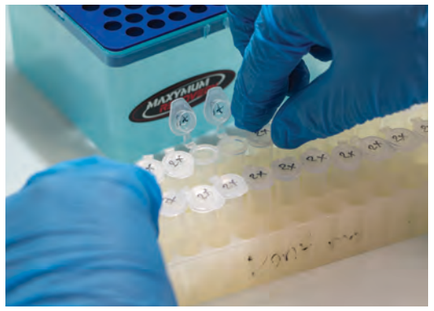
On a more positive note we were able to increase our research and training activities throughout 2022. The pandemic also gave us a push to do more whole-genome sequencing in LOMWRU. With funding from the Wellcome Trust, we have been sequencing SARS-CoV-2 viruses from Lao patients as part of the national genomic surveillance effort led by the National Centre for Laboratory and Epidemiology. We have now shared sequence data from more than 700 Lao strains with GISAID (Global Initiative on Sharing Avian Influenza Data) and GenBank sequence databases. COVID has also underlined the importance of a One Health approach to tackling infectious diseases and drug resistance.

From *left*: Mahosot Hospital Deputy Director Dr Khaysy Rassavong, Director Dr Susath Vongphachanh, and Deputy Directors Dr Xaysana Sombandith, Mrs Bouavanh Pathoumthong, and Dr Bounhome Kanthavong. © LOMWRU 2023. Photographers: Gerhard Jørén (*left photo*) and Bounhome Kanthavong (*right*).

We were delighted to hold the first ever *Pint of Science* event in Laos in 2022 which was led by Matt Robinson. This is a global science festival during which researchers share their work with anyone who is interested in a relaxed venue like a café.







The UK Minister for Asia at the Foreign, Commonwealth & Development Office, Amanda Milling was in Laos from 30 March to 2 April 2022 to boost collaboration on global health, climate change and trade and dropped in to see us at Mahosot Hospital. She was very interested to hear more about the UK Fleming Fund Laos Country grant to strengthen AMR surveillance in Laos which we are a part of.

Finally, I would like to thank Dr Susath Vongphachanh, Director of Mahosot Hospital, Deputy Directors Mrs Bouavanh Pathoumthong, Dr Xaysana Sombandith, Dr Bounhome Kanthavong and Dr Khaysy Rassavong, and all other departments for their continued collaboration and support.

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Best wishes,

Professor Elizabeth A Ashley
Director

May 2023

Research highlights in 2022

ຜົນການຄົ້ນຄວ້າທີ່ພົ້ນເດັ່ນໃນປີຜ່ານມາ

ໃນນີ້ ພວກເຮົາຂໍຍົກຜົນໄດ້ຮັບຈາກການຄົ້ນຄວ້າບາງບົດຂອງ LOMWRU ແລະ ຄູ່ຮ່ວມງານຈາກອົງການຈັດຕັ້ງຕ່າງໆ ທີ່ໄດ້ຮັບການຕີພິມໃນປີ 2021. ບົດຄົ້ນຄວ້າ ແລະ ບົດລັດຫຍໍ້ທັງໝົດ ແມ່ນສາມາດເບິ່ງໄດ້ຢູ່ລາຍງານສະບັບນີ້ ໃນພາກບົດຕີພິມຂອງ LOMWRU ປະຈຳປີ 2022

ພະຍາດໄຂ້ສະໝອງອັກເສບໃນເດັກນ້ອຍ

ການຕິດເຊື້ອໃນລະບົບປະສາດສ່ວນກາງໄດ້ສົ່ງຜົນກະທົບທີ່ຮ້າຍແຮງຕໍ່ເດັກນ້ອຍໃນທົ່ວໂລກ. ພະຍາດໄຂ້ສະໝອງອັກເສບອາດຈະນຳໄປສູ່ຄວາມຮ້າຍແຮງເຖິງຂັ້ນເສຍຊີວິດ ຫຼື ຜົນທີ່ຕາມມາດ້ານພັດທະນາການທາງລະບົບປະສາດໃນໄລຍະຍາວ. ເຖິງແມ່ນວ່າຈະມີການເຂົ້າເຖິງເຄື່ອງມືໃນການບົ່ງມະຕິທີ່ດີທີ່ສຸດແຕ່ສາເຫດທີ່ແທ້ຈິງກໍ່ມັກຈະບໍ່ສາມາດລະບຸໄດ້. ພວກເຮົາໄດ້ເຂົ້າຮ່ວມໂຄງການພະຍາດໄຂ້ສະໝອງອັກເສບອາຊີຕາເວັນອອກສຽງໃຕ້ (SouthEast Asia Encephalitis), ເຊິ່ງເປັນການສຶກສາໃນຫຼາຍປະເທດທີ່ນຳພາໂດຍສະຖາບັນປາສເຕີ (Institut Pasteur) ໃນປະເທດກຳປູເຈຍ, ທີ່ມີຈຸດປະສົງເພື່ອຊອກຫາສາເຫດຂອງພະຍາດໄຂ້ສະໝອງອັກເສບໃນເດັກນ້ອຍທີ່ເຂົ້າຮັບການປິ່ນປົວໃນໂຮງໝໍໃນທົ່ວຂົງເຂດພາກພື້ນລຸ່ມແມ່ນ້ຳຂອງໂດຍນຳໃຊ້ການບົ່ງມະຕິທີ່ທັນສະໄໝ. ໃນລະຫວ່າງປີ 2014 ຫາປີ 2017, ພົບວ່າມີເດັກນ້ອຍທີ່ເປັນພະຍາດໄຂ້ສະໝອງອັກເສບຈຳນວນ 664 ຄົນໃນປະເທດລາວ ຫວຽດນາມ ກຳປູເຈຍ ແລະ ມຽນມາ ໄດ້ເຂົ້າຮ່ວມໃນການສຶກສາ. ໂດຍມີລະບຸສາເຫດທີ່ໄດ້ຮັບການຢືນຢັນ ຫຼື ຄວາມເປັນໄປໄດ້ຂອງພະຍາດໄຂ້ສະໝອງອັກເສບໃນຄົນເຈັບຈຳນວນ 425 (64%).

ສາເຫດຕົ້ນຕໍແມ່ນເຊື້ອໄວຣັສໄຂ້ສະໝອງອັກເສບຍີ່ປຸ່ນໃນ 216 ຄົນ (33%) ຂອງຈຳນວນ 664 ກໍລະນີ, ໄຂ້ເລືອດອອກ 27 ຄົນ (4%), ເຊື້ອໄຂ້ຫວັດໃຫຍ່ 26 ຄົນ (4%), ເຊື້ອໄວຣັສ herpes simplex virus 1 ຈຳນວນ 24 ຄົນ (4%), ເຊື້ອວັນນະໂລກ 18 ຄົນ (3%), ເຊື້ອ *Streptococcus pneumoniae* 17 ຄົນ (3%), ແລະ ເຊື້ອ enterovirus A71 ຈຳນວນ 17 ຄົນ (3%). ຄົນເຈັບ 6 ຄົນ (1%) ໄດ້ຮັບການບົ່ງມະຕິວ່າເປັນພະຍາດໄຂ້ສະໝອງອັກເສບຈາກພູມຄຸ້ມກັນຜິດປົກກະຕິ. ເດັກນ້ອຍ 62 ຄົນໃນການສຶກສາທີ່ມາຈາກປະເທດລາວ (ໄດ້ຮັບການບົ່ງມະຕິຢັ້ງຢືນວ່າເປັນພະຍາດໄຂ້ສະໝອງອັກເສບຍີ່ປຸ່ນ 14 ຄົນ, ເຊື້ອວັນນະໂລກ 5 ຄົນ, ໄຂ້ເລືອດອອກ 2 ຄົນ, ເຊື້ອໄຂ້ຫວັດໃຫຍ່ 2 ຄົນ, ອື່ນໆ 8 ຄົນ).

ພະຍາດໄຂ້ສະໝອງອັກເສບຈາກພູມຄຸ້ມກັນແມ່ນໄດ້ຮັບການຍອມຮັບຫຼາຍຂຶ້ນວ່າມີຄວາມສຳພັນກັນກັບພະຍາດໄຂ້ສະໝອງອັກເສບໃນເດັກນ້ອຍ. ໃນການສຶກສາແຍກໃນນະຄອນຫຼວງວຽງຈັນເຊິ່ງກວດຊອກຫາ ທາດກາຍຕ້ານ (auto-antibodies) ໃນນ້ຳໄຂສັນຫຼັງ ແລະ ເຊຣຳຂອງຄົນເຈັບ 134 ຄົນທີ່ສົງໄສວ່າມີການຕິດເຊື້ອທາງລະບົບປະສາດສ່ວນກາງ ລວມເຖິງເຊຣຳຂອງການຄວບຄຸມສຸຂະພາບ. ຄົນເຈັບ 2 ຄົນທີ່ມີທາດກາຍຕ້ານແມ່ນມີການສະແດງອອກທາງດ້ານອາການສາດໂດຍທົ່ວໄປຂອງພະຍາດໄຂ້ສະໝອງອັກເສບຈາກພູມຄຸ້ມກັນຜິດປົກກະຕິ. ຢ່າງໃດກໍ່ຕາມ, ຄົນເຈັບອີກ 3 ຄົນທີ່ມີທາດກາຍຕ້ານທີ່ກວດພົບແມ່ນມີສາເຫດອື່ນສຳລັບການສະແດງອອກທາງລະບົບປະສາດສ່ວນກາງ, ໂດຍເນັ້ນໜັກເຖິງສິ່ງທ້າທາຍໃນການບົ່ງມະຕິພະຍາດນີ້.

Childhood encephalitis in the Greater Mekong region (the SouthEast Asia Encephalitis Project): a multicentre prospective study. Pommier JD, Gorman C, Crabol Y, Bleakley K, Sothy H, Santy K, Tran HTT, Nguyen LV, Bunnakea E, Hlaing CS, Aye AMM, Cappelle J, Herrant M, Piola P, Rosset B, Chevalier V, Tarantola A, Channa M, Honnorat J, Pinto AL, Rattanavong S, Vongsouvath M, Mayxay M, Phangmanixay S, Phongsavath K, Tin OS, Kyaw LL, Tin HH, Linn K, Tran TMH, Pérot P, Thuy NTT, Hien N, Phan PH, Buchy P, Dussart P, Laurent D, Eloit M, Dubot-Pérès A, Lortholary O, de Lamballerie X, Newton PN, Lecuit M; SEAe Consortium. *Lancet Glob Health*. 2022 Jul;10(7): e989-e1002. doi: 10.1016/S2214-109X(22)00174-7. PMID: 35714649; PMCID: PMC9210261.

Detection and significance of neuronal autoantibodies in patients with meningoencephalitis in Vientiane, Lao PDR. Uy CE, Mayxay M, Harrison R, Al-Diwani A, Jacobson L, Rattanavong S, Dubot-Pérès A, Vongsouvath M, Davong V, Chansamouth V, Phommasone K, Waters P, Irani SR, Newton PN. *Trans R Soc Trop Med Hyg*. 2022 Oct 2;116(10):959-965. doi: 10.1093/trstmh/trac023. PMID: 35385878; PMCID: PMC9526827.

ການຕິດເຊື້ອລະບົບຫາຍໃຈ ໃນ ສປປ ລາວ

ການຕ້ອຍດັ່ງ, ຄໍ ແມ່ນໄດ້ເພີ່ມຄວາມສາມາດຂອງພວກເຮົາ ໃນການບົ່ງມະຕິລະດັບໂມເລກຸນ ຂອງສາເຫດການຕິດເຊື້ອຂອງລະບົບຫາຍໃຈ. ຢ່າງໃດກໍຕາມ, ໃນລະບົບຫາຍໃຈພາກສ່ວນເທິງຂອງຄົນທີ່ແຂງແຮງນັ້ນ ອາດຈະມີເຊື້ອບັກເຕີຣີ ແລະ ໄວຣັສ ປະຈຳຖິ່ນຢູ່ແລ້ວ ເຊິ່ງອາດຈະເປັນການຍາກທີ່ຈະໝັ້ນໃຈວ່າ ບັກເຕີຣີ ແລະ ໄວຣັສນັ້ນໆ ເປັນສາເຫດທີ່ແທ້ຈິງຂອງພະຍາດ. ໃນລະຫວ່າງວັນທີ 24 ມີຖຸນາ 2019 ຫາ 24 ມີຖຸນາ 2020, ພວກເຮົາໄດ້ເອົາຄົນເຈັບເຂົ້າການສຶກສາທີ່ມາກວດຢູ່ໂຮງໝໍແຂວງຊຽງຂວາງ ດ້ວຍອາການສະແດງ ຂອງການຕິດເຊື້ອລະບົບຫາຍໃຈ ທັງໝົດ 205 ຄົນ. ຄົນເຈັບແຕ່ລະຄົນທີ່ເຂົ້າການສຶກສາ ຈະມີຄົນເຈັບປຽບທຽບໜຶ່ງຄົນທີ່ມາຈາກບ້ານດຽວກັນ ເພດດຽວກັນ ແລະ ອາຍຸໃກ້ຄຽງກັນ. ພວກເຮົາຈະໄດ້ເຮັດການຕ້ອຍດັ່ງ ໃນກຸ່ມຄົນເຈັບ ແລະ ກຸ່ມປຽບທຽບ(ບໍ່ເປັນພະຍາດ) ທຸກຄົນເພື່ອຊອກຫາເຊື້ອທີ່ມີຄວາມເປັນໄປໄດ້ທີ່ຈະເປັນພະຍາດ 33 ເຊື້ອ ດ້ວຍການເຮັດ PCR. ພວກເຮົາພົບ influenza B virus, influenza A virus, human metapneumovirus (HMPV) ແລະ respiratory syncytial virus (RSV) ໃນກຸ່ມຄົນເຈັບຫຼາຍກວ່າ ກຸ່ມປຽບທຽບ, ໃນຂະນະທີ່ *Streptococcus pneumoniae* 41% ພົບໃນກຸ່ມຄົນເຈັບ ແລະ 61% ໃນກຸ່ມປຽບທຽບ.

ຄົນເຈັບທີ່ເຂົ້ານອນໂຮງໝໍ ຍ້ອນຊຶມເຊື້ອລະບົບຫາຍໃຈສະທັນຫັນ ມີສາເຫດຈາກ influenza B virus, influenza A virus, human metapneumovirus (HMPV), and respiratory syncytial virus (RSV) in 17.8%, 17.2%, 7.5% ແລະ 6.5% ຂອງຄົນເຈັບ, ຕາມລຳດັບ. ພວກເຮົາບໍ່ SARS-CoV-2 ທັງ 2 ກຸ່ມ.

ຫຼັງຈາກການເຮັດການຄົ້ນຄວ້າຄັ້ງນີ້, ພວກເຮົາຍັງສືບຕໍ່ເຝົ້າລະວັງໄວຣັສຂອງລະບົບຫາຍໃຈຂອງຄົນເຈັບໃນ ແລະ ນອກ ຂອງໂຮງໝໍແຂວງຊຽງຂວາງ, ຫຼວງນ້ຳທາ ແລະ ອັດຕະປື ເຊິ່ງເຮົາສາມາດລວບລວມຂໍ້ມູນຂອງ COVID-19 ຈາກຫຼາຍໆແຫ່ງທົ່ວປະເທດ ຈາກປີ 2020 ຮອດປັດຈຸບັນ. ເຊິ່ງຂໍ້ມູນເຫຼົ່ານັ້ນ ແມ່ນມີຄວາມສຳຄັນສຳລັບ national genomic surveillance ແລະ ພວກເຮົາໄດ້ສົ່ງຕໍ່ໃຫ້ທາງ the International Severe Acute Respiratory and emerging Infection Consortium (ISARIC). ຊຸດຂໍ້ມູນຂອງ ISARIC COVID-19 ແມ່ນໄດ້ຮຽບຮຽງໃນຂະນະທີ່ມີການລະບາດຂອງ COVID-19 ແລະ ໄດ້ລວມເອົາຂໍ້ມູນຂອງຄົນເຈັບຫຼາຍກວ່າ 705,000 ຄົນ, ຈາກຫຼາຍກວ່າ 60 ປະເທດ ແລະ 1500 ສູນ ໃນທົ່ວໂລກ.

ນັກສຶກສາແພດຊ່ຽວຊານ ແລະ ຄູ່ມືການໃຫ້ຢາຕ້ານເຊື້ອສະບັບໃໝ່ © 2023 LOMWRU.
ຮູບພາບໂດຍ: ດຣ ວິລະດາ ຈັນສະໝຸດ

A case-control study of the causes of acute respiratory infection among hospitalized patients in Northeastern Laos. Phommasone K, Xaiyaphet X, Garcia-Rivera JA, Hontz RD, Pathavongsa V, Keomoukda P, Vongsouvath M, Mayxay M, Vongsouvath M, Newton PN, Ashley EA, Dubot-Pérès A. *Sci Rep*. 2022 Jan 18;12(1):939. doi: 10.1038/s41598-022-04816-9. PMID: 35042900; PMCID: PMC8766494.

ISARIC-COVID-19 dataset: A Prospective, Standardized, Global Dataset of Patients Hospitalized with COVID-19. ISARIC Clinical Characterization Group; Garcia-Gallo E, Merson L, Kennon K, Kelly S, Citarella BW, Fryer DV, Shrapnel S, Lee J, Duque S, Fuentes YV, Balan V, Smith S, Wei J, Gonçalves BP, Russell CD, Sigfrid L, Dagens A, Olliaro PL, Baruch J, Kartsonaki C, Dunning J, Rojek A, Rashan A, Beane A, Murthy S, Reyes LF. *Sci Data*. 2022 Jul 30;9(1):454. doi: 10.1038/s41597-022-01534-9. PMID: 35908040; PMCID: PMC9339000.

ภาบต้านต่ยาต้านเชื้อจุละชีบ และ ภาบใช้ยาต้านเชื้อจุละชีบ

ภาบต้านต่ยาต้านเชื้อจุละชีบ ยังถืงเป้นบับหาสำคับทางด้านสาทาละนะสุภ และ อัดตาของเชื้อ *E. coli* ที่ผะลิดสาบ extended-spectrum beta lactamase และเชื้อ *Staphylococcus aureus* ทิต้านต่ยา methicillin ยังสืบต่เพิ่มขึ้นย่างต่ำเมื่องในลาว. ปัดไจหนึ่งที่เธ็ดให้ภาบต้านต่ยาต้านจุละชีบ เพิ่มขึ้น แม่น ภาบนำใช้ยาต้านจุละชีบ. โดยภาบลอบลอมของ ท่าน นาง ดธ. วิละดา จันสะมุด เชิ่งได้เธ็ดภาบสำหลอดภาบนำใช้ยาต้านเชื้อและใบสั่งจ่ายยาต้านเชื้อจุละชีบนะจุดเอลาใดหนึ่ง, ได้แก่ 1 โธงหมสูนกาง และ 6 โธงหม แดอง ในส.ป.ป.ลาอ และ ได้ลายงานผินว่าลาอเป้นหนึ่งในปะเทดที่มีภาบสั่งจ่ายยาต้านเชื้อ จุละชีบสูงที่สุดในโลก, ปะมาบ 70% ของถ้นเจ็บบอนโธงหมได้ธับยาต้านเชื้อนะจุด เอลาใดหนึ่ง.

โธงหมะโทสิด ได้แบ่งปับข้มูน 20 ปี ใช้กับโดงภาบ Global Research on Antimicrobial Resistance (GRAM) จุดปะสิงแม่นเพื่อปะเม็นบับหา (พาละ) ของ AMR ในทั่วโลภ. ภาบค้นพิบ นี้ได้ถูกตีพิมลิงในอาละสานภาบแผด *Lancet*. มีภาบคาดภาบว่าในปี 2019 จะมีผู้เสยชีวิดในทั่ว โลภปะมาบ 4.95 ล้านถ้น (3.62-6.57) จาภเชื้อจุละชีบที่ต้านต่ยา.

ภาบต้านต่ยาต้านเชื้อแม่นหนึ่งในอวยภางานสุขะพาบหนึ่งดวย, ซึ่งสิ่งผินกะทับต่สัด และ สิ่งแวดล้อม ตะหลอด ธอดสุขะพาบของถ้น. Colistin (Polymyxin E) แม่นยาต้านเชื้อทางเลือกสุดท้าย ที่ใช้เข้า ในภาบป้นป้อ พะยาดฉีมเชื้อ จาภเชื้อต้านต่ยาหลายชะนิดซึ่งบ่มีอยู่ในลาอ. เถิงย่างใดก่ตามมับยังได่ถูกนำใช้เข้าในภาบป้นป้อสัดในขิงเขดอาชิตาเอ้นออกสยงใต้ และ เป้นต้อช่อยกะตุ้นภาบจะเลินเติบใหย่ของสัด. พอกเธา ได้มีภาบเลือกเก้บ 673 ต้อย่างจาภถ้น (ต้วยธูกะอาบ), ไก่, หมา, แมงอ้น และ น้ำในอวยจัน และ ได้กอดหา เชื้อ *E. coli* ที่ต้านต่ยา colistin เพื่อชอกหา gene (*mcr*) ที่ต้านต่ยา colistin. พอกเธาพิบเชื้อ *E. coli* ที่ต้านต่ยา colistin 14.6% ของต้อย่างทั้งหมิด (ลวมมิ 45,9% (45/98) ต้อย่างจาภถ้น, 14.3% (2/14) ในอาจิมของหมา, 12.0% (24/200) ในแมงอ้น, 11.0% (11/100) ในชิ้นไก่, 8.9% (8/90) ธูกะอาบไก่, 8.0% (4/50) ไส้ติ่ง/ไส้ต้นไก่, และ 7.5% (4/53) ในน้ำเสย).

มิถอามจำเป้นย่างธีบถ่อนในภาบผัดทะบายาต้านเชื้อจุละชีบชะนิดใหม่ และ ยังมิถอามพะยายามที่จะป่วนจุดปะสิงของยาเก่าที่บ่ได้นำใช้ป้นป้อภาบฉีมเชื้อในถ้น. Apramycin แม่นยาต้านเชื้อเก่าที่อยู่ในกุ่ม aminoglycoside ซึ่งก่อมพ้านี้ถูกนำใช้ในสัด และ ในภาบสึกสาของ preclinical ได้สะแดงให้เห้น ปะสิดทิพาบในภาบต้านต่เชื้อจุลินชี ภลามลิบ และ เชื้อที่ต้านต่ยาหลายชะนิด. พอกเธาได้เธ็ดภาบทิดสอบ ยาชะนิดนี้กับเชื้อจุลินชีที่เธาเก้บแยกได้จาภต้วอย่างถ้นเจ็บฉีมเชื้อที่ห้องวิเดาะจุลินชีโธงหมะโทสิด. มันออกลิดได้ดีหลายต่ำกับเชื้อจุลินชี ภลามลิบที่ต้านต่ยา gentamicin, carbapenems และ ยาลุ่มที่ 3 ของ cephalosporins และ กำลังอยู่ในละหว่างภาบผันขะหยายผักทะบาหางคลินิกเพิ่มติ่ม.

Evaluation of trends in hospital antimicrobial use in the Lao PDR using repeated point-prevalence surveys-evidence to improve treatment guideline use. Chansamouth V, Chommanam D, Roberts T, Keomany S, Paphasiri V, Phamisith C, Sengsavang S, Detleuxay K, Phoutsavath P, Bouthavong S, Douangnouvong A, Vongsouvath M, Rattana S, Keohavong B, Day NPJ, Turner P, van Doorn HR, Mayxay M, Ashley EA, Newton PN. *Lancet Reg Health West Pac*. 2022 Jul 9;27:100531. doi: 10.1016/j.lanwpc.2022.100531. PMID: 35846979; PMCID: PMC9283659.

Global burden of bacterial antimicrobial resistance in 2019: a systematic analysis. Antimicrobial Resistance Collaborators. *Lancet*. 2022 Feb 12;399(10325):629-655. doi: 10.1016/S0140-6736(21)02724-0. Epub 2022 Jan 19. Erratum in: *Lancet*. 2022 Oct 1;400(10358):1102. PMID: 35065702; PMCID: PMC8841637.

A One-Health Sampling Strategy to Explore the Dissemination and Relationship Between Colistin Resistance in Human, Animal, and Environmental Sectors in Laos. Zhou Y, Farzana R, Sihalath S, Rattanavong S, Vongsouvath M, Mayxay M, Sands K, Newton PN, Dance DAB, Hassan B, Walsh TR. *Engineering*, Volume 15, 2022, Pages 45-56. ISSN 2095-8099, https://doi.org/10.1016/j.eng.2022.01.013.

Apramycin susceptibility of multidrug-resistant Gram-negative blood culture isolates in five countries in Southeast Asia. Gysin M, Hon PY, Tan P, Sengduangphachanh A, Simmalavong M, Hinfonthong P, Kaewphanderm N, Pham TD, Nguyen TH, Haldimann K, Becker K, van Doorn HR, Hopkins J, Simpson AJH, Ashley EA, Kesteman T, Tran HH, Vasoo S, Ling CL, Roberts T, Turner P, Hobbie SN. *Int J Antimicrob Agents*. 2022 Oct;60(4):106659. doi: 10.1016/j.ijantimicag.2022.106659. Epub 2022 Aug 18. PMID: 35988665.

