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LOMWRU
Annual Report 2020

Lao-Oxford-Mahosot Hospital-Wellcome Trust Research Unit

Designed by:
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Cover photos: Malavanh Vongsouvath (top) and Padthana Kiedsathid (centre) perform COVID-19 PCR testing in the Molecular lab (photographer: Matthew Robinson). In the bottom photo, participants in an interactive COVID-19 ICU training organised by Dr Rebecca Inglis (photographer: Rebecca Inglis). All photos © LOMWRU 2021.

LOMWRU.

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

ທີມງານ LOMWRU ຕໍ່ໜ້າພະແນກຈຸລິນຊີວິທະຍາ. ຮູບພາບໂດຍ Mickaël Perier. © LOMWRU.

LOMWRU team shown in front of the Microbiology Laboratory. Photographer: Mickaël Perier © LOMWRU.

ກ່ຽວກັບໜ່ວຍງານຄົ້ນຄວ້າຂອງພວກເຮົາ

ໂຄງການຮ່ວມມືຄົ້ນຄວ້າດ້ານພະຍາດເຂດຮ້ອນລະຫວ່າງໂຮງໝໍມະໂຫສົດ - ມະຫາວິທະຍາໄລອ໋ອກຟອດ-ແວວຄຳທີ່ຕັ້ສ ຫຼື The Lao-Oxford-Mahosot Hospital-Wellcome Trust Research Unit (LOMWRU) ແມ່ນໜ່ວຍງານຄົ້ນຄວ້າທີ່ມີການຮ່ວມມືລະຫວ່າງມະຫາວິທະຍາໄລອ໋ອກຟອດ ແລະ ໂຮງໝໍມະໂຫສົດ, ນະຄອນຫຼວງວຽງຈັນ, ສປປ ລາວ ໂດຍໄດ້ຮັບທຶນຊ່ວຍເຫຼືອຫຼັກ ຈາກແວວຄຳຕັ້ສ ປະເທດອັງກິດ. ພວກເຮົາຍັງແມ່ນສ່ວນໜຶ່ງຂອງເຄືອຂ່າຍໜ່ວຍງານຄົ້ນຄວ້າພະຍາດເຂດຮ້ອນ (MORU Tropical Health Network) ທີ່ມີສູນຄົ້ນຄ້ວາ ຕັ້ງຢູ່ ປະເທດໄທ, ກຳປູເຈຍ, ສປປ ລາວ, ພະມ້າ ແລະ ສາທາລະນະລັດ ປະຊາທິປະໄຕ ຄອງໂກ.

ປະຈຸບັນ ພວກເຮົາມີພະນັກງານທັງໝົດ 77 ຄົນ ຊຶ່ງລວມມີ ພະນັກງານທີ່ເຮັດວຽກປະຈຳຢູ່ນະຄອນຫຼວງວຽງຈັນ ແລະ ຕ່າງ ແຂວງ ທີ່ເປັນໜຶ່ງໃນວຽກງານການຮ່ວມມືຄົ້ນຄ້ວາ, ແລະ ໃນນັ້ນຍັງມີ ພະນັກງານພາກລັດຈາກພະແນກຈຸລິນຊີວິທະຍາ ຈຳນວນ 20 ຄົນ ໂດຍມີ ດຣ ມະນີວັນ ວົງສຸວັດ ເປັນຫົວໜ້າພະແນກ. ໜ່ວຍງານຄົ້ນຄວ້າ LOMWRU ມີ ຫ້ອງວິເຄາະທາງພັນທຸກຳ, ຫ້ອງວິເຄາະເຊໂຣໂລຊີ ແລະ ຫ້ອງວິເຄາະຄວາມປອດໄພລະດັບ 3 (BSL3) ສຳລັບປຸກເຊື້ອ Rickettsial, Mycobacterium spp., B. pseudomallei ແລະ ເຊື້ອໄວຣັສ. ສຈ. ປອ. ດຣ ມາຍຟອງ ມາຍຊາຍ, ຮອງອະທິການບໍດີ ມະຫາວິທະຍາໄລ ວິທະຍາສາດສຸຂະພາບ ຊ່ວຍຊີ້ນຳວຽກງານຮ່ວມມືຄົ້ນຄວ້າກັບບັນດາ ແຂວງ ແລະ ວຽກງານຄົ້ນຄວ້າພາກສະໜາມ.

ໜ່ວຍງານຄົ້ນຄວ້າ LOMWRU ໄດ້ສະໜັບສະໜຸນການບິ່ງມະຕິພະຍາດທີ່ເກີດຈາກເຊື້ອຈຸລະຊີບໃນ ສ.ປ.ປ ລາວ, ສະໜັບສະໜຸນການຝຶກອົບຮົມ ບັນດານັກເຕັກນິກ ແລະ ນັກວິທະຍາສາດການແພດລາວ ແລະ ຍັງຈັດຕັ້ງປະຕິບັດການສຶກສາຄົ້ນຄວ້າ ໂດຍສະເພາະຂົງເຂດທີ່ກ່ຽວກັບພະຍາດຊຶມເຊື້ອ.

Who We Are

The Lao-Oxford-Mahosot Hospital-Wellcome Trust Research Unit (LOMWRU) is a research collaboration between Oxford University and Mahosot Hospital in Vientiane, Lao PDR with core funding from the Wellcome Trust in the UK. We are part of the MORU Tropical Health Network which has research units in Thailand, Cambodia, Laos, Myanmar and Democratic Republic of Congo.

Currently there is a team of 77 research and support staff in the capital and the provinces working on projects as part of the collaboration, including 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 and Engagement 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.

ຮູບພາບລຽນຕາມເຂັ້ມໂມງ; ຈາກດ້ານເທິງຊ້າຍ ດຣ ມະນີວັນ ວົງສຸວັດ (ຫົວໜ້າພະແນກຈຸລິນຊີວິທະຍາ ໂຮງໝໍມະໂຫສົດ ນັ່ງຂ້າງ ນາງ ຫຼ້າ ນ້ອຍ ສີລິສັກ), ຕໍ່ມາແມ່ນຮູບພາບ ບັນດານັກເຕັກນິກວິເຄາະການແພດຂອງໜ່ວຍງານວິເຄາະຈຸລິນຊີ, ຕໍ່ດ້ວຍຮູບພາບ ດຣ ພູດທະສອນ ກວຍ ເກສອນ (ຜູ້ຈັດການດ້ານຄຸນນະພາບຂໍ້ມູນປະຈຳ LOMWRU) ແລະ ດຣ ສຸພາພອນ ວັນນະຈອນ (ວິຊາການຄົ້ນຄວ້າປະຈຳ LOMWRU) ແລະ ສຸດທ້າຍ ແມ່ນຮູບພາບພູມປຸກເຊື້ອໃນຫ້ອງວິເຄາະຈຸລິນຊີ. ຮູບພາບໂດຍ Mickaël Perier. © LOMWRU.

Shown, *clockwise from top left:* Dr Manivanh Vongsouvath, Head of Mahosot Hospital Microbiology Laboratory, seated next to Ms Lanoi Silichack; Mahosot Microbiology laboratory technicians hard at work; LOMWRU Data Quality Manager Dr Phoudthasone Kouaykesone with LOMWRU Research Physician Dr Souphaphone Vannachone; and agar plates in the Microbiology laboratory. Photographer: Mickaël Perier © LOMWRU 2021.

MESSAGE FROM THE DIRECTOR

ຄຳເຫັນຂອງທ່ານ **Professor Elizabeth Ashley**

ໃນໄລຍະປີ 2020, ທົ່ວໂລກໄດ້ຮັບຜົນກະທົບຈາກແຜ່ລະບາດຂອງພະຍາດ COVID-19, ເຊັ່ນດຽວກັນກັບປະເທດລາວ. ປະເທດລາວໄດ້ມີວິທີຈັດການເພື່ອສະກັດກັ້ນການແຜ່ລະບາດຂອງເຊື້ອພະຍາດ SARS-CoV-2 ຕະຫລອດປີ 2020 ແລະ ລັດຖະບານໄດ້ຈັດຕັ້ງລະບົບການຄັດກອງ ແລະ ລະບົບການກັກໂຕ ເພື່ອຮັກສາລະບົບສາທາລະນະສຸກພາຍຫຼັງປິດປະເທດໃນໄລຍະເດືອນ ເມສາ 2020 ທີ່ຜ່ານມາ, ທັ້ງປະເທດເລີ່ມກັບສູ່ສະພາບໃກ້ຄຽງກັບປົກກະຕິແຕ່ເສດຖະກິດຫຼາຍພາກສ່ວນກໍໄດ້ຮັບຜົນກະທົບທີ່ຮຸນແຮງໂດຍສະເພາະພາກສ່ວນການທ່ອງທ່ຽວ ເນື່ອງຈາກຈຳນວນນັກທ່ອງທ່ຽວທີ່ຫຼຸດລົງ. ການກວດສອບຊອກຫາເຊື້ອພະຍາດທົ່ວປະເທດ ສ່ວນໃຫຍ່ແມ່ນສູນລະບາດວິທະຍາແຫ່ງຊາດເປັນຜູ້ຮັບຜິດຊອບ, ພ້ອມດ້ວຍຫ້ອງວິເຄາະຈາກບັນດາໂຮງໝໍແຂວງ ກໍໄດ້ກວດຄັດກອງແຮງງານຕາມເຂດຊາຍແດນທີ່ກັບຄືນສູ່ປະເທດລາວ. ໂຮງໝໍມະໂຫສົດ ກໍໄດ້ຊ່ວຍສະໜັບສະໜູນການກວດຫາເຊື້ອພະຍາດ SARS-CoV-2. ໜ່ວຍງານປິ່ງມະຕິໄວຣັສ ຂອງໂຮງໝໍມະໂຫສົດແມ່ນໄດ້ຮັບການສະໜັບສະໜູນຈາກ LOMWRU ແລະ ໜ່ວຍງານສຸກເສີນດ້ານໄວຣັສ ທີ່ Marseille ປະເທດຝຣັ່ງ. ໃນໄລຍະປີ 2020 ໜ່ວຍງານໄວຣັສພວກເຮົາໄດ້ກວດຕົວຢ່າງ ຈຳນວນ 1,191 ຕົວຢ່າງຈາກຄົນເຈັບ ແລະ ຜູ້ທີ່ບໍ່ສະແດງອາການທີ່ມາເຂົ້າມາໃຊ້ບໍລິການໃນໂຮງໝໍມະໂຫສົດ, ໂຮງໝໍແຂວງຫຼວງນ້ຳທາ, ໂຮງໝໍແຂວງຊຽງຂວາງ ແລະ ໂຮງໝໍແຂວງສາລະວັນ. ຈາກການກວດຕົວທັງໝົດ, ພົບຜົນກວດທີ່ເປັນບວກທັງໝົດພຽງແຕ່ 3 ກໍລະນີ, ເຊິ່ງແມ່ນຕົວຢ່າງມາຈາກນະຄອນຫຼວງວຽງຈັນ, ພ້ອມນີ້ຕົວຢ່າງທີ່ເປັນບວກຍັງໄດ້ຮັບການກວດຢັ້ງຢືນຄືນຈາກສູນລະບາດວິທະຍາແຫ່ງຊາດ.

ໃນປີ 2020 ນີ້, ດຣ ໄຊຍະເພັດ ຣັດຕະນະວົງ ຮອງຫົວໜ້າພະແນກຈຸລິນຊີ ໄດ້ຍົກຍ້າຍໄປປະຈຳການທີ່ໂຮງໝໍແຂວງສະຫວັນນະເຂດ ຍ້ອນເງື່ອນໄຂທາງດ້ານຄອບຄົວ ການຍົກຍ້າຍຂອງເພິ່ນ ໄດ້ເຮັດໃຫ້ໜ່ວຍງານພວກເຮົາຂາດເພື່ອນຮ່ວມງານທີ່ດີໄປອີກ 1 ຄົນ. ດຣ ໄຊຍະເພັດ ໄດ້ປະກອບສ່ວນໃນວຽກງານການເຮັດການສຶກສາຄົ້ນຄວ້າ ແລະນຳພາທີມງານຄລີນິກໃນ LOMWRU ຕະຫຼອດໄລຍະ 10 ປີທີ່ໄດ້ເຮັດວຽກໃນໂຮງໝໍມະໂຫສົດ. ດຣ Céline Caillet, ຜູ້ປະສານງານຫຼັກຂອງໜ່ວຍງານຄຸນນະພາບຢາ ພ້ອມດ້ວຍຄອບຄົວ ກໍໄດ້ກັບຄືນໄປຍັງບ້ານເກີດ ທີ່ປະເທດຝຣັ່ງ ຫຼັງຈາກທີ່ໄດ້ໃຊ້ຊີວິດ ແລະ ເຮັດວຽກຢູ່ລາວເປັນໄລຍະເວລາ 5 ປີ ແລະ ໄດ້ໄປປະຈຳການທີ່ Oxford, ປະເທດອັງກິດ ເຊິ່ງໄດ້ຮັບການແຕ່ງຕັ້ງເປັນຮອງຫົວໜ້າໜ່ວຍງານຄຸນນະພາບຢາ ແລະ ຍັງໄດ້ສືບຕໍ່ເຮັດວຽກກັບ Professor Paul Newton. ດຣ Céline ຍັງຄົງຮັບຜິດຊອບຊີ້ນຳໜ່ວຍງານຄຸນນະພາບຢາຢູ່ວຽງຈັນເຊັ່ນເດີມໃນຮູບແບບທາງໄກ.

ນອກນັ້ນ ພວກເຮົາຍັງມີຄວາມປຶ້ມປິຕິຍິນດີທີ່ສຸດ ທີ່ ທ່ານ ສຈ. ປອ. ດຣ ມາຍຟອງ ມາຍຊາຍ, ຫົວໜ້າໜ່ວຍງານສຶກສາຄົ້ນຄວ້າ ແລະ ໜ່ວຍງານສົ່ງເສີມສຸຂະພາບຂອງ LOMWRU ທີ່ໄດ້ຮັບນາມມະຍົດສາດສະດາຈານພິເສດດ້ານພະຍາດເຂດຮ້ອນ ຈາກ ມະຫາວິທະຍາໄລ Oxford. ດຣ Matt Robinson ໄດ້ຮັບການແຕ່ງຕັ້ງເປັນອາຈານທາງດ້ານການສຶກສາຄົ້ນຄວ້າຂອງມະຫາວິທະຍາໄລ Oxford ພາຍຫຼັງທີ່ໄດ້ປະກອບສ່ວນໃນວຽກງານຄົ້ນຄວ້າຢ່າງໃຫຍ່ຫຼວງມາໄລຍະໜຶ່ງ.

ຜົນງານທາງດ້ານການສຶກສາຄົ້ນຄວ້າທີ່ພົ້ນເດັ່ນ

ໜ່ວຍງານພວກເຮົາ ໄດ້ເອົາໃຈໃສ່ຕໍ່ວຽກງານການຕ້ານຂອງເຊື້ອພະຍາດຕໍ່ຢາຕ້ານເຊື້ອ ແລະ ໄດ້ຮ່ວມງານກັບກົມປິ່ນປົວ ແລະ ຟື້ນຟູໜ້າທີ່ການ, ກະຊວງສາທາລະນະສຸກ ພ້ອມດ້ວຍບັນດາອາຈານແພດປິ່ນປົວ ເພື່ອສ້າງແບບຄູ່ມືການໃຊ້ຢາຕ້ານເຊື້ອຈຸລະຊີບແຫ່ງຊາດ ເຊິ່ງເລີ່ມທົດລອງນຳໃຊ້ໃນ 5 ໂຮງໝໍແຂວງ ແລະ 1 ໂຮງໝໍສູນກາງ. ພວກເຮົາຍັງໄດ້ສືບຕໍ່ເຮັດການສຶກສາຄົ້ນຄວ້າດ້ານລະບາດວິທະຍາ ແລະ ການຄຸ້ມຄອງອາການໄຂ້ທີ່ບໍ່ແມ່ນໄຂ້ມາລາເຣຍ ແລະ ໄດ້ເລີ່ມໂຄງການໃໝ່ທີ່ແຂວງສາລະວັນ ແລະ ສະຫວັນນະເຂດ ໂດຍມີຈຸດປະສົງເພື່ອຊອກຫາ biomarkers ຂອງການຊຶມເຊື້ອເລືອດໃນເດັກນ້ອຍ. ນັກຄົ້ນຄວ້າຈາກ LOMWRU ແລະ ຈາກຜູ້ຮ່ວມງານອື່ນໆ ໄດ້ຕີພິມບົດຄວາມທາງວິຊາການທັງໝົດ ຈຳນວນ 71 ສະບັບໃນປີ 2020.

ຜົນງານທາງດ້ານການເຝິກອົບຮົມທີ່ພົ້ນເດັ່ນ ແລະ ຕິດພັນກັບ LOMWRU

ດຣ ກຸແກ້ວ ພິມມະສອນ, ດຣ Risara Jaksuwan ແລະ ດຣ Audrey Rachlin ໄດ້ສຳເລັດການສຶກສາໃນລະດັບປະລິນຍາເອກ ແລະ Soo Kai Ter ແລະ Le Hong Dai ກໍໄດ້ສຳເລັດການສຶກສາໃນລະດັບປະລິນຍາໂທ. ນັກຄົ້ນຄວ້າ,

ໃນເດືອນມັງກອນ ປີ 2020, Prof Elizabeth Ashley (ຜູ້ທີ 4 ນັບຈາກດ້ານຂວາ), ດຣ ມະນີວັນ ວົງສຸວັດ (ຜູ້ທີ 2 ນັບຈາກດ້ານຂວາ), ດຣ ນ້ອຍກະເສີມສີ ສິດທິວົງ (ຜູ້ທີ 3 ນັບຈາກດ້ານຂວາ, ຫົວໜ້າຂະແໜງວິເຄາະວິທະຍາ, ສູນວິເຄາະ ແລະ ລະບາດວິທະຍາ, ກະຊວງສາທາລະນະສຸກ, ສປປ ລາວ) ແລະ Dr Risara Jaksuwan (ຜູ້ສຸດທ້າຍເບື້ອງຂວາ) ໄດ້ທຳການເຂົ້າຢ້ຽມຢາມຄະນະເຫັນການແພດ, ມະຫາວິທະຍາໄລຊຽງໃໝ່ (ນຳພາໂດຍ Dr Ratchada Cressey, ຜູ້ຊ່ວຍຄະນະບໍດີຝ່າຍວິໄຈຄົ້ນຄວ້າ ແລະ ພົວພັນຕ່າງປະເທດ (Research and International Relations), ຜູ້ທີ 4 ນັບຈາກດ້ານຊ້າຍ) ເພື່ອປຶກສາຫາລືກ່ຽວກັບການຈັດຕັ້ງຫລັກສູດເຝິກອົບຮົມແບບເລັ່ງລັດ ເປັນໄລຍະເວລາ 6 ເດືອນ ສຳລັບການປິ່ງມະຕິທາງດ້ານຈຸລິນຊີວິທະຍາ ໃຫ້ແກ່ພະນັກງານຫ້ອງວິເຄາະຈາກ ສປປ ລາວ.

ດຣ Weerawat Phuklia ແລະ ດຣ ວິລະຍຸດ ພິມົນສານຸຊິດ ໄດ້ຮັບທຶນ Wellcome Fellowships ເພື່ອເຮັດການສຶກສາຄົ້ນຄວ້າ. ດຣ Rebecca Inglis, ນັກສຶກສາປະລິນຍາເອກ ຈາກມະຫາວິທະຍາໄລ Oxford ໄດ້ເຮັດການສຶກສາກ່ຽວກັບການເບິ່ງແຍງຮັກສາຄົນເຈັບໜັກໃນ ສ.ປ.ປ ລາວ ເຊິ່ງເພິ່ນໄດ້ສຳເລັດການລົງເກັບກຳຂໍ້ມູນ ແລະໄດ້ຮັບການສະໜັບສະໜູນຈາກອົງການອະນາໄມໂລກໃນການຈັດເຝິກອົບຮົມເພື່ອເປັນຮຸບແບບປະຕິບັດໃນທົ່ວປະເທດ.

ແຜນໃນອະນາຄົດ

ໃນປີ 2020, ທາງ Wellcome Trust ໄດ້ສົ່ງຄະນະກຳມະການດ້ານການຄົ້ນຄວ້າໄປບາງກອກ ແລະ ແມ່ສອດ ປະເທດໄທ ເພື່ອຂະຫຍາຍເຄືອຂ່າຍການເຮັດການສຶກສາຄົ້ນຄວ້າ ແລະ ແບບແຜນໃນອະນາຄົດ ແລະ ເພື່ອເປັນບ່ອນອີງໃນການຊອກຫາທຶນເພື່ອການສຶກສາຄົ້ນຄວ້າໃນອະນາຄົດ. ພວກເຮົາມີຄວາມຍິນດີທີ່ຈະແຈ້ງໃຫ້ຮັບຮູ້ວ່າ ພວກເຮົາໄດ້ຮັບການສະໜັບສະໜູນທຶນການສຶກສາຄົ້ນຄວ້າຈົນເຖິງປີ 2025. ໃນປີ 2020ນີ້ ເປັນປີທີ່ຄົບຮອບ 65 ປີ ສາຍສຳພັນທາງການທູດລະຫວ່າງປະເທດອັງກິດ ແລະ ສ.ປ.ປ ລາວ. ສະຖານທູດອັງກິດປະຈຳລາວ ໄດ້ເປັນເຈົ້າພາບຮັບຕ້ອນໂອກາດພິເສດນີ້ ໃນວັນທີ 25 ພະຈິກ 2020. ການກໍ່ສ້າງໂຮງໝໍມະໂຫສົດໃໝ່ ທີ່ໄດ້ຮັບການຊ່ວຍເຫຼືອຈາກລັດຖະບານຈີນ ໄດ້ມີຄວາມຊັກຊ້າຍ້ອນບັນຫາການແຜ່ລະບາດຂອງເຊື້ອພະຍາດ COVID-19 ເຊິ່ງພວກເຮົາຫວັງວ່າຈະສາມາດຍົກຍ້າຍເຂົ້າຕຶກໃໝ່ໄດ້ພາຍໃນທ້າຍປີ 2021. ພວກເຮົາຍັງຂໍສະແດງຄວາມຂອບໃຈ ດຣ ພິສິດ ພຸດສະຫວັດ ແລະ ບັນດາພະນັກງານໃນໂຮງໝໍມະໂຫສົດທີ່ໄດ້ໃຫ້ການສະໜັບສະໜູນພວກເຮົາຕະຫຼອດປີ 2020.

Professor Elizabeth A Ashley
ຜູ້ອຳນວຍການ LOMWRU

MESSAGE FROM THE DIRECTOR

Message from Professor Elizabeth Ashley

In Laos, as in the rest of the world, most of 2020 was overshadowed by the COVID-19 pandemic. Laos managed to avoid sustained community transmission of SARS-CoV-2 throughout 2020 and the government introduced a screening and quarantine system early on to safeguard the health system. After a short lockdown in April 2020, work in the country gradually returned to something approaching normal, although certain sectors of the economy have been very badly affected by the loss of tourism. Most of the testing nationally is being done by the National Centre for Laboratory Epidemiology (NCLE), with provincial hospital laboratories also screening workers crossing the border to return to Laos. Mahosot Hospital is also supporting national testing for SARS-CoV-2. The virology diagnostic service in Mahosot Hospital is supported by LOMWRU and the Unit for Emerging Viruses in Marseille, France. In 2020 the laboratory ran 1191 tests from patients and asymptomatic individuals presenting to Mahosot Hospital, Luang Namtha, Xieng Khuang and Salavan Provincial Hospitals. Only three specimens from Vientiane were positive, which were specimens sent for repeat testing from NCLE early on in the pandemic.

We were very sorry to see some colleagues leave Vientiane in 2020. Dr Sayaphet Rattanavong, the Deputy Head of the Microbiology Laboratory, moved to a post in Savannakhet Provincial Hospital to be closer to his family. While working at Mahosot Hospital for 10 years, Dr Sayaphet made a massive contribution to LOMWRU collaborative research as well as leading the clinical team and is greatly missed. Dr Céline Caillet, Medicine Quality Scientific Group Coordinator, her partner Martial and son Raphaël had to rush to catch one of the last flights out of Vientiane back to France after 5 years in Laos. They have moved to Oxford in the UK where Céline is the Deputy Head of the Medicine Quality Research Group, working with Professor Paul Newton. Céline continues to supervise MQ team members in the Vientiane office remotely.

There were still a few occasions worth celebrating in 2020. Professor Mayfong Mayxay, Head of LOMWRU Field Research and Engagement was made a Visiting Professor of Tropical Medicine by the University of Oxford. The title of University Research Lecturer was conferred on Dr Matt Robinson, following a Recognition of Distinction exercise by Oxford.

RESEARCH HIGHLIGHTS

We increased our work on antimicrobial resistance and worked with the Curative Department of the Ministry of Health and several senior Lao clinicians to develop national antimicrobial prescribing guidelines which are being pilot tested in six provincial or central hospitals. We also continued to study the epidemiology and management of non-malaria febrile illnesses and started a new project in Salavan and Savannakhet which aims to discover biomarkers which predict sepsis in children. LOMWRU researchers and collaborators published 71 papers in 2020.

TRAINING HIGHLIGHTS

Dr Koukeo Phommasone, Dr Risara Jaksuwan and Dr Audrey Rachlin graduated with PhDs in 2020 and Mr Soo Kai Ter and Mr Le Hong Dai were awarded Master's degrees. Two scientists, Dr Weerawat Phuklia and Dr Vilayouth Phimolsarnnousith, were awarded prestigious Wellcome Fellowships to

In Jan 2020, Prof Elizabeth Ashley (*4th from right*), Dr Manivanh Vongsouvath (*2nd right*), Dr Noikaseumsy Sithivong (*3rd right*), Chief of Laboratory Section, National Center for Laboratory and Epidemiology, Ministry of Health, Lao PDR) and Dr Risara Jaksuwan (*far right*) visited the Faculty of Associated Medical Sciences, Chiang Mai University (led by Dr Ratchada Cressey, Assistant Dean for Research and International Relations, *4th from left*) to discuss setting up a six-month intensive training course in diagnostic microbiology for Lao lab technicians.

continue their research. Dr Rebecca Inglis, a DPhil student from Oxford working on a critical care project in Laos, finished her field work and was seconded to WHO where she worked to develop a training course which has been rolled out across the country.

LOOKING AHEAD

In 2020 the Wellcome Trust sent a committee of scientists to Bangkok and Mae Sot to assess the research of the network and our future plans and to make a recommendation about future funding. I'm pleased to say they renewed our funding until 2025. 2020 marked the 65th Anniversary of UK and Laos diplomatic friendship. The British Embassy hosted a reception to mark this special occasion on Wednesday 25th November. Completing building of the new Mahosot Hospital, funded by the Chinese government, has been delayed by the pandemic so we expect to move at the end of 2021. We remain very grateful to Dr Phisith Phouthsavath and all staff at Mahosot Hospital for their continued support throughout 2020.

Best wishes to all our colleagues and collaborators,

Professor Elizabeth A Ashley

Professor Mayfong Mayxay made a Visiting Professor of Oxford University

ຮູບພາບ ສຈ ດຣ ມາຍຟອງ ມາຍຊາຍ ໃນພະແນກຈຸລິນຊີວິທະຍາ ໂຮງໝໍມະໂຫສົດ ຮູບພາບໂດຍ Gerhard Jørén.
Professor Mayfong Mayxay, shown in the Microbiology Laboratory, Mahosot Hospital.
Photographer: Gerhard Jørén.

ທ່ານ ປອ. ດຣ ມາຍຟອງ ມາຍຊາຍ ໄດ້ຮັບນາມມະຍົດ ສາດສະດາຈານພິເສດ ສາຂາພະຍາດເຂດຮ້ອນຈາກມະຫາວິທະຍາໄລອ໋ອກຟອດ, ປະເທດອັງກິດ

ໃນວັນຈັນ, ວັນທີ 27 ເດືອນ ກໍລະກົດ ປີ 2020 ໄດ້ມີພິທີສະເຫຼີມສະຫຼອງອັນສຳຄັນເພື່ອປະກາດນາມມະຍົດທາງດ້ານວິຊາການໃຫ້ແກ່ທ່ານສາດສະດາຈານ ມາຍຟອງ ມາຍຊາຍ, ຮອງອະທິການບໍດີ, ມະຫາວິທະຍາໄລວິທະຍາສາດສຸຂະພາບ ເຊິ່ງທ່ານໄດ້ຮັບນາມມະຍົດສາດສະດາຈານພິເສດສາຂາການແພດເຂດຮ້ອນ ຈາກຄະນະແພດສາດນາບຟິວ (Nuffield Department of Medicine), ມະຫາວິທະຍາໄລອ໋ອກຟອດ ປະເທດອັງກິດ. ໃນພິທີ ພະນະທ່ານ ຮອງສາດສະດາຈານ ບຸນກອງ ສີຫາວົງ, ລັດຖະມົນຕີກະຊວງສາທາລະນະສຸກ ແລະ ພະນະທ່ານ ຈອນ ເພຍສັນ, ເອກອັກຄະລັດຖະທູດ ປະເທດອັງກິດປະຈຳ ສປປ ລາວ ກໍໃຫ້ກຽດເຂົ້າຮ່ວມ. ພາຍໃນພິທີ, ທ່ານສາດສະດາຈານ ມາຍຟອງ ມາຍຊາຍ ໄດ້ນຳສະເໜີວຽກງານການເຄື່ອນໄຫວອັນພົ້ນເດັ່ນໃນໄລຍະຜ່ານມາ, ເຊິ່ງລວມເຖິງປະສົບການຊີວິດໃນໄວເດັກ ທີ່ເລີ່ມຕົ້ນຈາກການເປັນເດັກນ້ອຍຍູ້ລໍ້ຂາຍຜັກເພື່ອຫາລາຍໄດ້ຊ່ວຍຄອບຄົວ.

ຕະຫຼອດໄລຍະເວລາຫຼາຍກວ່າ 20 ປີທີ່ຜ່ານມາຈົນເຖິງປະຈຸບັນ ທ່ານສາດສະດາຈານ ມາຍຟອງ ມາຍຊາຍ ເປັນຜູ້ນຳໜ້າທາງວິຊາການດ້ານສາທາລະນະສຸກໃນລາວ ແລະ ເປັນໜຶ່ງໃນຜູ້ກໍ່ຕັ້ງໂຄງການຮ່ວມມືຄົ້ນຄວ້າດ້ານພະຍາດເຂດຮ້ອນລະຫວ່າງໂຮງໝໍມະໂຫສົດ-ແອວຄຳຕັ໊ສ, ປະເທດອັງກິດ. ປັດຄົ້ນຄ້ວາຂອງ ທ່ານສາດສະດາຈານ ມາຍຟອງ ມາຍຊາຍ

ຮູບພາບ ພິທີມອບ-ຮັບນາມມະຍົດ ວິທະຍາຖານະທາງວິຊາການ ສາດສະດາຈານພິເສດ “Visiting Professor” ຈາກ ມະຫາວິທະຍາໄລ ອ໋ອກຟອດ ເຊິ່ງໄດ້ຈັດຂຶ້ນທີ່ ມະຫາວິທະຍາໄລ ວິທະຍາສາດ ສຸຂະພາບ

A ceremony to mark Professor Mayfong’s appointment as a Visiting Professor to Oxford University was held at the University of Health Sciences.