One Health

ยู่ใน สปป ลาอ ตะหลาดสิดถืเป้นบ่อนที่มีภาบซื้ขายสัดป่าก้บหลาย. ในไลยะผ่านมา มีภาบสึกสาที่ชี้ให้เห้นว่า ภาบซื้ขายชิ้นสัดป่ายู่ลาอมีปะมาบ 70,000 kg ต่ำปี, สำงลายธับได้เกือบ $550,000. ภาบอางขายสัดป่าในตะหลาดสิด เธ็ดให้สัดหลากหลายสายพ้นยู่ธ่อมก้นในสะพาบแวดล้อมที่แออัด และ บ่ถูกต้องตามหล้กภาบสุขาพิบาบ, เป้นภาบเพิ่มคอามเสงในภาบปะสิม, ภาบขะหยาย และ ภาบแผ่เชื้อพะยาดละหว่างสัด และ สัดที่เป้นต๊อนำเชื้อพะยาด ลอมเถิงถ้นเธา. ภาบสึกสาผ่านมายังสะแดงให้เห้นอ่า มีพงุ่ถ้นจำนอมหม้อยที่ตะหม้กเถิงคอามสงุ่ตำ่สุขะพาบ ละหว่างๆ ผู้ขาย และ ผู้บ่ลิโพสัดป่า. ภาบสึกสาถิ้งนี้พะยายามที่จะละบุหาคอามสงุ่เหิ่านั้นโดยจะถ้ดภองเอิาสัดป่าที่ขายในตะหลาด เพื่อนำมาหาเชื้อจุละชีบที่ก่ำให้เกิดพะยาด. ในละหว่างเดือนท้นอา 2014 หา เดือน ก้นยา 2017 เชิ่งเป้นส่อนหนึ่งของโดงภาบ Lacanet ที่ได้ธับเงินสะหม้บสะหมุนจาภสะหะพาบเอิธิบ, พอกเธาได้เก้บต๊อย่างจาภแหล่งซื้ขายสัดป่า 11 แห่งทั่วปะเทดลาอ และ เก้บต๊อย่างสัดที่ถูกยึดโดยเจ้าหน้าที่ห้องภาบป่าไม้ขั้นแดอง 3 แห่ง. สามาดละบุสายพ้นเชื้อจุละชีบที่ก่ำให้เป้นพะยาดได้ 359 ต๊อย่าง จาภต๊อย่างที่เก้บได้ทั้งหมิด 717 ต๊อย่าง. โดยพิบในสัดป่าหลายกว่า 37 สายพ้น เชิ่งโตภะธอกากอมเอิา 73%. ต๊อย่างที่เก้บจาภตะหลาดสิดนั้น, พิบเห้นเชื้อจุละชีบ *Leptospira* spp., ปะมาบ 20.1%, เชื้อจุละชีบ *Rickettsia* spp., 9.8% และ จำนอน 4.9% แม่นมีเชื้อ *Anaplasmataceae*. จาภต๊อย่างสัดที่เจ้าหน้าที่ห้องภาบป่าไม้ขั้นแดองยึดได้นั้น พิบว่า จำนอน 71.4% มีเชื้อที่ก่ำให้เกิดพะยาดหลายกว่าหนึ่งชะนิด ในนี้ 25% แม่นเชื้อจุละชีบ *Leptospira* spp., หลายกว่า 57% แม่นเชื้อจุละชีบ *Rickettsia* spp., พิบเห้นเชื้อจุละชีบ *Orientia tsutsugamushi* ยู่ในสองต๊อย่าง, และ 17% แม่นมีเชื้อ *Anaplasmataceae*. สามาดบิ่งชี้เชื้อจุละชีบที่ภอดพิบได้แก่ *R. typhi*, *R. felis*, *R. conorii*, กุ่มพะยาด Anaplasma (*A. centrale*, *A. capra*, หื *A. marginale*), *A. platy*, *A. bovis*, *A. phagocytophilum*, *Ehrlichia chaffeensis*, *Lactococcus garvieae*, และ *Kurthia populi*. ภาบสึกสาถิ้งนี้สะแดงใช้เห้นว่าเชื้อที่ก่ำให้เกิดพะยาด *Leptospira* พิบหลายในสัดป่า 2 ชะนิดถื ภะธอภ และ เหง้น ภอมเอิาหลายกว่า 45% เชิ่งภาบสึกสาผ่านมาก่อนพ้านี้ก็ได้ยั้งยืนว่าภะธอภเป้นสัดที่มีภาบซื้ขายก้นหลายที่สุดยู่ในตะหลาดสิด โดยผู้ถ้นมักซื้ภะธอภเป้นจำนอนหลาย ปะมาบ 2-3 โตขึ้นไป. ภาบคำนอนคอามสงุ่ชี้ให้เห้นว่าโดยสะเล่ยแล้วถ้นที่ซื้ภะธอภ ปะมาบ 3 โต มีโอภาดสูงเถิง 83% ที่จะมีภะธอภที่มีเชื้อพะยาด หลายกว่า 1 โต. โดยปิภาะติ บ่ค่อยจะธู้ก่ยวกับเชื้อพะยาดจาภสัดป่าที่แผ่ละขาดในลาอ, ภาบก่ำนิดเชื้อพะยาดที่มียู่ในสัดป่าที่มีภาบซื้ขายก้น และ ยู่ในคอามสงุ่ยที่สิ่งผินต่ำสุขะพาบเป้นสิ่งสำคับ เพื่อก่ำนิดมาดตะภาบชี้นำที่เหมาะสึมในภาบสะก้ดก้บพะยาดติดต่ำจาภสัดสู่ถ้น, เป้นภาบธิภสาติ่นทึนทางสังคึม และ สิ่งแวดล้อมต่ภาบค้าสัดป่า. บิดถอามนี้เป้นหนึ่งในสามของลายละอยดก่ยวกับภาบค้าสัดป่า และ ถอามสงุ่ยของพะยาดติดต่ำในลาอ เชิ่งเป้นส่อนหนึ่งของโดงภาบ *Lancet*.

แผงขายสัดป่าในตะหลาดค้าขายสัดป่าแห่งหนึ่งใน สปป ลาอ เชิ่งมีจำพอกสัดเลือดนม, ภะธอภ และ สัดปีกที่อาไสในป่าหลายชะนิดเผื่อจำหน่าย. ภาบค้าขายสัดป่าได้เธ็ดให้สัดหลายชะนิดเกิดมิภาบสำผัดก้น, โดยสะเพาะยู่ในสะพาบขาแหน้นแออัด และ บ่สะอาด, ก่ำให้เกิดถอามสงุ่ในภาบป้นเป้อนเชื้อพะยาด, ภาบขะหยายติอ และ ภาบแผ่ภะจายของเชื้อพะยาดไปสู่ขับดาสัดชะนิดอื่นๆ, ลอมทั้งมะนุดด้อย.
ธูบพาบโดย: K. Yoganand/World Wildlife Fund via AP.

Zoonotic Pathogens in Wildlife Traded in Markets for Human Consumption, Laos. Nawtaisong P, Robinson MT, Khammavong K, Milavong P, Rachlin A, Dittrich S, Dubot-Pérès A, Vongsouvath M, Horwood PF, Dussart P, Theppangna W, Douangngeum B, Fine AE, Pruvot M, Newton PN. *Emerg Infect Dis*. 2022 Apr;28(4):860-864. doi: 10.3201/eid2804.210249. PMID: 35318932; PMCID: PMC8962878.

Medicine quality

ຢາປອມເປັນບັນຫາທາງດ້ານສາທາລະນະສຸກທີ່ສຳຄັນຂອງໂລກ, ແຕ່ວ່າງານວິໄຈທາງດ້ານນະວັດຕະກຳ ເພື່ອໃຫ້ເຂົ້າໃຈກ່ຽວກັບຕົ້ນກຳເນີດແຫຼ່ງທີ່ມາຂອງຢາປອມຫຼາຍຂຶ້ນມີໜ້ອຍ. ເນື່ອງຈາກປະສິດທິຜົນການວິເຄາະສານພັນທຸກຳ (DNA) ໄດ້ຊ່ວຍໃນການພິສູດຫຼັກຖານທາງດ້ານນິຕິວິທະຍາສາດເພື່ອແກ້ໄຂຄະດີທາງດ້ານອາຊະຍາກຳ, ທີມງານຂອງເຮົາຈຶ່ງຕັ້ງຂໍ້ສົມມຸດຕິຖານວ່າເຕັກນິກເຫຼົ່ານີ້ສາມາດໃຊ້ເພື່ອກວດສອບຕົ້ນກຳເນີດແຫຼ່ງທີ່ມາຂອງຢາປອມ ແລະ ສ່ວນປະສົມຕ່າງໆ ຂອງຢາເຫຼົ່ານີ້ໄດ້ເຊັ່ນດຽວກັນ. ທີມງານຂອງເຮົາໄດ້ສະແດງໃຫ້ເຫັນເຖິງຄຸນປະໂຫຍດຂອງເກສອນດອກໄມ້ (pollen) ໃນການກວດສອບຫາແຫຼ່ງທີ່ມາຂອງຢາເມັດ artesunate ປອມ ທີ່ເປັນໄພຂົ່ມຂູ່ອັນໃຫຍ່ຫຼວງໃນອາຊີຕາເວັນອອກສຽງໃຕ້. ຝຸ່ນລະອອງ (pollen) ແລະ ຫຼັກຖານອື່ນໆຂອງສິ່ງແວດລ້ອມຢູ່ໃນບໍລິເວນທີ່ເປັນແຫຼ່ງທີ່ມາຂອງສ່ວນປະສົມ ແລະ ບ່ອນຜະລິດຢາ ຈະຖືກຫຸ້ມຫໍ່ຢູ່ພາຍໃນແຜງຢາ (blister-packages). ທີມງານຂອງເຮົາໄດ້ຮ່ວມມືກັບມະຫາວິທະຍາໄລ Flinders ແລະ ມະຫາວິທະຍາໄລ Adelaide ປະເທດ Australia, ດຳເນີນການສຶກສາທົດລອງແບບປິດບັງ (blinded pilot study) ເພື່ອກວດສອບວ່າ DNA ສິ່ງແວດລ້ອມ (eDNA) ດັ່ງກ່າວ ທີ່ກວດພົບໃນຢາເມັດຕ້ານມາລາເຣຍ artesunate ປອມ ແລະ artesunate ແທ້ ທີ່ເກັບມາຈາກອາຊີຕາເວັນອອກສຽງໃຕ້ ສາມາດຊີ້ບອກເຖິງຕົ້ນກຳເນີດແຫຼ່ງທີ່ມາ ຫຼື ສະຖານທີ່ຜະລິດ ຂອງຢາເຫຼົ່ານີ້. Massively Parallel Sequencing (MPS) ໄດ້ນຳໃຊ້ເພື່ອລະບຸລັກສະນະຄວາມຫຼາກຫຼາຍຂອງຈຸລິນຊີ (Microbial) ແລະ ຢູຄາລີໂອດ (eukaryote). ຄວາມແຕກຕ່າງທີ່ສຳຄັນໃນສານພັນທຸກຳ (DNA) ຂອງໂຄງສ້າງໂດຍທົ່ວໄປໃນບັກເຕີຣີ (bacterial) ແລະ ຢູຄາລີໂອດ (Eukaryote) ໄດ້ຖືກກວດສອບໃນຢາເມັດ artesunate ແທ້ ແລະ artesunate ປອມ ແລະ ໃນເຄື່ອງຫຸ້ມຫໍ່ທີ່ແຕກຕ່າງກັນຂອງ artesunate ປອມ. ການກວດສອບໂດຍໃຊ້ MPS ໄດ້ພົບສານພັນທຸກຳ (DNA) ຂອງມະນຸດ ທີ່ຄ້າຍຄືກັບເຊື້ອສາຍຂອງຊາວອາຊີຕາເວັນອອກໃນຢາເມັດປອມ. ການສຶກສາແບບທົດລອງ ຂອງ ‘pharmabiome’ ໄດ້ສະແດງໃຫ້ເຫັນສັກກະຍະພາບຂອງ DNA ສິ່ງແວດລ້ອມ (eDNA) ໃນການເປັນເຄື່ອງມືທາງນິຕິວິທະຍາສາດທີ່ສຳຄັນເຊິ່ງຊ່ວຍໃນການລະບຸຕົ້ນຕໍຂອງສິ່ງແວດລ້ອມ, ດັ່ງນັ້ນ ສະຖານທີ່ ແລະ ເວລາ ຂອງແຫຼ່ງທີ່ມາ ແລະ ການຜະລິດຢາປອມ ແມ່ນໄດ້ສ້າງຄວາມເຊື່ອມໂຍງໃນການຈັບກຸມ ແລະ ເປັນເຄື່ອງມືເພີ່ມເຕີມທີ່ຊ່ວຍສະແດງໃຫ້ເຫັນຊັດເຈນເຖິງເສັ້ນທາງໃນການຄ້າຂາຍແບບຜິດກົດໝາຍ. ເຕັກນິກນີ້ແມ່ນມີຄວາມສັບຊ້ອນ ເນື່ອງຈາກມີສິ່ງຕ່າງໆທີ່ອາດນຳ DNA ສິ່ງແວດລ້ອມ (eDNA) ເຂົ້າສູ່ຢາເມັດໃນລະຫວ່າງການຜະລິດ ແລະ ການຄົ້ນຫາສານພັນທຸກຳ (DNA) ຂອງມະນຸດ ໃນຢາເມັດແມ່ນເຮັດໃຫ້ເກີດບັນຫາທາງຈະລິຍະທຳທີ່ສຳຄັນເຊິ່ງຈຳເປັນຕ້ອງໄດ້ຮັບການແກ້ໄຂ. ທີມງານຂອງເຮົາກຳລັງສືບຕໍ່ການສຶກສານີ້ຮ່ວມກັບມະຫາວິທະຍາໄລ Edinburgh ແລະ Huddersfield ແລະ ພະແນກເຜີຍແຜ່ວິທະຍາຂອງ MORU ເຊິ່ງເປັນສ່ວນໜຶ່ງຂອງໂຄງການຮ່ວມມືຂອງ Wellcome Award FORESFA.

Environmental DNA as an innovative technique to identify the origins of falsified antimalarial tablets-a pilot study of the pharmabiome. Young JM, Liddicoat C, van Dijk KJ, Tabernero P, Caillet C, White NJ, Linacre A, Austin JJ, Newton PN. *Sci Rep*. 2022 Dec 20;12(1):21997. doi: 10.1038/s41598-022-25196-0. PMID: 36539480; PMCID: PMC9764312.

ໃນເດືອນມິຖຸນາ 2022, ພະນັກງານຂອງ LOMWRU ໄດ້ເຂົ້າມອບປຶ້ມຕຳລາຢາຂອງປະເທດອັງກິດ ປີ 2022 (British Pharmacopoeia 2022) ໃຫ້ແກ່ ດຣ ຈັນສະໝາ ປາມະນີວົງ (ຜູ້ທີ່ສີ່ ຈາກດ້ານຂວາ) ແລະ ທີມງານວິໄຈອາຫານ ແລະ ຢາແຫ່ງຊາດ, ເປັນຂອງຂວັນຈາກທາງ ໜ່ວຍງານກວດກາຄຸນນະພາບຢາຈາກ MORU ເພື່ອຊຸກຍູ້ວຽກງານໃນການກວດສອບຄຸນນະພາບຂອງຢາ ສຳລັບປະຊາຊົນລາວ. ປຶ້ມຕຳລາຢາຂອງປະເທດອັງກິດ ແມ່ນ ປຶ້ມເກັບກຳຂໍ້ມູນກ່ຽວກັບ ມາດຕະຖານທາງການຂອງສ່ວນປະກອບຂອງຢາ ແລະ ຜະລິດຕະພັນຢາ ເຊິ່ງເປັນຂໍ້ມູນທີ່ສຳຄັນໃນການອ້າງອີງໃຫ້ກັບ ການຄົ້ນຄວ້າທີ່ກ່ຽວກັບຢາ, ການພັດທະນາ, ການຜະລິດ ແລະ ການຄວບຄຸມຄຸນນະພາບ ແລະ ການວິໄຈຢາ. © 2022 LOMWRU. ຮູບພາບໂດຍ: FN LN.

Research highlights in 2022

Here we highlight a selection of research outputs of LOMWRU and partner organisations published in 2022. The complete list with abstracts is found in the LOMWRU Publications in 2022 section of the report.

Childhood encephalitis

Central nervous system infections have a devastating impact on children globally. Encephalitis may lead to fatal outcomes or long-lasting neurodevelopmental sequelae. Even with access to the best diagnostic tools, the underlying cause is frequently not identified. We participated in the SouthEast Asia Encephalitis Project, a multi-country study led by Institut Pasteur in Cambodia, which aimed to determine the causes of encephalitis in children admitted to hospitals across the Greater Mekong Subregion (GMS) using state-of-the-art diagnostics. Between 2014 and 2017, 664 children with encephalitis in Laos, Vietnam, Cambodia and Myanmar were enrolled in the study. A confirmed or probable cause of encephalitis was identified in 425 (64%) patients.

Leading causes were Japanese encephalitis virus in 216 (33%) of 664 cases, dengue in 27 (4%), influenza in 26 (4%), herpes simplex virus 1 in 24 (4%), *Mycobacterium tuberculosis* in 18 (3%), *Streptococcus pneumoniae* in 17 (3%), and enterovirus A71 in 17 (3%). Six patients (1%) were diagnosed with autoimmune encephalitis. Sixty-two children in the study were from Laos (confirmed diagnoses included 14 Japanese encephalitis, 5 *Mycobacterium tuberculosis*, 2 dengue, 2 influenza, 8 other).

Autoimmune encephalitis is increasingly recognized as being responsible for a significant proportion of childhood encephalitis. In a separate study in Vientiane we tested for neuronal autoantibodies in CSF and serum of 134 patients with suspected CNS infection as well as the serum of healthy controls. Two patients with antibodies had a clinical presentation typical of autoimmune encephalitis. However, three other patients with detectable antibodies had another cause for their CNS presentation identified, highlighting the challenges of diagnosing this disease.

Childhood encephalitis in the Greater Mekong region (the SouthEast Asia Encephalitis Project): a multicentre prospective study. Pommier JD, Gorman C, Crabol Y, Bleakley K, Sothy H, Santy K, Tran HTT, Nguyen LV, Bunnakea E, Hlaing CS, Aye AMM, Cappelle J, Herrant M, Piola P, Rosset B, Chevalier V, Tarantola A, Channa M, Honnorat J, Pinto AL, Rattanavong S, Vongsouvath M, Mayxay M, Phangmanixay S, Phongsavath K, Tin OS, Kyaw LL, Tin HH, Linn K, Tran TMH, Pérot P, Thuy NTT, Hien N, Phan PH, Buchy P, Dussart P, Laurent D, Eloit M, Dubot-Pérès A, Lortholary O, de Lamballerie X, Newton PN, Lecuit M; SEAe Consortium. *Lancet Glob Health*. 2022 Jul;10(7): e989-e1002. doi: 10.1016/S2214-109X(22)00174-7. PMID: 35714649; PMCID: PMC9210261.

Detection and significance of neuronal autoantibodies in patients with meningoencephalitis in Vientiane, Lao PDR. Uy CE, Mayxay M, Harrison R, Al-Diwani A, Jacobson L, Rattanavong S, Dubot-Pérès A, Vongsouvath M, Davong V, Chansamouth V, Phommasone K, Waters P, Irani SR, Newton PN. *Trans R Soc Trop Med Hyg*. 2022 Oct 2;116(10):959-965. doi: 10.1093/trstmh/trac023. PMID: 35385878; PMCID: PMC9526827.

Respiratory infections in Lao PDR

Molecular diagnostic methods on nose, throat or nasopharyngeal swabs have improved our ability to identify the cause of respiratory tract infections. However, the upper respiratory tract of healthy people may also be colonized by a variety of bacteria and viruses so it can be difficult to be sure whether the detected bacterium or virus is really the cause of the illness. From 24 June 2019 to 24 June 2020, we enrolled 205 patients presenting to Xieng Khuang Provincial Hospital with signs and symptoms of respiratory tract infection. For every patient included we included one age- and sex-matched control from the same village. All cases and controls had a nasopharyngeal swab performed which was tested for 33 potential pathogens by PCR. We found influenza B virus, influenza A virus, human metapneumovirus (HMPV), and respiratory syncytial virus (RSV) were much more likely to be found in cases than controls, while *Streptococcus pneumoniae* was found in 41% cases and 61% controls.

Acute respiratory infections in admitted patients were attributed to influenza B virus, influenza A virus, human metapneumovirus (HMPV), and respiratory syncytial virus (RSV) in 17.8%, 17.2%, 7.5%, and 6.5% of participants, respectively. SARS-CoV-2 was not detected in any cases or controls.

After this study we continued respiratory virus surveillance in inpatients and outpatients with our partners in Xieng Khuang, Luang Namtha, Salavan and Attapeu Provincial Hospitals which enabled us to gather data on COVID-19 from different sites around the country from 2020 until now. These data were useful for national genomic surveillance and were also shared with the International Severe Acute Respiratory and emerging Infection Consortium (ISARIC). The ISARIC COVID-19 dataset was compiled during the COVID-19 pandemic and includes data from more than 705,000 patients, collected in more than 60 countries and 1,500 centres worldwide.

Lao resident doctors with the new Lao antimicrobial prescribing guidelines. © 2023 LOMWRU. Photographer: Vilada Chansamouth.

A case-control study of the causes of acute respiratory infection among hospitalized patients in Northeastern Laos. Phommasone K, Xaiyaphet X, Garcia-Rivera JA, Hontz RD, Pathavongsa V, Keomoukda P, Vongsouvath M, Mayxay M, Vongsouvath M, Newton PN, Ashley EA, Dubot-Pérès A. *Sci Rep*. 2022 Jan 18;12(1):939. doi: 10.1038/s41598-022-04816-9. PMID: 35042900; PMCID: PMC8766494.

ISARIC-COVID-19 dataset: A Prospective, Standardized, Global Dataset of Patients Hospitalized with COVID-19. ISARIC Clinical Characterization Group; Garcia-Gallo E, Merson L, Kennon K, Kelly S, Citarella BW, Fryer DV, Shrapnel S, Lee J, Duque S, Fuentes YV, Balan V, Smith S, Wei J, Gonçalves BP, Russell CD, Sigfrid L, Dagens A, Olliaro PL, Baruch J, Kartsonaki C, Dunning J, Rojek A, Rashan A, Beane A, Murthy S, Reyes LF. *Sci Data*. 2022 Jul 30;9(1):454. doi: 10.1038/s41597-022-01534-9. PMID: 35908040; PMCID: PMC9339000.

Antimicrobial resistance and antimicrobial use

Antimicrobial resistance (AMR) remains a high priority public health issue and rates of extended-spectrum beta lactamase producing *E. coli* and methicillin resistant *Staphylococcus aureus* continue to increase in Laos. One driver of increasing AMR is antimicrobial use. Dr Vilada Chansamouth led repeated point-prevalence surveys of antimicrobial prescriptions in six provincial and/or central hospitals in Laos and reported that Laos has one of the highest prescribing rates globally, with around 70% of inpatients on antibiotics at any point in time.

Mahosot Hospital shared 20 years of data with the Global Research on Antimicrobial Resistance (GRAM) project which aimed to estimate the global burden of AMR. These findings were published in the *Lancet* medical journal. It was estimated that in 2019 4.95 million (3.62–6.57) deaths globally were associated with bacterial AMR.

AMR is a One Health issue, affecting animals and the environment as well as human health. Colistin (Polymyxin E) is an antibiotic of last resort used to treat multidrug resistant infections which is not available in Laos. However, it is used to treat animals in Southeast Asia and as a growth promoter. We collected 673 samples from humans (rectal swabs), chickens, dogs, flies and water in Vientiane and tested them for the presence of colistin-resistant *E. coli*, looking for the mobile colistin resistance gene (*mcr*). We found colistin-resistant *E. coli* in 14.6% of all specimens (including 45.9% (45/98) human specimens, 14.3% (2/14) in dog faeces, 12.0% (24/200) in flies, 11.0% (11/100) in chicken meat, 8.9% (8/90) in chicken cloacae, 8.0% (4/50) in chicken caeca, and 7.5% (4/53) in wastewater).

There is an urgent need to develop new antimicrobials and there are also efforts to repurpose older agents which are not being used to treat human infections. Apramycin is an old antibiotic from the aminoglycoside class which was used in animals and has shown efficacy against gentamicin-resistant and multidrug-resistant Gram-negative bacteria in preclinical studies. We tested this antibiotic against stored bacterial isolates from human infections in the Mahosot Hospital laboratory. It demonstrated very good activity against Gram-negative bacteria resistant to gentamicin, carbapenems and third-generation cephalosporins and is undergoing further clinical development.

Evaluation of trends in hospital antimicrobial use in the Lao PDR using repeated point-prevalence surveys-evidence to improve treatment guideline use. Chansamouth V, Chommanam D, Roberts T, Keomany S, Paphasiri V, Phamisith C, Sengsavang S, Detleuxay K, Phoutsavath P, Bouthavong S, Douangnouvong A, Vongsouvath M, Rattana S, Keohavong B, Day NPJ, Turner P, van Doorn HR, Mayxay M, Ashley EA, Newton PN. *Lancet Reg Health West Pac*. 2022 Jul 9;27:100531. doi: 10.1016/j.lanwpc.2022.100531. PMID: 35846979; PMCID: PMC9283659.

Global burden of bacterial antimicrobial resistance in 2019: a systematic analysis. Antimicrobial Resistance Collaborators. *Lancet*. 2022 Feb 12;399(10325):629-655. doi: 10.1016/S0140-6736(21)02724-0. Epub 2022 Jan 19. Erratum in: *Lancet*. 2022 Oct 1;400(10358):1102. PMID: 35065702; PMCID: PMC8841637.

A One-Health Sampling Strategy to Explore the Dissemination and Relationship Between Colistin Resistance in Human, Animal, and Environmental Sectors in Laos. Zhou Y, Farzana R, Sihalath S, Rattanavong S, Vongsouvath M, Mayxay M, Sands K, Newton PN, Dance DAB, Hassan B, Walsh TR. *Engineering*, Volume 15, 2022, Pages 45-56. ISSN 2095-8099, https://doi.org/10.1016/j.eng.2022.01.013.

Apramycin susceptibility of multidrug-resistant Gram-negative blood culture isolates in five countries in Southeast Asia. Gysin M, Hon PY, Tan P, Sengduangphachanh A, Simmalavong M, Hinfonthong P, Kaewphanderm N, Pham TD, Nguyen TH, Haldimann K, Becker K, van Doorn HR, Hopkins J, Simpson AJH, Ashley EA, Kesteman T, Tran HH, Vasoo S, Ling CL, Roberts T, Turner P, Hobbie SN. *Int J Antimicrob Agents*. 2022 Oct;60(4):106659. doi: 10.1016/j.ijantimicag.2022.106659. Epub 2022 Aug 18. PMID: 35988665.

One Health

Wildlife is often traded in wet markets in Laos. Estimates by previous work have suggested over 70,000 kg of wildlife meat may be traded by a single market per year, with a revenue of nearly $550,000 USD. Trading wildlife at markets brings diverse species into contact, usually in dense and unsanitary conditions, increasing the risk of mixing, amplification, and transmission of pathogens among host species, including humans. Despite this risk, a previous study has shown very little awareness among vendors and consumers as to the health risks involved with trading and handling wildlife. This study attempted to identify what those risks were, by screening wildlife sold at markets for pathogenic bacteria. Between December 2014 and September 2017, as part of the EU-funded Lacanet project, we collected samples from 11 wildlife trade hotspots across Laos, as well as sampling animals confiscated by three regional Provincial Offices for Forestry Inspection (POFI). In total, 359 animals were sampled, with a total of 717 samples being tested for pathogenic bacterial species. Over 37 species of animals were identified, with 73% being squirrels. From wet markets, 20.1% of animals were positive for *Leptospira* spp., 9.8% were positive for *Rickettsia* spp., and 4.9% positive for Anaplasmataceae. Of animals confiscated by POFI, 71.4% were positive for >1 pathogen with over 25% positive for *Leptospira* spp., over 57% positive for *Rickettsia* spp., two individuals positive for *Orientia tsutsugamushi*, and 17% positive for Anaplasmataceae. Speciation of the pathogens detected identified *R. typhi*, *R. felis*, *R. conorii*, an *Anaplasma* species (either *A. centrale*, *A. capra*, or *A. marginale*), *A. platys*, *A. bovis*, *A. phagocytophilum*, *Ehrlichia chaffeensis*, *Lactococcus garvieae*, and *Kurthia populi*. This work showed that pathogenic *Leptospira* were extremely common in the two most frequently traded animals, squirrels and civet cats, with over 45% of animals testing positive. Previous work has confirmed that squirrels are the most frequently traded animal at wet markets, often being purchased in batches of 2 to 3 squirrels. Calculating the risk suggests that on average someone purchasing 3 variable squirrels would have an 83% likelihood of buying more than one infected squirrel. Little is known of the pathogens infecting wildlife in Laos, and determining the pathogens present in traded wildlife and the potential risk to health, is vital to guide appropriate measures to combat zoonotic diseases and document societal and environmental costs of wildlife trade. This manuscript is one of three detailing wildlife trading and risk of infectious diseases in Laos, as part of the Lacanet project.

A stall at a wildlife market in Laos with lizards, squirrels and wild birds for sale. Trading wildlife at markets brings diverse species into contact, usually in dense and unsanitary conditions, increasing the risk of mixing, amplification, and transmission of pathogens among host species, including humans. Photo: K. Yoganand/World Wildlife Fund via AP.

Zoonotic Pathogens in Wildlife Traded in Markets for Human Consumption, Laos. Nawtaisong P, Robinson MT, Khammavong K, Milavong P, Rachlin A, Dittrich S, Dubot-Pérès A, Vongsouvath M, Horwood PF, Dussart P, Theppangna W, Douangngeum B, Fine AE, Pruvot M, Newton PN. *Emerg Infect Dis*. 2022 Apr;28(4):860-864. doi: 10.3201/eid2804.210249. PMID: 35318932; PMCID: PMC8962878.

In June 2022, LOMWRU staff presented the British Pharmacopoeia 2022 to Dr Chansapha Pamanivong (*4th from right*) and his team at the National Center for Food and Drug Analysis, Lao PDR, as a gift from the MORU Medicine Quality Research Group (MQRG) to support their work in assuring the quality of medicines for the people of Lao PDR. The British Pharmacopoeia is a collection of official standards for pharmaceutical substances and medicinal products. It is an important reference for all that are involved in pharmaceutical research, development, manufacture, and quality control and analysis. © 2022 LOMWRU.

Medicine quality

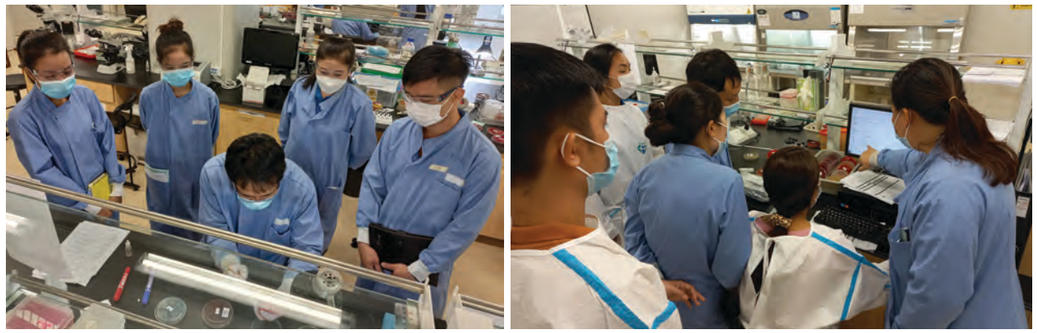
Although falsified medicines are a major threat to global health there has been minimal innovative research to more objectively understand their origins. As DNA analysis has revolutionized forensic criminology, we hypothesized that these techniques could also be used to investigate the origins of falsified medicines and their ingredients. We demonstrated the utility of pollen analysis in estimating the source of falsified oral artesunate that was a major scourge in SE Asia. We looked within sealed blister-packages for pollen and other evidence of the environment where the ingredients were sourced and the medicines were manufactured. We conducted, with Flinders University and the University of Adelaide, Australia, a blinded pilot study to determine if such environmental DNA (eDNA) could be detected in falsified and genuine artesunate antimalarial tablets, collected in SE Asia, which could be indicative of origin. Massively Parallel Sequencing (MPS) was used to characterize microbial and eukaryote diversity. Significant differences in bacterial and eukaryote DNA community structures were observed between genuine and falsified tablets and between different packaging types of falsified artesunate. Human DNA, which was indicative of likely east Asian ancestry, was found in falsified tablets. This pilot study of the 'pharmabiome' shows the potential of environmental DNA as a powerful forensic tool to assist with the identification of the environments, and hence location and timing, of the source and manufacture of falsified medicines, establish links between seizures and complement existing tools to build a more complete picture of criminal trade routes. The technique is complicated by different potential sites of ingress of eDNA into tablets during production, and the finding of human DNA in tablets raises important ethical issues that need to be addressed. We are expanding this work, with the Universities of Edinburgh and Huddersfield and with the Pharmacology Dept of MORU, as a part of the Wellcome Collaborative Award FORESFA project.

Environmental DNA as an innovative technique to identify the origins of falsified antimalarial tablets-a pilot study of the pharmabiome. Young JM, Liddicoat C, van Dijk KJ, Tabernero P, Caillet C, White NJ, Linacre A, Austin JJ, Newton PN. *Sci Rep*. 2022 Dec 20;12(1):21997. doi: 10.1038/s41598-022-25196-0. PMID: 36539480; PMCID: PMC9764312.

Training highlights 2022

UK Fleming Fund Lao country grant

The Fleming Fund is a UK Aid programme helping tackle antimicrobial resistance (AMR) in low- and middle-income countries (LMICs) around the world. The aim of the Fleming Fund is to support the strengthening of national AMR surveillance systems and laboratories, develop global frameworks, support AMR governance, and improve public awareness of AMR and global data use. In Laos, the Fleming Fund country grant is organised by Fondation Mérieux and run in partnership with LOMWRU/Mahosot Hospital microbiology laboratory and the National Centre for Laboratory and Epidemiology (NCLE). The project started in May 2020 with LOMWRU/Mahosot Hospital initially supporting three sites (Xieng Khuang, Salavan and Luang Namtha) with two more sites added in June 2022 (Savannakhet and Vientiane Province). Fondation Mérieux and the NCLE support another five sites in other provincial hospital laboratories in Laos.



Senior Laboratory Technician Phonepasith Panyanouvong (*centre, seated)* training provincial hospital staff on culture techniques. Quality Control/Senior Laboratory Technician Amphonsavanh Sengduangchanh training provincial staff on SOPs. © 2022 LOMWRU. Photographer: Tamalee Roberts.

This year saw a lot of activity for the LOMWRU and Mahosot Hospital supported sites for Fleming Fund. There were two onsite training sessions at each of the five sites. Mahosot Hospital laboratory staff Amphonesavanh Sengduangchanh, Joy Silisouk, Sao Vang and Phonepasith Panyanouvong visited the various sites doing hands-on training for two weeks initially in May-July and another week in November-December with training on basic microbiology techniques, specimen reception and processing, quality control, and the laboratory database WHONET. Goats were also introduced to the sites as a source of blood to make agar plates. In July, blood culture processing using automated blood culture machines (BACTEC) were introduced to four of the sites. The automated blood culture machines will improve blood culture processing and the work-flow in the laboratories. In August, two laboratory staff from each of the sites travelled to Mahosot Hospital for two weeks for intensive laboratory training. In total, 13 laboratory staff from the five provincial sites had training in 2022.

As part of the Fleming Fund activities, there was also diagnostic stewardship training held at each of the sites. In May-July and December, Dr Koukeo Phommasone, Dr Sayaphet Rattanavong and Dr Anousone Douangnouvong travelled to the sites to demonstrate how to take clean blood cultures, explain the importance of taking samples for diagnosing infection, and how to interpret laboratory results. These session included talks, learning aids and practical sessions. These sessions were a great success with over 180 nurses and clinicians were involved in these training sessions in 2022.

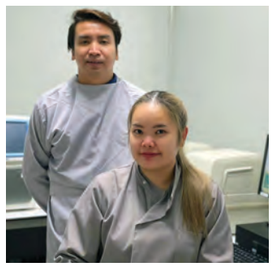
Asst Prof Prapan Luangsook and Asst Prof Chayada Sutthidet Tharinjaroen and their nine Lao students at the workshop at Mahosot Hospital. © 2022 LOMWRU. Photographer: Tamalee Roberts.

Following on from the 6-month clinical microbiology laboratory course held at Chiang Mai University in 2021, there was a follow-up visit 11-16 June 2022 to Laos by two of the Thai professors from the course. Asst Prof Prapan Luangsook and Asst Prof Chayada Sutthidet Tharinjaroen came to Laos for 10 days. They visited their previous students in Luang Prabang and Xieng Kuang Hospitals, and at the National Centre for Laboratory and Epidemiology (NCLE), where they did hands-on training with the staff. They then ran a two-day workshop at Mahosot Hospital laboratory. The nine students who attended the Chiang Mai course in 2021 travelled to Mahosot Hospital and participated in sessions on the impact the course had on their current work, challenges in the laboratory, and refresher training on laboratory processes and quality control. It was a fun workshop and all students were happy to see their old professors again.

As part of the Fleming Fund, Mahosot Hospital and LOMWRU are also supporting training for two Fleming Fund Fellows by running lectures and workshops. Dr Manivanh Vongsouvath, Head of Mahosot Microbiology Department is also a Fleming Fund Fellow and travelled to France for three weeks where she attended the Antimicrobial Resistance Course (AMR) - A One Health Challenge 3rd edition on 7-11 November 2022 in Annecy, as well as meetings with her mentors and training at the Centre Hospitalier de Valence.

Dr Manivanh Vongsouvath (*centre*) with her mentors, Dr Julien Saison (*left*) and Elodie Hamel Dorangeon. © LOMWRU.

Postgraduate Training



Postdoctoral researchers

Dr Weerawat Phuklia, LOMWRU Postdoctoral Scientist and Wellcome Trust International Training Fellow, returned to LOMWRU from Washington State University in the laboratory of Dr Anders Omsland where he worked to develop a new cell-free culture medium for *Rickettsia* bacteria.

Dr Weerawat is shown with Laboratory Technician Ms Kaisone Padith. © 2022 LOMWRU. Photographer: Latsaniphone Boutthasavong.

Doctoral students

Dr Vilada Chansamouth (*right*) started 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. She went on maternity leave at the end of 2022 after the birth of her baby, Malida.

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Photographer: Vilada Chansamouth.

© 2022 LOMWRU. Photographer: Gerhard Jørén.

Master's students

We hosted two Master's students from the 21st batch of the International Master's Course in Tropical Medcine and International Health at the Lao Tropical and Public Health Institute in 2022. Both worked on dengue-related projects under the supervision of Dr Audrey Dubot-Pérès. Dr Sengdavanh Sydalay's project was on *Factors associated with dengue clinical presentation among children admitted at Mahosot Hospital and Children Hospital*. Dr Somphavan Duanghorm's topic was on *Understanding the relative contribution of asymptomatic transmission of dengue in the rainy season in Vientiane Capital, Lao People's Democratic Republic*. On 25 and 26 January, all students defended their thesis projects in front of an international jury. This was closely followed by the graduation ceremony, presided over by HE the Vice Minister of Health, Dr Sanong Thongsana. Congratulations to Dr Sengdavanh (*left*) and Dr Somphavan (*right*), who came in the top 5 of this year's graduates!

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Dr Vilayouth Phimolsarnnousith (*left)* passed his MSc in Microbiology and Virology from the London School of Hygiene & Tropical Medicine (LSHTM) in 2022. This was funded by a Wellcome International Master's Fellowship which also supports him to undertake a fellowship project on *Intra-host dengue virus genetic diversity among primary and secondary infections in Laos*. He travelled to Marseille in September 2022 where he was working on the laboratory aspects of this project under the supervision of Dr Audrey Dubot-Pérès (*right*).

Both photos © 2023 LOMWRU.

Dr Manophab Luangraj (*left*) has been in London, UK since October 2022 studying for a Master's in Epidemiology at the London School of Hygiene & Tropical Medicine (LSHTM). Mr Vanheuang Phommadeechack, LOMWRU molecular bacteriology junior scientist is in Bangkok studying for a Master's in Tropical Medicine at Mahidol University. He was awarded the Sylvia Meek scholarship for Entomology. The scholarship was set up in 2016 in memory of Dr Sylvia Meek, a highly respected scientist and well known for her contributions to the fight against infectious diseases, and malaria in particular. The scholarship supports students from across the world to study entomology at universities in Nigeria, South Africa and Thailand. Vanheuang was the only student to be awarded the scholarship this year at Mahidol.

Other training

In 2022, we hosted Dr Vilaiphone Phomsisavath, a veterinarian who was awarded a Fellowship by the Southeast Asia One Health University Network (SEAOHUN) and is investigating *Escherichia coli* isolates from pigs and humans in Lao PDR for colistin resistance. She was awarded a travel scholarship to present her preliminary findings at the 7th World One Health Congress in Singapore in November 2022.

© 2022 LOMWRU. Photographer: Matthew Robinson.

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Ms Manilung Nalongsack (*second from left*), LOMWRU Research Pharmacist, is currently an intern at the Health Intervention and Technology Assessment Program (HITAP) in Thailand. Her long term aim is to conduct Health Technology Assessment (HTA) research in Lao PDR in support of the new Unit for Health Evidence and Policy (UHEP).

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Ms Malavanh Vongsouvath, a Mahosot Microbiology and Virology Laboratory technician, spent two months at the Unit for Emerging Viruses in Marseille, France, under the supervision of Dr Audrey Dubot-Pérès where she studied more advanced laboratory virology techniques. Pictured, *from left*: Malavanh Vongsouvath, Dr Manivanh Vongsouvath, Audrey Dubot-Pérès and Vilayouth Phimolsarnnousith in the Unit for Emerging Viruses in Marseille.

LOMWRU publications in 2022

In 2022, LOMWRU published 58 articles or letters in peer-reviewed journals and had seven conference abstracts accepted. Abstracts are reproduced below with articles grouped by theme.

Microbiology including antimicrobial resistance (AMR)

Global burden of bacterial antimicrobial resistance in 2019: a systematic analysis. Antimicrobial Resistance Collaborators. *Lancet*. 2022 **399**(10325): 629–655. doi: 10.1016/S0140-6736(21)02724-0. PMID: 35065702. PMCID: PMC8841637.

This comprehensive analysis describes the global burden of AMR, including estimates of death and morbidity. In 2019, of 4.95 million deaths associated with AMR, 1.27 million were directly attributable to AMR. Results are presented region-by-region, and the roles of key pathogens are also considered individually. Knowledge gaps are highlighted, and the implications for policy are discussed.

BACKGROUND:	Antimicrobial resistance (AMR) poses a major threat to human health around the world. Previous publications have estimated the effect of AMR on incidence, deaths, hospital length of stay, and health-care costs for specific pathogen-drug combinations in select locations. To our knowledge, this study presents the most comprehensive estimates of AMR burden to date.
METHODS:	We estimated deaths and disability-adjusted life-years (DALYs) attributable to and associated with bacterial AMR for 23 pathogens and 88 pathogen-drug combinations in 204 countries and territories in 2019. We obtained data from systematic literature reviews, hospital systems, surveillance systems, and other sources, covering 471 million individual records or isolates and 7585 study-location-years. We used predictive statistical modelling to produce estimates of AMR burden for all locations, including for locations with no data. Our approach can be divided into five broad components: number of deaths where infection played a role, proportion of infectious deaths attributable to a given infectious syndrome, proportion of infectious syndrome deaths attributable to a given pathogen, the percentage of a given pathogen resistant to an antibiotic of interest, and the excess risk of death or duration of an infection associated with this resistance. Using these components, we estimated disease burden based on two counterfactuals: deaths attributable to AMR (based on an alternative scenario in which all drug-resistant infections were replaced by drug-susceptible infections), and deaths associated with AMR (based on an alternative scenario in which all drug-resistant infections were replaced by no infection). We generated 95% uncertainty intervals (UIs) for final estimates as the 25th and 975th ordered values across 1000 posterior draws, and models were cross-validated for out-of-sample predictive validity. We present final estimates aggregated to the global and regional level.
FINDINGS:	On the basis of our predictive statistical models, there were an estimated 4·95 million (3·62-6·57) deaths associated with bacterial AMR in 2019, including 1·27 million (95% UI 0·911-1·71) deaths attributable to bacterial AMR. At the regional level, we estimated the all-age death rate attributable to resistance to be highest in western sub-Saharan Africa, at 27·3 deaths per 100 000 (20·9-35·3), and lowest in Australasia, at 6·5 deaths (4·3-9·4) per 100 000. Lower respiratory infections accounted for more than 1·5 million deaths associated with resistance in 2019, making it the most burdensome infectious syndrome. The six leading pathogens for deaths associated with resistance (*Escherichia coli*, followed by *Staphylococcus aureus*, *Klebsiella pneumoniae*, *Streptococcus pneumoniae*, *Acinetobacter baumannii*, and *Pseudomonas aeruginosa*) were responsible for 929 000 (660 000-1 270 000) deaths attributable to AMR and 3·57 million (2·62-4·78) deaths associated with AMR in 2019. One pathogen-drug combination, meticillin-resistant *S aureus*, caused more than 100 000 deaths attributable to AMR in 2019, while six more each caused 50 000-100 000 deaths: multidrug-resistant excluding extensively drug-resistant tuberculosis, third-generation cephalosporin-resistant *E coli*, carbapenem-resistant *A baumannii*, fluoroquinolone-resistant *E coli*, carbapenem-resistant *K pneumoniae*, and third-generation cephalosporin-resistant *K pneumoniae*.
INTERPRETATION:	To our knowledge, this study provides the first comprehensive assessment of the global burden of AMR, as well as an evaluation of the availability of data. AMR is a leading cause of death around the world, with the highest burdens in low-resource settings. Understanding the burden of AMR and the leading pathogen-drug combinations contributing to it is crucial to making informed and location-specific policy decisions, particularly about infection prevention and control programmes, access to essential antibiotics, and research and development of new vaccines and antibiotics. There are serious data gaps in many low-income settings, emphasising the need to expand microbiology laboratory capacity and data collection systems to improve our understanding of this important human health threat.

Evaluation of trends in hospital antimicrobial use in the Lao PDR using repeated point-prevalence surveys-evidence to improve treatment guideline use. Chansamouth V, Chommanam D, Roberts T, Keomany S, Paphasiri V, Phamisith C, Sengsavang S, Detleuxay K, Phoutsavath P, Bouthavong S, Douangnouvong A, Vongsouvath M, Rattana S, Keohavong B, Day NPJ, Turner P, van Doorn HR, Mayxay M, Ashley EA and Newton PN. *Lancet Reg Health West Pac*. 2022 **27**: 100531. doi: 10.1016/j.lanwpc.2022.100531. PMID: 35846979. PMCID: PMC9283659.

Point-prevalence surveys conducted over 4 years at 6 sites in Lao PDR revealed that nearly three-quarters of all in-patients received antibiotics, and that only 26% of antibiotic use was compliant with local guidelines. Enhanced stewardship interventions are required.

BACKGROUND:	Antimicrobial use (AMU) is a key driver of antimicrobial resistance (AMR). There are few data on AMU, to inform optimizing antibiotic stewardship, in the Lao PDR (Laos).
METHODS:	Point prevalence surveys (PPS) of AMU were conducted at four-month intervals in six general hospitals across Laos from 2017 to 2020, using modified Global-PPS data collection tools. The surveys focused on AMU amongst hospitalized inpatients.
FINDINGS:	The overall prevalence of inpatient AMU was 71% (4,377/6,188), varying by hospital and survey round from 50·4% (135/268) to 88·4% (61/69). Of 4,377 patients, 44% received >one antimicrobial. The total number of prescriptions assessed was 6,555. Ceftriaxone was the most commonly used (39·6%) antimicrobial, followed by metronidazole (17%) and gentamicin (10%). Pneumonia was the most common diagnosis among those prescribed antimicrobials in both children aged ≤5 years (29% among aged ≤1 year and 27% among aged >1 to ≤5years) and adults aged ≥15 years at 9%. The percentage of

	antimicrobial use compliant with local treatment guidelines was 26%; inappropriate use was mainly found for surgical prophylaxis (99%). Adult patients received ACCESS group antimicrobials less commonly than children (47% vs 63%, p-value<0·0001). Most WATCH group prescriptions (99%) were without a microbiological indication.
INTERPRETATION:	AMU among hospitalized patients in Laos is high with frequent inappropriate use of antimicrobials, especially as surgical prophylaxis. Continued monitoring and enhanced antimicrobial stewardship interventions are needed in Lao hospitals.

Apramycin susceptibility of multidrug-resistant Gram-negative blood culture isolates in five countries in South-East Asia. Gysin M, Hon PY, Tan P, Sengduangphachanh A, Simmalavong M, Hinfonthong P, Kaewphanderm N, Pham TD, Nguyen TH, Haldimann K, Becker K, van Doorn HR, Hopkins J, Simpson AJH, Ashley EA, Kesteman T, Tran HH, Vasoo S, Ling CL, Roberts T, Turner P, Hobbie SN. *Int J Antimicrob Agents*. 2022 **60**(4): 106659. doi: 10.1016/j.ijantimicag.2022.106659. PMID: 35988665.

The novel aminoglycoside antibiotic apramycin was active against almost all multidrug-resistant Gram-negative bacteria tested, including colistin-resistant isolates. Activity was maintained against all Acinetobacter baumannii *and* Pseudomonas aeruginosa *isolates.*

Bloodstream infections (BSIs) are a leading cause of sepsis, a life-threatening condition that contributes significantly to the mortality of bacterial infections. Aminoglycoside antibiotics such as gentamicin or amikacin are essential medicines in the treatment of BSIs, but their clinical efficacy is increasingly compromised by antimicrobial resistance. The aminoglycoside apramycin has demonstrated preclinical efficacy against aminoglycoside- and multidrug-resistant (MDR) Gram-negative bacilli (GNB) and is currently in clinical development for the treatment of critical systemic infections. Here, we collected a panel of 470 MDR GNB isolates from health care facilities in Cambodia, Laos, Singapore, Thailand, and Vietnam for a multi-centre assessment of their antimicrobial susceptibility to apramycin in comparison to other aminoglycosides and colistin by broth microdilution assays. Apramycin and amikacin MICs ≤ 16 µg/mL were found for 462 (98.3%) and 408 (86.8%) GNB isolates, respectively. Susceptibility to gentamicin and tobramycin (MIC ≤ 4 µg/mL) was significantly lower at 122 (26.0%) and 101 (21.5%) susceptible isolates, respectively. Of note, all carbapenem and third-generation cephalosporin (3GC) resistant Enterobacterales, all *Acinetobacter baumannii*, and all *Pseudomonas aeruginosa* isolates tested in this study appeared to be susceptible to apramycin. Of the 65 colistin-resistant isolates tested, only four (6.2%) had an apramycin MIC > 16 µg/mL. Apramycin demonstrated best-in-class activity against a panel of GNB isolates with resistances to other aminoglycosides, carbapenems, 3GC, and colistin, warranting continued consideration of apramycin as a drug candidate for the treatment of multidrug-resistant BSIs.

***Haemophilus influenzae* serotype b seroprevalence in central Lao PDR before and after vaccine introduction.** Hefele L, Lai J, Vilivong K, Bounkhoun T, Chanthaluanglath V, Chanthongthip A, Balloch A, Black AP, Hübschen JM, Russell FM, Muller CP. *PLoS One*. 2022 **17**(9): e0274558. doi: 10.1371/journal.pone.0274558. PMID: 36107979. PMCID: PMC9477263.

All children, whether vaccinated against Haemophilus influenzae *type b or not, had protective antibodies – suggesting ongoing circulation of this pathogen. Short-term protection was associated with increased time since vaccination, and nutritional status. We recommend ongoing surveillance of this infection and vaccine efficacy.*

INTRODUCTION:	Vaccination has dramatically reduced invasive *Haemophilus influenzae* type b (Hib) disease worldwide. Hib vaccination was introduced in the Lao PDR in 2009, as part of the pentavalent vaccine. To contribute to the understanding of the epidemiology of Hib in Lao PDR and the protection levels before and after the introduction of the vaccination, we tested serum samples from existing cohorts of vaccine age-eligible children and unvaccinated adolescents for antibodies against Hib.
METHODS:	Serum samples from 296 adolescents born before vaccine introduction and from 1017 children under 5 years (vaccinated and unvaccinated) were tested for anti-Hib antibodies by ELISA. Bivariate analyses were performed to investigate factors associated with long-term protection.
RESULTS:	The vast majority of all participants showed evidence of short (42.7%) or long-term (56.1%) protection against Hib. Almost all of the unvaccinated adolescents had antibody titers indicating short-term protection and almost half (45.6%) were long-term protected. Nearly all children (>99.0%) were at least short-term protected, even those that were unvaccinated or whose vaccination status was unknown. Among vaccinated children, participants vaccinated more than 1 or 2 years ago and with a mid-upper arm circumference z-score < -2 were less likely to be long-term protected.
DISCUSSION:	Nearly all adolescents born before the introduction of Hib vaccination in the Lao PDR had antibody titers corresponding to at least short-term protection, indicating a high burden of Hib disease at that time. After vaccine introduction, all but four children (>99%) showed at least short-term protection. Possible explanations for the proportion of protected, yet apparently unvaccinated children, may be past infections, cross-reacting antibodies or faulty vaccination documentation. Our results highlight the need for robust surveillance and reporting of invasive Hib disease to determine the burden of disease despite vaccination.

Antibiotic knowledge, attitudes and reported practice during pregnancy and six months after birth: a follow-up study in Lao PDR. Kounnavong S, Yan W, Sihavong A, Sychareun V, Eriksen J, Hanson C, Chaleunvong K, Keohavong B, Vongsouvath M, Mayxay M, Brauner A, Stålsby Lundborg C, Machowska A. *BMC Pregnancy Childbirth*. 2022 **22**(1): 701. doi: 10.1186/s12884-022-05018-x. PMID: 36096811. PMCID: PMC9465860.

Pregnant women and mothers had limited knowledge about antibiotics. Mothers used antibiotics during pregnancy and for their children more appropriately than for themselves, but antibiotic use was frequent for the common cold.