ຫຼາຍກວ່າ 180 ປົດໄດ້ຮັບການຕີພິມເຜີຍແຜ່ໃນວາລະສານການແພດສາກົນທີ່ມີຊື່ສຽງ. ຜົນງານການຄົ້ນຄ້ວາທຳອິດຂອງທ່ານ ແມ່ນໄດ້ສຶກສາກ່ຽວກັບພະຍາດໄຂ້ຍຸງ ຫລື ໄຂ້ມາລາເຣຍ ເຊິ່ງຜົນການຄົ້ນຄວ້າດັ່ງກ່າວໄດ້ຖືກນຳໃຊ້ເຂົ້າໃນການປັບປຸງແຜນນະໂຍບາຍແຫ່ງຊາດໃນການປິ່ນປົວໄຂ້ຍຸງ. ໃນອະນາຄົດ, ທ່ານໄດ້ວາງແຜນນະໂຍບາຍເພື່ອນຳເອົາວິທີການປະເມີນເຕັກໂນໂລຍີທາງດ້ານສາທາລະນະສຸກເຂົ້າມາໃນລາວ ພ້ອມນັ້ນ, ປະຈຸບັນທ່ານໄດ້ສ້າງໜ່ວຍງານຄົ້ນຄວ້າຫຼັກຖານດ້ານວິທະຍາສາດ ແລະ ນະໂຍບາຍທາງດ້ານສາທາລະນະສຸກ ທີ່ມະຫາວິທະຍາໄລວິທະຍາສາດສຸຂະພາບ ໂດຍໄດ້ຮັບທຶນສະໜັບສະໜູນຈາກກອງທຶນແວວຄຳຕັ໊ສ, ປະເທດອັງກິດ.

A special ceremony was held for Professor Mayfong Mayxay on Monday 27th July, 2020, at the University of Health Sciences where he is Vice-President, in honour of his appointment as a Visiting Professor of Tropical Medicine by the Nuffield Department of Medicine of the University of Oxford in the UK. Their Excellencies Associate Professor Dr Bounkong Syhavong, Minister of Health, and Mr John Pearson, British Ambassador to Laos, were in attendance to celebrate this important achievement. Professor Mayfong gave a moving lecture covering highlights of his career, including his humble beginnings as a cart-boy in Vientiane to help support his family.

Professor Mayfong was a founding member of LOMWRU more than 20 years ago and is now a leading academic in the Lao PDR with more than 180 publications in peer-reviewed journals. His early research was on malaria and led to changes in national treatment policy. He is aiming to introduce health technology assessment into Laos and recently created a Unit for Health Evidence and Policy in the University of Health Sciences, with funding from Wellcome.

RESEARCH HIGHLIGHTS

ຮູບພາບ ດຣ ວິລະດາ ຈັນສະມຸດ ນຳສະເໜີປຶ້ມຄູ່ມືການນຳໃຊ້ຢາຕ້ານເຊື້ອ ສຳລັບເດັກ (ປຶ້ມຫົວສີຂຽວ) ແລະ ສຳລັບຜູ້ໃຫຍ່ (ປຶ້ມຫົວສີຟ້າ)

ຜົນການຄົ້ນຄວ້າທີ່ພົ້ນເດັ່ນໃນປີຜ່ານມາ

ພວກເຮົາສືບຕໍ່ທຳການສຶກສາຄົ້ນຄວ້າຮ່ວມກັບໂຮງໝໍແຂວງຫຼາຍໆແຫ່ງໃນ ສ.ປ.ປ ລາວ ແລະ ອົງກອນຕ່າງໆ ໃນຫົວຂໍ້ການຕ້ານຕໍ່ຢາຕ້ານເຊື້ອຂອງເຊື້ອຈຸລະຊີບ ແລະ ລະບາດວິທະຍາຂອງໄຂ້ ໃນປີ 2020. ບາງເນື້ອໃນທີ່ພົ້ນເດັ່ນແມ່ນໄດ້ອະທິບາຍທາງດ້ານລຸ່ມນີ້. ທ່ານສາມາດເຂົ້າເບິ່ງຜົນການຄົ້ນຄວ້າທັງໝົດທີ່ LOMWRU ໄດ້ເຮັດຜ່ານມາ, ພ້ອມດ້ວຍບົດຄັດຫຍໍ້ ຢູ່ທີ່ຫົວຂໍ້ Publications (ການຕີພິມເຜີຍແຜ່) ໃນທ້າຍບົດລາຍງານສະບັບນີ້.

ການຕ້ານຕໍ່ຢາຕ້ານເຊື້ອຈຸລະຊີບ & ຄູ່ມືການນຳໃຊ້ຢາຕ້ານເຊື້ອຈຸລະຊີບແຫ່ງຊາດ

ຄວາມຕື່ນຕົວຕໍ່ບັນຫາການຕ້ານຕໍ່ຢາຕ້ານເຊື້ອຈຸລະຊີບຢູ່ໃນ ສ.ປ.ປ ລາວ ໄດ້ນັບມື້ນັບເພີ່ມຂຶ້ນ ໄປຄຽງຄູ່ກັບອັດຕາການເພີ່ມຂຶ້ນຂອງເຊື້ອ Escherichia coli ທີ່ຜະລິດອັ້ງຊີມ extended spectrum beta-lactamase (ESBL) ແລະ ເຊື້ອ Escherichia coli ທີ່ຕ້ານຕໍ່ຢາຕ້ານເຊື້ອຫລາຍຊະນິດ (multi-drug resistant). ໃນປີ 2020, ພວກເຮົາໄດ້ເຮັດວຽກຮ່ວມກັບກົມປິ່ນປົວ ແລະ ຝຶ້ນຟູໜ້າທີ່ການ, ກະຊວງສາທາລະນະສຸກ ແລະ ທ່ານໝໍຫຼາຍໆທ່ານທີ່ມີປະສົບການສູງ ຢູ່ ສ.ປ.ປ ລາວ, ໃນການຮ່າງປຶ້ມຄູ່ມືການນຳໃຊ້ຢາຕ້ານເຊື້ອຈຸລະຊີບແຫ່ງຊາດ ສະບັບຜູ້ໃຫຍ່ ແລະ ສະບັບເດັກນ້ອຍ. ປຶ້ມຄູ່ມືທັງສອງສະບັບນີ້ ແມ່ນໄດ້ຖືການຳໃຊ້ໃນເບື້ອງຕົ້ນ ຢູ່ 6 ໂຮງໝໍ ໃນ ສ.ປ.ປ ລາວ, ແລະ ໄດ້ທຳການເຜີຍແຜ່ເພື່ອນຳໃຊ້ໂດຍ ດຣ ວິລະດາ ຈັນສະມຸດ (ສະແດງທາງດ້ານເທິງ) ເຊິ່ງເປັນນັກຄົ້ນຄວ້າປະລິນຍາເອກ ທີ່ໄດ້ຮັບທຶນ Wellcome International Training Fellow. ດຣ ວິລະດາ ຈັນສະມຸດ ຈະໄດ້ທຳການປະເມີນການນຳໃຊ້ຢາຕ້ານເຊື້ອຂອງທ່ານໝໍວ່າ ສອດຄ່ອງກັບຄູ່ມືການນຳໃຊ້ຢາຕ້ານເຊື້ອທີ່ໄດ້ມີການແຈກຢາຍໃຫ້ ຫຼືບໍ່, ດ້ວຍວິທີການເກັບກຳຂໍ້ມູນການນຳໃຊ້ຢາຕ້ານເຊື້ອຂອງທ່ານໝໍຢ່າງເປັນໄລຍະ ຢ່າງສະໝ່ຳສະເໝີ. ພ້ອມນີ້, ດຣ ວິລະດາ ຈັນສະມຸດ ຍັງໄດ້ເຮັດວຽກຮ່ວມກັບ Olivier Celhay ເຊິ່ງເປັນຜູ້ທີ່ມີຄວາມຊ່ຽວຊານດ້ານຂໍ້ມູນ, ເພື່ອສ້າງຖານຂໍ້ມູນຂອງການຕ້ານຕໍ່ຢາຕ້ານເຊື້ອຈຸລະຊີບ ແລະ ການນຳໃຊ້ຢາຕ້ານເຊື້ອຈຸລະຊີບເພື່ອໃຫ້ທຸກຄົນສາມາດເຂົ້າເຖິງຂໍ້ມູນ ໃນຮູບແບບທີ່ເຂົ້າໃຈໄດ້ງ່າຍ.

ລະບາດວິທະຍາ ແລະ ການຄຸ້ມຄອງອາການໄຂ້ ແລະ ຕົວບົ່ງຊີ້ທາງຊີວະພາບໃໝ່ສຳຫຼັບພາວະຕິດເຊື້ອໃນກະແສເລືອດ.

ວັນທີ 31 ຕຸລາ ປີ 2020 ທີ່ຜ່ານມາ ເຮົາສຳເລັດການສຶກສາໃນຄົນເຈັບ ຈຳນວນ 1973 ຄົນ ທີ່ໂຮງໝໍແຂວງວຽງຈັນ ເພື່ອຫາສາເຫດຂອງໄຂ້ທີ່ມີພະຍາດປົນຊ້ອນຕ່າງກັນຫຼາຍສະຖານທີ່, FIEBRE (Febrile Illness Evaluation in a Broad Range of Endemicities), ໂດຍໄດ້ຮັບການສະໜັບສະໜູນຈາກ ມະຫາວິທະຍາໄລ London School of Hygiene & Tropical Medicine, ລອນດອນ, ປະເທດອັງກິດ. ການສຶກສາ FIEBRE ມີເປົ້າໝາຍເພື່ອຊອກຫາສາເຫດຫຼັກຂອງອາການໄຂ້ ໃນປະເທດເຂດ ຊາຮາຣາ ອາຟຣິກາກາງ ແລະ ອາຊີຕາເວັນອອກສຽງໃຕ້. ການສຶກສານີ້ ຈະໄດ້ຮັບຜົນພາຍໃນປີ 2021 ນີ້. ລະຫວ່າງ ວັນທີ 10 ຕຸລາ ຫາ 14 ກຸມພາ 2020, ເຮົາໄດ້ເປັນເຈົ້າພາບໃນການຈັດກອງປະຊຸມຜູ້ດຳເນີນສຶກສາໂດຍມີຜູ້ເຂົ້າຮ່ວມ ມາຈາກສະຖານທີ່ເຮັດການສຶກສາອື່ນ ເຊັ່ນ ປະເທດໂມແຊມບິກ, ມາລາວີ ແລະ ຊິມບັບເວ.

ຮູບພາບ ບັນດາຜູ້ຈັດຕັ້ງປະຕິບັດການຄົ້ນຄວ້າທີ່ໄດ້ຮ່ວມໂຕກັນຕໍ່ໜ້າໂຮງໝໍແຂວງວຽງຈັນ. ການຢ້ຽມຢາມຄັ້ງນີ້ ເປັນສ່ວນໜຶ່ງໃນກອງປະຊຸມຂອງບັນດາຜູ້ຈັດຕັ້ງປະຕິບັດການຄົ້ນຄວ້າ ແລະ ໄດ້ຮັບກຽດເຂົ້າຮ່ວມຈາກຫຼາຍປະເທດທີ່ເຮັດການຄົ້ນຄວ້າເຊັ່ນ ປະເທດ Malawi, Mozambique, Zimbabwe, ນອກນັ້ນ ຍັງມີທີມງານການເປັນຜູ້ນຳ ຈາກ LSHTM.

Hopkins H, Bassat Q, Chandler CI, et al; FIEBRE Consortium. Febrile Illness Evaluation in a Broad Range of Endemicities (FIEBRE): protocol for a multisite prospective observational study of the causes of fever in Africa and Asia. *BMJ Open* 2020; 10(7): e035632. Published online: 21 July 2020. doi: 10.1136/bmjopen-2019-035632.

ໃນເດືອນ ກັນຍາ ປີ 2020, ພວກເຮົາໄດ້ເລີ່ມຮັບຄົນເຈັບເຂົ້າຮ່ວມການສຶກສາ Spot Sepsis ທີ່ໂຮງໝໍແຂວງສາລະວັນ. ການສຶກສາໃນຫຼາຍສະຖານທີ່ນີ້ ໄດ້ຮັບການສະໜັບສະໜູນໂດຍ ການແພດບໍ່ມີພົມແດນ Médecins Sans Frontières ແລະ ກອງທຶນ Wellcome (ຜູ້ຮ່ວມດຳເນີນການສຶກສາ Sakib Burza ແລະ Yoel Lubell) ໂດຍມີຈຸດປະສົງເພື່ອສຶກສາ ກຸ່ມຄົນເຈັບເດັກນ້ອຍ ຈຳນວນ 4,900 ຄົນ ແລະ ເພື່ອຜັດທະນາຂັ້ນຕອນວິທີ ປະເມີນຄວາມສ່ຽງ, ສົມທົບກັນການວັດແທກຕົວຊີ້ວັດທາງຊີວະພາບ ແລະ ອາການສະແດງຂອງຄົນເຈັບທີ່ຈຸດກວດຄົນເຈັບ, ໃນເດັກອາຍຸ ລະຫວ່າງ 1 ເດືອນ ຫາ 5 ປີ ທີ່ມີອາການໄຂ້ກະທັນຫັນ, ໃນສະພາບແວດລ້ອມທີ່ມີຂໍ້ຈຳກັດ. ສະພາບການລະບາດຂອງພະຍາດ COVID-19, ໄດ້ເຮັດໃຫ້ໂຄງການມີຄວາມຊັກຊ້າອອກໄປ, ເຊິ່ງຕາມແຜນແມ່ນຈະດຳເນີນການສຶກສາ ທີ່ ສ.ປ.ປ ລາວ (ແຂວງ ສາລະວັນ ແລະ ສະຫວັນນະເຂດ), ເຊັ່ນດຽວກັນກັບທີ່ ປະເທດ ກຳປູເຈຍ, ອິນໂດເນເຊຍ, ຟີລິບປິນ, ຫວຽດນາມ ແລະ ບັງກລາເທດ.

ການເຝົ້າລະວັງແບບງ່າຍດາຍ ຕໍ່ເຊື້ອຈຸລະໂລກທີ່ມີສາເຫດມາຈາກແມງໄມ້ຕີນຂໍ (Arboviruses) ໃນເຂດຊົນນະບົດ

ໃນປີ 2020, ດຣ ມະນີວັນ ວົງສຸວັດ ໄດ້ເຜີຍແຜ່ຂໍ້ມູນເອກະສານການປະເມີນສັກກະຍາພາບໃນການນຳໃຊ້ຊຸດກວດບົ່ງມະຕິແບບໄວຂອງພະຍາດໄຂ້ເລືອດອອກ (dengue RDT) ເພື່ອໃຊ້ເຂົ້າໃນການເຝົ້າລະວັງພະຍາດໄຂ້ເລືອດອອກ (Dengue), ພະຍາດໄຂ້ຊິກ້າ (Zika) ແລະ ພະຍາດໄຂ້ປວດຂໍ້ກະດູກ (Chikungunya). ການສຶກສາຄັ້ງນີ້ ແມ່ນໃຊ້ຕົວຢ່າງເລືອດທີ່ມີເຊື້ອຈຸລະໂລກທັງສາມຊະນິດທີ່ຖືກເກັບບັນຈຸໄວ້ໃນຊຸດກວດ dengue RDT. ຂໍ້ຈຳກັດຂອງການກວດຫາພະຍາດCHIKVແມ່ນຕ່ຳກວ່າ2ລ໋ອກໂຟ(logfold)ແລະຕ່ຳກວ່າ1ລ໋ອກໂຟ(logfold)ໃນພະຍາດZIKVເມື່ອສົມທຽບຈາກການສະກັດເອົາຈາກຕົວຢ່າງໂດຍກົງ. ສຳລັບການເກັບກຳຂໍ້ມູນຄວາມສະຖຽນຂອງອຸນຫະພູມ, ຕົວຢ່າງຂອງ DENV ໄດ້ຖືກກະກຽມ ແລະ ເກັບໄວ້ໃນຊຸດກວດ (dengue RDT), ແລະ ເກັບຮັກສາໄວ້ເປັນເວລາຫຼາຍກວ່າ 2 ເດືອນ

ຢູ່ທີ່ອຸນຫະພູມ -80°C, 4°C, ຫຼື 35°C ກ່ອນທີ່ຈະມີການທົດສອບ. ຊຸດກວດທີ່ບັນຈຸຕົວຢ່າງ ແລະ ເກັບໄວ້ 2 ເດືອນ ທີ່ອຸນຫະພູມ 35°C ແມ່ນບໍ່ໄດ້ສົ່ງຜົນເສຍຫາຍຫຼາຍໃນການກວດຊອກຫາ RNA ໂດຍໃຊ້ເທັກນິກ RT-qPCR, ພົບພຽງ ແຕ່ການເສື່ອມໂຊມຂອງຊຸດກວດເລັກນ້ອຍ. ການຄົ້ນຄວ້າຄັ້ງນີ້ສະແດງໃຫ້ເຫັນວ່າການນຳໃຊ້ຊຸດກວດບົ່ງມະຕິແບບ ໄວຂອງພະຍາດໄຂ້ເລືອດອອກ (dengue RDT) ແມ່ນມີຄວາມຈຳເປັນ ໃນການເຝົ້າລະວັງພະຍາດ DENV/CHIKV/ ZIKV ຢູ່ຂົງເຂດທີ່ບໍ່ສາມາດເຂົ້າເຖິງການກວດທາງຫ້ອງວິເຄາະ.

Vongsouvath M, Bharucha T, Seephonelee M, de Lamballerie X, Newton PN, Dubot-Pérès A. Harnessing Dengue Rapid Diagnostic Tests for the Combined Surveillance of Dengue, Zika, and Chikungunya Viruses in Laos. *Am J Trop Med Hyg* 2020; 102(6): 1244-8. Published online: 09 March 2020. doi: 10.4269/ajtmh.19-0881.

ການຕິດຕາມເກັບກຳຂໍ້ມູນກ່ຽວກັບຜົນກະທົບຕໍ່ເນື່ອງໄລຍະຍາວ ໃນຄົນເຈັບທີ່ຕິດເຊື້ອ ພະຍາດໄຂ້ສະໝອງອັກເສບຍີ່ປຸ່ນ (Japanese Encephalitis)

ພວກເຮົາໄດ້ເຮັດການຕິດຕາມຍ້ອນຫຼັງຄົນເຈັບທີ່ຕິດເຊື້ອພະຍາດໄຂ້ສະໝອງອັກເສບຍີ່ປຸ່ນ (JEV) ຈຳນວນ 123 ກໍລະນີ (ເດັກນ້ອຍອາຍຸຕ່ຳກວ່າ 15 ປີ 70 ກໍລະນີ ແລະ ຜູ້ໃຫ່ຍອາຍຸຫຼາຍກວ່າ 15 ປີ 53 ກໍລະນີ) ທີ່ມານອນປິ່ນປົວຢູ່ ໂຮງໝໍ ມະໂຫສົດ, ນະຄອນຫຼວງວຽງຈັນ, ໃນລະຫວ່າງປີ 2003 ຫາ 2013. ການບົ່ງມະຕິ JEV ແມ່ນ ໂດຍການກວດຫາທາດ ພາຍຕ້ານຂອງເຊື້ອພະຍາດແບບສະເພາະເຈາະຈົງ (anti-JEV IgM) ໃນຕົວຢ່າງນ້ຳໄຂສັນຫຼັງ ແລະ/ຫຼື ການກວດຫາທາດ ພາຍຕ້ານອີກແບບໜຶ່ງທີ່ເອີ້ນວ່າ IgM seroconversion. ການປະເມີນຜົນກະທົບຕໍ່ເນື່ອງທາງດ້ານລະບົບປະສາດແມ່ນ ນຳໃຊ້ຄະແນນປະເມີນຈາກ Liverpool Outcome Score(LOS), ຄະແນນທັງໝົດ (total) (ສູງສຸດ = 75), ແລະ ຄະແນນສຸດທ້າຍ (final) (ສູງສຸດ = 5). ຄ່າເຄິ່ງກາງ (interquartile range (IQR)) ຂອງຄົນເຈັບແມ່ນ 12.0 ປີ (7.5-18.8 ປີ), ແລະ 57% ແມ່ນເພດຊາຍ. ຄ່າສະເລ່ຍໄລຍະເວລາຂອງການຕິດຕາມເກັບກຳຂໍ້ມູນຂອງຄົນເຈັບແມ່ນ 4.5 ປີ (3.2-7.3 ປີ). ຈາກຄົນເຈັບທັງໝົດ, 10/123 (8.1%) ເສຍຊີວິດໃນລະຫວ່າງນອນຮັບການປິ່ນປົວຢູ່ໂຮງໝໍ, ແລະ 13/123 (10.6%) ເສຍຊີວິດຫຼັງຈາກອອກໂຮງໝໍກັບບ້ານ. ປະເມີນອັດຕາການເສຍຊີວິດປະມານ 18.7% (23/123); (33 [26.8%] ບໍ່ສາມາດຕິດຕາມເກັບກຳຂໍ້ມູນໄດ້). ຄົນເຈັບທີ່ໄດ້ຮັບຜົນກະທົບຕໍ່ເນື່ອງທາງລະບົບ ປະສາດຈາກການຕິດຕາມຄັ້ງສຸດທ້າຍແມ່ນພົບ 61.2% (ຜູ້ໃຫ່ຍ 48.4% ແລະ ເດັກນ້ອຍ 69.4%, P = 0.135). ອັດຕາສ່ວນຂອງຄົນເຈັບທີ່ໄດ້ຮັບຜົນກະທົບເຮັດໃຫ້ເກີດມີຄວາມບົກຜ່ອງທາງດ້ານການເຄື່ອນເໜັງໃນການຕິດຕາມຄັ້ງ ສຸດທ້າຍແມ່ນພົບໃນເດັກຫຼາຍກວ່າຢ່າງຊັດເຈນເຖິງ (25%) ເມື່ອສົມທຽບກັບຜູ້ໃຫ່ຍ (6.5%), P = 0.042. ເຄິ່ງໜຶ່ງ ຂອງຄົນເຈັບທີ່ຍັງມີຊີວິດຢູ່ໃນຊ່ວງຂອງການຕິດຕາມຂໍ້ມູນຄັ້ງສຸດທ້າຍຈຳນວນ 67 ຄົນ ແລະ ການປະເມີນຂອງຄະແນນ ທັງໝົດ (total) ແລະ ຄະແນນສຸດທ້າຍ (final) ຂອງຄົນເຈັບທີ່ອອກໂຮງໝໍ ແລະ ຈາກຜູ້ທີ່ໄດ້ຖືກຕິດຕາມປະເມີນຄັ້ງ ສຸດທ້າຍ 22 ຄົນແມ່ນມີອາການດີຂຶ້ນ. ຄະແນນທັງໝົດ ແລະ ຄະແນນສຸດທ້າຍຂອງຄົນເຈັບທີ່ອອກໂຮງໝໍແມ່ນທັງຜູ້ ໃຫ່ຍ ແລະ ເດັກນ້ອຍແມ່ນບໍ່ມີຄວາມແຕກຕ່າງຢ່າງຊັດເຈນ, ແຕ່ຄະແນນທັງໝົດຂອງການຕິດຕາມຄັ້ງສຸດທ້າຍໃນຜູ້ ໃຫ່ຍ ແມ່ນສູງກວ່າເດັກນ້ອຍຢ່າງຊັດເຈນ (ຄ່າເຄິ່ງກາງ [IQR]: 74.5 [73-75] ຕໍ່ກັບ 73.0 [73-75], P = 0.019).

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ການປ່ຽນແປງທາງພູມຄຸ້ມກັນຂອງຮ່າງກາຍຕໍ່ການຕິດເຊື້ອພະຍາດ *RICKETTSIA TYPHI*

ການສຶກສາໄລຍະຍາວຄັ້ງກ່າວນີ້ ໄດ້ສຶກສາເຖິງການຕອບສະໜອງຂອງຮ່າງກາຍພ້ອມທັງການປິ່ນປົວພະຍາດ murine typhus ທີ່ບໍ່ມີອາການສິນ. ຄົນເຈັບຈຳນວນ 90 ຄົນໃນກຸ່ມຍ່ອຍທີ່ໄດ້ຮັບການຄັດເລືອກຈາກການທົດລອງແບບສຸ່ມເພື່ອ ສຶກສາປະສິດທິພາບໃນການປິ່ນປົວ ໂດຍນຳໃຊ້ສາມວິທີການປິ່ນປົວພະຍາດ murine typhus ທີ່ບໍ່ມີອາການສິນ ເຊິ່ງ ໄດ້ແກ່ (ໃຫ້ doxycycline 7 ມື້, ໃຫ້ doxycycline 3 ມື້ ຫຼື ໃຫ້ azithromycin 3 ມື້). ບັນດາຄົນເຈັບດັ່ງກ່າວແມ່ນ ໄດ້ຖືກຕິດຕາມຫຼັງຈາກໄດ້ຮັບການປິ່ນປົວໃນມື້ທີ 7, 14, 28, 90, 180 ແລະ 365, ແລະ ພ້ອມທັງໄດ້ກວດທາງເຊໂຣໂລ ຊີ (IFA) ຫາ IgM ແລະ IgG ຕໍ່ເຊື້ອ murine typhus ໃນແຕ່ລະເທື່ອຂອງຕິດຕາມ. ໃນຄົນເຈັບທັງໝົດ 90 ຄົນ, ລະດັບ ຄວາມເຂັ້ມຂຸ້ນຂອງທາດພາຍຕ້ານຂອງ R. typhi IgM ແລະ IgG ແມ່ນຢູ່ລະຫວ່າງ <400 ຫາ ≥3200. ຄ່າເຄິ່ງຊີວິດ ຂອງ R. typhi IgM ແມ່ນ 126 ມື້ (ຄ່າຂອງ interquartile ແມ່ນຢູ່ໃນລະຫວ່າງ 36-204 ມື້) ແລະ IgG ແມ່ນ 177 ມື້ (ຄ່າຂອງ interquartile ແມ່ນຢູ່ໃນລະຫວ່າງ 134-355ມື້). ຄ່າເຄິ່ງກາງຂອງຄົນເຈັບທີ່ມີລະດັບຄວາມເຂັ້ມຂຸ້ນຂອງ R. typhi IgM ແລະ IgG ແມ່ນມີຄວາມແຕກຕ່າງກັນຫຼາຍ ($p < 0.0001$) ແລະພ້ອມທັງການເກັບຕົວຢ່າງໃນແຕ່ລະເທື່ອ (ຄ່າລະຫວ່າງ $p<0.0001$ ຫາ $p=0.0411$). ການວິເຄາະຂໍ້ມູນໂດຍນຳໃຊ້ແບບຈຳລອງBayesianlatentclassmodel ເຫັນວ່າຄ່າກຳນົດຂອງການກວດທາງເຊໂຣໂລຊີ (IFA) ຂອງຄົນເຈັບທີ່ໄດ້ຮັບການປິ່ນປົວແມ່ນມີລະດັບຄວາມເຂັ້ມຂຸ້ນ ຂອງ IgM ແມ່ນ 1:800 ແລະ ສຳລັບ IgG ແມ່ນ 1:1600. ຂໍ້ມູນດັ່ງກ່າວນີ້ມີຄວາມສຳຄັນໃນການບົ່ງມະຕິການຕິດ ເຊື້ອພະຍາດ murine typhus ແບບກະທັນຫັນໃນປະເທດລາວ ໂດຍມີການກຳນົດຄ່າທີ່ເໝາະສົມ. ນອກຈາກນີ້, ການ ສຶກສານີ້ຍັງໄດ້ເນັ້ນໃຫ້ເຫັນເຖິງການຄົງຕົວຂອງທາດພາຍຕ້ານຕໍ່ພະຍາດ murine typhus ອີກດ້ວຍ.

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ໄຂ້ທໍລະພິດທີ່ຍັງສາມາດປິ່ນປົວຫາຍດີດ້ວຍຢາຕ້ານເຊື້ອຕົວເລືອກທຳອິດ (First-line anthibiotic therapy) ຢູ່ໃນ ສປປ ລາວ

ດັ່ງທີ່ໄດ້ມີການສຶນທະນາກ່ຽວກັບປະສິດທິພາບຂອງວັກຊີນປ້ອງກັນພະຍາດ Typhoid ເພື່ອສະເໜີໃຫ້ນຳເຂົ້າໃນໂຄງການ ສັກວັກຊີນປ້ອງກັນພະຍາດແຫ່ງຊາດລາວ, ພວກເຮົາໄດ້ເຮັດການສຶກສາໃນຈຳນວນຄົນເຈັບທີ່ເປັນພະຍາດ typhoid ຢູ່ໂຮງໝໍມະໂຫສົດ ໄລຍະ 18 ປີຜ່ານມາ. ມີຈຳນວນ 913 ຕົວຢ່າງທີ່ພົບເຊື້ອ S. Typhi ຈາກ 60,384 ຕົວຢ່າງທັງໝົດ ທີ່ໄດ້ປຸກເລືອດ. ຜົນທົດສອບຢາຕ້ານເຊື້ອທີ່ສາມາດໃຊ້ໄດ້ ສະແດງໃຫ້ເຫັນວ່າມັນຕ່າງຈາກຊ່ວງທີ່ມີການລະບາດໃນປີ 2004, ເຊື້ອພະຍາດ S. Typhi ຕ້ານຕໍ່ຢາຕ້ານເຊື້ອຫຼາຍຕົວແມ່ນພົບໜ້ອຍ (resistant to ampicillin, ciprofloxacin and nalidixic acid) ແລະ ມີການຕ້ານຕໍ່ຢາ fluoroquinolone ແມ່ນຕ່ຳກວ່າ 10%. ຈາກຜົນການສຶກສາທີ່ສອງ ທີ່ໄດ້ປະຕິບັດເພື່ອປະເມີນອັດຕາການຕິດເຊື້ອພະຍາດ S. Typhi and S. Paratyphi A ປະຈຳປີໃນນະຄອນຫຼວງພົບວ່າ typhoid ມີ 3.8 ກໍລະນີ ໃນຈຳນວນ 100,000 ຄົນ ແລະ paratyphoid ພົບ 1.4 ກໍລະນີ ໃນ 100,000 ຄົນ.

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ໄຂ້ມາລາເຣຍ

ພາຍຫຼັງທີ່ ເຊື້ອໄຂ້ຍຸງຊະນິດ P. falciparum ຕ້ານຕໍ່ຢາ artemisinin ແລະ ຢາປະສົມຂອງມັນ ຢູ່ບັນດາປະເທດທີ່ຢູ່ ເຂດລຸ່ມແມ່ນ້ຳຂອງ (Greater Mekong Subregion), ຈຶ່ງໄດ້ເຮັດການສຶກສາແບບທົດລອງ ໂດຍການໃຫ້ຢາປິ່ນປົວ ໄຂ້ມາລາເຣຍທົ່ວປ່ອງຊິນ ຢູ່ເມືອງນອງ ແຂວງສະຫວັນນະເຂດ ເຊິ່ງການສຶກສາໄດ້ສະແດງໃຫ້ເຫັນວ່າການໃຫ້ຢາ ທົ່ວປ່ອງຊິນສາມາດຫຼຸດອຸບັດການເປັນພະຍາດ ແລະ ອັດຕາຊຸກຊຸມຂອງເຊື້ອ P. falciparum. ໃນການວິເຄາະຂໍ້ ມູນຂັ້ນສອງ ເຊິ່ງ ດຣ. ກຸແກ້ວ ພົມມະສອນ ໄດ້ປະເມີນຜົນຂອງການໃຫ້ຢາທົ່ວປ່ອງຊິນ ຕໍ່ກັບເຊື້ອຊະນິດ P. vivax, ຈຳນວນຜູ້ເຂົ້າຮ່ວມທັງໝົດ 3,790 (86%) ຄົນທີ່ຢູ່ໃນບ້ານທີ່ໄດ້ຮັບການກິນຢາທົ່ວປ່ອງຊິນ ແມ່ນໄດ້ເຂົ້າຮ່ວມໃນການ ກິນຢາຢ່າງນ້ອຍໜຶ່ງຮອບ, ເຊິ່ງໃນຈຳນວນດັ່ງກ່າວ 2,520 (57%) ແມ່ນເຂົ້າຮ່ວມໃນການກິນຢາຄົບ 3 ຮອບ. ອັດຕາ ຊຸກຊຸມຂອງເຊື້ອຊະນິດ P. vivax ຫຼຸດລົງຈາກ 9.31% ເຖິງ 0.89% ຢູ່ເດືອນ ທີ 3 ແຕ່ ອັດຕາດັ່ງກ່າວໄດ້ກັບມາ ເພີ່ມຂຶ້ນຄືນເຖິງ 5.81% ກ່ອນເດືອນທີ່ 6. ການສຶກສານີ້ພົບວ່າ ບໍ່ມີຫຼັກຖານຢັ້ງຢືນວ່າ ການໃຫ້ຢາທົ່ວປ່ອງຊິນໂດຍ ການໃຫ້ແຕ່ຢາຂ້າແຕ່ເຊື້ອ schizonts ສາມາດຫຼຸດອັດຕາການຕິດເຊື້ອສະສົມ ຂອງເຊື້ອໄຂ້ຍຸງຊະນິດ P. vivax (95% ຊ່ວງຄວາມເຊື່ອໝັ້ນ [CI]. ການໃຫ້ຢາທົ່ວປ່ອງຊິ້ນ ໂດຍການໃຫ້ຢາຂ້າເຊື້ອ schizonts ແມ່ນມີຜົນໄລຍະຍາວຕໍ່ເຊື້ອ ໄຂ້ຍຸງຊະນິດ P. falciparum ແຕ່ມີຜົນໄລຍະສັ້ນຕໍ່ເຊື້ອໄຂ້ຍຸງຊະນິດ P. vivax. ການປິ່ນປົວແບບຖອນຮາກຖອນ ໂຄນ ດ້ວຍການຕື່ມຢາ 8-aminoquinoline ແມ່ນມີຄວາມຈຳເປັນ ເພື່ອກຳຈັດເຊື້ອໄຂ້ຍຸງຊະນິດ P. vivax ຢ່າງໄວ ວາ.

ການປະສົມຢາຕ້ານເຊື້ອມາລາເຣຍ ສາມຕົວຢາ (Triple antimalarial drug combinations ຫຼື TACTs), ໂດຍ ການປະສົມຢາຮ່ວມທີ່ມີປະຈຸບັນ (ACTs) ກັບຢາຮ່ວມຊະນິດທີສອງ ເຊິ່ງເປັນຢາທີ່ຖືກຂັບອອກຈາກຮ່າງກາຍຊ້າ, ໄດ້

ຖືກສະເໜີໃຫ້ເປັນຍຸດທະສາດໃນການຊະລໍການເກີດ ແລະ ການແຜ່ກະຈາຍເຊື້ອ Plasmodium falciparum ທີ່ຕ້ານຕໍ່ຢາ artemisinin ແລະ ຢາປະສົມຂອງມັນ. ສ.ປ.ປ ລາວ ກໍໄດ້ປະກອບສ່ວນເຂົ້າໃນການສຶກສາທົດລອງ ແບບສຸ່ມ-ເປີດ ທີ່ເຮັດຢູ່ຫຼາຍປະເທດ (NCT02453308), ເຊິ່ງການສຶກສາດັ່ງກ່າວໄດ້ເອົາຄົນເຈັບ ທີ່ເປັນໄຂ້ມາລາເຣຍ ຊະນິດ Plasmodium falciparum ທີ່ບໍ່ມີອາການສົມ ເຂົ້າໃນການສຶກສາ ແລະ ສຸ່ມຄົນເຈັບ ວ່າຈະໄດ້ຢາປິ່ນປົວແບບ ມາດຕະຖານ ຫຼື ຢາ TACT. ຢູ່ລາວ ແມ່ນສົມທຽບຢາ artemether-lumefantrine ກັບຢາ artemether-lumefantrine ຮ່ວມກັບ amodiaquine. ປະສິດທິພາບຂອງຢາ artemether-lumefantrine ຮ່ວມກັບ amodiaquine ຢູ່ມື້ທີ 42 ພາຍຫຼັງທີ່ມີການດັດປັບກັບຜົນກວດທາງດ້ານ PCR ແມ່ນ (98% [281 of 286; 95% CI 97 to 99]) ເຊິ່ງປະສິດທິຜົນແມ່ນຄ້າຍຄືການໃຫ້ຢາ artemether-lumefantrine (97% [279 of 289; 95% CI 94 to 98]; risk difference 2%, 95% CI -1 to 4; p=0.30). ຜູ້ເຂົ້າຮ່ວມສາມາດ ຮັບຢາ TACTs ໄດ້ເປັນຢ່າງດີ. Dihydroartemisinin-piperaquine ຮ່ວມກັບ mefloquine ແລະ artemether-lumefantrine ຮ່ວມກັບ amodiaquine TACTs ແມ່ນມີປະສິດທິພາບ ແລະ ເປັນການປິ່ນປົວ ເຊິ່ງຄົນເຈັບທີ່ເປັນໄຂ້ມາລາເຣຍຊະນິດ P. falciparum ແບບບໍ່ມີອາການສົມ ສາມາດຮັບຢາໄດ້, ລວມທັງເຂດທີ່ເຊື້ອຕ້ານຕໍ່ຢາ artemisinin ແລະ ACT.

Phommasone K, van Leth F, Peto TJ et al. Mass drug administrations with dihydroartemisinin-piperaquine and single low dose primaquine to eliminate Plasmodium falciparum have only a transient impact on *Plasmodium vivax*: Findings from randomised controlled trials. *PLoS One* 2020; 15(2): e0228190. Published online: 05 February 2020. doi: 10.1371/journal.pone.0228190.

van der Pluijm RW, Tripura R, Hoglund RM et al. Triple artemisinin-based combination therapies versus artemisinin-based combination therapies for uncomplicated *Plasmodium falciparum* malaria: a multicentre, open-label, randomised clinical trial. *Lancet* 2020; 395(10233): 1345-60. Published online: 11 March 2020. doi: 10.1016/s0140-6736(20)30552-3.

ການຮ່ວມມືເຮັດການຄົ້ນຄວ້າ

ພວກເຮົາກຳລັງຮ່ວມມືກັບອົງການຫຼັກຂອງພວກເຮົາ ກໍຄື ໜ່ວຍວິໄຈພະຍາດເຂດຮ້ອນມະຫິດົນ-ອ໊ອກຟອດ, ມະຫາວິທະຍາໄລມະຫິດົນ, ບາງກອກ, ປະເທດໄທ (Mahidol Oxford Tropical Medicine Research Unit; MORU) ໃນໂຄງການສຶກສາ ການຄາດຄະເນຄວາມຮຸນແຮງຂອງພະຍາດໃນເດັກນ້ອຍທີ່ມີໄຂ້ກະທັນຫັນໃນສະພາບທີ່ມີຂໍ້ຈຳກັດດ້ານຊັບພະຍາກອນ ຫຼື ເອີ້ນວ່າ Spot Sepsis ແລະ ໂຄງການສຶກສາກ່ຽວກັບພະຍາດໄຂ້ມາລາເຣຍ ສອງໂຄງການຄື: GenRe ແລະ ENDGAME, ໂດຍຮ່ວມມືກັບສູນໄຂ້ຍຸງ, ແມ່ນາຟາ ແລະ ແມງໄມ້ (Centre of Malariology, Parasitology and Entomology; CMPE).

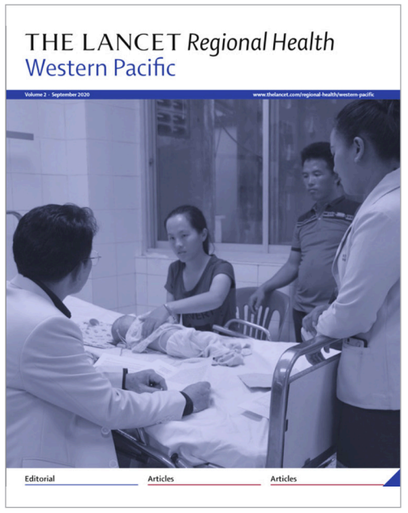
ການຮ່ວມມືໄລຍະຍາວຂອງພວກເຮົາ ຮ່ວມກັບ ສະຖາບັນຄົ້ນຄວ້າເພື່ອການພັດທະນາ (Institut de recherche pour le développement; IRD) ຍັງໄດ້ສືບຕໍ່ໃນໂຄງການສຶກສາໄວຣັສວິທະຍາທາງຄລີນິກ ຕະຫຼອດເຖິງການວິໄຈນິເວດວິທະຍາຂອງດິນ ແລະ Burkholderia pseudomallei.

ໂຄງການເຝົ້າລະວັງພະຍາດຕິດເຊື້ອ NAMRU-2 ໄດ້ຫັນປ່ຽນໄປເນັ້ນໃນການດຳເນີນການຕິດເຊື້ອໄວຣັສຂອງລະບົບຫາຍໃຈກະທັນຫັນ ໃນປີ 2020, ແຕ່ຍັງໄດ້ຮ່ວມມືກັບສາມໂຮງໝໍແຂວງຄື: ໂຮງໝໍແຂວງຊຽງຂວາງ, ຫຼວງນ້ຳທາ ແລະ ສາລະວັນ.

ການຮ່ວມມືທີ່ຍາວນານຂອງພວກເຮົາ ແລະ ທ່ານສາສະດາຈານ Fiona Russell ພ້ອມດ້ວຍທີມງານຈາກໜ່ວຍງານ Pacific Health Research Group ທີ່ສະຖາບັນຄົ້ນຄວ້າ Murdoch Children's Research Institute (MCRI), ເມືອງເມວເບີນ ປະເທດອົດສະຕາລີ ເຊິ່ງໄດ້ຮັບທຶນສະໜັບສະໜຸນງົບປະມານຈາກ Wellcome Impact of Vaccines on Antimicrobial Resistance. ຫົວຂໍ້ໂຄງການໄລຍະເວລາ 3 ປີຄື: 'ການສຶກສາລະບາດວິທະຍາ ແລະ ກົນໄກກ່ຽວກັບບົດບາດຂອງວັກແຊັງ pneumococcal conjugate vaccine ໃນການຕ້ານຕໍ່ຢາຕ້ານເຊື້ອຈຸລະຊີບ

ຮູບພາບ NAMRU-2 ແລະ LOMWRU ໄດ້ລົງຢ້ຽມຢາມໂຮງໝໍແຂວງສາລະວັນ. ຮູບພາບລຽນຈາກຊ້າຍຫາຂວາ: CDR Karen Corson, LCDR Jose Garcia, ສຈ ດຣ Elizabeth Ashley, ດຣ ກອງສິດ ອຸ່ນຈິດ (ຜູ້ອຳນວຍການໂຮງໝໍແຂວງສາລະວັນ), ດຣ ສົມໝາຍ ແກ້ວມະນີ (ຮອງອຳນວຍການໂຮງໝໍແຂວງສາລະວັນ), ດຣ ມະນີວັນ ວົງສຸວັດ, ດຣ ກຸແກ້ວ ພິມມະສອນ.

ໃນລາວ (Epidemiological and mechanistic studies on the role of pneumococcal conjugate vaccine in antimicrobial resistance in Laos)' ເຊິ່ງຈະຊ່ວຍສືບຕໍ່ດຳເນີນການສຶກສາ ການຕິດເຊື້ອໄວຣັສຂອງລະບົບຫາຍໃຈກະທັນຫັນໃນເດັກນ້ອຍທີ່ໂຮງໝໍມະໂຫສົດ.



ຮູບພາບ ການເຮັດວຽກຂອງທີມ ARIVI/Pneu-CAPTIVE ທີ່ໄດ້ຮັບການຕີພິມຂຶ້ນປົກວາລະສານ The Lancet Regional Health Western Pacific ປະຈຳເດືອນ ກັນຍາ 2020.

ການຮ່ວມມືທີ່ຜ່ານມາໄວໆນີ້ ໄດ້ສະແດງໃຫ້ເຫັນວ່າການນຳໃຊ້ a novel test-negative approach ສຳລັບ 13-valent pneumococcal conjugate vaccine (PCV13) ມີປະສິດທິພາບໃນການປ້ອງກັນພະຍາດອັກເສບປອດທີ່ຂາດອົກຊີໃນເດັກໃນລາວ ແລະ ໄດ້ແນະນຳວ່າຄວນໃຫ້ຄວາມສຳຄັນຂອງວັກແຊັງໃນໂຄງການສັກຢາກັນພະຍາດແຫ່ງຊາດໃນອາຊີ

Weaver R, Nguyen CD, Chan J, Vilivong K, Lai JYR, Lim R, Satzke C, Vongsakid M, Newton PN, Mulholland K, Gray A, Dubot-Pérès A, Dance DAB, Russell FM. The effectiveness of the 13-valent pneumococcal conjugate vaccine against hypoxic pneumonia in children in Lao People's Democratic Republic: An observational hospital-based test-negative study. *Lancet Regional Health - Western Pacific* 2020; 2: 100014. Published online: 06 September 2020. doi: 10.1016/j.lanwpc.2020.100014.

RESEARCH HIGHLIGHTS

Dr Vilada Chansamouth holding copies of the Lao National Paediatric (green) and Adult (blue) treatment guidelines.

We continued to study antimicrobial resistance and the epidemiology of febrile illness in 2020 and partnered with several provincial hospitals in Laos as well as external organisations. A few highlights are described below. The complete list of LOMWRU outputs with abstracts is found in the publications section of the report.

ANTIMICROBIAL DRUG RESISTANCE (AMR) & NEW NATIONAL PRESCRIBING GUIDELINES

Awareness of AMR is increasing in Laos, along with rising rates of extended spectrum beta-lactamase (ESBL) producing, multi-drug resistant *Escherichia coli*. In 2020, we worked with the Curative Department of the Ministry of Health to draft national adult and paediatric antimicrobial prescribing guidelines with senior clinicians in the country. These are being piloted in six hospitals, led by Dr Vilada Chansamouth (*shown above*), a Wellcome International Training Fellow. Dr Vilada will assess adherence to the guidelines in six hospitals by conducting regular point prevalence surveys of antimicrobial use (AMU). She has also worked with Olivier Celhay, a data scientist, to create dashboards for visualisation of AMR and AMU data.

FEBRILE ILLNESS EPIDEMIOLOGY & MANAGEMENT & NEW BIOMARKERS FOR SEPSIS

On 31 October 2020 we finished recruiting 1973 patients at Phonhong Hospital in Vientiane Province to the multicountry FIEBRE (Febrile Illness Evaluation in a Broad Range of Endemicities) study, sponsored by the London School of Hygiene & Tropical Medicine. FIEBRE aims to reveal leading causes of fever in sub-Saharan Africa and southeast Asia, with results available in 2021. Between 10-14 February 2020, we hosted the third FIEBRE Investigators' Meeting with participants from the other sites in Mozambique, Malawi and Zimbabwe.

Hopkins H, Bassat Q, Chandler CI, et al; FIEBRE Consortium. Febrile Illness Evaluation in a Broad Range of Endemicities (FIEBRE): protocol for a multisite prospective observational study of the causes of fever in Africa and Asia. *BMJ Open* 2020; 10(7): e035632. Published online: 21 July 2020. doi: 10.1136/bmjopen-2019-035632.

In September 2020, we started recruiting patients for the Spot Sepsis study in Salavan Provincial Hospital. This multicentre study sponsored by Médecins Sans Frontières and Wellcome (Co-PIs Sakib Burza and Yoel Lubell) aims to study 4,900 children and develop a risk prediction algorithm, combining measurements of host biomarkers and clinical features at the point-of-triage, for children aged between 1 month and 5 years with an acute febrile illness in resource-limited settings. COVID-19 led to significant delays in the project which is planned to take place in two sites in Laos (Salavan and Savannakhet), as well as Cambodia, Indonesia, The Philippines, Vietnam and Bangladesh.

FIEBRE investigators gathered in front of Vientiane Provincial Hospital. The visit was organised as part of an Investigators' meeting and was attended by participants from other study sites in Malawi, Mozambique, Zimbabwe, as well as the leadership team from LSHTM.

Chandna A, Aderie EM, Ahmad R, Arguni E, Ashley EA, Cope T, et al. Prediction of disease severity in young children presenting with acute febrile illness in resource-limited settings: a protocol for a prospective observational study. *BMJ Open* 2021; 11(1): e045826. Published online: 25 January 2021. doi: 10.1136/bmjopen-2020-045826.

SIMPLIFYING SURVEILLANCE FOR ARBOVIRUSES IN RURAL AREAS

In 2020 Dr Manivanh Vongsouvath published an evaluation of the potential for using used dengue rapid diagnostic tests for the combined surveillance of dengue, Zika and chikungunya. In this proof-of principle study, dengue RDTs were inoculated with spiked blood samples containing the three viruses. The limit of detection was two logfold lower for CHIKV and one logfold lower for ZIKV compared to direct extracts. For analysis of temperature stability, DENV dilutions were spotted on RDTs and stored for up to 2 months at -80°C, 4°C, or 35°C before testing. Storage of RDTs for 2 months at 35°C did not compromise detection of RNA by RT-qPCR; only minimal degradation was observed. This proof-of-principle study demonstrates the potential of using dengue RDTs for DENV/CHIKV/ZIKV combined surveillance in areas without access to laboratory facilities.

Vongsouvath M, Bharucha T, Seephonelee M, de Lamballerie X, Newton PN, Dubot-Pérès A. Harnessing Dengue Rapid Diagnostic Tests for the Combined Surveillance of Dengue, Zika, and Chikungunya Viruses in Laos. *Am J Trop Med Hyg* 2020; 102(6): 1244-8. Published online: 09 March 2020. doi: 10.4269/ajtmh.19-0881.

DOCUMENTING THE LONGER-TERM SEQUELAE OF JAPANESE ENCEPHALITIS INFECTION

We prospectively followed up 123 Japanese encephalitis virus (JEV)-infected patients (70 children ≤ 15 years and 53 adults ≥ 15 years) admitted at Mahosot Hospital, Vientiane, from 2003 to 2013. JEV infection was diagnosed by the detection of anti-JEV IgM in cerebrospinal fluid and/or IgM seroconversion. Neurological sequelae were assessed using the Liverpool Outcome Score (LOS), total (maximum score = 75), and final (maximum score = 5). The median (interquartile range [IQR])

age of the patients was 12.0 (7.5-18.8) years, and 57% were male. The median (IQR) duration of patients' follow-up was 4.5 (3.2-7.3) years. Of all patients, 10/123 (8.1%) died during hospitalization, and 13/123 (10.6%) died at home after discharge, giving a mortality of 18.7% (23/123); (33 [26.8%] patients were lost to follow-up). The frequency of neurological sequelae at the last follow-up was 61.2% (48.4% in adults and 69.4% in children, P = 0.135). The proportion of patients with severe and moderate functional impairment at the last follow-up was significantly higher in children (25%) than adults (6.5%), P = 0.042. Half of the patients who were still alive at the last follow-up (67) and for whom LOS data were available (22) had improvements in their total and final LOS between discharge and the last follow-up. The total and final LOS at discharge were not significantly different between children and adults, but total LOS at the last follow-up was significantly higher in adults than children (median [IQR]: 74.5 [73-75] versus 73.0 [73-75], P = 0.019).

Mayxay M, Douangdala P, Vilayhong C, Phommasone K, Chansamouth V, Vongsouvath M, Rattanavong S, Chang K, Sengvilaipaseuth O, Chanthongthip A, Thongpaseuth S, Newton PN, Dubot-Pérès A. Outcome of Japanese Encephalitis Virus (JEV) Infection in Pediatric and Adult Patients at Mahosot Hospital, Vientiane, Lao PDR. *Am J Trop Med Hyg* 2021; 104(2): 567-75. Published online: 21 December 2020. doi: 10.4269/ajtmh.20-0581.

TEMPORAL DYNAMICS OF HUMORAL IMMUNITY TO RICKETTSIA TYPHI INFECTION

This longitudinal study looked at the humoral response following treatment of uncomplicated murine typhus. A subset of 90 patients were selected from an ongoing open, randomized trial looking at the therapeutic efficacy of three treatment regimens for treatment of uncomplicated murine typhus (7 days of doxycycline, 3 days of doxycycline or 3 days of azithromycin). These patients were followed up after patient admission at days 7, 14, 28, 90, 180, and 365, and murine typhus IgM and IgG IFAs were carried out at each time point. For all 90 individuals, reciprocal *R. typhi* IgM and IgG antibody titres ranged from <400 to ≥3200. The median half-life of *R. typhi* IgM was 126 days (interquartile range 36-204 days) and IgG was 177 days (interquartile range 134-355 days). Median patient titres for *R. typhi* IgM and IgG were significantly different both overall ($p < 0.0001$) and also at each temporal sample collection point (range $p < 0.0001$ to $p = 0.0411$). Using Bayesian latent class model analysis, the optimal diagnostic cut-off IFA titer on patient admission for IgM was identified as 1:800 and for IgG at 1:1600. This data is valuable for local diagnosis of acute murine typhus infections in Laos, with the determination of appropriate cut-offs. In addition this study highlights the longevity of antibodies against murine typhus.

Phakhounthong K, Mukaka M, Dittrich S, Tanganuchitcharnchai A, Day NPJ, White LJ, Newton PN, Blacksell SD. The temporal dynamics of humoral immunity to *Rickettsia typhi* infection in murine typhus patients. *Clin Microbiol Infect* 2020; 26(6): 781.e9-16. Published online: 31 October 2019. doi: 10.1016/j.cmi.2019.10.022.

ENTERIC FEVER IN LAOS REMAINS TREATABLE WITH FIRST-LINE AGENTS

As discussions about the potential for typhoid vaccination to be introduced into the national immunisation program in Lao PDR were beginning, we carried out a study looking at the number of typhoid cases from Mahosot Hospital in the last 18 years. A total of 913 from 60,384 blood cultures were positive for *S.* Typhi. Antimicrobial susceptibility results showed that apart from an outbreak in 2004, multi-drug resistant *S.* Typhi (resistant to ampicillin, ciprofloxacin and nalidixic acid) was rare and that less than 10% of isolates were fluoroquinolone resistant. A second study was carried out to estimate the annual incidence of *S.* Typhi and *S.* Paratyphi A in Vientiane and found an estimated annual incidence of typhoid of 3.8 cases per 100,000 people and paratyphoid was 1.4 cases per 100,000 people.

Roberts T, Rattanavong S, Phommasone K, Chansamouth V, Davong V, Keoluangkhot V, Hongsakhone S, Bounsavath N, Mayxay M, Vongsouvath M, Dance DAB, Newton PN. Typhoid in Laos: An 18-Year Perspective. *Am J Trop Med Hyg* 2020; 102(4): 749-57. Published online: 27 January 2020. doi: 10.4269/ajtmh.19-0637.

NAMRU-2 and LOMWRU visit Salavan Provincial Hospital. Shown L to R: CDR Karen Corson, LCDR Jose Garcia, Elizabeth Ashley, Dr Kongsith Ounchit (Director of Salavan Hospital), Dr Sommay Keomany (Director of Salavan Hospital), Dr Manivanh Vongsouvath, Dr Koukeo Phommasone.

Chanthavilay P, Mayxay M, Xongmixay P, Roberts T, Rattanavong S, Vongsouvath M, Newton PN, Crump JA. Estimation of Incidence of Typhoid and Paratyphoid Fever in Vientiane, Lao People's Democratic Republic. *Am J Trop Med Hyg* 2020; 102(4): 744-748. Published online: 02 March 2020. doi: 10.4269/ajtmh.19-0634.

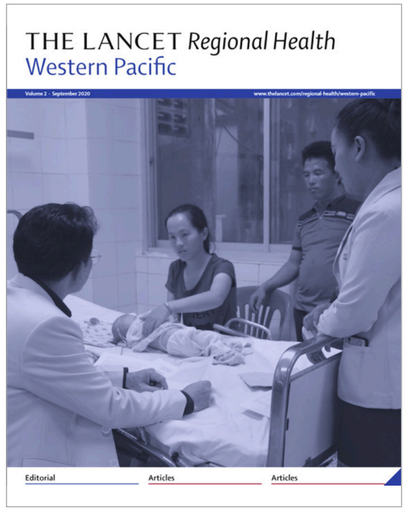
MALARIA

After the emergence of artemisinin and partner drug resistance in countries in the Greater Mekong Subregion, pilot evaluations of mass drug administration have been conducted and shown to reduce the incidence and prevalence of *P. falciparum* infections, including one study in Nong District, Savannakhet Province in southern Laos. In a secondary data analysis, Dr Koukeo Phommasone assessed the impact of the MDA on P. *vivax* infections. A total of 3,790 (86%) residents in the intervention villages participated in at least one MDA round, of whom 2,520 (57%) participated in three rounds. The prevalence of *P. vivax* infections fell from 9.31% to 0.89% at

month 3 but rebounded by six months to 5.81%. There was no evidence that the intervention reduced the cumulative incidence of *P. vivax* infections (95% confidence interval [CI] MDA with schizontocidal drugs has a lasting effect on *P. falciparum* infections but only a transient effect on the prevalence of *P. vivax* infections. Radical cure with an 8-aminoquinoline will be needed for the rapid elimination of vivax malaria.

Triple antimalarial drug combinations (TACTs), which combine existing co-formulated ACTs with a second partner drug that is slowly eliminated, have been proposed as a strategy to delay the emergence and spread of artemisinin and partner drug resistance in *Plasmodium falciparum*. Laos was one site of a multicentre, open-label, randomised trial (NCT02453308), in which patients with uncomplicated falciparum malaria were assigned to either standard treatment of a TACT. In Laos this was artemether-lumefantrine or artemether-lumefantrine plus amodiaquine. The overall 42-day PCR-corrected efficacy of artemether-lumefantrine plus amodiaquine (98% [281 of 286; 95% CI 97 to 99]) was similar to that of artemether-lumefantrine (97% [279 of 289; 95% CI 94 to 98]; risk difference 2%, 95% CI -1 to 4; p=0.30). TACTs were well tolerated. Dihydroartemisinin-piperaquine plus mefloquine and artemether-lumefantrine plus amodiaquine TACTs were efficacious and well tolerated treatments of uncomplicated *P. falciparum* malaria, including in areas with artemisinin and ACT partner-drug resistance.

Phommasone K, van Leth F, Peto TJ et al. Mass drug administrations with dihydroartemisinin-piperaquine and single low dose primaquine to eliminate *Plasmodium falciparum* have only a transient impact on *Plasmodium vivax*: Findings from randomised controlled trials. *PLoS One* 2020; 15(2): e0228190. Published online: 05 February 2020. doi: 10.1371/journal.pone.0228190.



van der Pluijm RW, Tripura R, Hoglund RM et al. Triple artemisinin-based combination therapies versus artemisinin -based combination therapies for uncomplicated *Plasmodium falciparum* malaria: a multicentre, open-label, randomised clinical trial. *Lancet* 2020; 395(10233): 1345-60. Published online: 11 March 2020. doi: 10.1016/s0140-6736(20)30552-3.

RESEARCH COLLABORATIONS

We are collaborating with our parent organization, the Mahidol Oxford Tropical Medicine Research Unit in the Faculty of Tropical Medicine, Mahidol University, Bangkok, Thailand on the Spot Sepsis project and on two malaria projects (GenRe and ENDGAME), in partnership with the Laos Centre of Malariology, Parasitology and Entomology (CMPE).

The work of the ARIVI/PneuCAPTIVE team was featured on the cover of the September 2020 issue of The Lancet Regional Health Western Pacific.

Our long-term collaboration with the Institut de recherche pour le développement (IRD) continues, working on clinical virology projects as well as research on soil ecology and *Burkholderia pseudomallei*.

Our program of infectious disease surveillance with NAMRU-2 switched focus to acute respiratory virus infections in 2020, but still with our provincial hospital collaborators in three locations (Xieng Khuang, Luang Namtha and Salavan).

Our long-standing collaboration (ARIVI/PneuCAPTIVE project) with Professor Fiona Russell and colleagues from the Asia-Pacific Health Research Group at the Murdoch Children's Research Institute (MCRI), in Melbourne, Australia, was boosted by the award to MCRI of a new Wellcome Impact of Vaccines on Antimicrobial Resistance grant. The title of the proposed 3-year project was 'Epidemiological and mechanistic studies on the role of pneumococcal conjugate vaccine in antimicrobial resistance in Laos', and this will allow our ongoing studies of acute respiratory infection in young children at Mahosot Hospital to continue.

The collaboration recently demonstrated, using a novel test-negative approach, that the 13-valent pneumococcal conjugate vaccine (PCV13) is effective against hypoxic pneumonia in children in Laos, and suggested that the vaccine should be prioritised for inclusion in national immunisation programs in Asia.