BACKGROUND:	Antibiotics are important medicines to prevent maternal and child morbidity and mortality. Women's knowledge and attitudes towards antibiotic use influence their practice. When they become mothers, this may be mirrored in the use of antibiotics for their newborn children. The current study aimed to assess knowledge, attitudes, and reported practice of pregnant women regarding antibiotic use and antibiotic resistance as well as their approach towards antibiotic use for their newborn babies.
METHODS:	This was a follow-up study with data collected via structured interviews between September 2019 and August 2020 in Feuang (rural) and Vangvieng (urban) districts in Vientiane province, Lao PDR. We identified and invited all women attending antenatal care in their third trimester of pregnancy in the

	selected areas. Using a structured questionnaire at third trimester of pregnancy we captured data on knowledge regarding antibiotic use and resistance. We collected information on attitudes and reported practice at two time points: (i) at third trimester of pregnancy and (ii) 6 months after birth. Univariate analysis and frequency distributions were used to study pattern of responses. Chi-square and Mann-Whitney tests were used to compare categorical and continuous variables respectively. P value < 0.05 was considered statistically significant.
RESULTS:	We surveyed 539 women with a mean age of 25 years. Two oral antibiotics, i) ampicillin and ii) amoxicillin were correctly identified by 68 and 47% of participants respectively. Only 24% of women (19% in Feuang and 29% in Vangvieng) answered correctly that antibiotics are effective against bacterial infections. The most prevalent response was "I don't know" suggesting the questions were challenging. Significantly less women would use antibiotics from a previous illness for their child than for themselves (16% vs 29%); however, they would be more willing to use antibiotics for their baby even in case of mild symptoms (29% vs 17% while pregnant). The majority of antibiotics were prescribed by healthcare providers and 46% of children with the common cold received antibiotics.
DISCUSSION:	Women's knowledge was sub-optimal, still, they manifested appropriate attitudes towards antibiotic use during pregnancy and for their child. Nearly half of children received antibiotics for the common cold. There is a need for context adapted programs aiming at improving women's knowledge, as well as healthcare providers, emphasising rational antibiotic prescribing during pregnancy and for children.

Invasive *Streptococcus agalactiae* ST283 infection after fish consumption in two sisters, Lao PDR. Luangraj M, Hiestand J, Rasphone O, Chen S, Davong V, Barkham T, Simpson A, Dance DAB, Keoluangkhot V. *Wellcome Open Research*. 2022 **7**: 148. doi: 10.12688/wellcomeopenres.17804.2. PMID: 36324702. PMCID: PMC9607938.

Invasive Group B Streptococcus *infection occurred simultaneously in two women who had shared a meal together. The presumed source was undercooked fish, highlighting its potential as a foodborne pathogen.*

BACKGROUND:	*Streptococcus agalactiae* is a normal commensal of the human gastro-intestinal and female genital tracts. It causes serious disease in neonates and pregnant women, as well as non-pregnant adults. Food-borne outbreaks have also been described. A link between invasive Group B streptococcus (GBS) infection in humans caused by S. agalactiae serotype III-4, sequence type 283 (ST283) and the consumption of raw fresh-water fish was first described in Singapore in 2015.
CASE PRESENTATION:	We report the simultaneous occurrence of acute fever and myalgia in two sisters who were visiting Laos. Both were found to have invasive GBS ST283 infection, confirmed by blood culture. Infection was temporally linked to fish consumption. They responded well to intravenous antibiotics within 48 hours.
CONCLUSIONS:	Food-borne transmission of *Streptococcus agalactiae* is an important and under-recognised source of serious human disease throughout Southeast Asia and possibly beyond.

Nitrofurantoin and glucose-6-phosphate dehydrogenase deficiency: a safety review. Recht J, Chansamouth V, White NJ and Ashley EA. *JAC Antimicrob Resist*. 2022 **4**(3): dlac045. doi: 10.1093/jacamr/dlac045. PMID: 35529053. PMCID: PMC9070801.

Haemolysis is associated with nitrofurantoin use in patients with glucose-6-phosphate dehydrogenase deficiency. Despite 245 million courses having been administered, only 318 cases of haemolytic anaemia and 10 deaths were reported – but it is not clear if nitrofurantoin was causally related. Short courses of nitrofurantoin are likely to be safe.

Nitrofurantoin, a broad-spectrum antibiotic available since 1953, is used widely for the treatment of urinary tract infections as it often retains activity against drug-resistant uropathogens. It is contraindicated in pregnant women at term, and in neonates. Like trimethoprim/sulfamethoxazole, nitrofurantoin carries a warning for patients with known sensitivity to oxidant drugs, notably glucose-6-phosphate dehydrogenase (G6PD) deficiency, in whom it may cause haemolytic anaemia. This is a barrier to uptake in tropical regions where there is a high burden of antimicrobial resistance and where G6PD deficiency is common. Early studies of erythrocyte survival following nitrofurantoin suggest it is less likely to cause oxidant haemolysis in individuals with G6PD deficiency than primaquine. Here we review reports of haemolysis associated with nitrofurantoin from the published literature and from USA (FDA Adverse Event Reporting System; FAERS) and European (VigiBase) pharmacovigilance databases. In total, 318 episodes of haemolytic anaemia were reported and 10 deaths, with 42 (13%) in individuals with confirmed or highly probable G6PD deficiency, out of at least 245 million exposures. A causal link between death and exposure was not reported and a precise risk estimation in G6PD-deficient individuals was not possible as there are few reports from regions where this enzymopathy is most prevalent. The evidence suggests a total daily dose of 200 mg nitrofurantoin may be used for short (3-5 day) course urinary tract infection treatment without G6PD screening when accompanied by appropriate advice. Pharmacovigilance in countries with high prevalence of G6PD-deficiency is recommended to monitor for serious adverse events.

Impact of delayed processing of positive blood cultures on organism detection: a prospective multi-centre study. Roberts T, Chandna A, Watthanaworawit W, Thaiprakong A, Soeng S, Simmalavong M, Phoumin P, Saengchun W, Khatta N, Hinfonthong P, Kaewpundoem N, Lee SJ, Perrone C, Amos B, Turner P, Ashley EA, Ling CL. *BMC Infect Dis*. 2022 **22**(1): 517. doi: 10.1186/s12879-022-07504-1. PMID: 35659576. PMCID: PMC9167519.

Delayed subculture of positive blood cultures results in reduced recovery of S. pneumoniae*, but not other bacterial species. Recovery was improved by maintaining cultures at 22-27 °C, and by using Amies bacterial transport swabs. This has implications for microbiology workflow.*

BACKGROUND:	Blood cultures remain the gold standard investigation for the diagnosis of bloodstream infections. In many locations, quality-assured processing of positive blood cultures is not possible. One solution is to incubate blood cultures locally, and then transport bottles that flag positive to a central reference laboratory for organism identification and antimicrobial susceptibility testing. However, the impact of delay between the bottle flagging positive and subsequent sub-culture on the viability of the isolate has received little attention.
METHODS:	This study evaluated the impact of delays to sub-culture (22 h to seven days) in three different temperature conditions (2-8 °C, 22-27 °C and 35 ± 2 °C) for bottles that had flagged positive in automated detection systems using a mixture of spiked and routine clinical specimens. Ninety spiked samples

	for five common bacterial causes of sepsis (*Escherichia coli*, *Haemophilus influenzae*, *Staphylococcus aureus*, *Streptococcus agalactiae* and *Streptococcus pneumoniae*) and 125 consecutive positive clinical blood cultures were evaluated at four laboratories located in Cambodia, Lao PDR and Thailand. In addition, the utility of transport swabs for preserving organism viability was investigated.
RESULTS:	All organisms were recoverable from all sub-cultures in all temperature conditions with the exception of *S. pneumoniae*, which was less likely to be recoverable after longer delays (> 46-50 h), when stored in hotter temperatures (35 °C), and from BacT/ALERT when compared with BACTEC blood culture bottles. Storage of positive blood culture bottles in cooler temperatures (22-27 °C or below) and the use of Amies bacterial transport swabs helped preserve viability of *S. pneumoniae*.
CONCLUSIONS:	These results have practical implications for the optimal workflow for blood culture bottles that have flagged positive in automated detection systems located remotely from a central processing laboratory, particularly in tropical resource-constrained contexts.

Antimicrobial resistance patterns in bacteria causing febrile illness in Africa, South Asia, and Southeast Asia: a systematic review of published etiological studies from 1980-2015. Roberts T, Dahal P, Shrestha P, Schilling W, Shrestha R, Ngu R, Huong VTL, van Doorn HR, Phimolsarnnousith V, Miliya T, Crump JA, Bell D, Newton PN, Dittrich S, Hopkins H, Stepniewska K, Guerin PJ, Ashley EA, Turner P. *Int J Infect Dis*. 2022 **122**: 612–621. doi: 10.1016/j.ijid.2022.07.018. PMID: 35817284.

This review demonstrates increasing amounts of AMR data globally, with worrying increases in the proportion of resistant isolates reported. Consistent surveillance data will require improvements to laboratory capacity, testing and reporting.

OBJECTIVE:	In this study, we aimed to conduct a systematic review to characterize antimicrobial resistance (AMR) patterns for bacterial causes of febrile illness in Africa and Asia.
METHODS:	We included published literature from 1980-2015 based on data extracted from two recent systematic reviews of nonmalarial febrile illness from Africa, South Asia, and Southeast Asia. Selection criteria included articles with full bacterial identification and antimicrobial susceptibility testing (AST) results for key normally sterile site pathogen-drug combinations. Pooled proportions of resistant isolates were combined using random effects meta-analysis. Study data quality was graded using the Microbiology Investigation Criteria for Reporting Objectively (MICRO) framework.
RESULTS:	Of 3475 unique articles included in the previous reviews, 371 included the target pathogen-drug combinations. *Salmonella enterica* tested against ceftriaxone and ciprofloxacin were the two highest reported combinations (30,509 and 22,056 isolates, respectively). Pooled proportions of resistant isolates were high for third-generation cephalosporins for *Klebsiella pneumoniae* and *Escherichia coli* in all regions. The MICRO grading showed an overall lack of standardization.
DISCUSSION:	This review highlights a general increase in AMR reporting and in resistance over time. However, there were substantial problems with diagnostic microbiological data quality. Urgent strengthening of laboratory capacity, standardized testing, and reporting of AST results is required to improve AMR surveillance.

Utility of InTray COLOREX Screen agar and InTray COLOREX ESBL agar for urine culture in the Lao PDR. Roberts T, Silisouk J, Sengdatka D, Sibounheuang B, Seljuk R, Vang X, Sengduangphachanh A, Davong V, Vongsouvath M, Malou N, Ferreyra C, Ashley EA, Simpson AJH. *JAC Antimicrob Resist*. 2022 4(1): dlac006. doi: 10.1093/jacamr/dlac006. PMID: 35146428. PMCID: PMC8826549.

We found InTray COLOREX Screen agar plates and COLOREX ESBL agar plates to be practical for culture of uropathogens and ESBL-producing organisms, respectively, with potential use in field sites.

BACKGROUND:	There is a need for simple microbiology diagnostics to enable antimicrobial resistance surveillance in low- and middle-income countries.
OBJECTIVES:	To investigate the field utility of InTray COLOREX plates for urine culture and ESBL detection.
METHODS:	Clinical urine samples from Mahosot Hospital, Vientiane, Lao PDR were inoculated onto chromogenic media and InTray COLOREX Screen plates between June and August 2020. Urine and isolates from other clinical specimens were inoculated onto COLOREX ESBL plates. A simulated field study investigating the field utility of the InTray COLOREX plates was also completed.
RESULTS:	In total, 355 urine samples were inoculated onto standard chromogenic agar and InTray COLOREX Screen plates, and 154 urine samples and 54 isolates from other clinical specimens on the COLOREX ESBL plates. Growth was similar for the two methods (COLOREX Screen 41%, standard method 38%) with 20% discordant results, mainly due to differences in colony counts or colonial appearance. Contamination occurred in 13% of samples, with the COLOREX Screen plates showing increased contamination rates, potentially due to condensation. ESBL producers were confirmed from 80% of isolates from the COLOREX ESBL plates, and direct plating provided rapid detection of presumptive ESBL producers. *Burkholderia pseudomallei* also grew well on the ESBL plates, a relevant finding in this melioidosis-endemic area.
CONCLUSIONS:	The InTray COLOREX Screen and ESBL plates were simple to use and interpret, permitting rapid detection of uropathogens and ESBLs, and have the potential for easy transport and storage from field sites and use in laboratories with low capacity.

Perceptions and reported practices of pregnant women and mothers of children under two years of age regarding antibiotic use and resistance in Vientiane province, Lao PDR: a qualitative study. Sychareun V, Phounsavath P, Sihavong A, Kounnavong S, Chaleunvong K, Machowska A, Keohavong B, Mayxay M, Eriksen J, Hanson C, Vongsouvath M, Brauner A, Durham J, Stålsby Lundborg C. *BMC Pregnancy Childbirth*. 2022 **22**(1): 569. doi: 10.1186/s12884-022-04894-7. PMID: 35842597. PMCID: PMC9287906.

Most mothers said they wanted to understand more about antibiotic use and resistance, but they misunderstood key concepts. The mismatch provides an opportunity to educate mothers as well as healthcare workers in the appropriate use of antibiotics.

BACKGROUND:	Understanding pregnant women and mothers' perceptions towards antibiotic use and resistance is essential for appropriate antibiotic use and limiting antibiotic resistance. This study aimed to explore perceptions and reported practices of pregnant women and mothers with children under two years of age regarding correct antibiotic use and antibiotic resistance in Vientiane Province, Lao PDR.

METHODS:	The study employed an exploratory qualitative research design using focus groups discussions (FGDs). Participants were purposively selected based on: being pregnant at third trimester and attending antenatal care and mothers with children under two years of age, attending the health facility for postpartum visit/vaccinations. Six focus group discussions were conducted in September 2019 with a total of 55 women. The FGDs were transcribed verbatim, data were analysed first by coding then categorizing the data as we looked for patterns and themes by using the qualitative content analysis.
RESULTS:	Most participants had some understanding of antibiotics but wrongly believed antibiotics can be used to treat viral disease. Over half of the participants had heard the term "antibiotic resistance", but often believed it was their bodies, not the bacteria that developed antibiotic resistance. During pregnancy and for their infants, women preferred to use antibiotics only when prescribed by a doctor. Outside of pregnancy, however, consuming antibiotics without a prescription was commonly reported. Participants wanted more information about the indications for antibiotic use and antibiotic resistance.
CONCLUSIONS:	More effort is required to increase the level of understanding, and practice of mothers to promote optimal antibiotic use. Mothers' desire to learn more, and their fundamental concern for their children, can be used to promote appropriate antibiotic use. Awareness raising should be complemented by efforts to address other determinants of inappropriate antibiotic use, including educating healthcare workers, and pharmacists and addressing health service determinants that contribute to inappropriate antibiotic use.

Antibiotic prescribing in connection to childbirth: an observational study in two districts in Lao PDR. Yan W, Machowska A, Sihavong A, Sychareun V, Chaleunvong K, Keohavong B, Eriksen J, Hanson C, Vongsouvath M, Brauner A, Mayxay M, Kounnavong S, Stålsby Lundborg C. *Antibiotics (Basel)*. 2022 **11**(4): 448. doi: 10.3390/antibiotics11040448. PMID: 35453200. PMCID: PMC9029038.

Every woman who gave birth, whether by vaginal delivery or caesarian section, in 2 district hospitals and 5 heath centres received antibiotics both while in hospital and on discharge. Appropriate antibiotic stewardship interventions are urgently required.

Overuse and misuse of antibiotics has frequently been reported for obstetric conditions and procedures, which may impact both the mother and the unborn baby and increase antibiotic resistance. This study aimed to investigate the antibiotic prescribing pattern in connection to childbirth in two districts in Lao PDR. It is a cross-sectional observational study. Antibiotic prescription data related to childbirth was collected via reviews of medical records in two district hospitals and five health centres in Lao PDR from September 2019 to November 2020. In total, antibiotic prescription data for 1777 women were extracted from their medical records. It was found that all women received antibiotics during in-patient care irrespective of delivery mode. When in hospital, 85.5% of the women who underwent a caesarean section got antibiotic treatment for 5 days and women who had a vaginal delivery usually had antibiotic treatment for one day or less. All the women got oral antibiotics for an additional 4-5 days upon discharge. Antibiotic prescription rate in connection to childbirth was very high in comparison with the WHO guidelines, and antibiotics were used extensively in the participating health facilities. Interventions to guide appropriate prescribing behaviour in relation to childbirth are urgently needed in Lao PDR.

A one-health sampling strategy to explore the dissemination and relationship between colistin resistance in human, animal, and environmental sectors in Laos. Zhou Y, Farzana R, Sihalath S, Rattanavong S, Vongsouvath M, Mayxay M, Sands K, Newton PN, Dance DAB, Hassan B, Walsh TR. *Engineering*. 2022 **15**(8): 45–56. doi: 10.1016/j.eng.2022.01.013.

Plasmids encoding colistin resistance are widespread in humans, animals and the environment. These plasmids transfer readily to new E. coli *strains, are stably maintained once acquired, and do not impose a fitness cost on their host. Infection control requirements in the One Health context are essential to limit on-going spread.*

This study was designed to investigate the molecular epidemiology of mobile colistin resistance (*mcr*) using a One Health approach in Laos and to predict whether any dominant plasmid backbone and/or strain type influences the dissemination of *mcr*. We collected 673 samples from humans (rectal normal flora), poultry, and the environment (water, flies, birds, etc.) in Vientiane, Laos, from May to September 2018. A total of 238 *Escherichia coli* (*E. coli*) isolated from non-duplicative samples, consisting of 98 MCR-positive *E. coli* (MCRPEC) ("*mcr*" denotes the gene encoding mobile colistin resistance, and "MCR" denotes the subsequent protein encoded by *mcr*) and 140 MCR-negative *E. coli* (MCRNEC), were characterized by phenotype and Illumina sequencing. A subset of MCRPEC was selected for MinION sequencing, conjugation assay, plasmid stability, and growth kinetics *in vitro*. The prevalence of MCRPEC was found to be 14.6% (98/673), with the highest prevalence in human rectal swabs (45.9% (45/98), $p < 0.0001$, odds ratio (OR): 0.125, 95% CI: 0.077–0.202). The percentages of MCRPEC from other samples were 14.3% (2/14) in dog faeces, 12.0% (24/200) in flies, 11.0% (11/100) in chicken meat, 8.9% (8/90) in chicken cloacal, 8.0% (4/50) in chicken caeca, and 7.5% (4/53) in wastewater. MCRPEC was significantly more resistant to co-amoxiclav, sulfamethoxazole-trimethoprim, levofloxacin, ciprofloxacin, and gentamicin than MCRNEC ($p < 0.05$). Genomic analysis revealed the distribution of MCRPEC among diverse clonal types. The putative plasmid Included types associated with *mcr-1* were IncX4, IncHI2, IncP1, IncI2, and IncFIA, and those associated with *mcr-3* were IncFII, IncFIA, IncFIB, IncP1, and IncR. Recovery of highly similar plasmids from both flies and other sampling sectors implied the role of flies in the dissemination of *mcr-1*. *mcr*-positive plasmids were shown to be conjugative, and a significantly high transfer rate into a hypervirulent clone ST1193 was observed. Plasmids containing *mcr* irrespective of Including type were highly stable and invariably did not exert a fitness effect upon introduction into a new host. These findings signify the urgent need for a standard infection control program to radically decontaminate the source of resistance.

Melioidosis

Detection and quantification of the capsular polysaccharide of *Burkholderia pseudomallei* in serum and urine samples from melioidosis patients. DeMers HL, Nualnoi T, Thorkildson P, Hau D, Hannah EE, Green HR, Pandit SG, Gates-Hollingsworth MA, Boutthasavong L, Luangraj M, Woods KL, Dance DAB, AuCoin DP. *Microbiol Spectr*. 2022 **10**(4): e00765-22. doi: 10.1128/spectrum.00765-22. PMID: 35924843. PMCID: PMC9430648.

New ELISA and lateral flow assays were evaluated for the diagnosis of melioidosis. The lateral flow device identified B. pseudomallei *in 40% of urine samples and 6% of serum samples, compared to 60% of urine samples and 50% of serum samples when tested by ELISA. Concentrating samples increased the sensitivity.*

BACKGROUND: *Burkholderia pseudomallei* is the causative agent of melioidosis, a life-threatening disease common in Southeast Asia and northern Australia. Melioidosis often presents with nonspecific symptoms and has a fatality rate of upwards of 70% when left untreated. The gold standard for diagnosis is culturing *B. pseudomallei* from patient samples. Bacterial culture, however, can take up to 7 days, and its sensitivity is poor, at roughly 60%. The successful administration of appropriate antibiotics is reliant on rapid and accurate diagnosis. Hence, there is a genuine need for new diagnostics for this deadly pathogen. The Active Melioidosis Detect (AMD) lateral flow immunoassay (LFI) detects the capsular polysaccharide (CPS) of *B. pseudomallei*. The assay is designed for use on various clinical samples, including serum and urine; however, there are limited data to support which clinical matrices are the best candidates for detecting CPS. In this study, concentrations of CPS in paired serum and urine samples from melioidosis patients were determined using a quantitative antigen capture enzyme-linked immunosorbent assay. In parallel, samples were tested with the AMD LFI, and the results of the two immunoassays were compared. Additionally, centrifugal concentration was performed on a subset of urine samples to determine if this method may improve detection when CPS levels are initially low or undetectable. The results indicate that while CPS levels varied within the two matrices, there tended to be higher concentrations in urine. The AMD LFI detected CPS in 40.5% of urine samples, compared to 6.5% of serum samples, suggesting that urine is a preferable matrix for point-of-care diagnostic assays.

IMPORTANCE: Melioidosis is very challenging to diagnose. There is a clear need for a point-of-care assay for the detection of *B. pseudomallei* antigen directly from patient samples. The Active Melioidosis Detect lateral flow immunoassay detects the capsular polysaccharide (CPS) of *B. pseudomallei* and is designed for use on various clinical samples, including serum and urine. However, there are limited data regarding which clinical matrix is preferable for the detection of CPS. This study addresses this question by examining quantitative CPS levels in paired serum and urine samples and relating them to clinical parameters. Additionally, centrifugal concentration was performed on a subset of urine samples to determine whether this might enable the detection of CPS in samples in which it was initially present at low or undetectable levels. These results provide valuable insights into the detection of CPS in patients with melioidosis and suggest potential ways forward in the diagnosis and treatment of this challenging disease.

The innate immune response in the marmoset during the acute pneumonic disease caused by *Burkholderia pseudomallei*. Ngugi S, Laws T, Simpson AJ, Nelson M. *Infect Immun*. 2022 **90**(3): e0055021. doi: 10.1128/iai.00550-21. PMID: 35041487. PMCID: PMC8929355.

The immune response of the marmoset to Burkholderia pseudomallei *was investigated. Key immune responses mirrored those seen in humans, were able to predict prognosis, and may prove useful for early diagnosis. The marmoset is a useful animal model for this disease.*

Burkholderia pseudomallei is the causative agent of melioidosis, a severe human infection that is difficult to treat with antibiotics and for which there is no effective vaccine. Development of novel treatments rely upon appropriately characterized animal models. The common marmoset (*Callithrix jacchus*) has been established at Defence Science and Technology laboratories (DSTL) as a model of melioidosis. Further analysis was performed on samples generated in these features described, (migration/activation of neutrophils and macrophages, activation of T cells, elevation of key cytokines IFNγ, TNF-α, IL-6, and IL-1β) have been observed in acute melioidosis human cases and correlated with prognosis. Expression of the MHCII marker (HLA-DR) on neutrophils showed potential as a diagnostic with 80% accuracy when comparing pre- and post-challenge levels in paired blood samples. Discriminant analysis of cell surface, activation markers on neutrophils combined with levels of key cytokines, differentiated between disease states from single blood samples with 78% accuracy. These key markers have utility as a prototype post-exposure, presymptomatic diagnostic. Ultimately, these data further validate the use of the marmoset as a suitable model for determining efficacy of medical countermeasures against *B. pseudomallei*.

Distribution of *Burkholderia pseudomallei* within a 300-cm deep soil profile: implications for environmental sampling. Pongmala K, Pierret A, Oliva P, Pando A, Davong V, Rattanavong S, Silvera N, Luangraj M, Boithias L, Xayyathip K, Menjot L, Macouin M, Rochelle-Newall E, Robain H, Vongvixay A, Simpson AJH, Dance DAB, Ribolzi O. *Sci Rep*. 2022 12(1): 8674. doi: 10.1038/s41598-022-12795-0. PMID: 35606475. PMCID: PMC9126866.

The preferred environmental niche of B. pseudomallei *needs to be fully understood to optimise sampling strategies, and to understand risk to populations.* B. pseudomallei *was preferentially found between 100cm and 200cm below the soil surface, and groundwater persistence appears to be important.*

The environmental distribution of *Burkholderia pseudomallei*, the causative agent of melioidosis, remains poorly understood. *B. pseudomallei* is known to have the ability to occupy a variety of environmental niches, particularly in soil. This paper provides novel information about a putative association of soil biogeochemical heterogeneity and the vertical distribution of *B. pseudomallei*. We investigated (1) the distribution of *B. pseudomallei* along a 300-cm deep soil profile together with the variation of a range of soil physico-chemical properties; (2) whether correlations between the distribution of *B. pseudomallei* and soil physico-chemical properties exist and (3) when they exist, what such correlations indicate with regards to the environmental conditions conducive to the occurrence of *B. pseudomallei* in soils. Unexpectedly, the highest concentrations of *B. pseudomallei* were observed between 100 and 200 cm below the soil surface. Our results indicate that unravelling the environmental conditions favourable to *B. pseudomallei* entails considering many aspects of the actual complexity of soil. Important recommendations regarding environmental sampling for *B. pseudomallei* can be drawn from this work, in particular that collecting samples down to the water table is of foremost importance, as groundwater persistence appears to be a controlling factor of the occurrence of *B. pseudomallei* in soil.

A novel lytic phage potentially effective for phage therapy against *Burkholderia pseudomallei* in the tropics. Wang Y, Li X, Dance DAB, Xia H, Chen C, Luo N, Li A, Li Y, Zhu Q, Sun Q, Wu X, Zeng Y, Chen L, Tian S, Xia Q. Infect Dis Poverty. 2022 **11**(1): 87. doi: 10.1186/s40249-022-01012-9. PMID: 35927751. PMCID: PMC9351088.