Weaver R, Nguyen CD, Chan J, Vilivong K, Lai JYR, Lim R, Satzke C, Vongsakid M, Newton PN, Mulholland K, Gray A, Dubot-Pérès A, Dance DAB, Russell FM. The effectiveness of the 13-valent pneumococcal conjugate vaccine against hypoxic pneumonia in children in Lao People's Democratic Republic: An observational hospital-based test-negative study. *Lancet Regional Health - Western Pacific* 2020; 2: 100014. Published online: 06 September 2020. doi: 10.1016/j.lanwpc.2020.100014.

TRAINING HIGHLIGHTS

LOMWRU has an active PhD and Master's programme for Lao and international students. Three PhD students graduated this year.

DOCTORAL STUDENTS

Dr Koukeo Phommasone getting ready to celebrate with LOMWRU colleagues after his successful University of Amsterdam Zoom PhD viva.

ດຣ ກຸແກ້ວ ພົມມະສອນ ສະເຫລີມສະຫລອງກັບເພື່ອນຮ່ວມງານພາຍໃນ LOMWRU ພາຍຫລັງປະສົບຜົນສຳເລັດຈາກການປ້ອງກັນປົດ ວິທະຍານິພົນປະຣິນຍາເອກ ຜ່ານທາງອອນລາຍ ຈາກມະຫາວິທະຍາໄລ Amsterdam.

Dr Koukeo Phommasone awarded a PhD by the University of Amsterdam

Dr Koukeo Phommasone, a Lao government scientist working with LOMWRU since 2009 was awarded a PhD by the University of Amsterdam in October 2020 for his thesis entitled "Studies to provide recommendations on the pre-elimination of *Plasmodium vivax* in Lao PDR." The COVID pandemic meant he was unable to travel to Amsterdam for his defence which took place over Zoom.

Dr Risara Jaksuwan awarded a PhD by Chiang Mai University

Dr Risara Jaksuwan, who works as a specialist advisor to the Microbiology Laboratory, was awarded a PhD in Clinical Epidemiology from Chiang Mai University on February 28, 2020.

Dr Risara Jaksuwan shown during a visit to Chiang Mai University, where she studied for her PhD.

ຮູບພາບ ດຣ Risara Jaksuwan ໄດ້ລົງຢ້ຽມຢາມ ມະຫາວິທະຍາໄລ ຊຽງໃໝ່ ເຊິ່ງເປັນສະຖານທີ່ ທີ່ເພິ່ນສຳເລັດການສຶກສາປະລິນຍາເອກ.

Dr Audrey Rachlin awarded a PhD by Menzies

Dr Audrey Rachlin was awarded her PhD (entitled "Next-generation sequencing for greater understanding of *Burkholderia pseudomallei* epidemiology and phylogeography in northern Australia and Vientiane, Laos") from the Menzies School of Health Research in Darwin, Australia. During her PhD, with the help of Dr Manophab Luangraj, she sampled mud and water in ditches and drains to look for *B. pseudomallei*, which was found to be widespread around Vientiane.

Dr Vilada Chansamouth

Dr Vilada Chansamouth is in the second year of her DPhil at the University of Oxford. Funded by Wellcome, Dr Vilada was awarded a prestigious International Training Fellowship in 2019. The subject of her research is antimicrobial resistance in Laos. She is evaluating the impact of introducing antimicrobial treatment guidelines on a mobile phone application on antibiotic prescribing in provincial and central hospitals in Laos in a stepped-wedge cluster randomised trial.

MASTER'S STUDENTS

Two Master's students graduated this year:

Mr Soo Kai Ter

Mr Soo Kai Ter graduated from the London School of Hygiene and Tropical Medicine in 2020 with a Master's in Medical Microbiology. He completed his MSc project at LOMWRU with the Molecular Bacteriology Group in 2019, looking at methods of detecting pathogens in culture-negative haemoculture fluids (subsequently published: Ter SK, Rattanavong S, *et al*. Am J Trop Med Hyg 2021;104(4):1582–5).

Mr Le Hong Dai

Mr Le Hong Dai, a Vietnamese student on the Master of Tropical Medicine and International Health course at the Lao Tropical and Public Health Institute, who did his project on recovery of *Leptospira* from blood samples with LOMWRU, graduated top of his year. Due to COVID-19 he had to rush back to Vietnam at short notice, sadly missing his graduation ceremony.

BACHELOR DEGREE

Ms Bountoy Sibounheuang

Ms Bountoy Sibounheuang, a laboratory technician in the Microbiology and Virology laboratories graduated from Khon Kaen University in Thailand with a Bachelor of Science (Medical Technology) degree.

The Mahosot microbiology team organised a "graduation ceremony" for Ms Bountoy Sibounheuang to mark the successful completion of her Bachelor degree at Khon Kaen University.

ໝ່ວຍງານຈຸລິນຊີ ໂຮງໝໍມະໂຫສົດ ໄດ້ຈັດພິທີສະຫລອງໃຫ້ແກ່ ນາງ ບຸນຕ້ອຍ ສີບຸນເຮືອງ ພາຍຫລັງ ສຳເລັດການສຶກສາລະດັບປະລິນຍາຕີ ທີ່ມະຫາວິທະຍາໄລຂອນແກ່ນ.

OTHER FELLOWSHIPS AND SCHOLARSHIPS

Two LOMWRU scientists were awarded fellowships by the Wellcome Trust in 2020.

Dr Weerawat Phuklia

In August, Dr Weerawat Phuklia, postdoctoral scientist at LOMWRU, was awarded a Wellcome International Training Fellowship for his planned research: Investigating antimicrobial susceptibility of *Rickettsia typhi*. He will develop ultrasensitive quantitative PCR-based methods to continue to investigate the susceptibility of *R. typhi* to frontline antibiotics in Laos, following on from a previous LOMWRU study which observed superior treatment responses following doxycycline compared to azithromycin.

Dr Vilayouth Phimolsarnnousith

Dr Vilayouth Phimolsarnnousith was awarded an International Master's Fellowship by the Wellcome Trust in December 2020. He will go to London for one year in September 2021 for the MSc in Medical Microbiology degree course at the London School of Hygiene and Tropical Medicine, and then complete his project on *Intra-host dengue virus genetic diversity among primary and secondary infections in Laos*.

Dr Laddaphone Bounvilay awarded a Master's Scholarship

Dr Laddaphone Bounvilay, a junior clinical researcher employed as part of the collaboration between the Murdoch Children's Research Institute (in Melbourne, Australia) and LOMWRU, was awarded a scholarship by the New Zealand Ministry of Foreign Affairs and Trade (MFAT). She will study for a Master of Public Health degree at the University of Otago in Dunedin.

TRAINING PROGRAMME FOR TRIAGE AND MANAGEMENT OF PATIENTS WITH COVID-19

Dr Rebecca Inglis, a Critical Care trainee from the UK, whose Oxford DPhil project was based at LOMWRU, spent 10 months seconded to the World Health Organization providing technical advice on the pandemic response in Laos. She developed a training programme for the triage and management of patients with COVID-19 that was implemented at central and provincial hospitals across the country and later cascaded to all 155 district hospitals.

Before then she had been based in Luang Prabang Provincial Hospital finishing off her DPhil fieldwork. Rebecca delivered Training of Trainers in Critical Care to three doctors, three nurses and one medical assistant, who went on to deliver the 6-day training to an additional 16 ICU nurses and doctors.

An interactive ICU training devised by Dr Rebecca Inglis.

ຮູບພາບ ການຝຶກອົບຮົມ ການປະຕິບັດແບບໂຕ້ຕອບ ທາງ ວຽກງານ ICU ໂດຍ Dr Rebecca Inglis

FLEMING FUND COUNTRY GRANT-LAOS

The Fleming Fund, established in 2015, is a £265 million UK aid programme supporting more than 20 low- and middle-income countries in Africa and Asia to tackle antimicrobial resistance by strengthening government institutions. Laos is a recipient of one of the country grants and the lead grantee is the United Nations Office for Project Services (UNOPS). LOMWRU was a sub-grantee and we have been working with provincial hospitals in Luang Namtha, Xieng Khouang and Salavan to help them strengthen their diagnostic microbiology and safety skills. Ten laboratory technicians spent a few weeks in Mahosot Hospital Microbiology Laboratory for training.

Dr Sayaphet Rattanavong (front row, *left*) and Dr Andy Simpson (seated, *third from left*) shown with medical and nursing staff of Xieng Khuang Hospital during a diagnostic stewardship training week as part of the Fleming Fund Laos Country Grant activities.

ຮູບພາບ ດຣ ໄຊຍະເພັດ ຣັດຕະນະວົງ (ດ້ານໜ້າຊ້າຍ) ແລະ ດຣ Andy Simpson (ຜູ້ທີສາມ ດ້ານໜ້ານັບຈາກຊ້າຍ) ພ້ອມດ້ວຍບັນດາ ພະນັກງານແພດ ແລະ ພະຍາບານ ໂຮງໝໍແຂວງຊຽງຂວາງ ໃນລະຫວ່າງການຝຶກອົບຮົມການບິ່ງມະຕິພະຍາດ ເຊິ່ງເປັນໜຶ່ງໃນກິດຈະກຳຂອງທຶນ Fleming Fund Laos Country Grant.

The National Antimicrobial Consumption meeting 2020 was held in the Vientiane Plaza Hotel.

ຮູບພາບ ກອງປະຊຸມການຊົມໃຊ້ຢາຕ້ານເຊື້ອຈຸລະຊີບແຫ່ງຊາດ ປີ 2020 ເຊິ່ງໄດ້ຈັດຂຶ້ນທີ່ ໂຮງແຮມວຽງຈັນພລາຊ່າ

ARBOSHIELD TRAINING WITH INSTITUT PASTEUR DU LAOS

Institut Pasteur du Laos (IPL) ran their Arboshield training courses again in 2020 for Lao Military Doctors and Lab Technicians. Dr Andrew Simpson and Dr Manophab Luangraj gave a talk on Melioidosis, whilst Dr Matthew Robinson and Mrs Anisone Chanthongthip (LOMWRU IDC Lab Manager) gave a talk and practical session on using bacterial RDTs. This was followed by a tour of the Mahosot Hospital Microbiology Laboratory (given by Mrs Viengmon Davong) and IDC. Arboshield is a three-year training program on surveillance and diagnosis of vector-borne diseases, organized by IPL teams and held at IPL. An average of 12 trainees per year, one third from civil organization and two third military staff, are following the curriculum.

FINAL LEG OF L-TEAM IN LUANG PRABANG

ຮູບພາບຈາກດ້ານຊ້າຍຫາຂວາ: ດຣ ໄຊຍະເພັດ ຣັດຕະນະວົງ, ດຣ ກຸແກ້ວ ພົມມະສອນ, ດຣ Andrew Simpson, ນາງ ພອນລາວັນ ພູມິນ, ດຣ ດານ້ອຍ ຈອມມະນາມ ໃນການຝຶກອົບຮົມ L-Team ເຊິ່ງໄດ້ຈັດຂຶ້ນທີ່ ແຂວງຫຼວງພະບາງ

From *left*: Dr Sayaphet Rattanavong, Dr Koukeo Phommasone, Dr Andrew Simpson. Ms Phonelavanh Phoumin, Dr Danoy Chommanam at the L-TEAM training in Luang Prabang , in January 2020, along with colleagues from the Mahosot Hospital Adult Infectious Diseases team and from MORU. This followed two previous workshops on Melioidosis in 2019, held in Vang Vieng and Pakse. This Lao Training Event for the Awareness of Melioidosis event was aimed principally at clinicians and hospital laboratory staff, as well as veterinary officers and epidemiologists, from the northern provinces of Laos. The well-attended workshop was funded by the US Government Defense Threat Reduction Agency (DTRA) Biological Threat Reduction Program (BTRP), in partnership with the Laos Ministry of Health, Department of Communicable Disease Control, and Department of Curative and Rehabilitation.

PREPARING FOR ORACLE

The LOMWRU admin team participated in many hours of online training in preparation for the introduction of the Oracle Business Process Management Suite across our network in 2021.

ETHICS IN RESEARCH TRAINING WITH UHS & NIOPH

On the 9th June 2020, Professor Mayfong Mayxay and Dr Vimalay Souvong attended a meeting at the National Institute of Public Health and Tropical Medicine to discuss improvement of the training curriculum on Health Ethics research.

The University of Health Sciences (Prof Mayfong Mayxay) conducted training on Ethics in Research on 9 September 2020. Dr Vimalay was one of the trainers and focused on principles of Good Clinical Practice (GCP), responsibilities of Principal investigators/coinvestigators and priority areas for study monitoring.

GOOD CLINICAL LABORATORY PRACTICE TRAINING

GCLP training was conducted by Risara Jaksuwan for laboratory staff between 3-6 August 2020, with 11 participants from various laboratories. Participants are shown discussing competency testing in the laboratory.

Mahosot laboratory technicians shown during the GCLP training.

ການຝຶກອົບຮົມການປະຕິບັດງານຄລີນິກດ້ານແລັບທີ່ດີ (GCLP) ຂອງນັກເຕັກນິກວິເຄາະການແພດ ທີ່ໂຮງໝໍມະໂຫສົດ

LOMWRU PUBLICATIONS IN 2020

In 2020, LOMWRU published 71 articles or letters in peer-reviewed journals. Abstracts from published articles are reproduced below, with articles grouped by theme.

MICROBIOLOGY (BACTERIAL INFECTIONS AND AMR)

Setting priorities for patient-centered surveillance of drug-resistant infections. Ashley EA, McLean A, Chiara F, Feasey N, Jaoko W, Opintan JA, Peacock SJ, Rupali P, Turner P. *Int J Infect Dis* 2020; 97: 60-5. Published online: 06 June 2020. doi: 10.1016/j.ijid.2020.05.121.

This study aimed to set priorities for tackling antimicrobial resistance in LMICs and found that most clinicians want more guidance on how best to treat drug-resistant infections.

METHODS: A priority-setting process (PSP) was launched to define priorities for patient-centered antimicrobial resistance (AMR) surveillance and research in low- and middle-income countries (LMICs). A list of uncertainties related to AMR surveillance in human health was generated using an online survey of stakeholders in LMICs, which asked for unanswered questions about diagnosis, treatment, or prevention of antibiotic resistance. **RESULTS:** A total of 445 respondents generated 1076 questions that were mapped to a final shortlist of 107 questions. The most common theme was the treatment of drug-resistant infections, followed by diagnosis, then prevention, and requests for local AMR data. The most asked question was a request for local AMR data, revealing the lack of basic information in many LMICs to guide actions to tackle AMR. The steering group recommended three research areas to be prioritized for funding in the next five years: infection prevention and control in LMICs, improved electronic patient records, starting with laboratory information management systems, and sustainable behavior change among doctors and other health care professionals with a focus on diagnostic stewardship.

The spread of chloramphenicol-resistant Neisseria meningitidis in Southeast Asia. Batty EM, Cusack TP, Thaipadungpanit J, Watthanaworawit W, Carrara V, Sihalath S, Hopkins J, Soeng S, Ling C, Turner P, Dance DAB. *Int J Infect Dis* 2020; 95: 198-203. Published online: 12 April 2020. doi: 10.1016/j.ijid.2020.03.081.

This study identified a single clone of chloramphenicol-resistant N. meningitidis and suggests that this organism is more widespread in southeast Asia than was realised previously.

OBJECTIVES: Invasive disease caused by *Neisseria meningitidis* is a significant health concern globally, but our knowledge of the prevailing serogroups, antimicrobial susceptibility patterns, and genetics of *N. meningitidis* in Southeast Asia is limited. Chloramphenicol resistance in *N. meningitidis* has rarely been reported but was first described in isolates from Vietnam in 1998. We aimed to characterise eight chloramphenicol resistant meningococcal isolates collected between 2007 and 2018 from diagnostic microbiology laboratories in Cambodia, Thailand and the Lao People's Democratic Republic (Laos). **METHODS:** Whole-genome sequencing was used to generate genome sequences from 18 meningococcal isolates including the eight chloramphenicol resistant isolates. We identified antimicrobial resistance genes present in these strains, and examined the phylogenetic relationships between strains. **RESULTS:** The eight resistant strains all contain the same chloramphenicol resistance gene first described in 1998, and are closely related to each other. Strains resistant to penicillin, tetracycline, and ciprofloxacin were also observed, including a chloramphenicol-resistant strain which has acquired penicillin and ciprofloxacin resistance. **CONCLUSIONS:** This study suggests that chloramphenicol-resistant *N. meningitidis* is more widespread than previously thought, and that the previously-identified resistant lineage is now found in multiple countries in Southeast Asia.

Bacteremia Caused by Extended-Spectrum Beta-Lactamase-Producing Enterobacteriaceae in Vientiane, Lao PDR: A 5-Year Study. Chang K, Rattanavong S, Mayxay M, Keoluangkhot V, Davong V, Vongsouvath M, Luangraj M, Simpson AJH, Newton PN, Dance DAB. *Am J Trop Med Hyg* 2020; 102(5): 1137-43. Published online: 09 March 2020. doi: 10.4269/ajtmh.19-0304.

This study demonstrated a rise in ESBL incidence, including as a cause of bacteraemia, at Mahosot Hospital between 2010 and 2014, and that treatment options may be very limited.

Although there has been an increasing incidence of bacteremia caused by extended-spectrum beta-lactamase (ESBL)-producing Enterobacteriaceae (ESBL-E) across South East Asia, there are sparse data from the Lao PDR, where laboratory capacity for antimicrobial resistance surveillance is limited. We, therefore, retrospectively reviewed bacteremia caused by ESBL-producing *Escherichia coli* and *Klebsiella pneumoniae* between 2010 and 2014 at Mahosot Hospital, Vientiane, Lao PDR. Clinical and laboratory data relating to all episodes of ESBL-E bacteremia were reviewed over the 5-year period and compared with non-ESBL-E bacteremia. Blood cultures positive for *E. coli* or *K. pneumoniae* were identified retrospectively from laboratory records. Clinical and laboratory data were extracted from research databases and case notes and analysed using STATA. Between 2010 and 2014, we identified 360 patients with *E. coli* (n = 249) or *K. pneumoniae* (n = 111) bacteremia, representing 34.8% of all patients with clinically significant bacteremia. Seventy-two (20%) isolates produced ESBL; *E. coli* accounted for 15.3% (55/360) and *K. pneumoniae* for 4.7% (17/360), respectively. The incidence of ESBL-producing *E. coli* bacteremia rose during the study period. By multiple logistic analysis, reported antibiotic use in the previous week was significantly associated with ESBL positivity (P < 0.001, odds ratio 3.89). Although multiresistant, most ESBL-producing *E. coli* and *K. pneumoniae* remained susceptible to meropenem (65/65; 100%) and amikacin (64/65; 98.5%). We demonstrated an alarming increase in the incidence of ESBL-E as a cause of bacteremia in Vientiane during the study period. This has implications for empiric therapy of sepsis in Laos, and ongoing surveillance is essential.

Estimation of Incidence of Typhoid and Paratyphoid Fever in Vientiane, Lao People's Democratic Republic. Chanthavilay P, Mayxay M, Xongmixay P, Roberts T, Rattanavong S, Vongsouvath M, Newton PN, Crump JA. *Am J Trop Med Hyg* 2020; 102(4): 744-8. Published online: 02 March 2020. doi: 10.4269/ajtmh.19-0634.

This study estimated the incidence of enteric fevers in Vientiane during 2019, in advance of policy decisions about the introduction of a typhoid vaccine. The incidence of both typhoid and paratyphoid fevers was low.

Typhoid conjugate vaccines represent a new tool for typhoid control. However, incidence data are needed to inform decisions about introduction. We sought to estimate typhoid and paratyphoid fever incidence in Vientiane, the capital and largest city of the Lao People's Democratic Republic (Lao PDR). We did a representative cluster survey of health-seeking behaviour for fever in Vientiane from January 15, 2019 through January 26, 2019. Multipliers derived from the survey were applied to data from *Salmonella* Typhi and *Salmonella* Paratyphi A bloodstream infection surveillance from Mahosot Hospital, Vientiane, for the period of January 1, 2015 through December 31, 2017, to estimate enteric fever incidence. A total of 336 households representing 1,740 persons were enrolled in the healthcare utilization survey, and multipliers were derived based on responses to questions about healthcare seeking in the event of febrile illness. Of 7,997 Vientiane residents receiving blood cultures over the 2-year surveillance period at Mahosot Hospital, we identified 16 (0.2%) with *Salmonella* Typhi and six (< 0.1%) with *Salmonella* Paratyphi A bloodstream infection. After applying multipliers, we estimated that the annual incidence of typhoid was 4.7 per 100,000 persons and paratyphoid was 0.5 per 100,000 persons. During the study period, the incidence of typhoid and paratyphoid fever was low in Vientiane. Ongoing surveillance is warranted to identify increases in future years. Similar studies elsewhere in the Lao PDR would be useful to understand the wider enteric fever situation in the country.

Establishing a critical care network in Asia to improve care for critically ill patients in low- and middle-income countries. CRIT CARE ASIA. *Crit Care* 2020; 24: 608. Published online: 15 October 2020. doi: 10.1186/s13054-020-03321-7.
Editorial.

Community-acquired Group B streptococcal meningitis in adults. Dance D, Zadoks RN, Luangraj M, Simpson A, Chen SL, Barkham T. *J Infect* 2020; 81(1): 175-6. Published online: 17 March 2020. doi: 10.1016/j.jinf.2020.03.009.
Letter (Correspondence).

Harnessing genomics in the battle against antimicrobial resistance and neglected tropical diseases. Dance DAB, Batty EM. *EBioMedicine* 2021; 63: 103178. Published online: 16 December 2020. doi: 10.1016/j.ebiom.2020.103178.
Commentary

Selection of Diagnostic Cutoffs for Murine Typhus IgM and IgG Immunofluorescence Assay: A Systematic Review. Dhawan S, Robinson MT, Stenos J, Graves SR, Wangrangsimakul T, Newton PN, Day NPJ, Blacksell SD. *Am J Trop Med Hyg* 2020; 103(1): 55-63. Published online: 06 April 2020. doi: 10.4269/ajtmh.19-0818.
This study demonstrated a lack of consensus in diagnostic cut-off titres between assays for serological diagnosis of murine typhus.
Murine typhus is a neglected but widespread infectious disease that results in acute fever. The immunofluorescence assay (IFA) is the "gold standard" to identify IgM or IgG antibodies, although there is a lack of standardization in methodologies. The objective of this review is to summarize 1) the differences in published methodologies, 2) the diagnostic cutoff titers, and 3) the justification of diagnostic cutoffs. Searches were performed by combining the following search terms: "murine typhus," "rickettsia typhi," "immunofluorescence," "IFA," and "serologic" with restrictions (i.e., "rickettsia typhi" or "murine typhus," and "IFA" or "immunofluorescence," or "serologic*"). The search identified 78 studies that used IFA or immunoperoxidase assay (IIP) antibody cutoffs to diagnose murine typhus, 39 of which were case series. Overall, 45 studies (57.7%) provided little to no rationale as to how the cutoff was derived. Variation was seen locally in the cutoff titers used, but a 4-fold or greater increase was often applied. The cutoffs varied depending on the antibody target. No consensus was observed in establishing a cutoff, or for a single-value diagnostic cutoff. In conclusion, there is a lack of consensus in the establishment of a single-value cutoff. Further studies will need to be executed at each distinct geographic location to identify region-specific cutoffs, while also considering background antibody levels to distinguish between healthy and infected patients.

A systematic review of the untreated mortality of murine typhus. Doppler JF, Newton PN. *PLoS Negl Trop Dis* 2020; 14(9): e0008641. Published online: 14 September 2020. doi: 10.1371/journal.pntd.0008641.
A literature review that suggests a high morbidity, with substantial hospitalisation rates, but a low mortality associated with murine typhus.
Murine typhus is an acute febrile, flea-borne disease caused by the bacteria *Rickettsia typhi*. The disease occurs worldwide but is likely underrecognised due to its non-specific symptoms, causing significant morbidity. A systematic review found disease complications in one-fourth of all patients and a long fever duration in those untreated. Although mortality in treated cases is estimated to be very low, some case series have shown a notably higher mortality in untreated patients. This study aimed to describe the outcomes and estimate the mortality of untreated murine typhus through a comprehensive systematic literature review. We systematically searched the literature for articles describing untreated murine typhus patients, excluding cases with no laboratory assay confirmed diagnosis, those who received efficacious treatment, had incomplete information on primary outcome and articles describing less than 10 patients and performed a narrative synthesis of the study findings. The study protocol followed the PRISMA guidelines and was part of a more extensive protocol registered at PROSPERO (CRD42018101991). Twelve studies including a total of 239 untreated patients matched the eligibility criteria. Only a single study reported one death in 28 patients, giving a patient series mortality of 3.6% and an overall mortality of 0.4% in 239 untreated patients. Complications were reported in 10 of the 12 studies and included involvement of the central nervous system, kidney and lung, with a hospitalisation rate of 70% and ICU admission rate of 27% in one study. The mean duration of fever in untreated patients was 15 days in two and 12.7 days in one study. Although the untreated mortality in this study was low, the sample size was small. Murine typhus caused significant morbidity when untreated, leading to high hospitalisation rates and highlighting the importance of early diagnosis and treatment of this neglected disease to reduce disease burden and health-care related costs.

Diagnostic accuracy of an in-house Scrub Typhus enzyme linked immunoassay for the detection of IgM and IgG antibodies in Laos. Elders PND, Dhawan S, Tanganuchitcharnchai A, Phommasone K, Chansamouth V, Day NPJ, Garcia-Rivera JA, Hertz JC, Mayxay M, Vongsouvath M, Dubot-Pérès A, Robinson MT, Newton PN, Blacksell SD. *PLoS Negl Trop Dis* 2020; 14(12): e0008858. Published online: 07 December 2020. doi: 10.1371/journal.pntd.0008858.
A novel in-house MORU scrub typhus IgG/M ELISA performed well in comparison with the reference IFA test, although further study is required.
Scrub typhus is a major cause of morbidity and mortality in Southeast Asia. Diagnosis of scrub typhus is difficult due to a lack of accessible validated diagnostic tools. Despite its objectivity, the diagnostic accuracy of ELISA tests is influenced by methodological and patient factors. This study aims to evaluate the performance of a novel in-house ELISA developed in the Mahidol Oxford Tropical Medicine Research Unit (MORU) for anti-scrub typhus group IgM and IgG compared to the "gold standard" reference IFA and PCR, and to determine whether the in-house ELISA can be used as a seroepidemiological screening tool and/or stand-alone test for scrub typhus. A total of 1,976 admission and 1,438 participant follow-up sera collected in the Lao PDR (Laos) were tested with ELISA for IgM and IgG. Samples with an ELISA OD>/=0.50 were tested with IFA for IgM and/or IgG. A strong positive relationship was present between ELISA ODs and IFA titers for admission IgM (r2: 0.70, p <0.005) and IgG (r2: 0.76, p<0.005), and for follow-up IgM and IgG (both r2: 0.76, p<0.005) samples. The best compromise between sensitivity and specificity for the ELISA OD cut-off is likely to be between 0.8-1.0 for IgM antibodies and 1.2-1.8 for IgG antibodies. These results demonstrate that the diagnostic accuracy of the MORU in-house scrub typhus group ELISA is comparable to that of IFA, with similar results as reported for the commonly used InBios Scrub Typhus Detect ELISA, validating the use of the in-house ELISA. The optimal ELISA cut-off would depend on the use of the test, and the desired sensitivity and specificity. Further studies are required to authenticate the use of these cut-offs in other endemic regions. This in-house ELISA has the potential to replace the imperfect IFA, which could ultimately reduce the burden of scrub typhus by improving the rate of scrub typhus diagnoses in endemic low-resource areas.

Serological evidence indicates widespread distribution of rickettsioses in Myanmar. Elders PND, Swe MMM, Pyae Phyo A, McLean ARD, Lin HN, Soe K, Htay WYA, Tanganuchitcharnchai A, Hla TK, Tun NN, Nwe TT, Moe MM, Thein WM, Zaw NN, Kyaw WM, Linn H, Htwe YY, Smithuis FM, Blacksell SD, Ashley EA. *Int J Infect Dis* 2021; 103: 494-501. Published online: 10 December 2020. doi: 10.1016/j.ijid.2020.12.013.
Rickettsial infections are common causes of fever in Myanmar, with high scrub typhus seroprevalence in the centre and north of the country.

BACKGROUND: Little research has been published on the prevalence of rickettsial infections in Myanmar. In this study, we determined the seroprevalence of IgG antibodies to rickettsial species in different regions of Myanmar. METHODS: We collected 700 leftover blood samples from patients of all age groups in primary care clinics and hospitals in seven different regions in Myanmar. Samples were screened for scrub typhus group, typhus group and spotted fever group IgG antibodies with ELISAs. A subsequent IFA was performed for the same rickettsial group to confirm seropositivity if ELISA was above a threshold of Optical Density (OD)>/=0.5. **RESULTS:** Overall IgG seroprevalence for scrub typhus was 19% (95% CI: 16-22%), for murine typhus was 5% (95% CI: 3-7%) and for spotted fever group was 3% (95% CI: 2-5%), with especially high scrub typhus seroprevalence in northern (59%) and central Myanmar (19-33%). Increasing age was associated with higher odds of seropositivity for scrub- and murine typhus (age per 10 years, unadjusted odds ratio estimates: 1.54, p < 0.01 and 1.24, p = 0.02 respectively). **CONCLUSION:** Our findings indicate that rickettsial infections are widespread in Myanmar, with especially high seroprevalence of scrub typhus in central and northern regions. Rickettsial infections should be considered by healthcare workers as common causes of fever in Myanmar.

Oxford Nanopore MinION Sequencing Enables Rapid Whole Genome Assembly of Rickettsia typhi in a Resource-Limited Setting. Elliott I, Batty EM, Ming D, Robinson MT, Nawtaisong P, de Cesare M, Newton PN, Bowden R. *Am J Trop Med Hyg* 2020; 102(2): 408-14. Published online: 09 December 2019. doi: 10.4269/ajtmh.19-0383.

This study reports the genome sequencing of a Rickettsia typhi strain using the MinION platform in Laos and Illumina sequencing in the UK.

The infrastructure challenges and costs of next-generation sequencing have been largely overcome, for many sequencing applications, by Oxford Nanopore Technologies' portable MinION sequencer. However, the question remains open whether MinION-based bacterial whole genome sequencing is by itself sufficient for the accurate assessment of phylogenetic and epidemiological relationships between isolates and whether such tasks can be undertaken in resource-limited settings. To investigate this question, we sequenced the genome of an isolate of *Rickettsia typhi*, an important and neglected cause of fever across much of the tropics and subtropics, for which only three genomic sequences previously existed. We prepared and sequenced libraries on a MinION in Vientiane, Lao PDR, using v9.5 chemistry, and in parallel, we sequenced the same isolate on the Illumina platform in a genomics laboratory in the United Kingdom. The MinION sequence reads yielded a single contiguous assembly, in which the addition of Illumina data revealed 226 base-substitution and 5,856 indel errors. The combined assembly represents the first complete genome sequence of a human *R. typhi* isolate collected in the last 50 years and differed from the genomes of existing strains collected over a 90-year time period at very few sites, with no rearrangements. Filtering based on the known error profile of MinION data improved the accuracy of the nanopore-only assembly. However, the frequency of false-positive errors remained greater than true sequence divergence from recorded sequences. Although nanopore-only sequencing cannot yet recover phylogenetic signals in *R. typhi*, such an approach may be applicable for more diverse organisms.

Point-of-Care Ultrasound in the Diagnosis of Melioidosis in Laos. Huson MAM, Kling K, Chankongsin S, Phongluxa K, Keoluangkhot V, Newton PN, Dance D, Heller T, Neumayr A. *Am J Trop Med Hyg* 2020; 103(2): 675-8. Published online: 01 June 2020. doi: 10.4269/ajtmh.20-0069.

Soft-tissue abscesses are common in melioidosis. This study demonstrated that abscess detection by ultrasound has a high predictive value and may aid early diagnosis and empiric treatment of melioidosis.

Melioidosis is endemic in many rural areas in Southeast Asia where facilities for culture and identification of *Burkholderia pseudomallei* are often limited. We performed a prospective observational study in patients presenting with fever to Mahosot Hospital, the primary referral hospital in Laos, to establish whether the detection of abscesses on ultrasound could support a presumptive diagnosis of melioidosis. All patients underwent ultrasound examination to detect abscesses in the liver, spleen, prostate, or, if indicated, subcutaneous tissue. We enrolled 153 patients, including 18 patients with melioidosis. Of these, 11 (61%) had an abscess at one or more sites, including five (28%) with splenic and/or liver abscesses. Absence of abscesses cannot rule out melioidosis, but the positive predictive value of abscesses for melioidosis was high at 93% (88-96%). Therefore, in endemic areas, the presence of abscesses in febrile patients should prompt empiric antibiotic therapy for melioidosis even in the absence of culture confirmation.

***Burkholderia pseudomallei* multi-centre study to establish EUCAST MIC and zone diameter distributions and epidemiological cut-off values.** Karatuna O, Dance DAB, Matuschek E, Åhman J, Turner P, Hopkins J, Amornchai P, Wuthiekanun V, Cusack T-P, Baird R, Hennessy J, Norton R, Armstrong M, Zange S, Zoeller L, Wahab T, Jacob D, Grunow R, Kahlmeter G. *Clin Microbiol Infect* 2021. Published online: 09 July 2020. doi: 10.1016/j.cmi.2020.07.001.

This study addressed a knowledge gap in the antimicrobial susceptibility testing of B. pseudomallei isolates, and contributed to the publication of EUCAST breakpoint guidelines during 2020.

OBJECTIVES: Melioidosis, caused by *Burkholderia pseudomallei*, requires intensive antimicrobial treatment. However, standardized antimicrobial susceptibility testing (AST) methodology based on modern principles for determining breakpoints and ascertaining performance of methods are lacking for *B. pseudomallei*. This study aimed to establish MIC and zone diameter distributions on which to set epidemiological cut-off (ECOFF) values for *B. pseudomallei* using standard EUCAST methodology for non-fastidious organisms. **METHODS:** Non-consecutive, non-duplicate clinical *B. pseudomallei* isolates (9-70 per centre) were tested at eight study centres against eight antimicrobials by broth microdilution (BMD) and the EUCAST disc diffusion method. Isolates without and with suspected resistance mechanisms were deliberately selected. The EUCAST Development Laboratory ensured the quality of study materials, and provided guidance on performance of the tests and interpretation of results. Aggregated results were analysed according to EUCAST recommendations to determine ECOFFs. **RESULTS:** MIC and zone diameter distributions were generated using BMD and disc diffusion results obtained for 361 *B. pseudomallei* isolates. MIC and zone diameter ECOFFs (mg/L; mm) were determined for amoxicillin-clavulanic acid (8; 22), ceftazidime (8; 22), imipenem (2; 29), meropenem (2; 26), doxycycline (2; none), tetracycline (8; 23), chloramphenicol (8; 22) and trimethoprim-sulfamethoxazole (4; 28). **CONCLUSIONS:** We have validated the use of standard BMD and disc diffusion methodology for AST of *B. pseudomallei*. The MIC and zone diameter distributions generated in this study allowed us to establish MIC and zone diameter ECOFFs for the antimicrobials studied. These ECOFFs served as background data for EUCAST to set clinical MIC and zone diameter breakpoints for *B. pseudomallei*.

Automating the Generation of Antimicrobial Resistance Surveillance Reports: Proof-of-Concept Study Involving Seven Hospitals in Seven Countries. Lim C, Miliya T, Chansamouth V, Aung MT, Karkey A, Teparrukkul P, Rahul B, Lan NPH, Stelling J, Turner P, Ashley E, van Doorn HR, Lin HN, Ling C, Hinjoy S, Iamsirithaworn S, Dunachie S, Wangrangsimakul T, Hantrakun V, Schilling W, Yen LM, Tan LV, Hlaing HH, Mayxay M, Vongsouvath M, Basnyat B, Edgeworth J, Peacock SJ, Thwaites G, Day NP, Cooper BS, Limmathurotsakul D. *J Med Internet Res* 2020; 22(10): e19762. Published online: 02 October 2020. doi: 10.2196/19762.

Report on the promising development and testing of an app (AMASS) to support the generation and sharing of AMR surveillance reports in local hospitals.

BACKGROUND: Reporting cumulative antimicrobial susceptibility testing data on a regular basis is crucial to inform antimicrobial resistance (AMR) action plans at local, national, and global levels. However, analysing data and generating a report are time consuming and often require trained personnel. **OBJECTIVE:** This study aimed to develop and test an application that can support a local hospital to analyse routinely collected electronic data independently and generate AMR surveillance reports rapidly. **METHODS:** An offline application to generate standardized AMR surveillance reports from routinely available microbiology and hospital data files was written in

the R programming language (R Project for Statistical Computing). The application can be run by double clicking on the application file without any further user input. The data analysis procedure and report content were developed based on the recommendations of the World Health Organization Global Antimicrobial Resistance Surveillance System (WHO GLASS). The application was tested on Microsoft Windows 10 and 7 using open access example data sets. We then independently tested the application in seven hospitals in Cambodia, Lao People's Democratic Republic, Myanmar, Nepal, Thailand, the United Kingdom, and Vietnam. **RESULTS:** We developed the AutoMated tool for Antimicrobial resistance Surveillance System (AMASS), which can support clinical microbiology laboratories to analyse their microbiology and hospital data files (in CSV or Excel format) onsite and promptly generate AMR surveillance reports (in PDF and CSV formats). The data files could be those exported from WHONET or other laboratory information systems. The automatically generated reports contain only summary data without patient identifiers. The AMASS application is downloadable from https://www.amass.website/. The participating hospitals tested the application and deposited their AMR surveillance reports in an open access data repository. **CONCLUSIONS:** The AMASS is a useful tool to support the generation and sharing of AMR surveillance reports.

Containment of Antibiotic REsistance-measures to improve antibiotic use in pregnancy, childbirth and young children (CAREChild): a protocol of a prospective, quasiexperimental interventional study in Lao PDR. Machowska A, Sihavong A, Eriksen J, Vongsouvath M, Marrone G, Sychareun V, Hanson C, Keohavong B, Brauner A, Mayxay M, Kounnavong S, Lundborg CS. *BMJ Open* 2020; 10(11): e040334. Published online: 19 November 2020. doi: 10.1136/bmjopen-2020-040334.

This is a protocol for a proposed study of the drivers of antibiotic use and AMR in pregnancy, during delivery and in children, in Laos. A subsequent interventional education campaign will then be evaluated.

INTRODUCTION: Antibiotics are essential to treat infections during pregnancy and to reduce both maternal and infant mortality. Overall use, but especially non-indicated use, and misuse of antibiotics are drivers of antibiotic resistance (ABR). High non-indicated use of antibiotics for uncomplicated vaginal deliveries is widespread in many parts of the world. Similarly, irrational use of antibiotics is reported for children. There is scarcity of evidence regarding antibiotic use and ABR in Lao PDR (Laos). The overarching aim of this project is to fill those knowledge gaps and to evaluate a quality improvement intervention. The primary objective is to estimate the proportion of uncomplicated vaginal deliveries where antibiotics are used and to compare its trend before and after the intervention. **METHODS AND ANALYSIS:** This 3-year, prospective, quasiexperimental study without comparison group includes a formative and interventional phase. Data on antibiotic use during delivery will be collected from medical records. Knowledge, attitudes and reported practices on antibiotic use in pregnancy, during delivery and for children, will be collected from women through questionnaires. Healthcare providers' knowledge, attitudes and practices of antibiotics administration for pregnant women, during delivery and for children, will be collected via adapted questionnaires. Perceptions regarding antibiotics will be explored through focus group discussions with women and individual interviews with key stakeholders. Faecal samples for culturing of Escherichia coli and Klebsiella spp. and antibiotic susceptibility testing will be taken before, during and 6 months after delivery to determine colonisation of resistant strains. The planned intervention will comprise training workshops, educational materials and social media campaign and will be evaluated using interrupted time series analysis. **ETHICS AND DISSEMINATION:** The project received ethical approval from the National Ethics Committee for Health Research, Ministry of Health, Laos. The results will be disseminated via scientific publications, conference presentations and communication with stakeholders. **TRIAL REGISTRATION NUMBER:** ISRCTN16217522; Pre-results.

The Isolation of Orientia tsutsugamushi and Rickettsia typhi from Human Blood through Mammalian Cell Culture: a Descriptive Series of 3,227 Samples and Outcomes in the Lao People's Democratic Republic. Ming DK, Phommadeechack V, Panyanivong P, Sengdatka D, Phuklia W, Chansamouth V, Roberts T, Blacksell SD, Newton PN, Robinson MT. *J Clin Microbiol* 2020; 58(12): e01553-20. Published online: 18 November 2020. doi: 10.1128/JCM.01553-20.

Review of the Mahosot Hospital experience of cell culture for rickettsial isolation from clinical samples over a six-year period. Overall success rate was 7.9%; sample type and speed of processing both influenced recovery rates.

In the Lao People's Democratic Republic (Laos), rickettsial infections, including scrub and murine typhus, account for a significant burden of fevers. The Mahosot Hospital Microbiology Laboratory in Vientiane, Laos, routinely performs rickettsial isolation from hospitalized patients with suspected rickettsioses using mammalian cell culture systems. We review the clinical and laboratory factors associated with successful *Orientia tsutsugamushi* and *Rickettsia typhi* isolations from this laboratory over a period of 6 years between 2008 and 2014. The overall isolation success was 7.9% for all samples submitted and 17.3% for samples for which the patient had a positive *O. tsutsugamushi* or *R. typhi* rapid diagnostic test (RDT), serology, or PCR. The frequency of successful isolation was highest for samples submitted in November, at the end of the wet season (28.3%). A longer median duration of reported illness, a positive result for a concurrent *Orientia* or *Rickettsia* spp. quantitative PCR, and the use of antibiotics by the patient in the week before admission were significantly associated with isolation success ($P < 0.05$). Buffy coat inoculation and a shorter interval between sample collection and inoculation in the laboratory were associated with a higher frequency of isolation (both $P < 0.05$). This frequency was highest if cell culture inoculation occurred on the same day as blood sample collection. Factors related to the initial rickettsial bacterial concentration are likely the main contributors to isolation success. However, modifiable factors do contribute to the rickettsial isolation success, especially delays in inoculating patient samples into culture.

Screening of ectoparasites from domesticated dogs for bacterial pathogens in Vientiane, Lao PDR. Nguyen HM, Theppannga W, Vongphayloth K, Douangngeun B, Blacksell SD, Robinson MT. *Zoonoses Public Health* 2020; 67(8): 862-8. Published online: 11 July 2020. doi: 10.1111/zph.12753.

This study screened ectoparasites, such as ticks, fleas and lice, from domestic dogs in urban Vientiane for bacterial pathogens, and suggests that these parasites have the potential to transmit zoonoses.

Arthropod-borne diseases are widespread worldwide and are a complex interaction between animals, humans and ectoparasites. The understanding of the diversity and epidemiology of organisms transmitted by arthropod vectors, and the role of hosts and vectors in transmission of infections remain limited in Lao PDR. What knowledge does exist is primarily focused on more rural regions of the country. This study screened ectoparasites from domestic dogs in Vientiane city for presence of bacterial pathogens of zoonotic importance. A total of 3,511 arthropod vectors were collected from 112 dogs. Vectors collected were *Rhipicephalus sanguineus* ticks, *Ctenocephalides felis felis* and *Ctenocephalides felis orientis* fleas and *Heterodoxus spiniger* lice. A sub-sample of vectors from each dog was analysed by PCR to identify the potential bacteria. From 129 vector pools, *Rickettsia* spp. was detected in 6.7% (7/105) pools of ticks, 86.4% (19/22) pools of fleas and both pools of lice. Sequencing analysis confirmed *Rickettsia felis* in 13 flea pools and one louse pool and *Rickettsia asembonensis* in six flea pools. Anaplasmataceae was identified in 14.3% (15/105) tick pools and 100% (22/22) flea pools. Sequencing revealed the presence of *Anaplasma platys* in ticks and *Wolbachia pipientis* in fleas. *Leptospira* spp. was detected in one tick and one louse pool, and *Brucella* spp. was detected in 12.4% (13/105) tick pools. All samples were negative for *Bartonella* spp., *Coxiella burnetii* and *Borrelia burgdorferi.* This is the first study providing evidence of *R. asembonensis* in fleas in Laos. Results from this study show arthropods are potential vectors to transmit zoonotic infection in Vientiane city, suggesting humans are at risk of zoonotic infections in the city.

The temporal dynamics of humoral immunity to Rickettsia typhi infection in murine typhus patients. Phakhounthong K, Mukaka M, Dittrich S, Tanganuchitcharnchai A, Day NPJ, White LJ, Newton PN, Blacksell SD. *Clin Microbiol Infect* 2020; 26(6): 781.e9-16. Published online: 31 October 2019. doi: 10.1016/j.cmi.2019.10.022.

This study characterised the temporal dynamics of humoral immunity to Rickettsia typhi infection in murine typhus patients in Laos and proposed diagnostic cut-offs for serological testing.

OBJECTIVES: This study examined individuals with *Rickettsia typhi* infection in the Lao People's Democratic Republic (Lao PDR) to (a) investigate humoral immune dynamics; (b) determine the differences in reference diagnostic results and recommend appropriate cut-offs; (c) determine differences in immune response after different antibiotic treatments; and (d) determine appropriate diagnostic cut-off parameters for indirect immunofluorescence assay (IFA). **METHODS:** Sequential serum samples from 90 non-pregnant, adults were collected at seven time-points (days 0, 7, 14, 28, 90, 180 and 365) as part of a clinical antibiotic treatment trial. Samples were tested using IFA to determine IgM and IgG antibody reciprocal end-point titres against *R. typhi* and PCR. RESULTS: For all 90 individuals, reciprocal *R. typhi* IgM and IgG antibody titres ranged from <400 to ≥3200. The median half-life of *R. typhi* IgM was 126 days (interquartile range 36-204 days) and IgG was 177 days (interquartile range 134-355 days). Overall median patient titres for *R. typhi* IgM and IgG were significantly different ($p < 0.0001$) and at each temporal sample collection point (range $p < 0.0001$ to p 0.0411). Using Bayesian latent class model analysis, the optimal diagnostic cut-off reciprocal IFA titer on patient admission for IgM was 800 (78.6%, 95% CI 71.6%-85.2% sensitivity; 89.9%, 95% CI 62.5%-100% specificity), and for IFA IgG 1600 (77.3%; 95% CI 68.2%-87.6% sensitivity; 99%, 95% CI 95%-100% specificity). **CONCLUSIONS:** This study suggests suitable diagnostic cut-offs for local diagnostic laboratories and other endemic settings and highlights antibody persistence following acute infection. Further studies are required to validate and define cut-offs in other geographically diverse locations.

Using Land Runoff to Survey the Distribution and Genetic Diversity of *Burkholderia pseudomallei* in Vientiane, Laos. Rachlin A, Luangraj M, Kaestli M, Rattanavong S, Phoumin P, Webb JR, Mayo M, Currie BJ, Dance DAB. *Appl Environ Microbiol* 2021; 87(4): e02112-20. Published online: 30 November 2020. doi: 10.1128/AEM.02112-20.

This study demonstrated that Burkholderia pseudomallei can be isolated from drains throughout urban Vientiane, and that Lao strains are genetically highly diverse (and thus well-established).

Melioidosis is a disease of significant public health importance that is being increasingly recognized globally. The majority of cases arise through direct percutaneous exposure to its etiological agent, *Burkholderia pseudomallei* In the Lao People's Democratic Republic (Laos), the presence and environmental distribution of *B. pseudomallei* are not well characterized, though recent epidemiological surveys of the bacterium have indicated that *B. pseudomallei* is widespread throughout the environment in the centre and south of the country and that rivers can act as carriers and potential sentinels for the bacterium. The spatial and genetic distribution of *B. pseudomallei* within Vientiane Capital, from where the majority of cases diagnosed to date have originated, remains an important knowledge gap. We sampled surface runoff from drain catchment areas throughout urban Vientiane to determine the presence and local population structure of the bacterium. *B. pseudomallei* was detected in drainage areas throughout the capital, indicating it is widespread in the environment and that exposure rates in urban Vientiane are likely more frequent than previously thought. Whole-genome comparative analysis demonstrated that Lao *B. pseudomallei* isolates are highly genetically diverse, suggesting the bacterium is well-established and not a recent introduction. Despite the wide genome diversity, one environmental survey isolate was highly genetically related to a Lao melioidosis patient isolate collected 13 years prior to the study. Knowledge gained from this study will augment understanding of *B. pseudomallei* phylogeography in Asia and enhance public health awareness and future implementation of infection control measures within Laos. **IMPORTANCE:** The environmental bacterium *B. pseudomallei* is the etiological agent of melioidosis, a tropical disease with one model estimating a global annual incidence of 165,000 cases and 89,000 deaths. In the Lao People's Democratic Republic (Laos), the environmental distribution and population structure of *B. pseudomallei* remain relatively undefined, particularly in Vientiane Capital from where most diagnosed cases have originated. We used surface runoff as a proxy for *B. pseudomallei* dispersal in the environment and performed whole-genome sequencing (WGS) to examine the local population structure. Our data confirmed that *B. pseudomallei* is widespread throughout Vientiane and that surface runoff might be useful for future environmental monitoring of the bacterium. *B. pseudomallei* isolates were also highly genetically diverse, suggesting the bacterium is well-established and endemic in Laos. These findings can be used to improve awareness of *B. pseudomallei* in the Lao environment and demonstrates the epidemiological and phylogeographical insights that can be gained from WGS.

***Elizabethkingia anophelis* Infection in Infants, Cambodia, 2012-2018.** Reed TAN, Watson G, Kheng C, Tan P, Roberts T, Ling CL, Miliya T, Turner P. *Emerg Infect Dis* 2020; 26(2): 320-2. Published online: 07 January 2020. doi: 10.3201/eid2602.190345

Case report and retrospective identification of previous isolates of E. anophelis, a recently identified opportunistic pathogen, in Cambodia and Thailand.

We describe 6 clinical isolates of *Elizabethkingia anophelis* from a pediatric referral hospital in Cambodia, along with 1 isolate reported from Thailand. Improving diagnostic microbiological methods in resource-limited settings will increase the frequency of reporting for this pathogen. Consensus on therapeutic options is needed, especially for resource-limited settings.

Typhoid in Laos: An 18-Year Perspective. Roberts T, Rattanavong S, Phommasone K, Chansamouth V, Davong V, Keoluangkhot V, Hongsakhone S, Bounsavath N, Mayxay M, Vongsouvath M, Dance DAB, Newton PN. *Am J Trop Med Hyg* 2020; 102(4): 749-57. Published online: 27 January 2020. doi: 10.4269/ajtmh.19-0637.

This study of over 900 Lao Salmonella Typhi isolates, collected over 18 years, demonstrated seasonality in incidence, but very little fluoroquinolone or multi-drug resistance.

Although typhoid is endemic to Southeast Asia, very little is known about the disease in Laos. Typhoid vaccination is not included in the national immunization program. Although sanitation has improved, one million people still do not have access to basic clean water sources. We describe the epidemiology and antimicrobial susceptibility patterns of *Salmonella enterica* serovar Typhi (*S.* Typhi) infection in Laos based on isolates accrued over 18 years at Mahosot Hospital, Vientiane. All blood cultures collected from patients presenting with fever submitted to the Microbiology Laboratory at Mahosot Hospital (February 2000-December 2018) were included. This included patients from Vientiane and four provincial hospitals and one typhoid outbreak investigation. A total of 913 (1.5%) of 60,384 blood cultures were positive for *S.* Typhi. The majority of isolates with data available (712/898, 79.3%) were susceptible to all antibiotics tested, with 59 (6.5%) multidrug-resistant (MDR) isolates, mostly from one outbreak. Of 854 isolates, 12 (1.4%) were fluoroquinolone resistant. Patient admissions peaked between March and June at the end of the dry season. Although there are key limitations, these data give the first detailed epidemiological evidence of typhoid in Laos. However, estimates will be greatly influenced by access to blood culture services and health-seeking behaviour. Although typhoid multidrug resistance and fluoroquinolone resistance are not currently major issues in Laos, continued surveillance and improved antibiotic stewardship are necessary to forestall worsening of the situation. Cost-effectiveness analysis is needed to inform decisions regarding typhoid vaccine introduction.

ACORN (A Clinically-Oriented Antimicrobial Resistance Surveillance Network): a pilot protocol for case based antimicrobial resistance surveillance. Turner P, Ashley EA, Celhay OJ, Douangnouvong A, Hamers RL, Ling CL, Lubell Y, Miliya T, Roberts T, Soputhy C, Ngoc Thach P, Vongsouvath M, Waithira N, Wannapinij P, van Doorn HR. *Wellcome Open Res* 2020; 5: 13. Published online: 01 June 2020. doi: 10.12688/wellcomeopenres.15681.2.

This publication describes the pilot phase protocol for the ACORN Study of AMR Surveillance. Mahosot Hospital is one of the Study Sites.

BACKGROUND: Antimicrobial resistance (AMR) / drug resistant infections (DRIs) are a major global health priority. Surveillance data is critical to inform infection treatment guidelines, monitor trends, and to assess interventions. However, most existing AMR / DRI surveillance systems are passive and pathogen-based with many potential biases. Addition of clinical and patient outcome data would provide considerable added value to pathogen-based surveillance. **METHODS:** The aim of the ACORN project is to develop an efficient clinically-oriented AMR surveillance system, implemented alongside routine clinical care in hospitals in low- and middle-income country settings. In an initial pilot phase, clinical and microbiology data will be collected from patients presenting with clinically suspected meningitis, pneumonia, or sepsis. Community-acquired infections will be identified by daily review of new admissions, and hospital-acquired infections will be enrolled during weekly point prevalence surveys, on surveillance wards. Clinical variables will be collected at enrolment, hospital discharge, and at day 28 post-enrolment using an electronic questionnaire on a mobile device. These data will be merged with laboratory data onsite using a flexible automated computer script. Specific target pathogens will be *Streptococcus pneumoniae*, *Staphylococcus aureus*, *Salmonella spp.*, *Klebsiella pneumoniae*, *Escherichia coli*, and *Acinetobacter baumannii*. A bespoke browser-based app will provide sites with fully interactive data visualisation, analysis, and reporting tools. **DISCUSSION:** ACORN will generate data on the burden of DRI which can be used to inform local treatment guidelines / national policy and serve as indicators to measure the impact of interventions. Following development, testing and iteration of the surveillance tools during an initial six-month pilot phase, a wider rollout is planned.

Case-based surveillance of antimicrobial resistance in the ACORN (A Clinically Oriented Antimicrobial Resistance Surveillance Network) study. van Doorn HR, Ashley EA, Turner P. *JAC-Antimicrob Resist* 2020; 2(1): dlaa018. Published online: 14 April 2020. doi: 10.1093/jacamr/dlaa018.
Letter (Correspondence).

The estimated burden of scrub typhus in Thailand from national surveillance data (2003-2018). Wangrangsimakul T, Elliott I, Nedsuwan S, Kumlert R, Hinjoy S, Chaisiri K, Day NPJ, Morand S. *PLoS Negl Trop Dis* 2020; 14(4): e0008233. Published online: 14 April 2020. doi: 10.1371/journal.pntd.0008233.
The burden of scrub typhus in Thailand is high, particularly in the northern provinces where disease incidence is rising.

BACKGROUND: Scrub typhus is a major cause of acute febrile illness in the tropics and is endemic over large areas of the Asia Pacific region. The national and global burden of scrub typhus remains unclear due to limited data and difficulties surrounding diagnosis. **METHODOLOGY/ PRINCIPAL FINDINGS:** Scrub typhus reporting data from 2003-2018 were collected from the Thai national disease surveillance system. Additional information including the district, sub-district and village of residence, population, geographical, meteorological and satellite imagery data were also collected for Chiangrai, the province with the highest number of reported cases from 2003-2018. From 2003-2018, 103,345 cases of scrub typhus were reported with the number of reported cases increasing substantially over the observed period. There were more men than women, with agricultural workers the main occupational group affected. The majority of cases occurred in the 15-64 year old age group (72,144/99,543, 72%). Disease burden was greatest in the northern region, accounting for 53% of the total reported cases per year (mean). In the northern region, five provinces-Chiangrai, Chiangmai, Tak, Nan and Mae Hong Son-accounted for 84% (46,927/55,872) of the total cases from the northern region or 45% (46,927/103,345) of cases nationally. The majority of cases occurred from June to November but seasonality was less marked in the southern region. In Chiangrai province, elevation, rainfall, temperature, population size, habitat complexity and diversity of land cover contributed to scrub typhus incidence. **INTERPRETATION:** The burden of scrub typhus in Thailand is high with disease incidence rising significantly over the last two decades. However, disease burden is not uniform with northern provinces particularly affected. Agricultural activity along with geographical, meteorological and land cover factors are likely to contribute to disease incidence. Our report, along with existing epidemiological data, suggests that scrub typhus is the most clinically important rickettsial disease globally.

Scrub Typhus and the Misconception of Doxycycline Resistance. Wangrangsimakul T, Phuklia W, Newton PN, Richards AL, Day NPJ. *Clin Infect Dis* 2020; 70(11): 2444-9. Published online: 01 October 2019. doi: 10.1093/cid/ciz972.
This report presents the case against the existence of doxycycline resistance in Orientia tsutsugamushi, the causative pathogen of scrub typhus.

Scrub typhus, a neglected infectious disease caused by the obligate intracellular bacterium *Orientia tsutsugamushi*, is a major cause of fever across the Asia Pacific region with more than a billion people at risk. Treatment with antibiotics such as doxycycline or chloramphenicol is effective for the majority of patients. In the 1990s, reports from northern Thailand raised a troubling observation; some scrub typhus patients responded poorly to doxycycline, which investigators attributed to doxycycline resistance. Despite the controversial nature of these reports, independent verification was neglected, with subsequent studies speculating on the role of doxycycline resistance in contributing to failure of treatment or prophylaxis. In this review, we have outlined the evidence for drug-resistant *Orientia tsutsugamushi*, assessed the evidence for doxycycline resistance, and highlight more recent findings unsupportive of doxycycline resistance. We conclude that doxycycline resistance is a misconception, with treatment outcome likely to be determined by other bacterial, host, and pharmacological factors.

Drug-Resistant Scrub Typhus. Wangrangsimakul T, Phuklia W, Newton PN, Richards AL, Day NPJ. *Clin Infect Dis* 2020; 71(6): 1580-1. Published online: 15 December 2019. doi: 10.1093/cid/ciz1192.
Letter (Correspondence).

The effectiveness of the 13-valent pneumococcal conjugate vaccine against hypoxic pneumonia in children in Lao People's Democratic Republic: An observational hospital-based test-negative study. Weaver R, Nguyen CD, Chan J, Vilivong K, Lai JYR, Lim R, Satzke C, Vongsakid M, Newton PN, Mulholland K, Gray A, Dubot-Pérès A, Dance DAB, Russell FM. *Lancet Regional Health - Western Pacific* 2020; 2: 100014. Published online: 06 September 2020. doi: 10.1016/j.lanwpc.2020.100014.
This study used a novel approach to demonstrate that the 13-valent pneumococcal conjugate vaccine (PCV13) is effective against hypoxic pneumonia in children in Laos, and should be prioritised for inclusion in national immunisation programs in Asia.

BACKGROUND: Pneumococcal pneumonia is a leading cause of childhood mortality. Pneumococcal conjugate vaccines (PCVs) have been shown to reduce hypoxic pneumonia in children. However, there are no studies from Asia examining the effectiveness of PCVs on hypoxic pneumonia. We describe a novel approach to determine the effectiveness of the 13-valent PCV (PCV13) against hypoxia in children admitted with pneumonia in the Lao People's Democratic Republic. **METHODS:** A prospective hospital-based, test-negative observational study of children aged up to 59 months admitted with pneumonia to a single tertiary hospital in Vientiane was undertaken over 54 months. Pneumonia was defined using the 2013 WHO definition. Hypoxia was defined as oxygen saturation < 90% in room air or requiring oxygen supplementation during hospitalisation. Test-negative cases and controls were children with hypoxic and non-hypoxic pneumonia, respectively. PCV13 status was determined by written record. Vaccine effectiveness was calculated using logistic regression. Propensity score and multiple imputation analyses were used to handle confounding and missing data. Findings: There were 826 children admitted with pneumonia, 285 had hypoxic pneumonia and 377 were PCV13-vaccinated. The unadjusted, propensity-score adjusted and multiple-imputation adjusted estimates of vaccine effectiveness against hypoxic pneumonia were 23% (95% confidence interval: -9, 46%; p = 0.14); 37% (6, 57%; p = 0.02) and 35% (7, 55%; p = 0.02) respectively. Interpretation: PCV13 is effective against hypoxic pneumonia in Asia, and should be prioritised for inclusion in national immunisation programs. This single hospital-based, test-negative approach can be used to assess vaccine effectiveness in other similar settings.

Myanmar *Burkholderia pseudomallei* strains are genetically diverse and originate from Asia with phylogenetic evidence of reintroductions from neighbouring countries. Webb JR, Win MM, Zin KN, Win KKN, Wah TT, Ashley EA, Smithuis F, Swe MMM, Mayo M, Currie BJ, Dance DAB. *Sci Rep* 2020; 10(1): 16260. Published online: 03 October 2020. doi: 10.1038/s41598-020-73545-8.