Phage therapy may be a useful adjunct in treatment melioidosis. Multiple phages were isolated from the environment and one was characterised in detail, including by genome sequencing. This phage was able to lyse 96% of B. pseudomallei *strains in vitro, and improved survival in a nematode model from 0% to 80%.*

BACKGROUND:	*Burkholderia pseudomallei* is a tropical pathogen that causes melioidosis. Its intrinsic drug-resistance is a leading cause of treatment failure, and the few available antibiotics require prolonged use to be effective. This study aimed to assess the clinical potential of *B. pseudomallei phages* isolated from Hainan, China.
METHODS:	*Burkholderia pseudomallei* strain (HNBP001) was used as the isolation host, and phages were recovered from domestic environmental sources, which were submitted to the host range determination, lytic property assays, and stability tests. The best candidate was examined via the transmission electron microscope for classification. With its genome sequenced and analysed, its protective efficacy against *B. pseudomallei* infection in A549 cells and Caenorhabditis elegans was evaluated, in which cell viability and survival rates were compared using the one-way ANOVA method and the log-rank test.
RESULTS:	A phage able to lyse 24/25 clinical isolates was recovered. It was classified in the Podoviridae family and was found to be amenable to propagation. Under the optimal multiplicity of infection (MOI) of 0.1, an eclipse period of around 20 min and a high titer (10(12) PFU/ml) produced within 1 h were demonstrated. This phage was found stabile at a wide range of temperatures (24, 37, 40, 50, and 60 °C) and pH values (3-12). After being designated as vB_BpP_HN01, it was fully sequenced, and the 71,398 bp linear genome, containing 93 open reading frames and a tRNA-Asn, displayed a low sequence similarity with known viruses. Additionally, protective effects of applications of vB_BpP_HN01 (MOI = 0.1 and MOI = 1) alone or in combination with antibiotics were found to improve viability of infected cells (70.6 ± 6.8%, 85.8 ± 5.7%, 91.9 ± 1.8%, and 96.8 ± 1.8%, respectively). A significantly reduced mortality (10%) and a decreased pathogen load were demonstrated in infected *C. elegans* following the addition of this phage.
CONCLUSIONS:	As the first *B. pseudomallei* phage was isolated in Hainan, China, phage vB_BpP_HN01 was characterized by promising lytic property, stability, and efficiency of bacterial elimination during the in vitro/vivo experiments. Therefore, we can conclude that it is a potential alternative agent for combating melioidosis.

Virology

The role of viral genomics in understanding COVID-19 outbreaks in long-term care facilities. Aggarwal D, Myers R, Hamilton WL, Bharucha T, Tumelty NM, Brown CS, Meader EJ, Connor T, Smith DL, Bradley DT, Robson S, Bashton M, Shallcross L, Zambon M, Goodfellow I, Chand M, O'Grady J, Török ME, Peacock SJ, Page AJ and The COVID-19 Genomics UK (COG-UK) Consortium. *Lancet Microbe*. 2022 **3**(2): e151–e158. doi: 10.1016/S2666-5247(21)00208-1. PMID: 34608459. PMCID: PMC8480962.

A review of genomic epidemiology studies shows that COVID-19 outbreaks in care facilities typically arise following one, or a few, index infections. Genomics methods allow outbreaks to be better characterised, but a significant number of studies used inadequate methods or did not release sequencing data.

We reviewed all genomic epidemiology studies on COVID-19 in long-term care facilities (LTCFs) that had been published to date. We found that staff and residents were usually infected with identical, or near identical, SARS-CoV-2 genomes. Outbreaks usually involved one predominant cluster, and the same lineages persisted in LTCFs despite infection control measures. Outbreaks were most commonly due to single or few introductions followed by a spread rather than a series of seeding events from the community into LTCFs. The sequencing of samples taken consecutively from the same individuals at the same facilities showed the persistence of the same genome sequence, indicating that the sequencing technique was robust over time. When combined with local epidemiology, genomics allowed probable transmission sources to be better characterised. The transmission between LTCFs was detected in multiple studies. The mortality rate among residents was high in all facilities, regardless of the lineage. Bioinformatics methods were inadequate in a third of the studies reviewed, and reproducing the analyses was difficult because sequencing data were not available in many facilities.

Immunoglobulin M seroneutralization for improved confirmation of Japanese encephalitis virus infection in a flavivirus-endemic area. Bharucha T, Ayhan N, Pastorino B, Rattanavong S, Vongsouvath M, Mayxay M, Changthongthip A, Sengvilaipaseuth O, Phonemixay O, Pommier JD, Gorman C, Zitzmann N, Newton PN, de Lamballerie X, Dubot-Pérès A. *Trans R Soc Trop Med Hyg*. 2022 **116**(11): 1032–1042. doi: 10.1093/trstmh/trac036. PMID: 35593182. PMCID: PMC9623734.

Cross-reactivity between IgM antibodies for Japanese encephalitis and IgG antibodies to other flaviviruses affects accuracy of diagnostic tests. Depleting serum of IgG antibodies increased test performance of Japanese encephalitis virus IgM neutralising tests, and improved diagnosis.

BACKGROUND:	The mainstay of diagnostic confirmation of acute Japanese encephalitis (JE) involves detection of anti-JE virus (JEV) immunoglobulin M (IgM) by enzyme-linked immunosorbent assay (ELISA). Limitations in the specificity of this test are increasingly apparent with the introduction of JEV vaccinations and the endemicity of other cross-reactive flaviviruses. Virus neutralization testing (VNT) is considered the gold standard, but it is challenging to implement and interpret. We performed a pilot study to assess IgG depletion prior to VNT for detection of anti-JEV IgM neutralizing antibodies (IgM-VNT) as compared with standard VNT.
METHODS:	We evaluated IgM-VNT in paired sera from anti-JEV IgM ELISA-positive patients (JE n=35) and negative controls of healthy flavivirus-naïve (n=10) as well as confirmed dengue (n=12) and Zika virus (n=4) patient sera. IgM-VNT was subsequently performed on single sera from additional JE patients (n=76).
RESULTS:	Anti-JEV IgG was detectable in admission serum of 58% of JE patients. The positive, negative and overall percentage agreement of IgM-VNT as compared with standard VNT was 100%. A total of 12/14 (86%) patient samples were unclassified by VNT and, with sufficient sample available for IgG depletion and IgG ELISA confirming depletion, were classified by IgM-VNT. IgM-VNT enabled JE case classification in 72/76 (95%) patients for whom only a single sample was available.
CONCLUSIONS:	The novel approach has been readily adapted for high-throughput testing of single patient samples and it holds promise for incorporation into algorithms for use in reference centres.

Mouse models of Japanese encephalitis virus infection: A systematic review and meta-analysis using a meta-regression approach. Bharucha T, Cleary B, Farmiloe A, Sutton E, Hayati H, Kirkwood P, Al Hamed L, van Ginneken N, Subramaniam KS, Zitzmann N, Davies G and Turtle L. *PLoS Negl Trop Dis*. 2022 **16**(2): e0010116. doi: 10.1371/journal.pntd.0010116. PMID: 35143497. PMCID: PMC8865681.

Studies of Japanese encephalitis using mouse models are heterogeneous and often of inadequate quality. Across 127 studies included in this meta-analysis, mouse age and strain, virus strain and dose, and route of inoculation were keep factors influencing mortality.

BACKGROUND:	Japanese encephalitis (JE) virus (JEV) remains a leading cause of neurological infection across Asia. The high lethality of disease and absence of effective therapies mean that standardised animal models will be crucial in developing therapeutics. However, published mouse models are heterogeneous. We performed a systematic review, meta-analysis and meta-regression of published JEV mouse experiments to investigate the variation in model parameters, assess homogeneity and test the relationship of key variables against mortality.
METHODOLOGY/ PRINCIPAL FINDINGS:	A PubMed search was performed up to August 2020. 1991 publications were identified, of which 127 met inclusion criteria, with data for 5026 individual mice across 487 experimental groups. Quality assessment was performed using a modified CAMARADES criteria and demonstrated incomplete reporting with a median quality score of 10/17. The pooled estimate of mortality in mice after JEV challenge was 64.7% (95% confidence interval 60.9 to 68.3) with substantial heterogeneity between experimental groups (I^2 70.1%, df 486). Using meta-regression to identify key moderators, a refined dataset was used to model outcome dependent on five variables: mouse age, mouse strain, virus strain, virus dose (in log10PFU) and route of inoculation. The final model reduced the heterogeneity substantially (I^2 38.9, df 265), explaining 54% of the variability.
CONCLUSION/ SIGNIFICANCE:	This is the first systematic review of mouse models of JEV infection. Better adherence to CAMARADES guidelines may reduce bias and variability of reporting. In particular, sample size calculations were notably absent. We report that mouse age, mouse strain, virus strain, virus dose and route of inoculation account for much, though not all, of the variation in mortality. This dataset is available for researchers to access and use as a guideline for JEV mouse experiments.

Flavivirus cross-reactivity would explain the apparent findings of Japanese encephalitis virus infection in Nigeria. Bharucha T, Zitzmann N, Newton P, Dubot-Pérès A, Turtle L. *J Immunoassay Immunochem*. 2022 **43**(4): 463–465. doi: 10.1080/15321819.2022.2039184. PMID: 35249461.

In this Letter to the Editor, we urge caution in interpreting positive IgG tests for Japanese encephalitis in a Nigerian cohort. Concurrent testing for other flaviviruses is necessary due to high levels of cross-reactivity and false-positive ELISA tests. This is especially important in settings where other flaviviruses are endemic, or where vaccination to flaviviruses is common. Reference laboratories are invaluable where local facilities do not permit confirmatory testing.

ISARIC-COVID-19 dataset: A prospective, standardized, global dataset of patients hospitalized with COVID-19. Garcia-Gallo E, Merson L, Kennon K, Kelly S, Citarella BW, Fryer DV, Shrapnel S, Lee J, Duque S, Fuentes YV, Balan V, Smith S, Wei J, Gonçalves BP, Russell CD, Sigfrid L, Dagens A, Olliaro PL, Baruch J, Kartsonaki C, Dunning J, Rojek A, Rashan A, Beane A, Murthy S, Reyes LF. *Sci Data*. 2022 **9**(1): 454. doi: 10.1038/s41597-022-01534-9. PMID: 35908040. PMCID: PMC9339000.

The ISARIC COVID-19 dataset includes clinical data from over 705,000 COVID-19 patients in more than 60 countries. This article explains the dataset design, accessibility, and ways to use this valuable resource.

The International Severe Acute Respiratory and Emerging Infection Consortium (ISARIC) COVID-19 dataset is one of the largest international databases of prospectively collected clinical data on people hospitalized with COVID-19. This dataset was compiled during the COVID-19 pandemic by a network of hospitals that collect data using the ISARIC-World Health Organization Clinical Characterization Protocol and data tools. The database includes data from more than 705,000 patients, collected in more than 60 countries and 1,500 centres worldwide. Patient data are available from acute hospital admissions with COVID-19 and outpatient follow-ups. The data include signs and symptoms, pre-existing comorbidities, vital signs, chronic and acute treatments, complications, dates of hospitalization and discharge, mortality, viral strains, vaccination status, and other data. Here, we present the dataset characteristics, explain its architecture and how to gain access, and provide tools to facilitate its use.

An international observational study to assess the impact of the Omicron variant emergence on the clinical epidemiology of COVID-19 in hospitalised patients. Gonçalves BP, Hall M, Jassat W, Balan V, Murthy S, Kartsonaki C, Semple MG, Rojek A, Baruch J, Reyes LF, Dasgupta A, Dunning J, Citarella BW, Pritchard M, Martín-Quiros A, Sili U, Baillie JK, Aryal D, Arabi Y, Rashan A, Angheben A, Caoili J, Carrier FM, Harrison EM, Gómez-Junyent J, Figueiredo-Mello C, Douglas JJ, Mat Nor MB, Chow YP, Wong XC, Bertagnolio S, Thwin SS, Streinu-Cercel A, Salazar L, Rishu A, Rangappa R, Ong DSY, Hashmi M, Carson G, Diaz J, Fowler R, Kraemer MUG, Wils EJ, Horby P, Merson L, Olliaro PL. *eLife*. 2022 **11**: e80556. doi: 10.7554/eLife.80556. PMID: 36197974. PMCID: PMC9534549.

To determine the clinical presentation of infections due to the Omicron variant of SARS-CoV-2, individual-patient-level clinical data was analysed with population-level data on circulating variants. This Omicron variant is associated with lower mortality compared to previous variants.

BACKGROUND:	Whilst timely clinical characterisation of infections caused by novel SARS-CoV-2 variants is necessary for evidence-based policy response, individual-level data on infecting variants are typically only available for a minority of patients and settings.
METHODS:	Here, we propose an innovative approach to study changes in COVID-19 hospital presentation and outcomes after the Omicron variant emergence using publicly available population-level data on variant relative frequency to infer SARS-CoV-2 variants likely responsible for clinical cases. We apply this method to data collected by a large international clinical consortium before and after the emergence of the Omicron variant in different countries.

RESULTS:	Our analysis, that includes more than 100,000 patients from 28 countries, suggests that in many settings patients hospitalised with Omicron variant infection less often presented with commonly reported symptoms compared to patients infected with pre-Omicron variants. Patients with COVID-19 admitted to hospital after Omicron variant emergence had lower mortality compared to patients admitted during the period when Omicron variant was responsible for only a minority of infections (odds ratio in a mixed-effects logistic regression adjusted for likely confounders, 0.67 [95% confidence interval 0.61-0.75]). Qualitatively similar findings were observed in sensitivity analyses with different assumptions on population-level Omicron variant relative frequencies, and in analyses using available individual-level data on infecting variant for a subset of the study population.
CONCLUSIONS:	Although clinical studies with matching viral genomic information should remain a priority, our approach combining publicly available data on variant frequency and a multi-country clinical characterisation dataset with more than 100,000 records allowed analysis of data from a wide range of settings and novel insights on real-world heterogeneity of COVID-19 presentation and clinical outcome.

COVID-19 vaccine boosters in the Asia-Pacific region in the context of Omicron. Hart JD, Chokephaibulkit K, Mayxay M, Ong-Lim ALT, Saketa ST, Russell FM. *Lancet Reg Health West Pac*. 2022 **20**: 100404. doi: 10.1016/j.lanwpc.2022.100404. PMID: 35187510. PMCID: PMC8847980.

In this Comment, we summarise the waning vaccine-derived immunity against the SARS-CoV-2 Delta variant, and the benefit of booster doses against the Omicron variant. We argue for booster doses in the Asia-Pacific region due to widespread use of less efficacious inactivated vaccines in primary regimens, and in the Pacific Island Countries due to highly prevalent risk factors for severe disease.

Factors associated with the opposition to COVID-19 vaccination certificates: a multi-country observational study from Asia. Sarin KC, Faradiba D, Sittimart M, Isaranuwatchai W, Ananthakrishnan A, Rachatan C, Dabak S, Shafie AA, Guerrero AM, Suwantika A, Kang G, Ahn J, Hsu LY, Mayxay M, Howard N, Wattanasri P, Nakamura R, George TK, Teerawattananon Y. *Travel Med Infect Dis*. 2022 **48**: 102358. doi: 10.1016/j.tmaid.2022.102358. PMID: 35595199. PMCID: PMC9113761.

A detailed questionnaire was deployed in 9 Asian countries to identify groups opposed to COVID-19 vaccine certificates and highlighted recurring themes. The findings enable policy-makers to address these concerns if acceptance of certificates is to be improved, and may require the personal benefits to be emphasized.

BACKGROUND:	There are ongoing calls to harmonise and increase the use of COVID-19 vaccination certificates (CVCs) in Asia. Identifying groups in Asian societies who oppose CVCs and understanding their reasons can help formulate an effective CVCs policy in the region. However, no formal studies have explored this issue in Asia.
METHODS:	The COVID-19 Vaccination Policy Research and Decision-Support Initiative in Asia (CORESIA) was established to address policy questions related to CVCs. An online cross-sectional survey was conducted from June to October 2021 in nine Asian countries. Multivariable logistical regression analyses were performed to identify potential opposers of CVCs.
RESULTS:	Six groups were identified as potential opposers of CVCs: (i) unvaccinated (Odd Ratio (OR): 2.01, 95% Confidence Interval (CI): 1.65-2.46); vaccine hesitant and those without access to COVID-19 vaccines; (ii) those not wanting existing NPIs to continue (OR: 2.97, 95% CI: 2.51-3.53); (iii) those with low level of trust in governments (OR: 1.25, 95% CI: 1.02-2.52); (iv) those without travel plans (OR: 1.58, 95% CI: 1.31-1.90); (v) those expecting no financial gains from CVCs (OR: 2.35, 95% CI: 1.98-2.78); and (vi) those disagreeing to use CVCs for employment, education, events, hospitality, and domestic travel.
CONCLUSIONS:	Addressing recurring public health bottlenecks such as vaccine hesitancy and equitable access, adherence to policies, public trust, and changing the narrative from 'societal-benefit' to 'personal-benefit' may be necessary and may help increase wider adoption of CVCs in Asia.

A multinational Delphi consensus to end the COVID-19 public health threat. Lazarus JV, Romero D, Kopka CJ, Karim SA, Abu-Raddad LJ, Almeida G, Baptista-Leite R, Barocas JA, Barreto ML, Bar-Yam Y, Bassat Q, Batista C, Bazilian M, Chiou ST, Del Rio C, Dore GJ, Gao GF, Gostin LO, Hellard M, Jimenez JL, Kang G, Lee N, Matičič M, McKee M, Nsanzimana S, Oliu-Barton M, Pradelski B, Pyzik O, Rabin K, Raina S, Rashid SF, Rathe M, Saenz R, Singh S, Trock-Hempler M, Villapol S, Yap P, Binagwaho A, Kamarulzaman A, El-Mohandes A. Nature. 2022 611(7935): 332–345. doi: 10.1038/s41586-022-05398-2. PMID: 36329272. PMCID: PMC9646517.

In the wake of 3 years of individual country-led strategies to combat Covid-19, a set of 41 consensus statements and 57 recommendations were devised by a diverse range of global stakeholders. It is hoped that this will enhance the global response.

Despite notable scientific and medical advances, broader political, socioeconomic and behavioural factors continue to undercut the response to the COVID-19 pandemic. Here we convened, as part of this Delphi study, a diverse, multidisciplinary panel of 386 academic, health, non-governmental organization, government and other experts in COVID-19 response from 112 countries and territories to recommend specific actions to end this persistent global threat to public health. The panel developed a set of 41 consensus statements and 57 recommendations to governments, health systems, industry and other key stakeholders across six domains: communication; health systems; vaccination; prevention; treatment and care; and inequities. In the wake of nearly three years of fragmented global and national responses, it is instructive to note that three of the highest-ranked recommendations call for the adoption of whole-of-society and whole-of-government approaches, while maintaining proven prevention measures using a vaccines-plus approach that employs a range of public health and financial support measures to complement vaccination. Other recommendations with at least 99% combined agreement advise governments and other stakeholders to improve communication, rebuild public trust and engage communities in the management of pandemic responses. The findings of the study, which have been further endorsed by 184 organizations globally, include points of unanimous agreement, as well as six recommendations with >5% disagreement, that provide health and social policy actions to address inadequacies in the pandemic response and help to bring this public health threat to an end.

Orthopoxvirus seroprevalence and infection susceptibility in France, Bolivia, Laos, and Mali. Luciani L, Lapidus N, Amroun A, Falchi A, Souksakhone C, Mayxay M, Dubot-Pérès A, Villarroel PMS, Diarra I, Koita O, Gallian P, de Lamballerie X. *Emerg Infect Dis*. 2022 **28**(12): 2463–2471. doi: 10.3201/eid2812.221136. PMID: 36343384. PMCID: PMC9707606.

Seroprevalence of anti-vaccinia antibodies was very low in Bolivia, Laos, and France, but modest in Mali. Cross-immunity was conferred to cowpox virus, and therefore protection likely extends to other orthopox viruses. The lack of immunity across 4 continents may have permitted the global monkeypox outbreak of 2022.

To determine a demographic overview of orthopoxvirus seroprevalence, we tested blood samples collected during 2003-2019 from France (n = 4,876), Bolivia (n = 601), Laos (n = 657), and Mali (n = 255) for neutralizing antibodies against vaccinia virus. In addition, we tested 4,448 of the 4,876 samples from France for neutralizing antibodies against cowpox virus. We confirmed extensive cross-immunity between the 2 viruses. Seroprevalence of antibodies was <1% in Bolivia, <5% in Laos, and 17.25% in Mali. In France, we found low prevalence of neutralizing antibodies in persons who were unvaccinated and vaccinated for smallpox, suggesting immunosenescence occurred in vaccinated persons, and smallpox vaccination compliance declined before the end of compulsory vaccination. Our results suggest that populations in Europe, Africa, Asia, and South America are susceptible to orthopoxvirus infections, which might have precipitated the emergence of orthopoxvirus infections such as the 2022 spread of monkeypox in Europe.

A systematic review of brain imaging findings in neurological infection with Japanese encephalitis virus compared with Dengue virus. Pichl T, Wedderburn CJ, Hoskote C, Turtle L, Bharucha T. *Int J Infect Dis*. 2022 **119**: 102–110. doi: 10.1016/j.ijid.2022.03.010. PMID: 35283297.

Brain imaging abnormalities, particularly thalamic lesions, are common in encephalitis caused by Japanese encephalitis virus and Dengue virus. No lesions are pathognomic of either viral infection, and microbiological testing is required to secure a diagnosis.

OBJECTIVES:	Japanese encephalitis virus (JEV) and dengue virus (DENV) represent important causes of encephalitis in Asia. Brain imaging may provide diagnostic clues about the etiology of infectious encephalitis. We performed a systematic review of brain imaging findings in Japanese encephalitis (JE) and DENV neurological infection (dengue) to identify characteristic lesions.
METHODOLOGY:	Five databases were searched. We included all study types and imaging techniques. Laboratory methods were categorized using diagnostic confidence levels. Imaging data were synthesized, and focal findings are presented as proportions for JE and dengue and for subgroups based on diagnostic confidence.
PRINCIPAL FINDINGS:	Thalamic lesions were the most reported magnetic resonance imaging finding in both diseases but appeared to occur more often in JE (74% in 23 studies) than dengue (29.4% in 58 studies). In cases diagnosed with antigen or nucleic acid tests, thalamic lesions were reported frequently in both JE (76.5% in 17 studies) and dengue (65.2% in 23 studies).
SIGNIFICANCE:	The results suggest that thalamic lesions frequently occur in both JE and dengue encephalitis. No radiological findings were found to be pathognomonic of either disease. Although brain imaging may support a diagnosis, laboratory confirmation with highly specific tests remains crucial.

Estimating the burden of hepatitis B virus infection in Laos between 2020 and 2021: A cross-sectional seroprevalence survey. Sitbounlang P, Deharo E, Latthaphasavang V, Marchio A, Soukhsakhone C, Soinxay V, Mayxay M, Steenkeste N, Vincelot P, Bertani S, Palamy S, Paboriboune P, Pineau P. *eClinicalMedicine*. 2022 **52**: 101582. doi: 10.1016/j.eclinm.2022.101582. PMID: 35923426. PMCID: PMC9340506.

A large seroprevalence study estimates that prevalence of chronic hepatitis B infection is between 5.0% and 6.0% in Lao PDR, downgrading the country's status from high to intermediate endemicity. Higher prevalence was noted in HIV-positive people, men, and in the north of the country.

BACKGROUND:	Laos is considered highly endemic for persistent infection with hepatitis B virus (HBV). To eliminate this burden, it has gradually implemented universal anti-hepatitis B immunisation of newborns over the past two decades.
METHODS:	Using VIKIA® HBsAg, a rapid test for the qualitative detection of the HBV surface antigen, we conducted between 1 Sept 2020 and 31 Aug 31 2021 the largest prospective prevalence survey ever in Laos. This survey included blood donors (BD, n = 42,277), patients attending care in capital and provincial hospitals (n = 37,347) including attending mothers (n = 20,548), HIV-infected patients (n = 7439, recruited from 2009 to 2020), students from the Health Sciences University (n = 609), and outpatients (n = 350) coming for diagnosis at the Center Infectiology Lao-Christophe Mérieux in Vientiane. In total, 88,022 persons were tested, representing approximately 1.22% of the national population. To reach a reasonable estimate of HBsAg prevalence in Laos, we segmented the population according to three variables, age (≤20 years as a cut-off), sex, and geographical origin. BD values were used to estimate HBsAg prevalence in patients aged <20 while hospital survey prevalence was used to estimate the prevalence in those aged older than 20 years.
FINDINGS:	We observed an HBsAg seroprevalence ranging from 2.6% in blood donors to 8.0% in HIV-infected patients. In BD, men were significantly more at risk to be carriers than women (RR = 1.2, P = 0.00063). For BD, attending mothers, or HIV-infected patients, HBsAg was significantly more prevalent in northern Laos (5.1-8.4%) than in central (2.0-8.1%) or southern parts of the country (2.2-6.9%), thereby delineating a North-to-South gradient.
INTERPRETATION:	We considered that HBsAg prevalence probably ranges between 5.0% and 6.0% of the total population. Thus, we consider that Laos may no longer be highly endemic for chronic HBV infection but rather a country with intermediate endemicity.

Malaria

An open dataset of *Plasmodium vivax* genome variation in 1,895 worldwide samples. Adam I, Alam MS, Alemu S, Amaratunga C, Amato R, Andrianaranjaka V, Anstey NM, Aseffa A, Ashley E, Assefa A, Auburn S, Barber BE, Barry A, Batista Pereira D, Cao J, Chau NH, Chotivanich K, Chu C, Dondorp AM, Drury E, Echeverry DF, Erko B, Espino F, Fairhurst R, Faiz A, Fernanda Villegas M, Gao Q, Golassa L, Goncalves S, Grigg MJ, Hamedi Y, Hien TT, Htut Y, Johnson KJ, Karunaweera N, Khan W, Krudsood S, Kwiatkowski DP, Lacerda M, Ley B, Lim P, Liu Y, Llanos-Cuentas A, Lon C, Lopera-Mesa T, Marfurt J, Michon P, Miotto O, Mohammed R, Mueller I, Namaik-Larp C, Newton PN, Nguyen TN, Nosten F, Noviyanti R, Pava Z, Pearson RD, Petros B, Phyo AP, Price RN, Pukrittayakamee S, Rahim AG, Randrianarivelojosia M, Rayner JC, Rumaseb A, Siegel SV, Simpson VJ, Thriemer K, Tobon-Castano A, Trimarsanto H, Urbano Ferreira M, Vélez ID, Wangchuk S, Wellems TE, White NJ, William T, Yasnot MF, Yilma D. *Wellcome Open Res*. 2022 **7**: 136. doi: 10.12688/wellcomeopenres.17795.1. PMID: 35651694. PMCID: PMC9127374.

This open-access database describes geographical variations in nearly 2000 P. vivax *genome sequences. Each genome is annotated with key resistance mutations, which were more prevalent in Southeast Asia.*

This report describes the MalariaGEN Pv4 dataset, a new release of curated genome variation data on 1,895 samples of *Plasmodium vivax* collected at 88 worldwide locations between 2001 and 2017. It includes 1,370 new samples contributed by MalariaGEN and VivaxGEN partner studies in addition to previously published samples from these and other sources. We provide genotype calls at over 4.5 million variable positions including over 3 million single nucleotide polymorphisms (SNPs), as well as short indels and tandem duplications. This enlarged dataset highlights major compartments of parasite population structure, with clear differentiation between Africa, Latin America, Oceania, Western Asia and different parts of Southeast Asia. Each sample has been classified for drug resistance to sulfadoxine, pyrimethamine and mefloquine based on known markers at the *dhfr*, *dhps* and mdr1 loci. The prevalence of all of these resistance markers was much higher in Southeast Asia and Oceania than elsewhere. This open resource of analysis-ready genome variation data from the MalariaGEN and VivaxGEN networks is driven by our collective goal to advance research into the complex biology of *P. vivax* and to accelerate genomic surveillance for malaria control and elimination.