Whole-genome sequencing suggests that B. pseudomallei was not introduced into Myanmar recently, as isolates show a high degree of diversity.

Melioidosis was first identified in Myanmar in 1911 but for the last century it has remained largely unreported there. *Burkholderia pseudomallei* was first isolated from the environment of Myanmar in 2016, confirming continuing endemicity. Recent genomic studies showed that *B. pseudomallei* originated in Australia and spread to Asia, with phylogenetic evidence of repeated reintroduction of *B. pseudomallei* across countries bordered by the Mekong River and the Malay Peninsula. We present the first whole-genome sequences of *B. pseudomallei* isolates from Myanmar: nine clinical and seven environmental isolates. We used large-scale comparative genomics to assess the genetic diversity, phylogeography and potential origins of *B. pseudomallei* in Myanmar. Global phylogenetics demonstrated that Myanmar isolates group in two distantly related clades that reside in a more ancestral Asian clade with high amounts of genetic diversity. The diversity of *B. pseudomallei* from Myanmar and divergence within our global phylogeny suggest that the original introduction of *B. pseudomallei* to Myanmar was not a recent event. Our study provides new insights into global patterns of *B. pseudomallei* dissemination, most notably the dynamic nature of movement of *B. pseudomallei* within densely populated Southeast Asia. The role of anthropogenic influences in both ancient and more recent dissemination of *B. pseudomallei* to Myanmar and elsewhere in Southeast Asia and globally requires further study.

Evidence for action: a One Health learning platform on interventions to tackle antimicrobial resistance. Wernli D, Jørgensen PS, Parmley EJ, Troell M, Majowicz S, Harbarth S, Léger A, Lambraki I, Graells T, Henriksson PJG, Carson C, Cousins M, Skoog Ståhlgren G, Mohan CV, Simpson AJH, Wieland B, Pedersen K, Schneider A, Chandy SJ, Wijayathilaka TP, Delamare-Deboutteville J, Vila J, Stålsby Lundborg C, Pittet D. *Lancet Infect Dis* 2020; 20(12): e307-11. doi: 10.1016/S1473-3099(20)30392-3. Epub 2020 Aug 24. PMID: 32853549; PMCID: PMC7444982.

Advocacy for an online AMR One Health learning platform and database of interventions.

Improving evidence for action is crucial to tackle antimicrobial resistance. The number of interventions for antimicrobial resistance is increasing but current research has major limitations in terms of efforts, methods, scope, quality, and reporting. Moving the agenda forwards requires an improved understanding of the diversity of interventions, their feasibility and cost-benefit, the implementation factors that shape and underpin their effectiveness, and the ways in which individual interventions might interact synergistically or antagonistically to influence actions against antimicrobial resistance in different contexts. Within the efforts to strengthen the global governance of antimicrobial resistance, we advocate for the creation of an international One Health platform for online learning. The platform will synthesise the evidence for actions on antimicrobial resistance into a fully accessible database; generate new scientific insights into the design, implementation, evaluation, and reporting of the broad range of interventions relevant to addressing antimicrobial resistance; and ultimately contribute to the goal of building societal resilience to this central challenge of the 21st century.

Genomic surveillance for hypervirulence and multi-drug resistance in invasive *Klebsiella pneumoniae* from South and Southeast Asia. Wyres KL, Nguyen TNT, Lam MMC, Judd LM, van Vinh Chau N, Dance DAB, Ip M, Karkey A, Ling CL, Miliya T, Newton PN, Lan NPH, Sengduangphachanh A, Turner P, Veeraraghavan B, Vinh PV, Vongsouvath M, Thomson NR, Baker S, Holt KE. *Genome Med* 2020; 12(1): 11. Published online: 16 January 2020. doi: 10.1186/s13073-019-0706-y.

This study used genomics-based surveillance and molecular profiles, such as sequence type and AMR genes, to demonstrate unique differences in K. pneumoniae isolates from south and southeast Asia.

BACKGROUND: *Klebsiella pneumoniae* is a leading cause of bloodstream infection (BSI). Strains producing extended-spectrum beta-lactamases (ESBLs) or carbapenemases are considered global priority pathogens for which new treatment and prevention strategies are urgently required, due to severely limited therapeutic options. South and Southeast Asia are major hubs for antimicrobial -resistant (AMR) *K. pneumoniae* and also for the characteristically antimicrobial-sensitive, community-acquired "hypervirulent" strains. The emergence of hypervirulent AMR strains and lack of data on exopolysaccharide diversity pose a challenge for *K. pneumoniae* BSI control strategies worldwide. **METHODS:** We conducted a retrospective genomic epidemiology study of 365 BSI *K. pneumoniae* from seven major healthcare facilities across South and Southeast Asia, extracting clinically relevant information (AMR, virulence, K and O antigen loci) using Kleborate, a *K. pneumoniae*-specific genomic typing tool. **RESULTS:** *K. pneumoniae* BSI isolates were highly diverse, comprising 120 multi-locus sequence types (STs) and 63 K-loci. ESBL and carbapenemase gene frequencies were 47% and 17%, respectively. The aerobactin synthesis locus (iuc), associated with hypervirulence, was detected in 28% of isolates. Importantly, 7% of isolates harbourediuc plus ESBL and/or carbapenemase genes. The latter represent genotypic AMR-virulence convergence, which is generally considered a rare phenomenon but was particularly common among South Asian BSI (17%). Of greatest concern, we identified seven novel plasmids carrying both iuc and AMR genes, raising the prospect of co-transfer of these phenotypes among K. pneumoniae. **CONCLUSIONS:** *K. pneumoniae* BSI in South and Southeast Asia are caused by different STs from those predominating in other regions, and with higher frequency of acquired virulence determinants. *K. pneumoniae* carrying both iuc and AMR genes were also detected at higher rates than have been reported elsewhere. The study demonstrates how genomics-based surveillance-reporting full molecular profiles including STs, AMR, virulence and serotype locus information-can help standardise comparisons between sites and identify regional differences in pathogen populations.

MALARIA

***Plasmodium falciparum* ATP4 inhibitors to treat malaria: worthy successors to artemisinin?** Ashley EA, Phyo AP. Lancet Infect Dis 2020; 20(8): 883-5. Published online: 07 April 2020. doi: 10.1016/S1473-3099(20)30139-0.

Comment.

Treatment and prevention of malaria in children. Ashley EA, Poespoprodjo JR. *Lancet Child Adolesc Health* 2020; 4(10): 775-89. Published online: 19 September 2020. doi: 10.1016/S2352-4642(20)30127-9.

Review of the management of malaria in children.

Malaria disproportionately affects children younger than 5 years. Falciparum malaria is responsible for more than 200 000 child deaths per year in Africa and vivax malaria is well documented as a cause of severe anaemia and excess mortality in children in Asia and Oceania. For the treatment of malaria in children, paediatric dosing recommendations for several agents, including parenteral artesunate and dihydroartemisinin-piperaquine, have belatedly been shown to be suboptimal. Worsening antimalarial resistance in *Plasmodium falciparum* in the Greater Mekong Subregion threatens to undermine global efforts to control malaria. Triple antimalarial combination therapies are being evaluated to try to impede this threat. The RTS,S/AS01 vaccine gives partial protection against falciparum malaria and is being evaluated in large, pilot studies in Ghana, Malawi, and Kenya as a complementary tool to other preventive measures. Seasonal malaria chemoprevention in west Africa has resulted in declines in malaria incidence and deaths and there is interest in scaling up efforts by expanding the age range of eligible recipients. Preventing relapse in *Plasmodium vivax* infection with primaquine is challenging because treating children who have G6PD deficiency with primaquine can cause acute haemolytic anaemia. The safety of escalating dose regimens for primaquine is being studied to mitigate this risk.

Seasonal malaria chemoprevention: closing the know-do gap. Ashley EA, Yeka A. *Lancet* 2020; 396(10265): 1778-9. Published online: 05 December 2020. doi: 10.1016/S0140-6736(20)32525-3. *Comment.*

Factors affecting the electrocardiographic QT interval in malaria: A systematic review and meta-analysis of individual patient data. Chan XHS, Win YN, Haeusler IL, Tan JY, Loganathan S, Saralamba S, Chan SKS, Ashley EA, Barnes KI, Baiden R, Bassi PU, Djimde A, Dorsey G, Duparc S, Hanboonkunupakarn B, Ter Kuile FO, Lacerda MVG, Nasa A, Nosten FH, Onyeji CO, Pukrittayakamee S, Siqueira AM, Tarning J, Taylor WRJ, Valentini G, van Vugt M, Wesche D, Day NPJ, Huang CL, Brugada J, Price RN, White NJ. *PLoS Med* 2020; 17(3): e1003040. Published online: 05 March 2020. doi: 10.1371/journal.pmed.1003040.

This large systematic review and meta-analysis (10,452 subjects) concludes that adjustment for malaria and fever-recovery-related QT lengthening is necessary to avoid misattributing malaria-related QT changes to antimalarial drug effects.

BACKGROUND: Electrocardiographic QT interval prolongation is the most widely used risk marker for ventricular arrhythmia potential and thus an important component of drug cardiotoxicity assessments. Several antimalarial medicines are associated with QT interval prolongation. However, interpretation of electrocardiographic changes is confounded by the coincidence of peak antimalarial drug concentrations with recovery from malaria. We therefore reviewed all available data to characterise the effects of malaria disease and demographic factors on the QT interval in order to improve assessment of electrocardiographic changes in the treatment and prevention of malaria. **METHODS AND FINDINGS:** We conducted a systematic review and meta-analysis of individual patient data. We searched clinical bibliographic databases (last on August 21, 2017) for studies of the quinoline and structurally related antimalarials for malaria-related indications in human participants in which electrocardiograms were systematically recorded. Unpublished studies were identified by the World Health Organization (WHO) Evidence Review Group (ERG) on the Cardiotoxicity of Antimalarials. Risk of bias was assessed using the Pharmacoepidemiological Research on Outcomes of Therapeutics by a European Consortium (PROTECT) checklist for adverse drug events. Bayesian hierarchical multivariable regression with generalised additive models was used to investigate the effects of malaria and demographic factors on the pretreatment QT interval. The meta-analysis included 10,452 individuals (9,778 malaria patients, including 343 with severe disease, and 674 healthy participants) from 43 studies. 7,170 (68.6%) had fever (body temperature >/= 37.5 degrees C), and none developed ventricular arrhythmia after antimalarial treatment. Compared to healthy participants, patients with uncomplicated falciparum malaria had shorter QT intervals (-61.77 milliseconds; 95% credible interval [CI]: -80.71 to -42.83) and increased sensitivity of the QT interval to heart rate changes. These effects were greater in s evere malaria (-110.89 milliseconds; 95% CI: -140.38 to -81.25). Body temperature was associated independently with clinically significant QT shortening of 2.80 milliseconds (95% CI: -3.17 to -2.42) per 1 degrees C increase. Study limitations include that it was not possible to assess the effect of other factors that may affect the QT interval but are not consistently collected in malaria clinical trials. **CONCLUSIONS:** Adjustment for malaria and fever-recovery-related QT lengthening is necessary to avoid misattributing malaria-disease-related QT changes to antimalarial drug effects. This would improve risk assessments of antimalarial-related cardiotoxicity in clinical research and practice. Similar adjustments may be indicated for other febrile illnesses for which QT-interval-prolonging medications are important therapeutic options.

The risk of *Plasmodium vivax* parasitaemia after *P. falciparum* malaria: An individual patient data meta-analysis from the WorldWide Antimalarial Resistance Network. Hossain MS, Commons RJ, Douglas NM, Thriemer K, Alemayehu BH, Amaratunga C, Anvikar AR, Ashley EA, Asih PBS, Carrara VI, Lon C, D'Alessandro U, Davis TME, Dondorp AM, Edstein MD, Fairhurst RM, Ferreira MU, Hwang J, Janssens B, Karunajeewa H, Kiechel JR, Ladeia-Andrade S, Laman M, Mayxay M, McGready R, Moore BR, Mueller I, Newton PN, Thuy-Nhien NT, Noedl H, Nosten F, Phyo AP, Poespoprodjo JR, Saunders DL, Smithuis F, Spring MD, Stepniewska K, Suon S, Suputtamongkol Y, Syafruddin D, Tran HT, Valecha N, Van Herp M, Van Vugt M, White NJ, Guerin PJ, Simpson JA, Price RN. *PLoS Med* 2020; 17(11): e1003393. Published online: 19 November 2020. doi: 10.1371/journal.pmed.1003393.

This meta-analysis suggests there is a high risk of P. vivax *parasitaemia after treatment of falciparum malaria, probably due to preventable relapses, but the risk is variable geographically.*

BACKGROUND: There is a high risk of *Plasmodium vivax* parasitaemia following treatment of falciparum malaria. Our study aimed to quantify this risk and the associated determinants using an individual patient data meta-analysis in order to identify populations in which a policy of universal radical cure, combining artemisinin-based combination therapy (ACT) with a hypnozoitocidal antimalarial drug, would be beneficial. **METHODS AND FINDINGS:** A systematic review of Medline, Embase, Web of Science, and the Cochrane Database of Systematic Reviews identified efficacy studies of uncomplicated falciparum malaria treated with ACT that were undertaken in regions coendemic for *P. vivax* between 1 January 1960 and 5 January 2018. Data from eligible studies were pooled using standardised methodology. The risk of *P. vivax* parasitaemia at days 42 and 63 and associated risk factors were investigated by multivariable Cox regression analyses. Study quality was assessed using a tool developed by the Joanna Briggs Institute. The study was registered in the International Prospective Register of Systematic Reviews (PROSPERO: CRD42018097400). In total, 42 studies enrolling 15,341 patients were included in the analysis, including 30 randomised controlled trials and 12 cohort studies. Overall, 14,146 (92.2%) patients had *P. falciparum* monoinfection and 1,195 (7.8%) mixed infection with *P. falciparum* and *P. vivax*. The median age was 17.0 years (interquartile range [IQR] = 9.0-29.0 years; range = 0-80 years), with 1,584 (10.3%) patients younger than 5 years. 2,711 (17.7%) patients were treated with artemether-lumefantrine (AL, 13 studies), 651 (4.2%) with artesunate-amodiaquine (AA, 6 studies), 7,340 (47.8%) with artesunate -mefloquine (AM, 25 studies), and 4,639 (30.2%) with dihydroartemisinin-piperaquine (DP, 16 studies). 14,537 patients (94.8%) were enrolled from the Asia-Pacific region, 684 (4.5%) from the Americas, and 120 (0.8%) from Africa. At day 42, the cumulative risk of vivax parasitaemia following treatment of *P. falciparum* was 31.1% (95% CI 28.9-33.4) after AL, 14.1% (95% CI 10.8-18.3) after AA, 7.4% (95% CI 6.7-8.1) after AM, and 4.5% (95% CI 3.9-5.3) after DP. By day 63, the risks had risen to 39.9% (95% CI 36.6-43.3), 42.4% (95% CI 34.7-51.2), 22.8% (95% CI 21.2-24.4), and 12.8% (95% CI 11.4-14.5), respectively. In multivariable analyses, the highest rate of *P. vivax* parasitaemia over 42 days of follow-up was in patients residing in areas of short relapse periodicity (adjusted hazard ratio [AHR] = 6.2, 95% CI 2.0-19.5; p = 0.002); patients treated with AL (AHR = 6.2, 95% CI 4.6-8.5; p < 0.001), AA (AHR = 2.3, 95% CI 1.4-3.7; p = 0.001), or AM (AHR = 1.4, 95% CI 1.0-1.9; p = 0.028) compared with DP; and patients who did not clear their initial parasitaemia within 2 days (AHR = 1.8, 95% CI 1.4-2.3; p < 0.001). The analysis was limited by heterogeneity between study populations and lack of data from very low transmission settings. Study quality was high. **CONCLUSIONS:** In this meta-analysis, we found a high risk of *P. vivax* parasitaemia after treatment of *P. falciparum* malaria that varied significantly between studies. These *P. vivax* infections are likely attributable to relapses that could be prevented with radical cure including a hypnozoitocidal agent; however, the benefits of such a novel strategy will vary considerably between geographical areas.

Molecular epidemiology of resistance to antimalarial drugs in the Greater Mekong subregion: an observational study. Imwong M, Dhorda M, Myo Tun K, Thu AM, Phyo AP, Proux S, Suwannasin K, Kunasol C, Srisutham S, Duanguppama J, Vongpromek R, Promnarate C, Saejeng A, Khantikul N, Sugaram R, Thanapongpichat S, Sawangjaroen N, Sutawong K, Han KT, Htut Y, Linn K, Win AA, Hlaing TM, van der Pluijm RW, Mayxay M, Pongvongsa T, Phommasone K, Tripura R, Peto TJ, von Seidlein L, Nguon C, Lek D, Chan XHS, Rekol H, Leang R, Huch C, Kwiatkowski DP, Miotto O, Ashley EA, Kyaw MP, Pukrittayakamee S, Day NPJ, Dondorp AM, Smithuis FM, Nosten FH, White NJ. *Lancet Infect Dis* 2020; 20(12): 1470-80. Published online: 14 July 2020. doi: 10.1016/S1473-3099(20)30228-0.

Artemisinin resistance in P. falciparum *is now prevalent across the Greater Mekong subregion, although this is not due to a single lineage.*

BACKGROUND: The Greater Mekong subregion is a recurrent source of antimalarial drug resistance in *Plasmodium falciparum* malaria. This study aimed to characterise the extent and spread of resistance across this entire region between 2007 and 2018. METHODS: *P. falciparum* isolates from Myanmar, Thailand, Laos, and Cambodia were obtained from clinical trials and epidemiological studies done between Jan 1, 2007, and Dec 31, 2018, and were genotyped for molecular markers (pfkelch, pfcrt, pfplasmepsin2, and pfmdr1) of antimalarial drug resistance. Genetic relatedness was assessed using microsatellite and single nucleotide polymorphism typing of flanking sequences around target genes. FINDINGS: 10 632 isolates were genotyped. A single long pfkelch Cys580Tyr haplotype (from -50 kb to +31.5 kb) conferring artemisinin resistance (PfPailin) now dominates across the eastern Greater Mekong subregion. Piperaquine resistance associated with pfplasmepsin2 gene amplification and mutations in pfcrt downstream of the Lys76Thr chloroquine resistance locus has also developed. On the Thailand-Myanmar border a different pfkelch Cys580Tyr lineage rose to high frequencies before it was eliminated. Elsewhere in Myanmar the Cys580Tyr allele remains widespread at low allele frequencies. Meanwhile a single artemisinin-resistant pfkelch Phe446Ile haplotype has spread across Myanmar. Despite intense use of dihydroartemisinin-piperaquine in Kayin state, eastern Myanmar, both in treatment and mass drug administrations, no selection of piperaquine resistance markers was observed. pfmdr1 amplification, a marker of resistance to mefloquine, remains at low prevalence across the entire region. **INTERPRETATION:** Artemisinin resistance in *P. falciparum* is now prevalent across the Greater Mekong subregion. In the eastern Greater Mekong subregion a multidrug resistant *P. falciparum* lineage (PfPailin) dominates. In Myanmar a long pfkelch Phe446Ile haplotype has spread widely but, by contrast with the eastern Greater Mekong subregion, there is no indication of artemisinin combination therapy (ACT) partner drug resistance from genotyping known markers, and no evidence of spread of ACT resistant *P. falciparum* from the east to the west. There is still a window of opportunity to prevent global spread of ACT resistance. FUNDING: Thailand Science Research and Innovation, Initiative 5%, Expertise France, Wellcome Trust.

The use of ultrasensitive quantitative-PCR to assess the impact of primaquine on asymptomatic relapse of *Plasmodium vivax* infections: a randomized, controlled trial in Lao PDR. Phommasone K, van Leth F, Imwong M, Henriques G, Pongvongsa T, Adhikari B, Peto TJ, Promnarate C, Dhorda M, Sirithiranont P, Mukaka M, Peerawaranun P, Day NPJ, Cobelens F, Dondorp AM, Newton PN, White NJ, von Seidlein L, Mayxay M. *Malar J* 2020; 19(1): 4. Published online: 03 January 2020. doi: 10.1186/s12936-019-3091-5.

An ultrasensitive PCR detection method was used in a successful trial of primaquine for preventing relapse of asymptomatic P. vivax *infections.*

BACKGROUND: Trials to assess the efficacy of the radical cure of *Plasmodium vivax* malaria with 8-aminoquinolines require that most post-treatment relapses are identified, but there is no consensus on the optimal duration of follow-up in either symptomatic or asymptomatic vivax malaria. The efficacy of a 14-day course of primaquine on the cumulative incidence of recurrent asymptomatic *P. vivax* infections detected by ultrasensitive quantitative PCR (uPCR) as a primary endpoint was assessed. **METHODS:** A randomized, placebo-controlled, single-blind trial was conducted in four villages of the Lao PDR during 2016-2018 nested in a larger project evaluating mass drug administrations (MDA) with dihydroartemisinin-piperaquine (DP) and a single low-dose primaquine to clear *Plasmodium falciparum* infections. In the nested sub-study, eligible participants with mono- or mixed *P. vivax* infections detected by uPCR were randomized to receive either 14 days of primaquine (0.5 mg/kg/day) or placebo during the last round of MDA (round 3) through directly observed therapy. Participants were checked monthly for 12 months for parasitaemia using uPCR. The primary outcome was cumulative incidence of participants with at least one recurrent episode of *P. vivax* infection. **RESULTS:** 20 G6PD-normal participants were randomized in each arm. 5 (29%) of 20 participants in the placebo arm experienced asymptomatic, recurrent *P. vivax* infections, resulting in a cumulative incidence at month 12 of 29%. None of the 20 participants in the intervention arm had recurrent infections (p = 0.047 Fisher's exact test). Participants with recurrent *P. vivax* infections were found to be parasitaemic for between one and five sequential monthly tests. The median time to recurrence of *P. vivax* parasitaemia was 178 days (range 62-243 days). **CONCLUSIONS**: A 14-day course of primaquine in addition to a DP-MDA was safe, well-tolerated, and prevented recurrent asymptomatic *P. vivax* infections. Long follow-up for up to 12 months is required to capture all recurrences following the treatment of asymptomatic vivax infection. To eliminate all malarias in settings where *P. vivax* is endemic, a full-course of an 8-aminoquinoline should be added to MDA to eliminate all malarias. Trial registration: This study was registered with ClinicalTrials.gov under NCT02802813 on 16th June 2016. https://clinicaltrials.gov/ct2/show/NCT02802813.

Mass drug administrations with dihydroartemisinin-piperaquine and single low dose primaquine to eliminate *Plasmodium falciparum* have only a transient impact on *Plasmodium vivax*: Findings from randomised controlled trials. Phommasone K, van Leth F, Peto TJ, Landier J, Nguyen T-N, Tripura R, Pongvongsa T, Lwin KM, Kajeechiwa L, Thwin MM, Parker DM, Wiladphaingern J, Nosten S, Proux S, Nguon C, Davoeung C, Rekol H, Adhikari B, Promnarate C, Chotivanich K, Hanboonkunupakarn B, Jittmala P, Cheah PY, Dhorda M, Imwong M, Mukaka M, Peerawaranun P, Pukrittayakamee S, Newton PN, Thwaites GE, Day NPJ, Mayxay M, Hien TT, Nosten FH, Cobelens F, Dondorp AM, White NJ, von Seidlein L. PLoS One 2020; 15(2): e0228190. Published online: 05 February 2020. doi: 10.1371/journal.pone.0228190.

Mass antimalarial drug administration (MDA) for P. falciparum *infections had only a transient effect on* P. vivax *prevalence. Radical cure will be required to eliminate vivax malaria in mass campaigns.*

BACKGROUND: Mass administrations of antimalarial drugs (MDA) have reduced the incidence and prevalence of *P. falciparum* infections in a trial in the Greater Mekong Subregion. Here we assess the impact of the MDA on *P. vivax* infections. **METHODS:** Between May 2013 and July 2017, four villages in each Myanmar, Vietnam, Cambodia and Lao PDR were selected based on high prevalence of *P. falciparum* infections. Eight of the 16 villages were randomly assigned to receive MDA consisting of three-monthly rounds of three-day courses of dihydroartemisinin-piperaquine and, except in Cambodia, a single low-dose of primaquine. Cross-sectional surveys were conducted at quarterly intervals to detect Plasmodium infections using ultrasensitive qPCR. The difference in the cumulative incidence between the groups was assessed through a discrete time survival approach, the difference in prevalence through a difference-in-difference analysis, and the difference in the number of participants with a recurrence of *P. vivax* infection through a mixed-effect logistic regression. **RESULTS:** 3,790 (86%) residents in the intervention villages participated in at least one MDA round, of whom 2,520 (57%) participated in three rounds. The prevalence of *P. vivax* infections fell from 9.31% to 0.89% at month 3 but rebounded by six months to 5.81%. There was no evidence that the intervention reduced the cumulative incidence of *P. vivax* infections (95% confidence interval [CI] Odds ratio (OR): 0.29 to 1.36). Similarly, there was no evidence of MDA related reduction in the number of participants with at least one recurrent infection (OR: 0.34; 95% CI: 0.08 to 1.42). **CONCLUSION:** MDA with schizontocidal drugs had a lasting effect on *P. falciparum* infections but only a transient effect on the prevalence of *P. vivax* infections. Radical cure with an 8-aminoquinoline will be needed for the rapid elimination of vivax malaria.

Pregnancy outcomes and risk of placental malaria after artemisinin-based and quinine-based treatment for uncomplicated falciparum malaria in pregnancy: a WorldWide Antimalarial Resistance Network systematic review and individual patient data meta-analysis. Saito M, Mansoor R, Kennon K, Anvikar AR, Ashley EA, Chandramohan D, Cohee LM, D'Alessandro U, Genton B, Gilder ME, Juma E, Kalilani-Phiri L, Kuepfer I, Laufer MK, Lwin KM, Meshnick SR, Mosha D, Muehlenbachs A, Mwapasa V, Mwebaza N, Nambozi M, Ndiaye J-LA, Nosten F, Nyunt M, Ogutu B, Parikh S, Paw MK, Phyo AP, Pimanpanarak M, Piola P, Rijken MJ, Sriprawat K, Tagbor HK, Tarning J, Tinto H, Valéa I, Valecha N, White NJ, Wiladphaingern J, Stepniewska K, McGready R, Guérin PJ. *BMC Med* 2020; 18(1): 138. Published online: 02 June 2020. doi: 10.1186/s12916-020-01592-z.

This review and meta-analysis suggests that many of the known effects of falciparum malaria on foetal development do not differ between commonly used artemisinin-based combination therapies, and concludes that malaria prevention is key in pregnancy.

BACKGROUND: Malaria in pregnancy, including asymptomatic infection, has a detrimental impact on foetal development. Individual patient data (IPD) meta-analysis was conducted to compare the association between antimalarial treatments and adverse pregnancy outcomes, including placental malaria, accompanied with the gestational age at diagnosis of uncomplicated falciparum malaria infection. **METHODS:** A systematic review and one-stage IPD meta-analysis of studies assessing the efficacy of artemisinin-based and quinine-based treatments for patent microscopic uncomplicated falciparum malaria infection (hereinafter uncomplicated falciparum malaria) in pregnancy was conducted. The risks of stillbirth (pregnancy loss at >/= 28.0 weeks of gestation), moderate to late preterm birth (PTB, live birth between 32.0 and < 37.0 weeks), small for gestational age (SGA, birthweight of < 10th percentile), and placental malaria (defined as deposition of malaria pigment in the placenta with or without parasites) after different treatments of uncomplicated falciparum malaria were assessed by mixed-effects logistic regression, using artemether-lumefantrine, the most used antimalarial, as the reference standard. Registration **PROSPERO:** CRD42018104013. RESULTS: Of the 22 eligible studies (n = 5015), IPD from16 studies were shared, representing 95.0% (n = 4765) of the women enrolled in literature. Malaria treatment in this pooled analysis mostly occurred in the second (68.4%, 3064/4501) or third trimester (31.6%, 1421/4501), with gestational age confirmed by ultrasound in 91.5% (4120/4503). Quinine (n = 184) and five commonly used artemisinin-based combination therapies (ACTs) were included: artemether-lumefantrine (n = 1087), artesunate-amodiaquine (n = 775), artesunate-mefloquine (n = 965), and dihydroartemisinin -piperaquine (n = 837). The overall pooled proportion of stillbirth was 1.1% (84/4361), PTB 10.0% (619/4131), SGA 32.3% (1007/3707), and placental malaria 80.1% (2543/3035), and there were no significant differences of considered outcomes by ACT. Higher parasitaemia before treatment was associated with a higher risk of SGA (adjusted odds ratio [aOR] 1.14 per 10-fold increase, 95% confidence interval [CI] 1.03 to 1.26, p = 0.009) and deposition of malaria pigment in the placenta (aOR 1.67 per 10-fold increase, 95% CI 1.42 to 1.96, p < 0.001). CONCLUSIONS: The risks of stillbirth, PTB, SGA, and placental malaria were not different between the commonly used ACTs. The risk of SGA was high among pregnant women infected with falciparum malaria despite treatment with highly effective drugs. Reduction of malaria-associated adverse birth outcomes requires effective prevention in pregnant women.

Efficacy and tolerability of artemisinin-based and quinine-based treatments for uncomplicated falciparum malaria in pregnancy: a systematic review and individual patient data meta-analysis. Saito M, Mansoor R, Kennon K, Anvikar AR, Ashley EA, Chandramohan D, Cohee LM, D'Alessandro U, Genton B, Gilder ME, Juma E, Kalilani-Phiri L, Kuepfer I, Laufer MK, Lwin KM, Meshnick SR, Mosha D, Mwapasa V, Mwebaza N, Nambozi M, Ndiaye J-LA, Nosten F, Nyunt M, Ogutu B, Parikh S, Paw MK, Phyo AP, Pimanpanarak M, Piola P, Rijken MJ, Sriprawat K, Tagbor HK, Tarning J, Tinto H, Valéa I, Valecha N, White NJ, Wiladphaingern J, Stepniewska K, McGready R, Guérin PJ. *Lancet Infect Dis* 2020; 20(8): 943-52. Published online: 29 April 2020. doi: 10.1016/S1473-3099(20)30064-5.

This review and meta-analysis concludes that the efficacy and tolerability of artemisinin-based combination therapies (ACTs) are better than quinine in pregnancy.

BACKGROUND: Malaria in pregnancy affects both the mother and the foetus. However, evidence supporting treatment guidelines for uncomplicated (including asymptomatic) falciparum malaria in pregnant women is scarce and assessed in varied ways. We did a systematic literature review and individual patient data (IPD) meta-analysis to compare the efficacy and tolerability of different artemisinin-based or quinine-based treatments for malaria in pregnant women. **METHODS:** We did a systematic review of interventional or observational cohort studies assessing the efficacy of artemisinin-based or quinine-based treatments in pregnancy. Seven databases (MEDLINE, Embase, Global Health, Cochrane Library, Scopus, Web of Science, and Literatura Latino Americana em Ciencias da Saude) and two clinical trial registries (International Clinical Trials Registry Platform and ClinicalTrials.gov) were searched. The final search was done on April 26, 2019. Studies that assessed PCR-corrected treatment efficacy in pregnancy with follow-up of 28 days or more were included. Investigators of identified studies were invited to share data from individual patients. The outcomes assessed included PCR-corrected efficacy, PCR-uncorrected efficacy, parasite clearance, fever clearance, gametocyte development, and acute adverse events. One-stage IPD meta-analysis using Cox and logistic regression with random-effects was done to estimate the risk factors associated with PCR-corrected treatment failure, using artemether-lumefantrine as the reference. This study is registered with PROSPERO, CRD42018104013. **FINDINGS:** Of the 30 studies assessed, 19 were included, representing 92% of patients in the literature (4968 of 5360 episodes). Risk of PCR-corrected treatment failure was higher for the quinine monotherapy (n=244, adjusted hazard ratio [aHR] 6.11, 95% CI 2.57-14.54, p<0.0001) but lower for artesunate-amodiaquine (n=840, 0.27, 95% 0.14-0.52, p<0.0001), artesunate-mefloquine (n=1028, 0.56, 95% 0.34-0.94, p=0.03), and dihydroartemisinin-piperaquine (n=872, 0.35, 95% CI 0.18-0.68, p=0.002) than artemether-lumefantrine (n=1278) after adjustment for baseline asexual parasitaemia and parity. The risk of gametocyte carriage on day 7 was higher after quinine-based therapy than artemisinin-based treatment (adjusted odds ratio [OR] 7.38, 95% CI 2.29-23.82). **INTERPRETATION:** Efficacy and tolerability of artemisinin-based combination therapies (ACTs) in pregnant women are better than quinine. The lower efficacy of artemether-lumefantrine compared with other ACTs might require dose optimisation. **FUNDING:** The Bill & Melinda Gates Foundation, ExxonMobil Foundation, and the University of Oxford Clarendon Fund.

Association between the proportion of *Plasmodium falciparum* and *Plasmodium vivax* infections detected by passive surveillance and the magnitude of the asymptomatic reservoir in the community: a pooled analysis of paired health facility and community data. Stresman G, Sepúlveda N, Fornace K, Grignard L, Mwesigwa J, Achan J, Miller J, Bridges DJ, Eisele TP, Mosha J, Lorenzo PJ, Macalinao ML, Espino FE, Tadesse F, Stevenson JC, Quispe AM, Siqueira A, Lacerda M, Yeung S, Sovannaroth S, Pothin E, Gallay J, Hamre KE, Young A, Lemoine JF, Chang MA, Phommasone K, Mayxay M, Landier J, Parker DM, Von Seidlein L, Nosten F, Delmas G, Dondorp A, Cameron E, Battle K, Bousema T, Gething P, D'Alessandro U, Drakeley C. *Lancet Infect Dis* 2020; 20(8): 953-63. Published online: 08 April 2020. doi: 10.1016/S1473-3099(20)30059-1.

This global study shows that malaria detection rates rise when transmission intensity is low. This has implications for the organization of malaria healthcare provision.

BACKGROUND: Passively collected malaria case data are the foundation for public health decision making. However, because of population-level immunity, infections might not always be sufficiently symptomatic to prompt individuals to seek care. Understanding the proportion of all *Plasmodium* spp infections expected to be detected by the health system becomes particularly paramount in elimination settings. The aim of this study was to determine the association between the proportion of infections detected and transmission intensity for *Plasmodium falciparum* and *Plasmodium vivax* in several global endemic settings. **METHODS:** The proportion of infections detected in routine malaria data, P(Detect), was derived from paired household cross-sectional survey and routinely collected malaria data within health facilities. P(Detect) was estimated using a Bayesian model in 431 clusters spanning the Americas, Africa, and Asia. The association between P(Detect) and malaria prevalence was assessed using log-linear regression models. Changes in P(Detect) over time were evaluated using data from 13 timepoints over 2 years from The Gambia. FINDINGS: The median estimated P(Detect) across all clusters was 12.5% (IQR 5.3-25.0) for *P falciparum* and 10.1% (5.0-18.3) for *P vivax* and decreased as the estimated log-PCR community prevalence increased (adjusted odds ratio [OR] for *P falciparum* 0.63, 95% CI 0.57-0.69; adjusted OR for *P vivax* 0.52, 0.47-0.57). Factors associated with increasing P(Detect) included smaller catchment population size, high transmission season, improved care-seeking behaviour by infected individuals, and recent increases (within the previous year) in transmission intensity.

INTERPRETATION: The proportion of all infections detected within health systems increases once transmission intensity is sufficiently low. The likely explanation for *P falciparum* is that reduced exposure to infection leads to lower levels of protective immunity in the population, increasing the likelihood that infected individuals will become symptomatic and seek care. These factors might also be true for *P vivax* but a better understanding of the transmission biology is needed to attribute likely reasons for the observed trend. In low transmission and pre-elimination settings, enhancing access to care and improvements in care-seeking behaviour of infected individuals will lead to an increased proportion of infections detected in the community and might contribute to accelerating the interruption of transmission. **FUNDING:** Wellcome Trust.

Comparison of Thiamin Diphosphate High-Performance Liquid Chromatography and Erythrocyte Transketolase Assays for Evaluating Thiamin Status in Malaria Patients without Beriberi. Taylor AJ, Talwar D, Lee SJ, Cox L, Mayxay M, Newton PN. *Am J Trop Med Hyg* 2020; 103(6): 2600-4. Published online: 28 September 2020. doi: 10.4269/ajtmh.20-0479.

HPLC detection of thiamin diphosphate performed well in comparison to more common indirect thiamin assays, such as erythrocyte transketolase activity, in patients with falciparum malaria.

Thiamin deficiency, or beriberi, is an increasingly re-recognized cause of morbidity and mortality in the developing world. Thiamin status has traditionally been measured through the erythrocyte activation assay (ETKA) or basal transketolase activity (ETK), which indirectly measure thiamin diphosphate (TDP). Thiamin diphosphate can also be measured directly by high-performance liquid chromatography (HPLC), which may allow a more precise estimation of thiamin status. We compared the direct measurement of TDP by HPLC with basal ETK activity and ETKA in 230 patients with *Plasmodium falciparum* malaria in rural southern Laos without overt clinical beriberi, as part of a trial of thiamin supplementation. Admission thiamin status measured by basal ETK activity and ETKA (alpha) were compared with thiamin status assessed by the measurement of TDP by HPLC. 55% of 230 included patients were male, and the median age was 10 (range 0.5-73) years. Using alpha >/= 25% as the gold standard of thiamin deficiency, the sensitivity of TDP < 275 ng/gHb as a measure of thiamin deficiency was 68.5% (95% CI: 54.4-80.5%), with specificity of 60.8 (95% CI: 53.2-68.1%). There was a significant inverse correlation between the results of the two tests (Kendall's tau = -0.212, P < 0.001). Basal ETK activity was also significantly positively correlated with TDP levels (Kendall's tau = 0.576, P < 0.001). Thiamin diphosphate measurement may have a role in measuring thiamin levels in clinical settings. Further studies evaluating TDP concentration in erythrocytes with basal ETK activity and ETKA (alpha) in beriberi patients would help establish comparative values of these assays.

Triple artemisinin-based combination therapies versus artemisinin-based combination therapies for uncomplicated *Plasmodium falciparum* malaria: a multicentre, open-label, randomised clinical trial. van der Pluijm RW, Tripura R, Hoglund RM, Pyae Phyo A, Lek D, Ul Islam A, Anvikar AR, Satpathi P, Satpathi S, Behera PK, Tripura A, Baidya S, Onyamboko M, Chau NH, Sovann Y, Suon S, Sreng S, Mao S, Oun S, Yen S, Amaratunga C, Chutasmit K, Saelow C, Runcharern R, Kaewmok W, Hoa NT, Thanh NV, Hanboonkunupakarn B, Callery JJ, Mohanty AK, Heaton J, Thant M, Gantait K, Ghosh T, Amato R, Pearson RD, Jacob CG, Goncalves S, Mukaka M, Waithira N, Woodrow CJ, Grobusch MP, van Vugt M, Fairhurst RM, Cheah PY, Peto TJ, von Seidlein L, Dhorda M, Maude RJ, Winterberg M, Thuy-Nhien NT, Kwiatkowski DP, Imwong M, Jittamala P, Lin K, Hlaing TM, Chotivanich K, Huy R, Fanello C, Ashley E, Mayxay M, Newton PN, Hien TT, Valecha N, Smithuis F, Pukrittayakamee S, Faiz A, Miotto O, Tarning J, Day NPJ, White NJ, Dondorp AM. *Lancet* 2020; 395(10233): 1345-60. Published online: 11 March 2020. doi: 10.1016/s0140-6736(20)30552-3.

Triple artemisinin-based combination therapies (dihydroartemisinin-piperaquine plus mefloquine and artemether-lumefantrine plus amodiaquine) are safe treatments of uncomplicated falciparum malaria, including in areas with known drug resistance.

BACKGROUND: Artemisinin and partner-drug resistance in *Plasmodium falciparum* are major threats to malaria control and elimination. Triple artemisinin-based combination therapies (TACTs), which combine existing co-formulated ACTs with a second partner drug that is slowly eliminated, might provide effective treatment and delay emergence of antimalarial drug resistance.

METHODS: In this multicentre, open-label, randomised trial, we recruited patients with uncomplicated *P falciparum* malaria at 18 hospitals and health clinics in eight countries. Eligible patients were aged 2-65 years, with acute, uncomplicated *P falciparum* malaria alone or mixed with non-falciparum species, and a temperature of 37.5 degrees C or higher, or a history of fever in the past 24 h. Patients were randomly assigned (1:1) to one of two treatments using block randomisation, depending on their location: in Thailand, Cambodia, Vietnam, and Myanmar patients were assigned to either dihydroartemisinin-piperaquine or dihydroartemisinin-nate-mefloquine or dihydroartemisinin-piperaquine plus mefloquine; and in Laos, Myanmar, Bangladesh, India, and the Democratic Republic of the Congo they were assigned to either artemether-lumefantrine or artemether-lumefantrine plus amodiaquine. All drugs were administered orally and doses varied by drug combination and site. Patients were followed-up weekly for 42 days. The primary endpoint was efficacy, defined by 42-day PCR-corrected adequate clinical and parasitological response. Primary analysis was by intention to treat. A detailed assessment of safety and tolerability of the study drugs was done in all patients randomly assigned to treatment. This study is registered at ClinicalTrials.gov, NCT02453308, and is complete. **FINDINGS:** Between Aug 7, 2015, and Feb 8, 2018, 1100 patients were given either dihydroartemisinin-piperaquine (183 [17%]), dihydroartemisinin-piperaquine plus mefloquine (269 [24%]), artesunate-mefloquine (73 [7%]), artemether-lumefantrine (289 [26%]), or artemether-lumefantrine plus amodiaquine (286 [26%]). The median age was 23 years (IQR 13 to 34) and 854 (78%) of 1100 patients were male. In Cambodia, Thailand, and Vietnam the 42-day PCR-corrected efficacy after dihydroartemisinin-piperaquine plus mefloquine was 98% (149 of 152; 95% CI 94 to 100) and after dihydroartemisinin-piperaquine was 48% (67 of 141; 95% CI 39 to 56; risk difference 51%, 95% CI 42 to 59; p<0.0001). Efficacy of dihydroartemisinin-piperaquine plus mefloquine in the three sites in Myanmar was 91% (42 of 46; 95% CI 79 to 98) versus 100% (42 of 42; 95% CI 92 to 100) after dihydroartemisinin-piperaquine (risk difference 9%, 95% CI 1 to 17; p=0.12). The 42-day PCR corrected efficacy of dihydroartemisinin-piperaquine plus mefloquine (96% [68 of 71; 95% CI 88 to 99]) was non-inferior to that of artesunate-mefloquine (95% [69 of 73; 95% CI 87 to 99]) in three sites in Cambodia (risk difference 1%; 95% CI -6 to 8; p=1.00). The overall 42-day PCR-corrected efficacy of artemether-lumefantrine plus amodiaquine (98% [281 of 286; 95% CI 97 to 99]) was similar to that of artemether-lumefantrine (97% [279 of 289; 95% CI 94 to 98]; risk difference 2%, 95% CI -1 to 4; p=0.30). Both TACTs were well tolerated, although early vomiting (within 1 h) was more frequent after dihydroartemisinin-piperaquine plus mefloquine (30 [3.8%] of 794) than after dihydroartemisinin-piperaquine (eight [1.5%] of 543; p=0.012). Vomiting after artemether-lumefantrine plus amodiaquine (22 [1.3%] of 1703) and artemether-lumefantrine (11 [0.6%] of 1721) was infrequent. Adding amodiaquine to artemether-lumefantrine extended the electrocardiogram corrected QT interval (mean increase at 52 h compared with baseline of 8.8 ms [SD 18.6] vs 0.9 ms [16.1]; p<0.01) but adding mefloquine to dihydroartemisinin-piperaquine did not (mean increase of 22.1 ms [SD 19.2] for dihydroartemisinin piperaquine vs 20.8 ms [SD 17.8] for dihydroartemisinin-piperaquine plus mefloquine; p=0.50). **INTERPRETATION:** Dihydroartemisinin-piperaquine plus mefloquine and artemether-lumefantrine plus amodiaquine TACTs are efficacious, well tolerated, and safe treatments of uncomplicated *P falciparum* malaria, including in areas with artemisinin and ACT partner-drug resistance. FUNDING: UK Department for International Development, Wellcome Trust, Bill & Melinda Gates Foundation, UK Medical Research Council, and US National Institutes of Health.

A cautionary note on the use of unsupervised machine learning algorithms to characterise malaria parasite population structure from genetic distance matrices. Watson JA, Taylor AR, Ashley EA, Dondorp A, Buckee CO, White NJ, Holmes CC. *PLoS Genet* 2020; 16(10): e1009037. Published online: 09 October 2020. doi: 10.1371/journal.pgen.1009037.

This paper advises caution when relying on computerized algorithms to characterize and interpret malaria parasite population structure from genetic surveillance.

Genetic surveillance of malaria parasites supports malaria control programmes, treatment guidelines and elimination strategies. Surveillance studies often pose questions about malaria parasite ancestry (e.g. how antimalarial resistance has spread) and employ statistical methods that characterise parasite population structure. Many of the methods used to characterise structure are unsupervised machine learning algorithms which depend on a genetic distance matrix, notably principal coordinates analysis (PCoA) and hierarchical agglomerative clustering (HAC). PCoA and HAC are sensitive to both the definition of genetic distance and algorithmic specification. Importantly, neither algorithm infers malaria parasite ancestry. As such, PCoA and HAC can inform (e.g. via exploratory data visualisation and hypothesis generation), but not answer comprehensively, key questions about malaria parasite ancestry. We illustrate the sensitivity of PCoA and HAC using 393 *Plasmodium falciparum* whole genome sequences collected from Cambodia and neighbouring regions (where antimalarial resistance has emerged and spread recently) and we provide tentative guidance for the use and interpretation of PCoA and HAC in malaria parasite genetic epidemiology. This guidance includes a call for fully transparent and reproducible analysis pipelines that feature (i) a clearly outlined scientific question; (ii) a clear justification of analytical methods used to answer the scientific question along with discussion of any inferential limitations; (iii) publicly available genetic distance matrices when downstream analyses depend on them; and (iv) sensitivity analyses. To bridge the inferential disconnect between the output of non-inferential unsupervised learning algorithms and the scientific questions of interest, tailor-made statistical models are needed to infer malaria parasite ancestry. In the absence of such models speculative reasoning should feature only as discussion but not as results.

VIROLOGY

A need to raise the bar - A systematic review of temporal trends in diagnostics for Japanese encephalitis virus infection, and perspectives for future research. Bharucha T, Shearer FM, Vongsouvath M, Mayxay M, de Lamballerie X, Newton PN, Zitzmann N, Gould E, Dubot-Pérès A. *Int J Infect Dis* 2020; 95: 444-56. Published online: 25 March 2020. doi: 10.1016/j.ijid.2020.03.039.
This review of diagnostics for Japanese encephalitis virus infections concludes that simple assays are still lacking but are much needed for future disease control.
OBJECTIVE: Japanese encephalitis virus infection (JE) remains a leading cause of neurological disease in Asia, mainly involving individuals living in remote areas with limited access to treatment centres and diagnostic facilities. Laboratory confirmation is fundamental for the justification and implementation of vaccination programs. We reviewed the literature on historical developments and current diagnostic capability worldwide, to identify knowledge gaps and instil urgency to address them. **METHODS:** Searches were performed in Web of Science and PubMed using the term 'Japanese encephalitis' up to 13October 2019. Studies reporting laboratory-confirmed symptomatic JE cases in humans were included, and data on details of diagnostic tests were extracted. A JE case was classified according to confirmatory levels (Fischer et al., 2008; Campbell et al., 2011; Pearce et al., 2018; Heffelfinger et al., 2017), where level 1 represented the highest level of confidence. **FINDINGS:** 20,212 published JE cases were identified from 205 studies. 15,167 (75%) of these positive cases were confirmed with the lowest-confidence diagnostic tests (level 3 or 4, or level 4). Only 109 (53%) of the studies reported contemporaneous testing for dengue-specific antibodies. **CONCLUSION:** A fundamental pre-requisite for the control of JEV is lacking - that of a simple and specific diagnostic procedure that can be adapted for point-of-care tests and readily used throughout JE-endemic regions of the world.

Modelling the potential effectiveness of interventions against coronavirus 2019 outbreak in the Lao PDR: a mathematical modelling approach. Chanthavilay P, Soukavong M, Aung YN, Tun STT, White LJ, Mayxay M. *Lao Med J* 2020; 11: 3-7.
Modelling of the effectiveness of different interventions in the event of a COVID-19 epidemic in Laos.

This is a policy brief article on the prediction of Covid-19 outbreak and its prevention and control for the possible second wave in the Lao PDR. Compartmental dynamic modelling was created to reflect the natural history of COVID-19. This included susceptible, symptomatic and asymptomatic cases and recovery or death. The simulation was done for one year and with two scenarios: 1) high transmission level (R0=5.2) and 2) mid-transmission level (R0=2.0). The model output showed that the size of the outbreak depended on the transmission level, and could reach to 85% of the Lao population with high transmission scenario. However, disease burden was predicted to be smaller with the interventions. Among these, voluntary home quarantine was found to be the most effective, but the prediction reverses in the mid-level transmission scenario. Social distancing is much more effective. If there are imported COVID-19 cases, a new wave could occur in two weeks to 2 months, depending on the size of pandemic and efficacy of the rest of interventions. Mid-level lockdown would result in new epidemic starting by July 2020, but the number of infected people would be less if travel bans and social distancing are maintaining. Only high-level lockdown would be able to stop community transmission in the country.

Dengue Seroprevalence and Seroconversion in Urban and Rural Populations in Northeastern Thailand and Southern Laos. Doum D, Overgaard HJ, Mayxay M, Suttiprapa S, Saichua P, Ekalaksananan T, Tongchai P, Rahman MS, Haque U, Phommachanh S, Pongvongsa T, Rocklöv J, Paul R, Pientong C. *Int J Environ Res Public Health* 2020; 17(23): 9134. Published online: 07 December 2020. doi: 10.3390/ijerph17239134.
This study reports very high dengue seroprevalence rates in residents of southern Laos and northeast Thailand, in both urban and rural areas.
Dengue is the most rapidly spreading mosquito-borne viral disease in the world. The detection of clinical cases enables us to measure the incidence of dengue infection, whereas serological surveys give insights into the prevalence of infection. This study aimed to determine dengue seroprevalence and seroconversion rates in northeastern Thailand and southern Laos and to assess any association of mosquito control methods and socioeconomic factors with dengue virus (DENV) infection. Cross-sectional seroprevalence surveys were performed in May and November 2019 on the same individuals. Blood samples were collected from one adult and one child, when possible, in each of 720 randomly selected households from two urban and two rural sites in both northeastern Thailand and southern Laos. IgG antibodies against DENV were detected in serum using a commercial enzyme-linked immunosorbent assay (ELISA) kit. Overall, 1071 individuals participated in the study. The seroprevalence rate was high (91.5%) across all 8 study sites. Only age and province were associated with seroprevalence rates. There were 33 seroconversions during the period from May to November, of which seven reported fever. More than half of the seroconversions occurred in the rural areas and in Laos. Dengue seroconversion was significantly associated with young age (<15 years old), female gender, province, and duration of living in the current residence. No socioeconomic factors or mosquito control methods were found to be associated with seroprevalence or seroconversion. Notably, however, the province with most seroconversions had lower diurnal temperature ranges than elsewhere. In conclusion, our study has highlighted the homogeneity of dengue exposure across a wide range of settings and most notably those from rural and urban areas. Dengue can no longer be considered to be solely an urban disease nor necessarily one linked to poverty.

Pragmatic Recommendations for Safety while Caring for Hospitalized Patients with Coronavirus Disease 2019 (COVID-19) in Low- and Middle-Income Countries. Inglis R, Barros L, Checkley W, Cizmeci EA, Lelei-Mailu F, Pattnaik R, Papali A, Schultz MJ, Ferreira JC, For The Covid-LMIC Task F. *Am J Trop Med Hyg* 2021; 104(3 Supplement): 12-24. Published online: 22 December 2020. doi: 10.4269/ajtmh.20-1128.
Infection control guidance is often expensive and unfeasible outside high-income countries. Practical recommendations are made for appropriate measures in LMICs.

Infection prevention and control measures to control the spread of COVID-19 are challenging to implement in many low- and middle-income countries (LMICs). This is compounded by the fact that most recommendations are based on evidence that mainly originates in high-income countries. There are often availability, affordability, and feasibility barriers to applying such recommendations in LMICs, and therefore, there is a need for developing recommendations that are achievable in LMICs. We used a modified version of the GRADE method to select important questions, searched the literature for relevant evidence, and formulated pragmatic recommendations for safety while caring for patients with COVID-19 in LMICs. We selected five questions related to safety, covering minimal requirements for personal protective equipment (PPE), recommendations for extended use and reuse of PPE, restriction on the number of times healthcare workers enter patients' rooms, hand hygiene, and environmental ventilation. We formulated 21 recommendations that are feasible and affordable in LMICs.

Baseline results of a living systematic review for COVID-19 clinical trial registrations [version 1; peer review: 2 approved]. Maguire BJ, McLean ARD, Rashan S, Antonio ES, Bagaria J, Bentounsi Z, Brack M, Caldwell F, Carrara VI, Citarella BW, Dahal P, Feteh VF, Guérin MHB, Kennon K, Lahaut KB, Makuka GJ, Ngu R, Obiesie S, Richmond C, Singh-Phulgenda S, Strudwick S, Tyrrell CSB, Schwinn A, King D, Newton PN, Price RN, Merson L, Stepniewska K, Guérin PJ. *Wellcome Open Res* 2020; 5: 116. Published online: 02 June 2020. doi: 10.12688/wellcomeopenres.15933.1.

This paper reported an early but ongoing review of COVID-19 clinical trials. Most were small studies, and probably unpowered for the purpose of providing good evidence for interventions.

BACKGROUND: Since the coronavirus disease 2019 (COVID-19) outbreak was first reported in December 2019, many independent trials have been planned that aim to answer similar questions. Tools allowing researchers to review studies already underway can facilitate collaboration, cooperation and harmonisation. The Infectious Diseases Data Observatory (IDDO) has undertaken a living systematic review (LSR) to provide an open, accessible and frequently updated resource summarising characteristics of COVID-19 study registrations. Methods: Review of all eligible trial records identified by systematic searches as of 3 April 2020 and initial synthesis of clinical study characteristics were conducted. In partnership with Exaptive, an open access, cloud-based knowledge graph has been created using the results. Results: There were 728 study registrations which met eligibility criteria and were still active. Median (25 (th), 75 (th) percentile) sample size was 130 (60, 400) for all studies and 134 (70, 300) for RCTs. Eight lower middle and low income countries were represented among the planned recruitment sites. Overall 109 pharmacological interventions or advanced therapy medicinal products covering 23 drug categories were studied. Majority (57%, 62/109) of them were planned only in one study arm, either alone or in combination with other interventions. There were 49 distinct combinations studied with 90% (44/49) of them administered in only one or two study arms. The data and interactive platform are available at https://iddo.cognitive.city/. **CONCLUSIONS:** Baseline review highlighted that the majority of investigations in the first three months of the outbreak were small studies with unique treatment arms, likely to be unpowered to provide solid evidence. The continued work of this LSR will allow a more dependable overview of interventions tested, predict the likely strength of evidence generated, allow fast and informative filtering of relevant trials for specific user groups and provide the rapid guidance needed by investigators and funders to avoid duplication of efforts.

Evaluation of the diagnostic accuracy of an affordable rapid diagnostic test for African Swine Fever antigen detection in Lao People's Democratic Republic. Matsumoto N, Siengsanan-Lamont J, Gleeson LJ, Douangngeun B, Theppangna W, Khounsy S, Phommachanh P, Halasa T, Bush RD, Blacksell SD. *J Virol Methods* 2020; 286: 113975. . Published online: 18 September 2020. doi: 10.1016/j.jviromet.2020.113975.

An African Swine Fever pen-side RDT showed promise for field application but further validation of performance characteristics is required.

African Swine Fever (ASF) is a transboundary animal disease of pigs and wild suids that appeared in Lao People's Democratic Republic (Lao PDR) in mid-2019, having spread across China and Vietnam in the months prior. Despite the scale of the Asian ASF pandemic and the availability of pen-side rapid diagnostic tests (RDT) on the market, few locally produced and easily available ASF RDTs have been evaluated for diagnostic accuracy. In this study, an ASF antigen detection RDT from Shenzhen Lvshiyuan Biotechnology Co. Ltd was evaluated using clinical field samples submitted to the National Animal Health Laboratory (NAHL) from ASF suspect cases between June and December 2019 in Lao PDR. Positive (n=57) and negative (n=50) samples of whole blood, serum and haemolysed serum were assessed by RDT and PCR, with the latter used as the gold standard reference comparator. Overall the RDT had a diagnostic sensitivity (DSe) of 65 %, 95 % CI [51-77] and diagnostic specificity (DSp) of 76 %, 95 % CI [62-87]. The RDT demonstrated improved performance on samples with lower PCR cycle threshold (ct) values with each additional cycle reducing the odds of the RDT returning a positive by 17 % relative to the previous cycle, 95 % CI [8 %-28 %] (P<0.01). While this test shows promise for field application, complete validation of diagnostic accuracy requires a larger sample size.

Infection in Pediatric and Adult Patients at Mahosot Hospital, Vientiane, Lao PDR. Mayxay M, Douangdala P, Vilayhong C, Phommasone K, Chansamouth V, Vongsouvath M, Rattanavong S, Chang K, Sengvilaipaseuth O, Chanthongthip A, Thongpaseuth S, Newton PN, Dubot-Pérès A. Outcome of Japanese Encephalitis Virus (JEV) *Am J Trop Med Hyg* 2021; 104(2): 567-575. Published online: 21 December 2020. doi: 10.4269/ajtmh.20-0581.

This study of patient outcomes following Japanese encephalitis virus infection in Laos demonstrated a mortality approaching 20% and high rates of neurological sequelae in survivors, especially in children.

Although Japanese encephalitis virus (JEV) infection is an important cause of acute febrile illness in Lao PDR (Laos), patient outcome has not been evaluated. We prospectively followed up 123 JEV-infected patients (70 children ≤ 15 years and 53 adults ≥ 15 years) admitted at Mahosot Hospital, Vientiane, from 2003 to 2013. Japanese encephalitis virus infection was diagnosed by the detection of anti-JEV IgM in cerebrospinal fluid and/or IgM seroconversion. Neurological sequelae were assessed using the Liverpool Outcome Score (LOS), total (maximum score = 75), and final (maximum score = 5). The median (interquartile range [IQR]) age of the patients was 12.0 (7.5-18.8) years, and 57% were male. The median (IQR) duration of patients' follow-up was 4.5 (3.2-7.3) years. Of all patients, 10/123 (8.1%) died during hospitalization, and 13/123 (10.6%) died at home after discharge, giving a mortality of 18.7% (23/123) (33 [26.8%] patients were lost to follow-up). The frequency of neurological sequelae at the last follow-up was 61.2% (48.4% in adults and 69.4% in children, P = 0.135). The proportion of patients with severe and moderate functional impairment at the last follow-up was significantly higher in children (25%) than adults (6.5%), P = 0.042. Half of the patients who were still alive at the last follow-up (67) and for whom LOS data were available (22) had improvements in their total and final LOS between discharge and the last follow-up. The total and final LOS at discharge were not significantly different between children and adults, but total LOS at the last follow-up was significantly higher in adults than children (median [IQR]: 74.5 [73-75] versus 73.0 [73-75], P = 0.019).

The emerging spectrum of COVID-19 neurology: clinical, radiological and laboratory findings. Paterson RW, Brown RL, Benjamin L, Nortley R, Wiethoff S, Bharucha T, Jayaseelan DL, Kumar G, Raftopoulos RE, Zambreanu L, Vivekanandam V, Khoo A, Geraldes R, Chinthapalli K, Boyd E, Tuzlali H, Price G, Christofi G, Morrow J, McNamara P, McLoughlin B, Lim ST, Mehta PR, Levee V, Keddie S, Yong W, Trip SA, Foulkes AJM, Hotton G, Miller TD, Everitt AD, Carswell C, Davies NWS, Yoong M, Attwell D, Sreedharan J, Silber E, Schott JM, Chandratheva A, Perry RJ, Simister R, Checkley A, Longley N, Farmer SF, Carletti F, Houlihan C, Thom M, Lunn MP, Spillane J, Howard R, Vincent A, Werring DJ, Hoskote C, Jäger HR, Manji H, Zandi MS. ***Brain*** 2020; 143(10): 3104-20. doi: 10.1093/brain/awaa240. PMID: 32637987; PMCID: PMC7454352.

COVID-19 infection is linked to multiple neurological syndromes, including acute disseminated encephalomyelitis, encephalitis and Guillain-Barré syndrome.