Comparison of antibody responses and parasite clearance in artemisinin therapeutic efficacy studies in Democratic Republic of Congo and Asia. Cutts JC, O'Flaherty K, Zaloumis SG, Ashley EA, Chan JA, Onyamboko MA, Fanello C, Dondorp AM, Day NP, Phyo AP, Dhorda M, Imwong M, Fairhurst RM, Lim P, Amaratunga C, Pukrittayakamee S, Hien TT, Htut Y, Mayxay M, Abdul Faiz M, Takashima E, Tsuboi T, Beeson JG, Nosten F, Simpson JA, White NJ, Fowkes FJI. *J Infect Dis*. 2022 **226**(2): 324–331. doi: 10.1093/infdis/jiac232. PMID: 35703955. PMCID: PMC9400417.

*Naturally acquired immunity to malaria complicates therapeutic efficacy studies and surveillance. In this study, anti-*P. falciparum *antibody titres in children from DRC did not affect parasite clearance rates. Parasite clearance was slower in Asian cohorts compared to the DRC cohort despite similar antibody titres, implicating other factors.*

BACKGROUND: Understanding the effect of immunity on *P. falciparum* clearance is essential for interpreting therapeutic efficacy studies designed to monitor emergence of artemisinin drug resistance. In low transmission areas of Southeast Asia, where resistance has emerged, *P. falciparum* antibodies confound parasite clearance measures. However, variation in naturally acquired antibodies across Asian and sub-Saharan African epidemiological contexts and their impact on parasite clearance, is yet to be quantified.

METHODS: In an artemisinin therapeutic efficacy study, antibodies to twelve pre-erythrocytic and erythrocytic *P. falciparum* antigens were measured in 118 children with uncomplicated *P. falciparum* malaria in Democratic Republic of Congo (DRC) and compared to responses in patients from Asian sites, described previously.

RESULTS: Parasite clearance half-life was faster in DRC patients (median 2 hours) compared to most Asian sites (median ranged from 2-7 hours), but *P. falciparum* antibody levels and seroprevalences were similar. There was no evidence for an association between antibody seropositivity and parasite clearance half-life (mean difference between seronegative and seropositive ranged from -0.14 and +0.40 h) in DRC patients.

CONCLUSIONS: In DRC, where artemisinin remains highly effective, the substantially faster parasite clearance time compared with Asia was not explained by differences in the *P. falciparum* antibody responses studied.

Forest malaria and prospects for anti-malarial chemoprophylaxis among forest goers: findings from a qualitative study in Lao PDR. Jongdeepaisal M, Inthasone S, Khonputsa P, Malaphone V, Pongsoipetch K, Pongvongsa T, Mayxay M, Chindavongsa K, Pell C, Maude RJ. *Malar J*. 2022 **21**(1): 8. doi: 10.1186/s12936-021-04027-z. PMID: 34983549. PMCID: PMC8727080.

Forest goers understand malaria risk and employ available protective measures. Antimalarial prophylaxis would be considered by both forest goers and stakeholders, subject to practical considerations. A holistic approach to malaria reduction requires improved local health care services, communication and logistics.

BACKGROUND: Despite significant decline in malarial incidence and mortality in countries across the Greater Mekong Subregion (GMS), the disease remains a public health challenge in the region; transmission continues mainly among people who visit forests in remote areas, often along international borders, where access to primary healthcare is limited. In the absence of effective vector-control measures and limited exposure periods, malaria chemoprophylaxis has been proposed as a strategy to protect forest goers. As a rarely used approach for indigenous populations, questions remain about its feasibility and acceptability. Drawing on in-depth interviews with forest goers and stakeholders, this article examines opportunities and challenges for implementation of anti-malarial chemoprophylaxis for forest goers in Lao PDR.

METHODS: In-depth interviews were conducted with 16 forest goers and 15 stakeholders in Savannakhet province, Lao PDR. Interview topics included experience of malaria prevention and health services, and perceptions of prophylaxis as a potential component of malaria elimination strategy. The interviews were transcribed and coded using inductive and deductive approaches for qualitative thematic analysis.

RESULTS: In ethnically and geographically diverse villages, awareness of malaria risk prompts forest goers to protect themselves, albeit sub-optimally using available preventive measures. Stakeholders highlighted challenges for targeting at-risk populations and approaches to address forest malaria in southern Lao PDR. Among policymakers, choice and cost of anti-malarials, particularly their efficacy and source of funding, were key considerations for the feasibility of malaria prophylaxis. Acceptability of prophylaxis among forest goers was also influenced by the complexity of the regimen, including the number of tablets and timing of doses. Implementation of prophylaxis may be affected by a lack of transportation and communication barriers in remote communities.

CONCLUSIONS: Adding prophylaxis to existing malaria control activities requires strengthening the capacity of local health workers in Lao PDR. Ideally, this would be part of an integrated approach that includes strategies to address the other febrile illnesses that forest goers describe as priority health concerns. The prophylactic regimen also requires careful consideration in terms of effectiveness and simplicity of dosing.

Keystone Malaria Symposium 2022: a vibrant discussion of progress made and challenges ahead from drug discovery to treatment. Kanai M, Hagenah LM, Ashley EA, Chibale K, Fidock DA. *Trends Parasitol*. 2022 **38**(9): 711–718. doi: 10.1016/j.pt.2022.06.005. PMID: 35864072. PMCID: PMC9631389.

In recent years, the field of malaria research has made substantial progress in the areas of antimalarial drug resistance and discovery. These efforts are essential to combatting the devastating impact of malaria, which, in 2020, resulted in an estimated 241 million cases and 627 000 deaths. Recent advances in this area were presented at a Keystone Symposium entitled 'Malaria: Confronting Challenges from Drug Discovery to Treatment', held in person in Breckenridge, Colorado, in April 2022. Herein, we present a summary of the proceedings of this vibrant scientific exchange, which brought together a superb group of faculty, postdocs, and students from around the globe.

Anti-gametocyte antigen humoral immunity and gametocytemia during treatment of uncomplicated falciparum malaria: a multi-national study. O'Flaherty K, Chan JA, Cutts JC, Zaloumis SG, Ashley EA, Phyo AP, Drew DR, Dondorp AM, Day NP, Dhorda M, Fairhurst RM, Lim P, Amaratunga C, Pukrittayakamee S, Hien TT, Htut Y, Mayxay M, Faiz MA, Mokuolu OA, Onyamboko MA, Fanello C, Takashima E, Tsuboi T, Theisen M, Nosten F, Beeson JG, Simpson JA, White NJ, Fowkes FJI. *Front Cell Infect Microbiol*. 2022 **12**: 804470. doi: 10.3389/fcimb.2022.804470. PMID: 35463638. PMCID: PMC9022117.

Presence of IgG antibodies to gametocyte antigens was correlated with presence and level of gametocytes in blood films of patients with falciparum malaria. These antigens are vaccine candidates and because the cognate IgG antibodies are known to block transmission, these results are important for vaccine development.

INTRODUCTION:	Understanding the human immune response to *Plasmodium falciparum* gametocytes and its association with gametocytemia is essential for understanding the transmission of malaria as well as progressing transmission blocking vaccine candidates.
METHODS:	In a multi-national clinical efficacy trial of artemisinin therapies (13 sites of varying transmission over Southeast Asia and Africa), we measured Immunoglobulin G (IgG) responses to recombinant *P. falciparum* gametocyte antigens expressed on the gametocyte plasma membrane and leading transmission blocking vaccine candidates Pfs230 (Pfs230c and Pfs230D1M) and Pfs48/45 at enrolment in 1,114 participants with clinical falciparum malaria. Mixed effects linear and logistic regression were used to determine the association between gametocyte measures (gametocytemia and gametocyte density) and antibody outcomes at enrolment.
RESULTS:	Microscopy detectable gametocytemia was observed in 11% (127/1,114) of participants at enrolment, and an additional 9% (95/1,114) over the follow-up period (up to day 42) (total 20% of participants [222/1,114]). IgG levels in response to Pfs230c, Pfs48/45 and Pfs230D1M varied across study sites at enrolment ($p < 0.001$), as did IgG seroprevalence for anti-Pfs230c and D1M IgG ($p < 0.001$), but not for anti-Pfs48/45 IgG ($p = 0.159$). In adjusted analyses, microscopy detectable gametocytemia at enrolment was associated with an increase in the odds of IgG seropositivity to the three gametocyte antigens (Pfs230c OR [95% CI], p: 1.70 [1.10, 2.62], 0.017; Pfs48/45: 1.45 [0.85, 2.46], 0.174; Pfs230D1M: 1.70 [1.03, 2.80], 0.037), as was higher gametocyte density at enrolment (per two-fold change in gametocyte density Pfs230c OR [95% CI], p: 1.09 [1.02, 1.17], 0.008; Pfs48/45: 1.05 [0.98, 1.13], 0.185; Pfs230D1M: 1.07 [0.99, 1.14], 0.071).
CONCLUSIONS:	Pfs230 and Pfs48/45 antibodies are naturally immunogenic targets associated with patent gametocytemia and increasing gametocyte density across multiple malaria endemic settings, including regions with emerging artemisinin-resistant *P. falciparum*.

Clinical impact of vivax malaria: a collection review. Phyo AP, Dahal P, Mayxay M, Ashley EA. *PLoS Med*. 2022 **19**(1): e1003890. doi: 10.1371/journal.pmed.1003890. PMID: 35041650. PMCID: PMC8765657.

The lack of standardized definitions of severe vivax malaria and inconsistent reporting frustrates attempts to quantify risks associated with P. vivax *infection. However, severe disease and death is increasingly recognised. This systematic review highlights the considerable morbidity that is seen in children with relapsing infections and pregnant woman; these groups should be prioritised for prevention of infection and treatment.*

BACKGROUND:	*Plasmodium vivax* infects an estimated 7 million people every year. Previously, vivax malaria was perceived as a benign condition, particularly when compared to falciparum malaria. Reports of the severe clinical impacts of vivax malaria have been increasing over the last decade.
METHODS AND FINDINGS:	We describe the main clinical impacts of vivax malaria, incorporating a rapid systematic review of severe disease with meta-analysis of data from studies with clearly defined denominators, stratified by hospitalization status. Severe anemia is a serious consequence of relapsing infections in children in endemic areas, in whom vivax malaria causes increased morbidity and mortality and impaired school performance. *P. vivax* infection in pregnancy is associated with maternal anemia, prematurity, foetal loss, and low birth weight. More than 11,658 patients with severe vivax malaria have been reported since 1929, with 15,954 manifestations of severe malaria, of which only 7,157 (45%) conformed to the World Health Organization (WHO) diagnostic criteria. Out of 423 articles, 311 (74%) were published since 2010. In a random-effects meta-analysis of 85 studies, 68 of which were in hospitalized patients with vivax malaria, we estimated the proportion of patients with WHO-defined severe disease as 0.7% [95% confidence interval (CI) 0.19% to 2.57%] in all patients with vivax malaria and 7.11% [95% CI 4.30% to 11.55%] in hospitalized patients. We estimated the mortality from vivax malaria as 0.01% [95% CI 0.00% to 0.07%] in all patients and 0.56% [95% CI 0.35% to 0.92%] in hospital settings. WHO-defined cerebral, respiratory, and renal severe complications were generally estimated to occur in fewer than 0.5% patients in all included studies. Limitations of this review include the observational nature and small size of most of the studies of severe vivax malaria, high heterogeneity of included studies which were predominantly in hospitalized patients (who were therefore more likely to be severely unwell), and high risk of bias including small study effects.
CONCLUSIONS:	Young children and pregnant women are particularly vulnerable to adverse clinical impacts of vivax malaria, and preventing infections and relapse in this group is a priority. Substantial evidence of severe presentations of vivax malaria has accrued over the last 10 years, but reporting is inconsistent. There are major knowledge gaps, for example, limited understanding of the underlying pathophysiology and the reason for the heterogeneous geographical distribution of reported complications. An adapted case definition of severe vivax malaria would facilitate surveillance and future research to better understand this condition.

STARTER checklist for antimalarial therapeutic efficacy reporting. Plucinski M, Ashley EA, Bassat Q, Venkatesan M, Rosenthal PJ, Halsey E. *Am J Trop Med Hyg*. 2022 **107**(1): 1–3. doi: 10.4269/ajtmh.22-0224. PMID: 35880678. PMCID: PMC9294688.

The WHO previously produced guidance documents that detail standardized methods for the design and analysis of malaria therapeutic efficacy studies, but these are frequently not adhered to. Poor quality research compromises national guidance and public health responses. Therefore, with engagement from key stakeholders, we have devised a checklist to support trial reporting.

STARTER checklist for antimalarial therapeutic efficacy reporting. Plucinski MM, Ashley EA, Bassat Q, Venkatesan M, Rosenthal PJ, Halsey ES. *Malar J*. 2022 **21**(1): 187. doi: 10.1186/s12936-022-04182-x. PMID: 35698123. PMCID: PMC9195280.

[As above]

Malaria outbreak in Laos driven by a selective sweep for *Plasmodium falciparum kelch13* R539T mutants: a genetic epidemiology analysis. Wasakul V, Disratthakit A, Mayxay M, Chindavongsa K, Sengsavath V, Thuy-Nhien N, Pearson RD, Phalivong S, Xayvanghang S, Maude RJ, Gonçalves S, Day NP, Newton PN, Ashley EA, Kwiatkowski DP, Dondorp AM, Miotto O. *Lancet Infectious Diseases*. 2022 S1473-3099(22)00697-1. doi: 10.1016/S1473-3099(22)00697-1. PMID: 36462526.

Genetic surveillance identified the remarkable explosion of P. falciparum *mutants within a single season in Lao PDR. The key mutations had been circulating for over a decade at low levels, but became dominant when first-line therapies changed, offering them a selective advantage. Such shifts in population structure can cause resurgence of infection in low-prevalence areas.*

BACKGROUND:	Malaria outbreaks are important public health concerns that can cause resurgence in endemic regions approaching elimination. We investigated a *Plasmodium falciparum* outbreak in Attapeu Province, Laos, during the 2020–21 malaria season, using genomic epidemiology methods to elucidate parasite population dynamics and identify its causes.
METHODS:	In this genetic analysis, 2164 P falciparum dried blood spot samples were collected from southern Laos between 1 January 2017 and 1 April 2021, which included 249 collected during the Attapeu outbreak between 1 April 2020 and 1 April 2021, by routine surveillance. Genetic barcodes obtained from these samples were used to investigate epidemiological changes underpinning the outbreak, estimate population diversity, and analyse population structure. Whole-genome sequencing data from additional historical samples were used to reconstruct the ancestry of outbreak strains using identity-by-descent analyses.
FINDINGS:	The outbreak parasite populations were characterised by unprecedented loss of genetic diversity, primarily caused by rapid clonal expansion of a multidrug-resistant strain (LAA1) carrying the kelch13 Arg539Thr (R539T) mutation. LAA1 replaced kelch13 Cys580Tyr (C580Y) mutants resistant to dihydroartemisinin–piperaquine (KEL1/PLA1) as the dominant strain. LAA1 inherited 58·8% of its genome from a strain circulating in Cambodia in 2008. A secondary outbreak strain (LAA2) carried the kelch13 C580Y allele, and a genome that is essentially identical to a Cambodian parasite from 2009. A third, low-frequency strain (LAA7) was a recombinant of KEL1/PLA1 with a kelch13 R539T mutant.
INTERPRETATION:	These results strongly suggest that the outbreak was driven by a selective sweep, possibly associated with multidrug-resistant phenotypes of the outbreak strains. Established resistant populations can circulate at low frequencies for years before suddenly overwhelming dominant strains when the conditions for selection become favourable—eg, when front-line therapies change. Genetic surveillance can support elimination by characterising key properties of outbreaks such as population diversity, drug resistance marker prevalence, and the origins of outbreak strains.

Have we really failed to roll back malaria? White NJ, Day NPJ, Ashley EA, Smithuis FM, Nosten FH. *Lancet*. 2022 **399**(10327): 799–800. doi: 10.1016/S0140-6736(22)00175-1. PMID: 35219391. PMCID: PMC8871413.

In this Correspondence, we advise caution in interpreting official statistics on case numbers and mortality due to malaria. Figures vary markedly depending on the assumptions and calculations used, and policy announcements often fail to accord with the data. Reliable and consistent reports are needed.

Haematological consequences of acute uncomplicated falciparum malaria: a WorldWide Antimalarial Resistance Network pooled analysis of individual patient data. The WorldWide Antimalarial Resistance Network Falciparum Haematology Study Group. *BMC Med*. 2022 **20**(1): 85. doi: 10.1186/s12916-022-02265-9. PMID: 35249546. PMCID: PMC8900374.

Analysis of global data highlighted the following risk factors for severe anaemia following treatment for malaria: moderately severe anaemia at baseline, young age, high parasitaemia, and delayed parasite clearance. Baseline haemoglobin was lowest in African cohorts, followed by Asian cohorts, and was highest in South American patients.

BACKGROUND:	*Plasmodium falciparum* malaria is associated with anaemia-related morbidity, attributable to host, parasite and drug factors. We quantified the haematological response following treatment of uncomplicated *P. falciparum* malaria to identify the factors associated with malarial anaemia.
METHODS:	Individual patient data from eligible antimalarial efficacy studies of uncomplicated P. *falciparum* malaria, available through the WorldWide Antimalarial Resistance Network data repository prior to August 2015, were pooled using standardised methodology. The haematological response over time was quantified using a multivariable linear mixed effects model with nonlinear terms for time, and the model was then used to estimate the mean haemoglobin at day of nadir and day 7. Multivariable logistic regression quantified risk factors for moderately severe anaemia (haemoglobin < 7 g/dL) at day 0, day 3 and day 7 as well as a fractional fall ≥ 25% at day 3 and day 7.
FINDINGS:	A total of 70,226 patients, recruited into 200 studies between 1991 and 2013, were included in the analysis: 50,859 (72.4%) enrolled in Africa, 18,451 (26.3%) in Asia and 916 (1.3%) in South America. The median haemoglobin concentration at presentation was 9.9 g/dL (range 5.0-19.7 g/dL) in Africa, 11.6 g/dL (range 5.0-20.0 g/dL) in Asia and 12.3 g/dL (range 6.9-17.9 g/dL) in South America. Moderately severe anaemia (Hb < 7g/dl) was present in 8.4% (4284/50,859) of patients from Africa, 3.3% (606/18,451) from Asia and 0.1% (1/916) from South America. The nadir haemoglobin occurred on day 2 post treatment with a mean fall from baseline of 0.57 g/dL in Africa

and 1.13 g/dL in Asia. Independent risk factors for moderately severe anaemia on day 7, in both Africa and Asia, included moderately severe anaemia at baseline (adjusted odds ratio (AOR) = 16.10 and AOR = 23.00, respectively), young age (age < 1 compared to ≥ 12 years AOR = 12.81 and AOR = 6.79, respectively), high parasitaemia (AOR = 1.78 and AOR = 1.58, respectively) and delayed parasite clearance (AOR = 2.44 and AOR = 2.59, respectively). In Asia, patients treated with an artemisinin-based regimen were at significantly greater risk of moderately severe anaemia on day 7 compared to those treated with a non-artemisinin-based regimen (AOR = 2.06 [95%CI 1.39-3.05], p < 0.001).

CONCLUSIONS: In patients with uncomplicated *P. falciparum* malaria, the nadir haemoglobin occurs 2 days after starting treatment. Although artemisinin-based treatments increase the rate of parasite clearance, in Asia they are associated with a greater risk of anaemia during recovery.

Temporal distribution of *Plasmodium falciparum* recrudescence following artemisinin-based combination therapy: an individual participant data meta-analysis. The WorldWide Antimalarial Resistance Network Methodology Study Group. *Malar J*. 2022 **21**(1): 106. doi: 10.1186/s12936-021-03980-z. PMID: 35331243. PMCID: PMC8943927.

Failure to detect late recrudescences leads to over-estimation of malaria treatment efficacy and risks missing emerging drug resistance. Molecular techniques now allow such recrudescences to be identified. We show that when restricting follow-up to WHO-recommended timeframes, treatment efficacy is overestimated by 2% – 3%.

BACKGROUND: The duration of trial follow-up affects the ability to detect recrudescent infections following anti-malarial treatment. The aim of this study was to explore the proportions of recrudescent parasitaemia as ascribed by genotyping captured at various follow-up time-points in treatment efficacy trials for uncomplicated *Plasmodium falciparum* malaria.

METHODS: Individual patient data from 83 anti-malarial efficacy studies collated in the WorldWide Antimalarial Resistance Network (WWARN) repository with at least 28 days follow-up were available. The temporal and cumulative distributions of recrudescence were characterized using a Cox regression model with shared frailty on study-sites. Fractional polynomials were used to capture non-linear instantaneous hazard. The area under the density curve (AUC) of the constructed distribution was used to estimate the optimal follow-up period for capturing a *P. falciparum* malaria recrudescence. Simulation studies were conducted based on the constructed distributions to quantify the absolute overestimation in efficacy due to sub-optimal follow-up.

RESULTS: Overall, 3703 recurrent infections were detected in 60 studies conducted in Africa (15,512 children aged < 5 years) and 23 studies conducted in Asia and South America (5272 patients of all ages). Using molecular genotyping, 519 (14.0%) recurrences were ascribed as recrudescent infections. A 28 day artemether-lumefantrine (AL) efficacy trial would not have detected 58% [95% confidence interval (CI) 47-74%] of recrudescences in African children and 32% [95% CI 15-45%] in patients of all ages in Asia/South America. The corresponding estimate following a 42 day dihydroartemisinin-piperaquine (DP) efficacy trial in Africa was 47% [95% CI 19-90%] in children under 5 years old treated with > 48 mg/kg total piperaquine (PIP) dose and 9% [95% CI 0-22%] in those treated with ≤ 48 mg/kg PIP dose. In absolute terms, the simulation study found that trials limited to 28 days follow-up following AL underestimated the risk of recrudescence by a median of 2.8 percentage points compared to day 63 estimates and those limited to 42 days following DP underestimated the risk of recrudescence by a median of 2.0 percentage points compared to day 42 estimates. The analysis was limited by few clinical trials following patients for longer than 42 days (9 out of 83 trials) and the imprecision of PCR genotyping which overcalls recrudescence in areas of higher transmission biasing the later distribution.

CONCLUSIONS: Restricting follow-up of clinical efficacy trials to day 28 for AL and day 42 for DP will miss a proportion of late recrudescent treatment failures but will have a modest impact in derived efficacy. The results highlight that as genotyping methods improve consideration should be given for trials with longer duration of follow-up to detect early indications of emerging drug resistance.

Artemisinin resistance in the malaria parasite, *Plasmodium falciparum*, originates from its initial transcriptional response. Zhu L, van der Pluijm RW, Kucharski M, Nayak S, Tripathi J, White NJ, Day NPJ, Faiz A, Phyo AP, Amaratunga C, Lek D, Ashley EA, Nosten F, Smithuis F, Ginsburg H, von Seidlein L, Lin K, Imwong M, Chotivanich K, Mayxay M, Dhorda M, Nguyen HC, Nguyen TNT, Miotto O, Newton PN, Jittamala P, Tripura R, Pukrittayakamee S, Peto TJ, Hien TT, Dondorp AM, Bozdech Z. *Commun Biol*. 2022 **5**(1): 274. doi: 10.1038/s42003-022-03215-0. PMID: 35347215. PMCID: PMC8960834.

The emergence and spread of artemisinin-resistant *Plasmodium falciparum*, first in the Greater Mekong Subregion (GMS), and now in East Africa, is a major threat to global malaria elimination ambitions. To investigate the artemisinin resistance mechanism, transcriptome analysis was conducted of 577 *P. falciparum* isolates collected in the GMS between 2016-2018. A specific artemisinin resistance-associated transcriptional profile was identified that involves a broad but discrete set of biological functions related to proteotoxic stress, host cytoplasm remodelling, and REDOX metabolism. The artemisinin resistance-associated transcriptional profile evolved from initial transcriptional responses of susceptible parasites to artemisinin. The genetic basis for this adapted response is likely to be complex.

Non-malaria febrile illness

A case-control study of the causes of acute respiratory infection among hospitalized patients in Northeastern Laos. Phommasone K, Xaiyaphet X, Garcia-Rivera JA, Hontz RD, Pathavongsa V, Keomoukda P, Vongsouvath M, Mayxay M, Vongsouvath M, Newton PN, Ashley EA, Dubot-Pérès A. *Sci Rep*. 2022 **12**(1): 939. doi: 10.1038/s41598-022-04816-9. PMID: 35042900. PMCID: PMC8766494.

Using a case-control study design, we distinguished cases of infection from asymptomatic carriage. In this cohort, respiratory viruses caused over half the hospitalisations due to acute respiratory infections, in particular influenza A and B, human metapneumovirus and respiratory syncytial virus.

With the advent of highly sensitive real-time PCR, multiple pathogens have been identified from nasopharyngeal swabs of patients with acute respiratory infections (ARIs). However, the detection of microorganisms in the upper respiratory tract does not necessarily indicate disease causation. We conducted a matched case-control study, nested within a broader fever aetiology project, to facilitate determination of the aetiology of ARIs in hospitalised patients in Northeastern Laos. Consenting febrile patients of any age admitted to Xieng Khuang Provincial Hospital

were included if they met the inclusion criteria for ARI presentation (at least one of the following: cough, rhinorrhoea, nasal congestion, sore throat, difficulty breathing, and/or abnormal chest auscultation). One healthy control for each patient, matched by sex, age, and village of residence, was recruited for the study. Nasopharyngeal swabs were collected from participants and tested for 33 pathogens by probe-based multiplex real-time RT-PCR (FastTrack Diagnostics Respiratory pathogen 33 kit). Attributable fraction of illness for a given microorganism was calculated by comparing results between patients and controls (= 100 * [OR - 1]/OR) (OR = odds ratio). From 24 June 2019 to 24 June 2020, 205 consenting ARI patients and 205 matching controls were recruited. After excluding eight pairs due to age mismatch, 197 pairs were included in the analysis. Males were predominant with sex ratio 1.2:1 and children < 5 years old accounted for 59% of participants. At least one potential pathogen was detected in 173 (88%) patients and 175 (89%) controls. ARI in admitted patients were attributed to influenza B virus, influenza A virus, human metapneumovirus (HMPV), and respiratory syncytial virus (RSV) in 17.8%, 17.2%, 7.5%, and 6.5% of participants, respectively. SARS-CoV-2 was not detected in any cases or controls. Determining ARI aetiology in individual patients remains challenging. Among hospitalised patients with ARI symptoms presenting to a provincial hospital in Northeastern Laos, half were determined to be caused by one of several respiratory viruses, in particular influenza A virus, influenza B virus, HMPV, and RSV.

Childhood encephalitis in the Greater Mekong region (the SouthEast Asia Encephalitis Project): a multicentre prospective study. Pommier JD, Gorman C, Crabol Y, Bleakley K, Sothy H, Santy K, Tran HTT, Nguyen LV, Bunnakea E, Hlaing CS, Aye AMM, Cappelle J, Herrant M, Piola P, Rosset B, Chevalier V, Tarantola A, Channa M, Honnorat J, Pinto AL, Rattanavong S, Vongsouvath M, Mayxay M, Phangmanixay S, Phongsavath K, Tin OS, Kyaw LL, Tin HH, Linn K, Tran TMH, Pérot P, Thuy NTT, Hien N, Phan PH, Buchy P, Dussart P, Laurent D, Eloit M, Dubot-Pérès A, Lortholary O, de Lamballerie X, Newton PN, Lecuit M, Buchy P, Bunnakea E, Cappelle J, Channa M, Chevalier V, Crabol Y, de Lamballerie X, Dubot-Pérès A, Dussart P, Eloit M, Gorman C, Herrant M, Hien N, Hlaing CS, Honnorat J, Hung TTM, Huong TTT, Kyaw LL, Lam NV, Laurent D, Lecuit M, Linn K, Lortholary O, Mayxay M, Min Aye AM, Newton P, Perot P, Phangmanixay S, Phongsavath K, Phuc PH, Pinto A-L, Piola P, Pommier J-D, Rattanavong S, Rosset B, Santy K, Sothy H, Tarantola A, Thuy NTT, Tin HH, Tin OS, Vongsouvath M, An PN, Anh DD, Bonnet P, Bun K, Chommanam D, Davong V, Debré P, Delfraissy J-F, Devaux C, Douangnouvong A, Duong V, Durand B, Eng C, Ferrant C, Fontenille D, Hafner L, Hai LT, Huong DT, Jouan M, July M, Lago M, Moatti J-P, Murgue B, Oo KY, Oum M, Phakhounthong K, Pham AT, Quyen D, Seephonelee M, Seguy M, Sibounheunang B, Sim K, Tan LM, Thair C, Thein W, Thuy PB, Tissot-Dupont H, Vongsouvath M. *Lancet Global Health*. 2022 **10**(7): e989–e1002. doi: 10.1016/S2214-109X(22)00174-7. PMID: 35714649. PMCID: PMC9210261.

Across 4 countries in southeast Asia, 64% of children with probable or confirmed encephalitis received a microbiological diagnosis. The commonest identified cause was Japanese encephalitis (33% of all cases). Overall in-hospital mortality was 13%, and 42% of cases were vaccine-preventable.

BACKGROUND:	Encephalitis is a worldwide public health issue, with a substantially high burden among children in southeast Asia. We aimed to determine the causes of encephalitis in children admitted to hospitals across the Greater Mekong region by implementing a comprehensive state-of-the-art diagnostic procedure harmonised across all centres, and identifying clinical characteristics related to patients' conditions.
METHODS:	fever (within the 72 h before or after presentation), one or more generalised or partial seizures (excluding febrile seizures), a new-onset focal neurological deficit, cerebrospinal fluid (CSF) white blood cell count of 5 per mL or higher, or brain imaging (CT or MRI) suggestive of lesions of encephalitis. Comprehensive diagnostic procedures were harmonised across all centres, with first-line testing was done on samples taken at inclusion and results delivered within 24 h of inclusion for main treatable causes of disease and second-line testing was done thereafter for mostly non-treatable causes. An independent expert medical panel reviewed the charts and attribution of causes of all the included children. Using multivariate analyses, we assessed risk factors associated with unfavourable outcomes (ie, severe neurological sequelae and death) at discharge using data from baseline and day 2 after inclusion. This study is registered with ClinicalTrials.gov, NCT04089436, and is now complete.
FINDINGS:	Between 28 July 2014 and 31 Dec 2017, 664 children with encephalitis were enrolled. Median age was 4·3 years (1·8–8·8), 295 (44%) children were female, and 369 (56%) were male. A confirmed or probable cause of encephalitis was identified in 425 (64%) patients: 216 (33%) of 664 cases were due to Japanese encephalitis virus, 27 (4%) were due to dengue virus, 26 (4%) were due to influenza virus, 24 (4%) were due to herpes simplex virus 1, 18 (3%) were due to *Mycobacterium tuberculosis*, 17 (3%) were due to *Streptococcus pneumoniae*, 17 (3%) were due to enterovirus A71, 74 (9%) were due to other pathogens, and six (1%) were due to autoimmune encephalitis. Diagnosis was made within 24 h of admission to hospital for 83 (13%) of 664 children. 119 (18%) children had treatable conditions and 276 (42%) had conditions that could have been preventable by vaccination. At time of discharge, 153 (23%) of 664 children had severe neurological sequelae and 83 (13%) had died. In multivariate analyses, risk factors for unfavourable outcome were diagnosis of *M tuberculosis* infection upon admission (odds ratio 3·23 [95% CI 1·04–10·03]), coma on day 2 (2·90 [1·78–4·72]), supplementary oxygen requirement (1·89 [1·25–2·86]), and more than 1 week duration between symptom onset and admission to hospital (3·03 [1·68–5·48]). At 1 year after inclusion, of 432 children who were discharged alive from hospital with follow-up data, 24 (5%) had died, 129 (30%) had neurological sequelae, and 279 (65%) had completely recovered.
INTERPRETATION:	In southeast Asia, most causes of childhood encephalitis are either preventable or treatable, with Japanese encephalitis virus being the most common cause. We provide crucial information that could guide public health policy to improve diagnostic, vaccination, and early therapeutic guidelines on childhood encephalitis in the Greater Mekong region.

A robust host-response-based signature distinguishes bacterial and viral infections across diverse global populations. Rao AM, Popper SJ, Gupta S, Davong V, Vaidya K, Chanthongthip A, Dittrich S, Robinson MT, Vongsouvath M, Mayxay M, Nawtaisong P, Karmacharya B, Thair SA, Bogoch I, Sweeney TE, Newton PN, Andrews JR, Relman DA, Khatri P. *Cell Reports Medicine*. 2022 **3**(12): 100842. doi: 10.1016/j.xcrm.2022.100842. PMID: 36543117. PMCID: PMC9797950.

An 8-gene signature that can distinguish bacterial from viral infections was identified using 69 transcriptome datasets. The diagnostic accuracy of this test exceeded WHO requirements, and crucially can discriminate between intracellular bacterial infections and viral infections.

Limited sensitivity and specificity of current diagnostics lead to the erroneous prescription of antibiotics. Host-response-based diagnostics could address these challenges. However, using 4,200 samples across 69 blood transcriptome datasets from 20 countries from patients with

bacterial or viral infections representing a broad spectrum of biological, clinical, and technical heterogeneity, we show current host-response-based gene signatures have lower accuracy to distinguish intracellular bacterial infections from viral infections than extracellular bacterial infections. Using these 69 datasets, we identify an 8-gene signature to distinguish intracellular or extracellular bacterial infections from viral infections with an area under the receiver operating characteristic curve (AUROC) > 0.91 (85.9% specificity and 90.2% sensitivity). In prospective cohorts from Nepal and Laos, the 8-gene classifier distinguished bacterial infections from viral infections with an AUROC of 0.94 (87.9% specificity and 91% sensitivity). The 8-gene signature meets the target product profile proposed by the World Health Organization and others for distinguishing bacterial and viral infections.

Childhood encephalitis in the Greater Mekong region: critical to public health policy. Thant KZ, Ngwe Tun MM. *Lancet Global Health*. 2022 **10**(7): e934–e935. doi: 10.1016/S2214-109X(22)00208-X. PMID: 35714635.

This Comment on the multicentre prospective study of childhood encephalitis published in the same issue sets it in a broader context. The 1-year mortality rate is about 20%, and one-third of children experience neurological sequelae. Therefore, we call for improvements in prevention, diagnosis and treatment of encephalitis, and rehabilitation for those affected.

Detection and significance of neuronal autoantibodies in patients with meningoencephalitis in Vientiane, Lao PDR. Uy CE, Mayxay M, Harrison R, Al-Diwani A, Jacobson L, Rattanavong S, Dubot-Pérès A, Vongsouvath M, Davong V, Chansamouth V, Phommasone K, Waters P, Irani SR, Newton PN. *Trans R Soc Trop Med Hyg*. 2022 **116**(10): 959–965. doi: 10.1093/trstmh/trac023. PMID: 35385878. PMCID: PMC9526827.

8/134 patients with meningoencephalitis had detectable neuronal antibodies in their serum, and 3 of these had accompanying antibodies in their CSF. 3 patients had proven CNS infections despite having positive neuronal antibodies in their serum, making diagnosis of autoimmune encephalitis complex. Immunotherapy should be considered if symptoms persist and infectious aetiologies have been excluded.

BACKGROUND:	The importance of autoimmune encephalitis and its overlap with infectious encephalitides are not well investigated in Southeast Asia.
METHODS:	We report autoantibody testing, using antigen-specific live cell-based assays, in a series of 134 patients (cerebrospinal fluid and sera) and 55 blood donor controls (sera), undergoing lumbar puncture for suspected meningoencephalitis admitted in Vientiane, Lao People's Democratic Republic (PDR).
RESULTS:	Eight of 134 (6%) patients showed detectable serum neuronal autoantibodies, against the N-methyl-D-aspartate and gamma-aminobutyric acid A receptors (NMDAR and GABAAR), and contactin-associated protein-like 2 (CASPR2). Three of eight patients had accompanying autoantibodies in cerebrospinal fluid (two with NMDAR and one with GABAAR antibodies), and in two of these the clinical syndromes were typical of autoimmune encephalitis. Three of the other five patients had proven central nervous system infections, highlighting a complex overlap between diverse infectious and autoimmune causes of encephalitis. No patients in this cohort were treated with immunotherapy, and the outcomes were poor, with improvement observed in a single patient.
CONCLUSIONS:	In Lao PDR, autoimmune encephalitis is underdiagnosed and has a poor prognosis. Empiric immunotherapy should be considered after treatable infectious aetiologies are considered unlikely. Awareness and diagnostic testing resources for autoimmune encephalitis should be enhanced in Southeast Asia.

Zoonoses

***Orientia tsutsugamushi* in chiggers and small mammals in Laos.** Elliott I, Kumlert R, Thangnimitchok N, Blacksell SD, Tanganuchitcharnchai A, Paris DH, Newton PN, Morand S. *Vector Borne Zoonotic Dis*. 2022 **22**(10): 505–511. doi: 10.1089/vbz.2022.0029. PMID: 36255415. PMCID: PMC7613890.

60% of small mammals in Vientiane were infested with chigger mites and one-third were sero-positive for O. tsutsugamushi*, demonstrating high levels of past infection. 1,609 chiggers were isolated but surprisingly only one pool tested positive for O. tsutsugamushi. Further understanding of the ecology of scrub typhus is our high-prevalence setting is needed.*

BACKGROUND:	Scrub typhus is a leading cause of febrile illness in Laos and accounts for a high burden of disease. There have been no previous studies on the causative agent, *Orientia tsutsugamushi*, in vector mites ("chiggers") or their small mammal hosts in Laos.
MATERIALS AND METHODS:	Small mammals and free-living chiggers were trapped in districts of Vientiane Province and Capital. Tissues were tested for O. tsutsugamushi by PCR and serum for IgG to *O. tsutsugamushi* by immunofluorescence assays (IFAs). Chiggers removed from small mammals and collected in their free-living stage using black plates were identified and tested for *O. tsutsugamushi* by PCR.
RESULTS:	Over an 18-month period, 131 small mammals of 14 species were collected in 5 districts. Seventy-eight of 131 small mammals were infested with chiggers, but all tissues were O. tsutsugamushi PCR negative. Eighteen species of chigger were identified and 1,609 were tested by PCR. A single pool of chiggers tested *O. tsutsugamushi* positive. Sera from 52 small mammals were tested by IFA, with 16 testing positive.
CONCLUSIONS:	These are the first molecular and serological data on *O. tsutsugamushi* in chiggers and small mammals in Laos. Further studies are needed to better understand the key vector species and ecology of scrub typhus in areas with high disease incidence in Laos.

Zoonotic pathogens in wildlife traded in markets for human consumption, Laos. Nawtaisong P, Robinson MT, Khammavong K, Milavong P, Rachlin A, Dittrich S, Dubot-Pérès A, Vongsouvath M, Horwood PF, Dussart P, Theppangna W, Douangngeum B, Fine AE, Pruvot M, Newton PN. *Emerg Infect Dis*. 2022 **28**(4): 860–864. doi: 10.3201/eid2804.210249. PMID: 35318932. PMCID: PMC8962878.

We tested animals from wildlife trade sites in Laos for the presence of zoonotic pathogens. Leptospira spp. *were the most frequently detected infectious agents, found in 20.1% of animals.* Rickettsia typhi *and* R. felix *were also detected. These findings suggest a substantial risk for exposure through handling and consumption of wild animal meat.*

Abattoir-based serological surveillance and spatial risk analysis of Foot-and-Mouth Disease, Brucellosis, and Q Fever in Lao PDR large ruminants. Siengsanan-Lamont J, Theppangna W, Phommachanh P, Khounsy S, Selleck PW, Matsumoto N, Gleeson LJ, Blacksell SD. *Trop Med Infect Dis*. 2022 **7**(5): 78. doi: 10.3390/tropicalmed7050078. PMID: 35622705. PMCID: PMC9145528.

There is low seroprevalence of Q fever (1.7%) and brucellosis (0.7%) in large ruminants in Lao PDR, with variation due to animal type, month of sampling, and origin and destination of the animal. Further investigations should be targeted on hotspots. Seroprevalence of Foot-and-Mouth Disease was 50%, which also varied by origin and destination of the animal.

A national animal disease surveillance network initiated by the Lao PDR government is adopted and reinforced by a joint research project between the National Animal Health Laboratory (NAHL), the Department of Livestock and Fisheries (DLF), and the Mahidol Oxford Tropical Medicine Research Unit (MORU). The network is strengthened by staff training and practical exercises and is utilised to provide zoonotic or high-impact disease information on a national scale. Between January and December 2020, large ruminant samples are collected monthly from 18 abattoirs, one in each province, by provincial and district agriculture and forestry officers. The surveillance network collected a total of 4247 serum samples (1316 buffaloes and 2931 cattle) over this period. Samples are tested for antibodies against *Brucella* spp., *Coxiella burnetii* (Q fever) and Foot-and-Mouth Disease Non-Structural Protein (FMD NSP) using commercial ELISA kits and the Rose Bengal test. Seroprevalences of Q fever and brucellosis in large ruminants are low at 1.7% (95% CI: 1.3, 2.1) and 0.7% (95% CI: 0.5, 1.0) respectively, while for FMD NSP it is 50.5% (95% CI: 49.0, 52.0). Univariate analyses show differences in seroprevalences of Q fever between destination (abattoir) province (p-value = 0.005), province of origin (p-value = 0.005), animal type (buffalo or cattle) (p-value = 0.0008), and collection month (p-value = 3.4 × 10(-6)). Similar to Q fever, seroprevalences of brucellosis were significantly different for destination province (p-value < 0.00001), province of origin (p-value < 0.00001), animal type (p-value = 9.9 × 10(-5)) and collection month (p-value < 0.00001), plus body condition score (p-value = 0.003), and age (p-value = 0.007). Additionally, risk factors of the FMD NSP dataset include the destination province (p-value < 0.00001), province of origin (p-value < 0.00001), sex (p-value = 7.97 × 10(-8)), age (p-value = 0.009), collection date (p-value < 0.00001), and collection month (p-value < 0.00001). Spatial analyses revealed that there is no spatial correlation of FMD NSP seropositive animals. High-risk areas for Q fever and brucellosis are identified by spatial analyses. Further investigation of the higher risk areas would provide a better epidemiological understanding of both diseases in Lao PDR. In conclusion, the abattoir serological survey provides useful information about disease exposure and potential risk factors. The network is a good base for field and laboratory staff training in practical technical skills. However, the sustainability of such a surveillance activity is relatively low without an external source of funding, given the operational costs and insufficient government budget. The cost-effectiveness of the abattoir survey could be increased by targeting hotspot areas, reducing fixed costs, and extending the focus to cover more diseases.

Medicine Quality

Out of the boxes, out of the silos: The need of interdisciplinary collaboration to reduce poor-quality medical products in the supply chain. Masini T, Macé C, Heide L, Hamill H, Hampshire K, Newton PN, Ravinetto R. *Res Social Adm Pharm*. 2022 **18**(9): 3694–3698. doi: 10.1016/j.sapharm.2022.03.006. PMID: 35317978.

In this paper, we argue that understanding and addressing the problem of poor-quality medical products requires a more interdisciplinary approach than has been evident to date. While prospective studies based on rigorous standardized methodologies are the gold standard for measuring the prevalence of poor-quality medical products and understanding their distribution nationally and internationally, they should be complemented by social science research to unpack the complex set of social, economic, and governance factors that underlie these patterns. In the following sections, we discuss specific examples of prospective quality surveys and of social science studies, highlighting the value of cross-sector partnerships in driving high-quality, policy-relevant research in this area.

A random survey of the prevalence of falsified and substandard antibiotics in the Lao PDR. Tabernero P, Swamidoss I, Mayxay M, Khanthavong M, Phonlavong C, Vilayhong C, Sichanh C, Sengaloundeth S, Green MD, Newton PN. *J Antimicrob Chemother*. 2022 77(6): 1770–1778. doi: 10.1093/jac/dkab435. PMID: 35137095.

909 samples of antibiotics from across the country were analysed. All except one contained the correct medication, but substandard antibiotics were common with drug amounts outside the expected range. Variation was seen between drugs, manufacturer and country of manufacture.

OBJECTIVES:	In 2012, a stratified random survey, using mystery shoppers, was conducted to investigate the availability and quality of antibiotics sold to patients in the private sector in five southern provinces of the Lao People's Democratic Republic (Laos).
METHODS:	A total of 147 outlets were sampled in 10 districts. The active pharmaceutical ingredient (API) content measurements for 909 samples, including nine APIs (amoxicillin, ampicillin, ceftriaxone, ciprofloxacin, doxycycline, ofloxacin, sulfamethoxazole, tetracycline and trimethoprim), were determined using HPLC.
RESULTS:	All the analysed samples contained the stated API and we found no evidence for falsification. All except one sample had all the units tested with %API values between 75% and 125% of the content stated on the label. However, we identified the presence of substandard antibiotics: 19.6% (201/1025) of samples had their units outside the 90%-110% content of the label claim and 18.3% (188/1025) of the samples had units outside the International Pharmacopoeia/United States Pharmacopoeia assay (percentage of label claim) specifications. Trimethoprim had a high number of samples [51.6% (64)] with units below the limit range, followed by ceftriaxone [42.9% (3)] and sulfamethoxazole [34.7% (43)]. Doxycycline, ofloxacin and ciprofloxacin had the highest number of samples with high API content: 43.7% (38), 14.7% (10) and 11.8% (2), respectively. Significant differences in %API were found between stated countries of manufacture and stated manufacturers.
CONCLUSIONS:	With the global threat of antimicrobial resistance on patient outcomes, greater understanding of the role of poor-quality antibiotics is needed. Substandard antibiotics will have reduced therapeutic efficacy, impacting public health and control of bacterial infections.

The quality of veterinary medicines and their implications for One Health. Vidhamaly V, Bellingham K, Newton PN, Caillet C. *BMJ Glob Health*. 2022 **7**(8): e008564. doi: 10.1136/bmjgh-2022-008564. PMID: 35918072. PMCID: PMC9351321.

In this review of the quality of veterinary medicines, 6.5% of all medications failed at least one quality test – commonly, unsatisfactory drug strength, lack of uniformity, or disintegration characteristics. This likely leads to animal suffering, and possibly antimicrobial resistance, but further research is needed to fully appreciate the wider impacts of substandard veterinary medications.

OBJECTIVES:	Substandard and falsified (SF) veterinary medicines affect animal health, agricultural production and food security and will influence antimicrobial resistance (AMR) in both animals and humans. Yet, our understanding of their extent and impact is poor. We assess the available public domain evidence on the epidemiology of SF veterinary medicines, to better understand their prevalence and distribution and their public health impact on animals and humans.
METHODS:	Searches were conducted in Embase, PubMed, MEDLINE, Global Health, Web of Science, CAB Abstracts, Scopus, Google Scholar, Google and websites with interest in veterinary medicines quality up to 28 February 2021. Identified articles in English and French were screened for eligibility. The Medicine Quality Assessment Reporting Guidelines were used to assess the quality of prevalence surveys.
RESULTS:	Three hundred and fourteen publications were included with a failure frequency (the percentage of samples that failed at least one quality test) of 6.5% (2335/35 733). The majority of samples were from post-marketing surveillance by medicines regulatory authorities of the Republic of Korea and China. A small proportion (3.5%) of samples, all anti-infectives, were from 20 prevalence surveys, with more than half (53.1%, 662/1246) collected in low-income and lower middle-income countries in Africa and Asia. The prevalence survey sample size ranged from 4 to 310 samples (median (Q1-Q3): 50 (27-80)); 55.0% of surveys used convenience outlet sampling methods. In 20 prevalence surveys more than half of the samples (52.0%, 648/1246) failed at least one quality test. The most common defects reported were out-of-specification active pharmaceutical ingredient(s) (API) content, failure of uniformity of units and disintegration tests. Almost half of samples (49.7%, 239/481) that failed API content tests contained at least one of the stated APIs below pharmacopoeial limits. Fifty-two samples (4.2% of all samples) contained one or more incorrect API. One hundred and twenty-three publications described incidents (recalls/seizures/case reports) of SF veterinary medicines in 29 countries.
CONCLUSIONS:	The data suggest that SF veterinary products are likely to be a serious animal and public health problem that has received limited attention. However, few studies of SF veterinary medicines are available and are geographically restricted. Lower API content and disintegration/dissolution than recommended by pharmacopoeial standards risks treatment failure, animal suffering and contribute to AMR. Our findings highlight the need of more research, with robust methodology, to better inform policy and implement measures to assure the quality of veterinary medicines within supply chains. The mechanism and impact of SF veterinary products on animal and human health, agricultural production, their economy and AMR need more transdisciplinary research.

Environmental DNA as an innovative technique to identify the origins of falsified antimalarial tablets—a pilot study of the pharmabiome. Young JM, Liddicoat C, van Dijk K-J, Tabernero P, Caillet C, White NJ, Linacre A, Austin JJ, Newton PN. *Scientific Reports*. 2022 **12**(1): 21997. doi: 10.1038/s41598-022-25196-0. PMID: 36539480. PMCID: PMC9764312.

Bacterial and eukaryotic DNA is trapped in medications during manufacture. We found that the composition of DNA found varied between genuine and falsified medications, and human DNA was also identified in falsified tablets. This powerful approach is a novel means to investigate the illegal supply of falsified medications.

Falsified medicines are a major threat to global health. Antimalarial drugs have been particularly targeted by criminals. As DNA analysis has revolutionized forensic criminology, we hypothesized that these techniques could also be used to investigate the origins of falsified medicines. Medicines may contain diverse adventitious biological contamination, and the sealed nature of blister-packages may capture and preserve genetic signals from the manufacturing processes allowing identification of production source(s). We conducted a blinded pilot study to determine if such environmental DNA (eDNA) could be detected in eleven samples of falsified and genuine artesunate antimalarial tablets, collected in SE Asia, which could be indicative of origin. Massively Parallel Sequencing (MPS) was used to characterize microbial and eukaryote diversity. Two mitochondrial DNA analysis approaches were explored to detect the presence of human DNA. Trace eDNA from these low biomass samples demonstrated sample specific signals using two target markers. Significant differences in bacterial and eukaryote DNA community structures were observed between genuine and falsified tablets and between different packaging types of falsified artesunate. Human DNA, which was indicative of likely east Asian ancestry, was found in falsified tablets. This pilot study of the 'pharmabiome' shows the potential of environmental DNA as a powerful forensic tool to assist with the identification of the environments, and hence location and timing, of the source and manufacture of falsified medicines, establish links between seizures and complement existing tools to build a more complete picture of criminal trade routes. The finding of human DNA in tablets raises important ethical issues that need to be addressed.

Substandard and falsified antibiotics: neglected drivers of antimicrobial resistance? Zabala GA, Bellingham K, Vidhamaly V, Boupha P, Boutsamay K, Newton PN, Caillet C. *BMJ Glob Health*. 2022 **7**(8): e008587. doi: 10.1136/bmjgh-2022-008587. PMID: 35981806. PMCID: PMC9394205.

Substandard and falsified antibiotics may lead to poor clinical outcomes and contribute to antimicrobial resistance. This quantitative analysis of 106 surveys revealed that 17% of medicines sampled failed at least one quality test, highlighting a clear need to strengthen regulatory and procurement processes.

OBJECTIVES:	Antimicrobial resistance (AMR) is a significant global health threat with substandard and falsified (SF) antibiotics being neglected contributing factors. With their relationships poorly understood, more research is needed in order to determine how interventions to reduce SF antibiotics should be ranked as priorities in national AMR action plans. We assessed the evidence available on the global prevalence of SF antibiotics, examined the quality of the evidence and discussed public health impact.
MATERIALS/ METHODS:	We searched PubMed, Embase, Google and Google Scholar for publications on antibiotic quality up to 31 December 2020. Publications reporting on the prevalence of SF antibiotics were evaluated for quantitative analysis and assessed using the Medicines Quality Assessment Reporting Guidelines.
RESULTS:	Of the 10 137 screened publications, 648 were relevant to antibiotic quality. One hundred and six (16.4%) surveys, published between 1992 and 2020 and conducted mainly in low-income and middle-income countries (LMICs) (89.9% (480/534) of the data points), qualified for quantitative analysis. The total number of samples tested for quality in prevalence surveys was 13 555, with a median (Q1-Q3) number of samples per survey of 47 (21-135). Of the 13 555 samples, 2357 (17.4%) failed at least one quality test and the median failure frequency (FF) per survey was 19.6% (7.6%-35.0%). Amoxicillin, sulfamethoxazole-trimethoprim and ciprofloxacin were the most surveyed antibiotics, with FF of 16.1% (355/2208), 26.2% (329/1255) and 10.4%

	(366/3511), respectively. We identified no SF survey data for antibiotics in the WHO 'Reserve' group. The mean Medicine Quality Assessment Reporting Guidelines score was 11 (95% CI 10.1 to 12.2) out of 26.
CONCLUSIONS:	SF antibiotics are widely spread with higher prevalence in LMICs. The quality of the evidence is poor, and these data are not generalisable that 17.4% of global antibiotic supply is SF. However, the evidence we have suggests that interventions to enhance regulatory, purchasing and financial mechanisms to improve the global antibiotic supply are needed.

Other topics

Factors associated with cervical cancer screening among women aged 25-60 years in Lao People's Democratic Republic. Phaiphichit J, Paboriboune P, Kunnavong S, Chanthavilay P. PLoS One. 2022 17(4): e0266592. doi: 10.1371/journal.pone.0266592. PMID: 35390098. PMCID: PMC8989294.

This case-control study demonstrated that symptoms of sexually transmitted infections, increased knowledge, and means to attend hospital led to higher uptake of cervical screening. Given the importance of cervical cancer in this key demographic group, there is scope for improved health promotion.

BACKGROUND:	Despite cervical cancer being a major public health concern in the Lao People's Democratic Republic (Lao PDR), screening coverage is very low. The reasons and factors for this are unknown. This study aimed to identify factors associated with uptake of cervical cancer screening among women aged 25-60 years.
METHODS:	The case-control study was conducted among women aged 25-60 years in Vientiane Capital and Luang Prabang province from 15 March to 31 May 2018. A total of 360 women were included in the study, a ratio of two controls per case. The cases were women who had undergone cervical cancer screening over the last five years. The controls were women who had never been screened or screened more than five years before, matched to the cases with residency and age (± five years). The cases were selected from central and provincial hospitals and the controls from the same community and districts where the cases resided. Conditional logistic regression was used to determine factors associated with cervical cancer screening.
RESULTS:	The mean age was 42.37±9.4 years (range: 25-60), 66.67% were women from Vientiane Capital, and 86.11% were married. The common reasons for not being screened were the absence of clinical signs and symptoms (45.28%) followed by never having heard about cervical cancer (13.33%). In the multivariable analyses, we found that having sexually transmitted infections (AOR = 3.93; 95% CI = 1.92-8.05), receiving recommendations for screening from health workers (AOR = 3.85; 95% CI = 1.90-7.78), a high score for knowledge (AOR = 7.90; 95% CI = 2.43-25.69) and attitude towards cervical cancer prevention and treatment (AOR = 2.26; 95% CI = 1.18-7.16), and having a car to travel (AOR = 2.97; 95% CI = 1.44-6.11) had a positive impact on undergoing cervical cancer screening.
CONCLUSIONS:	Gynaecological consultations, increased knowledge and positive attitudes result in women undergoing screening. Therefore, health education and advocacy for cervical cancer prevention should be provided to women.

Conference and meeting abstracts

International Symposium on Pneumococci and Pneumococcal Diseases,
Toronto, Canada, 19-23 June, 2022
Five years of pneumonia surveillance in Lao PDR. Laddaphone Bounvilay L, Simpson A, Ryan K, Vilivong K, Bounkhoun T, Chanthalaunglath V, Phonemexay O, Hart JD, Lai JYR, Chan J, Dunne EM, Fox K, Newton PN, Mayxay M, Xeuatvongsa A, Mulholland EK, Satzke C, A. Dubot-Pérès A, Dance DAB, Russell FM. Poster presentation. **No abstract available.**

The 7th World One Health Congress in Singapore,
November 2022
Abstract No: 15170
Investigation of *Escherichia coli* isolates from pigs and humans in Lao PDR for colistin resistance. Phomsisavath V, Chansamouth V, Roberts T, Robinson MT, Vongsouvath M, Theppangna W, Christensen P, Blacksell S, Mayxay M; Ashley EA.

INTRODUCTION AND OBJECTIVES OR PURPOSE:	Antimicrobial resistance (AMR) is a significant public health threat that should be tackled using One Health approach. Colistin is not available in Laos to treat human infections, only for animal treatment. The first report of colistin-resistant *E. coli* in human in Laos was in 2012, possibly acquired by horizontal transmission from a pig. However, it is unknown when colistin resistance in *E. coli* emerged and what the proportion of invasive isolates in humans is. Therefore, this study seeks to investigate colistin-resistant *Escherichia coli*, determine the prevalence, characterize antimicrobial susceptibility, and detect their genes from pigs and humans in Laos.
METHODS:	To investigate this, between August and November 2022, we will study up to 1900 samples from pigs and humans in Laos. Rectal swabs from approximately 900 domestic pigs and 1000 stored *E. coli* isolates from blood cultures from patients from all over Laos admitted to Mahosot Hospital between 2000 to 2022 will be included. Potential colistin-resistant *E. coli* isolates will be identified using selective colistin chromogenic agar. The minimal inhibitory concentration will be calculated for all isolates that grow on the selective agar using microbroth dilution (ComASPTM Colistin, Liofilchem®) following EUCAST guidelines. The clinical breakpoint for defining colistin resistance will be >2 mg/liter. Isolates will also be tested by Real-Time Polymerase Chain Reaction to detect plasmid-mediated genes (*mcr*-1, *mcr*-2, *mcr*-3).
RESULTS OR FOCUS:	We will present data on colistin-resistant *E. coli* in humans and pigs in Laos from representative regions of the country and describe when colistin resistance in clinical invasive isolates emerged. Demographic and geographic results will be analysed to show trends and risk factors for resistance.
CONCLUSION OR SCOPE:	Results will provide evidence of a link between colistin use in animals and invasive human infection and may inform policies for antibiotic usage both in the human and animal sectors.

Abstract No: 14797
Seropositivity and seroconversion to endemic zoonotic pathogens among market vendors in the Lao PDR. Senvanpan N, Phimolsarnnousith V, Rattanavong S, Blacksell SD, Mayxay M, Reinharz D, Pruvot M, Newton P, Robinson MT.

INTRODUCTION AND OBJECTIVES OR PURPOSE:	Interactions between humans and animals in the process of hunting, selling and consuming wild animal meat raises public health concerns, yet perception of health risks is often low. In Lao markets 23% of wildlife meat vendors said their produce could transmit disease, and 86% did not consider their health was at risk from their occupation. To understand the risks associated with exposure to wild animal meat, we conducted a one-year longitudinal serosurvey of market vendors to characterise the frequency of seropositivity and seroconversion to three endemic zoonotic bacterial pathogens in Laos: Rickettsia typhi, *Orientia tsutsugamushi,* and Leptospira spp.
METHODS:	150 vendors in three markets, selling vegetables, farmed meat or wildlife meat (and combinations thereof) consented to provide a blood sample up to three times between March 2017 and June 2018. Samples were tested for the presence of IgG against the target pathogens.
RESULTS OR FOCUS:	Twenty individuals (13.3%; 95% CI: 8.5–20.1) sero-converted for at least one pathogen during 15 months. The prevalence of anti-Leptospira IgG across all occasions was 12.0% (95% CI: 7.5-18.6), whilst against R. typhi was 24% (95% CI: 17.6-31.8) using ELISA and 12.7% (95% CI: 8.0-19.3) by IFA. Anti-O. tsutsugamushi IgG prevalence was 20% (95% CI: 14.1-27.5) using ELISA and 12% (95% CI: 7.5-18.6) using IFA, and significantly differed between vendor types (p=0.047), with vegetable and wild meat vendors (21.7% and 27.3%, respectively) having higher prevalence than farmed meat vendors (8.5%).
CONCLUSION OR SCOPE:	A significant number of vendors seroconverted (~10% per year) for key endemic zoonotic bacterial pathogens, which are often detected in wild vertebrates. The pattern of seropositivity suggests links with what the vendor sells and warrants further investigation to identify transmission pathways between wildlife and humans, and the risk attributable to wildlife trade and consumption and different practices along the supply chain.

The International Congress for Tropical Medicine and Malaria 2020 (ICTMM),
24-28 October 2022 in Bangkok, Thailand
Robinson MT, Oral presentation as part of symposium, **Fever in the Tropics: Advances in POCTs for febrile illness**.

Often clinical testing is done in specific laboratories resulting in a delay from a few hours to days before the result is reported to the clinical team. By this time the patient may already have been treated using broad range or non-specific drugs or given completely the wrong medication, putting their lives at risk. This lack of specified and tailored treatment also adds to the pressure of increasing drug resistance and the use of valuable resources in an already stretched environment. Point-of-Care Testing (POCT) enables the fast diagnosis of disease, close to the location of the patient. This allows a reduction of time to diagnosis, and allows treatment plans to be tailored to the patients' unique needs prior to starting treatment. The aim of POCT is that the test is simple and easy to perform by the bed-side in the ward. Many POCT we use today evolved from much larger or more complex assays and equipment, and have only become available after recent advances in a number of different technologies. Technology is rapidly changing, allowing improvement to existing POCT as well as introduction of newer simpler assays for harder to diagnose diseases. I will review some of the current and new-to-market POCT technologies available for febrile illnesses, and look at what novel technologies may soon be available and what we may look forward to in the way of diagnostic testing and patient monitoring.

Joint International Tropical Medicine Meeting,
Bangkok, 7-9 Dec 2022
Multiplex qPCR for screening leptospirosis and other tropical infectious diseases. Wongrattanapipat S, Huangsuranun W, Perrone C, Robinson MT, Suputtamongkol Y, Batty EM, Day NPJ, Lubell Y, Thaipadungpanit J.

INTRODUCTION:	Leptospirosis and rickettsiosis (LR) are endemic in South and Southeast Asia (SEA). Pathogenic Leptospira causes human leptospirosis. *R. typhi* of typhus group rickettsiae causes murine typhus. Orientia tsutsugamushi causes human scrub typhus. *R. conorii*, *R. felis*, *R. honei*, and *R. rickettsii* of the spotted fever group were also commonly found in SEA. These diseases show a wide range of symptoms from flu-like to severe diseases. Serology assays are used for disease confirmation using paired sera. Even the window of positivity is in days 1-5 post-onset acute infection; nucleic acid amplification tests (NAAT) are developed for early diagnosis and treatment. Sometimes there was no agreement between serology and NAAT results. It might be the diversity of bacterial serotypes or target sequences. In this study, we aim to develop multiplex real-time PCR detecting these bacterial infections to investigate the fever aetiology in SEA populations in rural areas.
METHODS:	Three modified primer and probe sets (used previously to screen leptospirosis, scrub typhus, and eubacteria infections) were combined with newly designed primers targeting Rickettsia spp. commonly identified in SEA. The multiplex PCR was optimised to archive the amplification efficiency and analytic sensitivity comparable to the simplex PCR assays. The assay accuracy was validated using clinical specimens confirmed LRD by serology tests or NAAT.
RESULTS AND CONCLUSION:	The diagnostic accuracy of multiplex PCR to screen leptospirosis and scrub typhus was comparable to the corresponding simplex PCR. Further optimisation and an increase in the accuracy of rickettsial diseases and other bacteria infections are needed.

American Society of Tropical Medicine and Hygiene (ASTMH) 71st Annual Meeting,
30 Oct-3 Nov 2022, Washington State Convention Center, Seattle, USA
Delayed onset of community transmission of SARS-CoV-2 and related trends in influenza A, influenza B and respiratory syncytial virus infections in Lao PDR: a hospital-based surveillance study. Danoy Chommanam, Nathaniel Christy, Touxiong Yiaye, Soulichanya Phoutthavong, Patsalin Keomoukda, Sompong Thammavong, Thipsavanh Bounphiengsy, Thongsavanh Lathsachack, Latsaniphone Bountthasavong, Bountoy Sibounheuang, Ooyanong Phonemixay, Siribun Panapruksachat, Viladeth Praphasiri, Sommay Keomany, Bounthavy Chaleunphon, Phouvieng Douangdala, Matthew T Robinson, Elizabeth Batty, Koukeo Phommasone, Manivanh Vongsouvath, Andrew Letizia, Mayfong Mayxay, Audrey Dubot-Pérès, Elizabeth A Ashley

ABSTRACT
The first cases of laboratory confirmed COVID-19 in Laos were reported on 23 March 2020. Following a nationwide lockdown from early April 2020 to May 2020, strict border controls and admission of all confirmed cases to hospital or quarantine centres were enforced, in order to prevent local transmission. We set up prospective case-based surveillance for respiratory virus infections in four provincial hospitals across the country.

We enrolled consenting patients of all ages who met our case definition (fever or history of fever AND cough or other respiratory symptoms/signs OR loss of smell and/or taste). Nasopharyngeal and throat swabs were collected and tested for SARS-CoV-2 N-gene, influenza A and B viruses and human respiratory syncytial virus (RSV) using probe based real-time RT-PCR assays. RNA extracts from specimens testing positive for SARS-CoV-2 with Ct ≤ 28 were sequenced (Oxford Nanopore).

Between 11 March 2021 and 31 May 2022 we enrolled 1960 patients at four provincial hospitals in Laos (Xieng Khuang, Luang Namtha, Salavan and Attapeu), of whom 938 (48%) were female. The majority (78%) were managed as outpatients. Median [range] age was 25 years [6 days-97y]. A total of 482 (25%) patients were diagnosed with SARS-CoV-2 infection, of whom 11 were co-infected with either RSV or influenza A, 15 patients had influenza A only, three influenza B, and 42 RSV. The number (%) cases testing positive for SARS-CoV2 by month increased from 3/79 (4%) in November 2021 to 187/240 (78%) in March 2022, before falling to 45/193 (23%) in May 2022. Whole-genome sequencing confirmed Delta as the predominant variant between December 2021 and February 2022 with Omicron BA.1 and Omicron BA.2 predominating from March 2022.

Laos successfully avoided widespread community transmission of SARS-CoV-2 until the arrival of new, more transmissible variants such as delta and omicron, by which time vaccination had started. Infections with other common respiratory viruses were very uncommon during this period, likely as a consequence of lockdown measures, including school closures, mask wearing, enhanced hand hygiene and social distancing.

An investigation of the etiology of seizures associated with fever in children from low- and middle-income countries: results from the FIEBRE study. Ajanovic A, Lal S, Mogeni P, Bramugy J, Valente M, Olaru I, Lungraj M, Phimolsarnnousith V, Chansamouth V, Chimenya M, Green E, Feasey N, Dubot-Pérès A, Mayxay M, Ashley EA, Newton P, Kranzer K, Yeung S, Hopkins H, Mabey D, Bassat Q.

Fever is a common symptom resulting in health care seeking worldwide. There is limited evidence of the epidemiology and underlying etiology of seizures associated with fever in children in low- and middle-income countries (LMICs). They can vary from mild conditions (benign febrile seizures) to the more serious life-threatening diseases such as bacterial meningitis and cerebral malaria. This analysis aims to provide a description of children with fever and seizures in the FIEBRE (Febrile Illness Evaluation in a Broad Range of Endemicities) observational study.

Child in- and outpatients were recruited and systematically investigated in Mozambique, Zimbabwe, Malawi and Lao PDR from 2018 to 2021. Clinical description, treatment and outcome were recorded for each participant. Point-of-care tests (including blood culture, urine dipstick and culture, and HIV and malaria tests) were systematically performed, and further samples were shipped to reference laboratories for gold standard testing for a broad range of infectious agents. Lumbar puncture was only performed when clinicians considered it necessary.

Across all sites 389 /3718 (4.9%) children aged 2 months to 14 years presented with seizures. The frequency among inpatients was uneven across the sites: 112/345 (32.4%) in Malawi, 122/533 (22.9%) in Mozambique, 46/355 (13%) in Zimbabwe, and 51/414 (12.3%) in Lao PDR. The frequencies in outpatients were 0.3%, 0.6%, 1.5% and 12.7% respectively. Of the 58 outpatients with seizures, 63.7% were categorized as "fever of unknown origin" by clinicians, 53.4% were prescribed with antibiotics and all of them who completed follow-up were alive by day 28. However, of 331 inpatients with seizures, 42.9% were diagnosed with malaria and 12.4% with suspected sepsis and/or meningitis. Among the 301 who completed D28 follow-up, mortality was 5%. We will present microbiology results stratified by clinical phenotypes, countries, and age groups.

Seizures on presentation are very frequent among febrile inpatients in LMICs. Detailed etiological diagnoses are crucial to better target the scarce therapeutic interventions available and improve survival.

Leptospirosis among patients presenting with fever in the multi-center Febrile Illness Evaluation in a Broad Range of Endemicities (FIEBRE) study. Crump J, Mogeni P, Newton PN, Houvert A, Sordoillet V, Lal S, Mayxay M, Green E, Valente M, Bramugy JM, Roberts C, DCW, Hopkins H, Picardeau M. Oral presentation. **No abstract available**

Application of liquid-chromatography mass-spectrometry and predictive modelling for identification of a protein signature of Japanese encephalitis virus in Lao PDR. In session 'Proteomics for identifying diagnostic biomarkers of central nervous system (CNS) infections in diverse settings' Tehmina Bharucha

ESCCAR International Intracellular Bacteria Meeting
23-26 Aug 2022, Lausanne, Switzerland
Epidemiology and treatment of scrub typhus and murine typhus. Paul Newton.

Other activities in 2022

Public engagement

LOMWRU continued its programme of community, public and policy engagement activities when COVID restrictions permitted in 2022

Pint of Science Laos

Images from the first Pint of Science event in Laos, held 9-10 May at SciPresso Café, Vientiane. © LOMWRU 2023. Photos: LOMWRU.

2022 saw the kick-off of the first ever Pint of Science festival in Laos. Pint of Science is an annual global science festival, held every May. The event started in the UK in 2013, with science talks held in local bars and aimed at the general public, and has since expanded to be held in 27 countries, with nearly 3,000 events held over the festivals' three days. Pint of Science aims to deliver interesting and relevant talks on the latest science research in an accessible format to the public – mainly across bars, pubs, cafés and other public spaces, where the audience can feel relaxed, and have an enjoyable evening. The aim is to provide a platform which allows people to discuss research with the people who carry it out within their local community, and no prior knowledge of the subject is required. Topics may range from human health to the natural environment, and from technology to social sciences.

LOMWRU organized the first Pint of Science event for Laos on Monday 9 and Tuesday 10 May at SciPresso Café, Vientiane's first science-themed café. Laos was one of only two Asian countries to take part in this year's global event. Each night showcased three researchers based in Vientiane. On Monday night, software developer Sylvain Dorey spoke about use of artificial intelligence and social media influencing, Dr Somphouthone Phimmachak (National University of Laos) shared her work on the Lao warty newt, and Dr Thitsamay Luangxay described her career as a cancer pathologist at Mittaphab Hospital. On Tuesday night, Micah Ingalls talked about the work of the Mekong Region Land Governance (MRLG) project, Dr Siriphone Virachith (Institut Pasteur du Laos) discussed how the COVID-19 pandemic impacted Laos, and Dr Matthew Robinson (LOMWRU) shared insights into zoonotic diseases in Laos. The event was organized and managed by the Pint of Science team made up of members of staff from LOMWRU. Each night was hosted by a senior and junior staff member: Monday was hosted by Matthew Robinson and Kaisone Padith, and Tuesday was hosted by Dr Vilada Chansamouth and Latsaniphone Boutthasavong. Each night had over 30 attendees, with the audience being made up of 14 nationalities (47% being Lao nationals). The majority of the audience had an interest in science but worked in non-science related jobs, 13% were students, and the remainder worked in science-related field. The evening was thoroughly enjoyed by everyone, with the chance for audience members to ask questions and interact with local scientists, as well as an opportunity to win the highly sought-after Pint of Science T-shirt with a knock-out game of heads-and-tails. The event received very supportive feedback from the audience, with requests for more such events. The Pint of Science team plan to continue, and look forward to hosting the 2023 event in May 2023. The Pint of Science Laos team included: Matthew Robinson (Country Director), Tamalee Roberts, Vayouly Vidhamaly, Kaisone Padith, Latsaniphone Boutthasavong, Manophab Luangraj, Padthana Kiedsathid, and Bountoy Sibounheuang.

Go Blue for AMR

LOMWRU staff demonstrate support for the WHO's Go Blue for AMR campaign to mark World Antibiotic Awareness Week (WAAW) in 2022.

LOMWRU joined the WHO's Go Blue for AMR campaign to mark World Antibiotic Awareness Week (WAAW) in 2022. WAAW is a global campaign celebrated annually to improve awareness and understanding of AMR and encourage best practices among the public, One Health stakeholders and policymakers, who all play a critical role in reducing the further emergence and spread of AMR. In 2022, the theme of WAAW was *Preventing Antimicrobial Resistance Together*. We call on all sectors to encourage the prudent use of antimicrobials and to strengthen preventive measures addressing AMR, working together collaboratively through a One Health approach.

Establishment of a Unit for Health Evidence & Policy (UHEP) in Lao PDR

The second meeting of UHEP was held on 1 September 2022, organised by the LOMWRU, UHS, and the Ministry of Health (MoH), Lao PDR, and was facilitated by the Health Intervention and Technology Assessment Program (HITAP) in Thailand. This meeting was designed to be a workshop with presentations and an interactive exercise session to promote peer-to-peer learning. The meeting aimed to promote the understanding of health technology assessment (HTA) topic prioritisation in Lao PDR via sharing knowledge on Thailand's experience of adopting the prioritisation processes. More importantly, it aimed to increase awareness on HTA and the topic prioritisation process.

Lao Medical Journal

LOMWRU continues to support publication of the *Lao Medical Journal*. The latest issue was published in June 2021.

Farewells

In November 2022, we bade Dr Anne Pando (*centre*, holding scroll) a very fond au revoir after four years in Laos working on soil-related projects, notably on factors influencing *Burkholderia pseudomallei* in the environment. She returns to IRD (Institut de Recherche pour le Développement) in France. © 2023 LOMWRU.

Organisational chart

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

Prof Elizabeth Ashley
Director of LOMWRU

Dr Manivanh Vongsouvath*
Director of Microbiology Laboratory & Deputy Head of Virology

Microbiology

Mrs Viengmon Davong*
Head Lab Technician & co-Deputy Head Microbiology Laboratory

Dr Koukeo Phommasone*
Co-Deputy Director of Microbiology Laboratory

Virology

Dr Audrey Dubot-Pérès***
Head of Virology

Molecular Bacteriology

Dr Matthew Robinson
Head of Molecular Bacteriology, Area Safety Officer & MORU Rickettsial Coordinator

Mrs Anisone Chanthongthip
Lab Manager

Clinical

Dr Koukeo Phommasone*
Research Physician & Head of Clinical Team

Dr Vilada Chansamouth*
Research Physician & Deputy Head of Clinical Team

Dr Sayaphet Rattanavong*
Research Physician

Malaria & Field Work

Prof Mayfong Mayxay*
Head of Field Research

Medicine Quality

Dr Céline Caillet**
MORU/IDDO MQ Coordinator

Administration

Mrs Olay Lattana
Micro Lab Administrator

Mrs Athirat Black
Operations Manager

Mr Sengkham Simanivong
Supplies /Logistics

Ms Sengmany Symanivong
Administrator

HR/Finance

IT

Legend

* Indicates Government of Lao PDR staff
** Based in Oxford, UK and reports to Prof Paul Newton, Head of MORU/IDDO MQ
*** Funded by and based at IRD, France

Annex A – LOMWRU collaborators in 2022

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. Hospital Directors and staff, Joint research projects, Mittaphab, Setthathirat, Children's, Mother & Child, Police and Army Hospitals, Vientiane, 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 Centre 2-Asia, 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 (UCLA), 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, NZ
35. Prof Nicole Zitzmann and Dr Bevin Gangadharan, Department of Biochemistry, University of Oxford, UK
36. Prof Philippe Guérin and the 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. 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. 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)
46. Institute of Medical Microbiology, University of Zurich, Switzerland
47. Institute for Health Metrics and Evaluation, USA
48. Médecins sans Frontières
49. Ecohealth Alliance, USA
50. Duke-NUS Medical School, Singapore
51. Clinton Health Access Initiative
52. Dr Martine Barons, University of Warwick
53. Health Intervention and Technology Assessment Program, Bangkok, Thailand
54. InBios International Inc. Innovative Diagnostics
55. Global Access Diagnostics

Annex B – LOMWRU staff in 2022

Elizabeth Ashley – Unit Director

Atsamouth, Aphaphone	Laboratory Technician
Bellingham, Khonsavath	Research Pharmacist, Medicine Quality Research Group
Black, Athirat	Operations Manager
Boutthasavong, Latsaniphone	Senior Laboratory Technician / Deputy IDC lab Manager
Bounkhoun, Toukta	Research Physician
Bounmanivong*	Cleaner
Bounphinegsy, Thipsavanh	Research Physician – Field
Bounvilay, Laddaphone	Research Physician
Buasy*	Cleaner
Caillet, Céline	Medicine Quality Research Group Coordinator / Research Scientist
Chansamouth, Vilada*	Senior Research Physician / PhD Student
Chanthaluanglath, Valin	Nurse – Patient Follow up
Chanthongthip, Anisone	IDC 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
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 Research
Opphalavong, Somphone	Security Guard
Panapruksachat, Siribun	Molecular Bacteriologist
Panyanouvong, Phonepasith*	Senior Laboratory Technician
Phalivong, Sonexay	Project Coordinator (CMPE)
Phianthanom, Bountherng*	Laboratory Technician
Phimolsannousith, Vilayouth	Research Physician
Phommadichak, Vanheuang	BSL3 Laboratory Manager
Phommahasay, Bounkhong*	Laboratory Technician
Phommasone, Koukeo*	Senior 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 Physician
Phoutthavong, Soulichanya	Research Physician – Field
Rattanavong, Sayaphet*	Senior Research Physician
Roberts, Tamalee	Microbiologist and Data Manager
Robinson, Matthew	Group Head Molecular Bacteriology & Area Safety Advisor
Seevanhthong, Khambang	Research Physician – Field
Sengdatka, Davanh*	Laboratory Technician
Sengduangphachanh, Amphonesavanh*	Quality Control/ Senior Laboratory Technician
Sengxeu, Noudy	Research Pharmacist, Medicine Quality Research Group
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
Souksavanh, Manila	Laboratory Technician
Solathtanavong, Tadam	Administrative and HR Officer
Soulivong Ailatda	Research Physician – Field
Souvong, Vimalay	CTSG Coordinator

Soukhammala, Sompasong	Finance and Admin trainee
Syhalath, Somsavanh*	Technician
Symanivong, Sengmany	Finance and HR Administrator
Thamavong, Sompong	Laboratory Technician – Field
Thammavongsa, Peeyanout	Research Physician
Thepbandith, Sompany	Finance Officer
Thongpaseuth, Souliyasack	Senior Laboratory Technician
Vang, Sao*	Laboratory Technician
Vannachone, Souphaphone	Research Physician
Vidhamaly, Vayouly	CTSG Coordinator
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
Yang, Pao	IT Helpdesk Support Manager
Yiaye, Touxiong	Research Physician – Field

* Indicates Government of Lao PDR staff

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PATH

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