Preliminary clinical data indicate that severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection is associated with neurological and neuropsychiatric illness. Responding to this, a weekly virtual coronavirus disease 19 (COVID-19) neurology multi-disciplinary meeting was established at the National Hospital, Queen Square, in early March 2020 in order to discuss and begin to understand neurological presentations in patients with suspected COVID-19-related neurological disorders. Detailed clinical and paraclinical data were collected from cases where the diagnosis of COVID-19 was confirmed through RNA PCR, or where the diagnosis was probable/possible according to World Health Organization criteria. Of 43 patients, 29 were SARS-CoV-2 PCR positive and definite, eight probable and six possible. Five major categories emerged: (i) encephalopathies (n = 10) with delirium/psychosis and no distinct MRI or CSF abnormalities, and with 9/10 making a full or partial recovery with supportive care only; (ii) inflammatory CNS syndromes (n = 12) including encephalitis (n = 2, para- or post-infectious), acute disseminated encephalomyelitis (n = 9), with haemorrhage in five, necrosis in one, and myelitis in two, and isolated myelitis (n = 1). Of these, 10 were treated with corticosteroids, and three of these patients also received intravenous immunoglobulin; one made a full recovery, 10 of 12 made a partial recovery, and one patient died; (iii) ischaemic strokes (n = 8) associated with a pro-thrombotic state (four with pulmonary thromboembolism), one of whom died; (iv) peripheral neurological disorders (n = 8), seven with Guillain-Barré syndrome, one with brachial plexopathy, six of eight making a partial and ongoing recovery; and (v) five patients with miscellaneous central disorders who did not fit these categories. SARS-CoV-2 infection is associated with a wide spectrum of neurological syndromes affecting the whole neuraxis, including the cerebral vasculature and, in some cases, responding to immunotherapies. The high incidence of acute disseminated encephalomyelitis, particularly with haemorrhagic change, is striking. This complication was not related to the severity of the respiratory COVID-19 disease. Early recognition, investigation and management of COVID-19-related neurological disease is challenging. Further clinical, neuroradiological, biomarker and neuropathological studies are essential to determine the underlying pathobiological mechanisms that will guide treatment. Longitudinal follow-up studies will be necessary to ascertain the long-term neurological and neuropsychological consequences of this pandemic.

Knowledge, Attitudes, and Practices on Climate Change and Dengue in Lao People's Democratic Republic and Thailand. Rahman MS, Overgaard HJ, Pientong C, Mayxay M, Ekalaksananan T, Aromseree S, Phanthanawiboon S, Zafar S, Shipin O, Paul RE, Phommachanh S, Pongvongsa T, Vannavong N, Haque U. *Environ Res* 2020: 110509. Published online: 24 November 2020. doi: 10.1016/j.envres.2020.110509.

This survey demonstrated that knowledge of the relationship between climate change and dengue was low in both Laos and Thailand.

BACKGROUND: Dengue is linked with climate change in tropical and sub-tropical countries including the Lao People's Democratic Republic (Laos) and Thailand. Knowledge about these issues and preventive measures can affect the incidence and outbreak risk of dengue. Therefore, the present study was conducted to determine the knowledge, attitudes, and practices (KAP) among urban and rural communities and government officials about climate change and dengue in Laos and Thailand. **METHODS:** A cross-sectional KAP survey about climate change and dengue were conducted in 360 households in Laos (180 urban and 180 rural), 359 households in Thailand (179 urban and 180 rural), and 20 government officials (10 in each country) using structured questionnaires. Data analysis was undertaken using descriptive methods, principal component analysis, Chi-square test or Fisher's exact test (as appropriate), and logistic regression. **RESULTS:** Significant differences among the selected communities in both countries were found in terms of household participant's age, level of education, socioeconomic status, attitude level of climate change and KAP level of dengue ($P < 0.05$; 95% CI). Overall, participants' KAP about climate change and dengue were low except the attitude level for dengue in both countries. The level of awareness among government officials regarding the climatic relationship with dengue was also low. In Lao households, participants' knowledge about climate change and dengue was significantly associated with the level of education and socioeconomic status (SES) ($P < 0.01$). Their attitudes towards climate change and dengue were associated with educational level and internet use ($P < 0.05$). Householders' climate change related practices were associated with SES ($P < 0.01$) and dengue related practices were associated with educational level, SES, previous dengue experience and internet use ($P < 0.01$). In Thailand, participants' knowledge about climate change was associated with the level of education and SES ($P < 0.01$). Their attitudes towards climate change were associated with residence status (urban/rural) and internet use ($P < 0.05$); climate change related practices were associated with educational level and SES ($P < 0.05$). Dengue related knowledge of participants was associated with SES and previous dengue experience ($P < 0.05$); participants' dengue related attitudes and practices were associated with educational level ($P < 0.01$).
CONCLUSION: The findings call for urgently needed integrated awareness programs to increase KAP levels regarding climate change adaptation, mitigation and dengue prevention to improve the health and welfare of people in these two countries, and similar dengue-endemic countries.

Spatial epidemiology of Japanese encephalitis virus and other infections of the central nervous system infections in Lao PDR (2003-2011): A retrospective analysis. Rattanavong S, Dubot-Pérès A, Mayxay M, Vongsouvath M, Lee SJ, Cappelle J, Newton PN, Parker DM. *PLoS Negl Trop Dis* 2020; 14(5): e0008333. Published online: 26 May 2020. doi: 10.1371/journal.pntd.0008333.

Patterns of central nervous system infections in space and time have multiple influences, including environmental, social, and geographic factors.

BACKGROUND: Central nervous system (CNS) infections are important contributors to morbidity and mortality and the causative agents for ~50% patients are never identified. The causative agents of some CNS infections have distinct spatial and temporal patterns. **METHODOLOGY/PRINCIPAL FINDINGS:** Here we present the results of a spatial epidemiological and ecological analysis of CNS infections in Lao PDR (2003-2011). The data came from hospitalizations for s uspected CNS infection at Mahosot Hospital in Vientiane. Out of 1,065 patients, 450 were assigned a confirmed diagnosis. While many communities in Lao PDR are in rural and remote locations, most patients in these data came from villages along major roads. Japanese encephalitis virus ((JEV); n = 94) and *Cryptococcus* spp. (n = 70) were the most common infections. JEV infections peaked in the rainy season and JEV patients came from villages with higher surface flooding during the same month as admission. JEV infections were spatially dispersed throughout rural areas and were most common in children. *Cryptococcus* spp. infections clustered near Vientiane (an urban area) and among adults. **CONCLUSIONS/SIGNIFICANCE:** The spatial and temporal patterns identified in this analysis are related to complex environmental, social, and geographic factors. For example, JEV infected patients came from locations with environmental conditions (surface water) that are suitable to support larger mosquito vector populations. Most patients in these data came from villages that are near major roads; likely the result of geographic and financial access to healthcare and also indicating that CNS diseases are underestimated in the region (especially from more remote areas). As Lao PDR is undergoing major developmental and environmental changes, the space-time distributions of the causative agents of CNS infection will also likely change. There is a major need for increased diagnostic abilities; increased access to healthcare, especially for rural populations; and for increased surveillance throughout the nation.

Chloroquine/ hydroxychloroquine prevention of coronavirus disease (COVID-19) in the healthcare setting; protocol for a randomised, placebo-controlled prophylaxis study (COPCOV) [version 1; peer review: 1 approved]. Schilling W, Callery JJ, Taylor W, Mukaka M, Ekkapongpisit M, Watson

J, Chandna A, Panapipat S, Tubprasert J, Yuentrakul P, Waithira N, Cope T, Dhorda M, Cruz C, von Seidlein L, Milton J, Llewelyn M, Adler A, Chotivanich K, Cheah PY, Ashley E, Mayxay M, Dondorp A, Phumratanaprapin W, Day N, White N. *Wellcome Open Research* 2020; 5: 241. Published online: 15 October 2020. doi: 10.12688/wellcomeopenres.15784.1.

Protocol for the COPCOV Study, a large multi-country investigation of prophylaxis against COVID-19, using chloroquine or hydroxychloroquine, in healthcare workers. Laos is ready to participate if community transmission occurs in future.

There is no proven preventative therapy or vaccine against COVID-19. The infection has spread rapidly and there has already been a substantial adverse impact on the global economy. Healthcare workers have been affected disproportionately in the continuing pandemic. Significant infection rates in this critical group have resulted in a breakdown of health services in some countries. Chloroquine, and the closely related hydroxychloroquine, are safe and well tolerated medications which can be given for years without adverse effects. Chloroquine and hydroxychloroquine have significant antiviral activity against SARS-CoV-2, and despite the lack of benefit of hydroxychloroquine treatment in patients hospitalised with severe COVID-19, these drugs could still work in prevention. The emerging infection paradigm of an early viral peak, and late inflammation where there is benefit from corticosteroids. If these direct acting antivirals are to work, they have the best chance given either early in infection and before infection occurs. We describe the study protocol for a multi-centre, multi-country randomised, double blind, placebo controlled trial to answer the question- can chloroquine/ hydroxychloroquine prevent COVID-19. 40,000 participants working in healthcare facilities or involved in the management of COVID-19 will be randomised 1:1 to receive chloroquine/ hydroxychloroquine or matched placebo as daily prophylaxis for three months. The primary objective is the prevention of symptomatic, virological or serologically proven coronavirus disease (COVID-19). The study could detect a 23% reduction from an incidence of 3% in the placebo group for either drug with 80% power. Secondary objectives are to determine if chloroquine/hydroxychloroquine prophylaxis attenuates severity, prevents asymptomaticCOVID-19 and symptomatic acute respiratory infections of another aetiology (non-SARS-CoV-2).

Harnessing Dengue Rapid Diagnostic Tests for the Combined Surveillance of Dengue, Zika, and Chikungunya Viruses in Laos. Vongsouvath M, Bharucha T, Seephonelee M, de Lamballerie X, Newton PN, Dubot-Pérès A. *Am J Trop Med Hyg* 2020; 102(6): 1244-8. Published online: 09 March 2020. doi: 10.4269/ajtmh.19-0881.

A novel laboratory-based study demonstrating that stored dengue RDTs can be utilised for subsequent RT-PCR detection of dengue, chikungunya or Zika virus infections, even after storage at 35 °C.

Recent expansions of vector-borne diseases highlight the need for improved surveillance, especially in resource-poor settings. Dengue virus (DENV), chikungunya virus (CHIKV), and Zika virus (ZIKV) share the same vectors as well as similar clinical presentations, suggesting that combined surveillance would be useful. We hypothesized that blood spotted on dengue rapid diagnostic tests (RDTs) could be harnessed for sample collection in remote areas for subsequent detection of DENV, CHIKV, and ZIKV by reverse transcription real-time polymerase chain reaction (RT-qPCR). CHIKV and ZIKV dilutions were spotted on dengue RDTs (SD BIOLINE Dengue DUO, Standard Diagnostics, Gyeonggi-do, Republic of Korea), dried, and extracted. As reference, aliquots of each viral dilution were directly extracted. Using specific RT-qPCR tests, both viruses were successfully detected from RDT extracts. However, the limit of detection was slightly lower in comparison to direct extracts, two logfold for CHIKV and one logfold for ZIKV. For analysis of temperature stability, DENV dilutions were spotted on RDTs and stored for up to 2 months at -80 degrees C, 4 degrees C, or 35 degrees C before testing. Storage of RDTs for 2 months at 35 degrees C did not compromise detection of RNA by RT-qPCR; only minimal degradation was observed. This proof-of-principle study demonstrates the potential of using dengue RDTs for DENV/CHIKV/ZIKV combined surveillance in areas without access to laboratory facilities. Further investigations are needed for evaluation of tri-viral surveillance under field conditions using patient samples. Large-scale implementation of surveillance for these viruses is of crucial public health importance for the early detection of epidemics. This method also has important implications for improving understanding of the molecular epidemiology of the three viruses.

CASE REPORT

A patient with emphysematous pyelonephritis presenting with acute kidney injury: A case report. Sengthavisouk N, Phanmalavong P, Chansamouth V, Chanthavilay P, Thongsana S. *Lao Med J* 2020; 11: 46-52.

Case Report of fatal emphysematous pyelonephritis caused by E. coli.

Emphysematous pyelonephritis (EPN) is an uncommon but life-threatening condition for which diabetic patients are at high risk. The most common chief complaint bringing patients to the hospital is upper urinary tract infection. Early clinical diagnosis with radiography is a key to reduce complications and death due emphysematous pyelonephritis. We present a case study of a 45-year old female patient who was presenting to the emergency room with left flank pain. Blood testing showed acute kidney injury, *E. coli* bacteremia, and the radiography demonstrated an abnormal image of the left kidney consistent with EPN. Symptomatic treatment and antibiotic were given, but no response and developed to heart failure and death at Emergency Room.

OTHER

STROBE-metagenomics: a STROBE extension statement to guide the reporting of metagenomics studies. Bharucha T, Oeser C, Balloux F, Brown JR, Carbo EC, Charlett A, Chiu CY, Claas ECJ, de Goffau MC, de Vries JJC, Eloit M, Hopkins S, Huggett JF, MacCannell D, Morfopoulou S, Nath A, O'Sullivan DM, Reoma LB, Shaw LP, Sidorov I, Simner PJ, Van Tan L, Thomson EC, van Dorp L, Wilson MR, Breuer J, Field N. *Lancet Infect Dis* 2020; 20(10): e251-60. Published online: 10 August 2020. doi: 10.1016/S1473-3099(20)30199-7.

Reporting Guidance from an Expert Group in the rapidly-evolving field of metagenomics.

The term metagenomics refers to the use of sequencing methods to simultaneously identify genomic material from all organisms present in a sample, with the advantage of greater taxonomic resolution than culture or other methods. Applications include pathogen detection and discovery, species characterisation, antimicrobial resistance detection, virulence profiling, and study of the microbiome and microecological factors affecting health. However, metagenomics involves complex and multistep processes and there are important technical and methodological challenges that require careful consideration to support valid inference. We co-ordinated a multidisciplinary, international expert group to establish reporting guidelines that address specimen processing, nucleic acid extraction, sequencing platforms, bioinformatics considerations, quality assurance, limits of detection, power and sample size, confirmatory testing, causality criteria, cost, and ethical issues. The guidance recognises that metagenomics research requires pragmatism and caution in interpretation, and that this field is rapidly evolving.

How many human pathogens are there in Laos? An estimate of national human pathogen diversity and analysis of historical trends. Clarkson MC, Aguas R, Sweet K, Roberts T, Strobel M, Newton PN. *BMJ Glob Health* 2020; 5(10): e002972. Published online: 24 October 2020. doi: 10.1136/bmjgh-2020-002972.

Review of the available historical medical literature and modelling were used to estimate human pathogen diversity in Laos.

OBJECTIVE: The emergence of infectious diseases poses major global health threats. Estimates of total in-country human pathogen diversity, and insights as to how and when species were described through history, could be used to estimate the probability of new pathogen discoveries. Data from the Lao People's Democratic Republic (Laos) were used in this proof-of-concept study to estimate national human pathogen diversity and to examine historical discovery rate drivers.

METHODS: A systematic survey of the French and English scientific and grey literature of pathogen description in Laos between 1874 and 2017 was conducted. The first descriptions of each known human pathogen in Laos were coded according to the diagnostic evidence available. Cumulative frequency of discovery across time informed the rate of discovery. Four distinct periods of health systems development in Laos were identified prospectively and juxtaposed to the unmodelled rate of discovery. A model with a time-varying rate of discovery was fitted to these data using a Markov-Chain-Monte-Carlo technique. **RESULTS:** From 6456 pathogen descriptions, 245 discoveries of known human pathogens in Laos, including repeat discoveries using different grades of evidence, were identified. The models estimate that the Laos human pathogen species diversity in 2017 is between 169 and 206. During the last decade, there has been a 33-fold increase in the discovery rate coinciding with the strengthening of medical research and microbiology. **CONCLUSION**: Discovery curves can be used to model and estimate country-level human pathogen diversity present in a territory. Combining this with historical assessment improves the understanding of the factors affecting local pathogen discovery. PROSPERO REGISTRATION NUMBER: A protocol of this work was registered on PROSPERO (ID:CRD42016046728).

Non-malarial febrile illness: a systematic review of published aetiological studies and case reports from Africa, 1980-2015. Elven J, Dahal P, Ashley EA, Thomas NV, Shrestha P, Stepniewska K, Crump JA, Newton PN, Bell D, Reyburn H, Hopkins H, Guerin PJ. *BMC Med* 2020; 18(1): 279. Published online: 21 September 2020. doi: 10.1186/s12916-020-01744-1.

This review summarises the published reports of non-malaria pathogens that may cause febrile illness in Africa. Dengue was more common than previously realised, but epidemics (e.g. Ebola) may bias reporting rates.

BACKGROUND: The availability of reliable point-of-care tests for malaria has heralded a paradigm shift in the management of febrile illnesses away from presumptive antimalarial therapy. In the absence of a definitive diagnosis, health care providers are more likely to prescribe empirical antimicrobials to those who test negative for malaria. To improve management and guide further test development, better understanding is needed of the true causative agents and their geographic variability. METHODS: A systematic review of published literature was undertaken to characterise the spectrum of pathogens causing non-malaria febrile illness in Africa (1980-2015). Literature searches were conducted in English and French languages in six databases: MEDLINE, EMBASE, Global Health (CABI), WHO Global Health Library, PASCAL, and Bulletin de la Societé Française de Parasitologie (BDSP). Selection criteria included reporting on an infection or infections with a confirmed diagnosis, defined as pathogens detected in or cultured from samples from normally sterile sites, or serological evidence of current or past infection. A number of published articles (rather than incidence or prevalence) reporting a given pathogen were presented. RESULTS: A total of 16,523 records from 48 African countries were screened, of which 1065 (6.4%) met selection criteria. Bacterial infections were reported in 564 (53.0%) records, viral infections in 374 (35.1%), parasitic infections in 47 (4.4%), fungal infections in nine (0.8%), and 71 (6.7%) publications reported more than one pathogen group. Age range of the study population was not specified in 233 (21.9%) publications. *Staphylococcus* aureus (18.2%), non-typhoidal *Salmonella* (17.3%), and Escherichia coli (15.4%) were the commonly reported bacterial infections whereas Rift Valley fever virus (7.4%), yellow fever virus (7.0%), and Ebola virus (6.7%) were the most commonly reported viral infections. Dengue virus infection, previously not thought to be widespread in Africa, was reported in 54 (5.1%) of articles. CONCLUSIONS: This review summarises the published reports of non-malaria pathogens that may cause febrile illness in Africa. As the threat of antimicrobial resistance looms, knowledge of the distribution of infectious agents causing fever should facilitate priority setting in the development of new diagnostic tools and improved antimicrobial stewardship. TRIAL REGISTRATION: PROSPERO, CRD42016049281.

Febrile Illness Evaluation in a Broad Range of Endemicities (FIEBRE): protocol for a multisite prospective observational study of the causes of fever in Africa and Asia. Hopkins H, Bassat Q, Chandler CIR, Crump JA, Feasey NA, Ferrand RA, Kranzer K, Lalloo DG, Mayxay M, Newton PN, Mabey D, FIEBRE Consortium. *BMJ Open* 2020; 10(7): e035632. Published online: 21 July 2020. doi: 10.1136/bmjopen-2019-035632.

Protocol for the FIEBRE Study of fever aetiology in Africa and Asia.

INTRODUCTION: Fever commonly leads to healthcare seeking and hospital admission in sub-Saharan Africa and Asia. There is only limited guidance for clinicians managing non-malarial fevers, which often results in inappropriate treatment for patients. Furthermore, there is little evidence for estimates of disease burden, or to guide empirical therapy, control measures, resource allocation, prioritisation of clinical diagnostics or antimicrobial stewardship. The Febrile Illness Evaluation in a Broad Range of Endemicities (FIEBRE) study seeks to address these information gaps. **METHODS AND ANALYSIS:** FIEBRE investigates febrile illness in paediatric and adult outpatients and inpatients using standardised clinical, laboratory and social science protocols over a minimum 12-month period at five sites in sub-Saharan Africa and Southeastern and Southern Asia. Patients presenting with fever are enrolled and provide clinical data, pharyngeal swabs and a venous blood sample; selected participants also provide a urine sample. Laboratory assessments target infections that are treatable and/or preventable. Selected point-of-care tests, as well as blood and urine cultures and antimicrobial susceptibility testing, are performed on site. On day 28, patients provide a second venous blood sample for serology and information on clinical outcome. Further diagnostic assays are performed at international reference laboratories. Blood and pharyngeal samples from matched community controls enable calculation of AFs, and surveys of treatment seeking allow estimation of the incidence of common infections. Additional assays detect markers that may differentiate bacterial from non-bacterial causes of illness and/or prognosticate illness severity. Social science research on antimicrobial use will inform future recommendations for fever case management. Residual samples from participants are stored for future use. **ETHICS AND DISSEMINATION:** Ethics approval was obtained from all relevant institutional and national committees; written informed consent is obtained from all participants or parents/guardians. Final results will be shared with participating communities, and in open-access journals and other scientific fora. Study documents are available online (https://doi.org/10.17037/PUBS.04652739).

COVID-19 and risks to the supply and quality of tests, drugs, and vaccines. Newton PN, Bond KC, on behalf of 54 signatories from 20 countries. *Lancet Glob Health* 2020; 8(6): e754-5. Published online: 09 April 2020. doi: 10.1016/s2214-109x(20)30136-4.

Comment.

Febrile illness mapping--much of the world without data and without evidence-based treatments. *Newton PN, Guerin PJ. BMC Med* 2020; 18(1): 287. Published online: 21 September 2020. doi: 10.1186/s12916-020-01747-y.

Editorial.

Perception of health risks in Lao market vendors. Philavong C, Pruvot M, Reinharz D, Mayxay M, Khammavong K, Milavong P, Rattanavong S, Horwood PF, Dussart P, Douangngeun B, Theppangna W, Fine AE, Robinson MT, Newton PN. *Zoonoses Public Health* 2020; 67(7): 796-804. Published online: 20 August 2020. doi: 10.1111/zph.12759.

Perception of disease risk is very low in Lao wet market vendors, even though wild animals (live and dead) are frequently for sale.

Wet markets are a critical part of South-East Asian culture and economy. However, their role in circulation and transmission of both endemic and emerging disease is a source of concern in a region considered a hotspot of disease emergence. In the Lao People's Democratic Republic (Lao PDR, Laos), live and dead wild animals are frequently found in wet markets, despite legislation against the bushmeat trade. This is generally considered to increase the risk of disease transmission and emergence, although whether or not wildlife vendors themselves have indeed increased

incidence of zoonotic disease has rarely been assessed. In preparation for a future longitudinal study of market vendors investigating vendors' exposure to zoonotic pathogens, we conducted a pilot survey of Lao market vendors of wildlife meat, livestock meat and vegetables, to identify demographic characteristics and potential control groups within markets. We also investigated baseline risk perception for infectious diseases among market vendors and assessed the association between risk perception and risk mitigation behaviours. The surveys conducted with 177 vendors revealed similar age, sex, ethnic background and geographical origin between vendor types, but differences in professional background and work history for livestock meat vendors. The perception of disease risk was very low across all vendors, as was the reported use of personal protective equipment, and the two appeared unrelated. Personal risk discounting and assumptions about transmission routes may explain this lack of association. This information will help inform the development of future research, risk communication and risk mitigation policy, especially in the light of the COVID-19 pandemic.

Non-malarial febrile illness: a systematic review of published aetiological studies and case reports from Southern Asia and South-eastern Asia, 1980-2015. Shrestha P, Dahal P, Ogbonnaa-Njoku C, Das D, Stepniewska K, Thomas NV, Hopkins H, Crump JA, Bell D, Newton PN, Ashley EA, Guerin PJ. *BMC Med* 2020; 18(1): 299. Published online: 21 September 2020. doi: 10.1186/s12916-020-01745-0.

This review summarises the published reports of non-malaria pathogens that may cause febrile illness in south and southeast Asia.

BACKGROUND: In the absence of definitive diagnosis, healthcare providers are likely to prescribe empirical antibacterials to those who test negative for malaria. This problem is of critical importance in Southern Asia (SA) and South-eastern Asia (SEA) where high levels of antimicrobial consumption and high prevalence of antimicrobial resistance have been reported. To improve management and guide further diagnostic test development, better understanding is needed of the true causative agents of fever and their geographical variability. **METHODS:** We conducted a systematic review of published literature (1980-2015) to characterise the spectrum of pathogens causing non-malarial febrile illness in SA and SEA. We searched six databases in English and French languages: MEDLINE, EMBASE, Global Health (CABI) database, WHO Global Health Library, PASCAL, and Bulletin de la Société Française de Parasitologie (BDSP). Selection criteria included reporting on an infection or infections with a confirmed diagnosis, defined as pathogens detected in or cultured from samples from normally sterile sites, or serological evidence of current or past infection. **RESULTS:** A total of 29,558 records from 19 countries in SA and SEA were screened, of which 2410 (8.1%) met the selection criteria. Bacterial aetiologies were reported in 1235 (51.2%) articles, viral in 846 (35.1%), parasitic in 132 (5.5%), and fungal in 54 (2.2%), and 143 (6.0%) articles reported more than one pathogen group. In descending order of frequency, *Salmonella* Typhi, *Escherichia coli*, *Staphylococcus aureus*, *Klebsiella pneumoniae*, and coagulase negative *Staphylococcus* were the commonly reported bacteria, while dengue virus, chikungunya virus, Japanese encephalitis virus, hepatitis B virus, and hepatitis C virus were common viral pathogens reported. Reports of rarely reported or emerging pathogens included a case report of *Borrelia burgdorferi* (Lyme disease) in India in 2010 and reports of Nipah virus in Singapore and India. **CONCLUSIONS:** This review summarises the reported non-malaria pathogens that may cause febrile illness in SA and SEA. The findings emphasise the need of standardising the reporting of aetiological studies to develop effective, evidence-based fever management and improved surveillance. Research and development of diagnostic tools would benefit from up-to-date epidemiological reporting of the regional diversities of non-malaria fever aetiologies. TRIAL REGISTRATION: PROSPERO registration, CRD42016049281.

Evaluation of the forum theatre approach for public engagement around antibiotic use in Myanmar. Swe MMM, Hlaing PH, Phyo AP, Aung HH, Smithuis F, Ashley EA, Cheah PY. *PLoS One* 2020; 15(7): e0235625. Published online: 09 July 2020. doi: 10.1371/journal.pone.0235625.

Public engagement using participatory forum theatre is effective for disseminating knowledge on appropriate use of antibiotics with the community.

INTRODUCTION: The risk of emergence and spread of antibiotic resistance is high in Southeast Asian countries and various strategies are being used to raise awareness about appropriate antibiotic use and antibiotic resistance within communities. Public engagement in science has not been widely practised in Myanmar. We describe the use of a forum theatre to engage with the community about antibiotic use. **METHODS:** The engagement activities took place in a peri-urban township in Yangon, Myanmar. Five preliminary story gathering workshops with the community were carried out to develop scripts and songs for the forum theatre. After that, we organised forum theatre plays between September and October 2018. Following each play we provided four simple key messages based on WHO's world antibiotic awareness week advocacy materials; 1) Antibiotics are medicines used to treat bacterial infections 2) Antibiotics are not useful for coughs and colds 3) Never use leftover antibiotics or share antibiotics with others 4) Prevent infections by regularly washing hands, preparing food hygienically, avoiding close contact with sick people, and keeping vaccinations up to date. We evaluated the engagement activities by conducting focus group discussions (FGD) with audience members. **RESULTS:** Ten forum theatre plays were performed on two topics; "Fever and antibiotics" and "Mixed medicines", reaching 1175 community members. Four themes emerged from our thematic analysis: 1) Knowledge dissemination, 2) Enjoyment and fun, 3) Willingness to support and recommendations for future engagement activities and 4) Preference over traditional methods of health education. We found improvement of antibiotic related knowledge and enjoyment among audience who were also willing to support future engagement activities and preferred forum theatre approach over formal health talks. **CONCLUSIONS:** We conclude that forum theatre is an effective innovative approach to engage and disseminate knowledge on appropriate use of antibiotics with the community in a participatory way.

A Bayesian phase 2 model based adaptive design to optimise antivenom dosing: Application to a dose-finding trial for a novel Russell's viper antivenom in Myanmar. Watson JA, Lamb T, Holmes J, Warrell DA, Thwin KT, Aung ZL, Oo MZ, Nwe MT, Smithuis F, Ashley EA. *PLoS Negl Trop Dis* 2020; 14(11): e0008109. Published online: 16 November 2020. doi: 10.1371/journal.pntd.0008109.

Proposal to use Bayesian modelling to aid clinical trial design and apply this to a dose-finding study for a new Russell's viper antivenom in Myanmar.

For most antivenoms there is little information from clinical studies to infer the relationship between dose and efficacy or dose and toxicity. Antivenom dose-finding studies usually recruit too few patients (e.g. fewer than 20) relative to clinically significant event rates (e.g. 5%). Model based adaptive dose-finding studies make efficient use of accrued patient data by using information across dosing levels, and converge rapidly to the contextually defined 'optimal dose'. Adequate sample sizes for adaptive dose-finding trials can be determined by simulation. We propose a model based, Bayesian phase 2 type, adaptive clinical trial design for the characterisation of optimal initial antivenom doses in contexts where both efficacy and toxicity are measured as binary endpoints. This design is illustrated in the context of dose-finding for *Daboia siamensis* (Eastern Russell's viper) envenoming in Myanmar. The design formalises the optimal initial dose of antivenom as the dose closest to that giving a pre-specified desired efficacy, but resulting in less than a pre-specified maximum toxicity. For *Daboia siamensis* envenoming, efficacy is defined as the restoration of blood coagulability within six hours, and toxicity is defined as anaphylaxis. Comprehensive simulation studies compared the expected behaviour of the model based design to a simpler rule based design (a modified '3+3' design). The model based design can identify an optimal dose after fewer patients relative to the rule based design. Open source code for the simulations is made available in order to determine adequate sample sizes for future adaptive snakebite trials. Antivenom dose-finding trials would benefit from using standard model based adaptive designs. Dose-finding trials where rare events (e.g. 5% occurrence) are of clinical importance necessitate larger sample sizes than current practice. We will apply the model based design to determine a safe and efficacious dose for a novel lyophilised antivenom to treat *Daboia siamensis* envenoming in Myanmar.

Marginalized mites: Neglected vectors of neglected diseases. Weitzel T, Makepeace BL, Elliott I, Chaisiri K, Richards AL, Newton PN. *PLoS Negl Trop Dis* 2020; 14(7): e0008297. Published online: 23 July 2020. doi: 10.1371/journal.pntd.0008297.
Viewpoint.

Patch test results in paediatric patients with atopic dermatitis in Laos. Wootton CI, Sodaly MK, Billamay SX, English JSC, Mayxay M. *PLoS One* 2020; 15(4): e0231455. Epub 2020/04/15. doi: 10.1371/journal.pone.0231455.
The first study of patch testing in Lao children with atopic dermatitis showed a wide range of potential allergens.
BACKGROUND: Dermatological services in Laos, South East Asia are limited mainly to the capital and patch testing is currently not available, so no data exists regarding the common cutaneous allergens in this population. **OBJECTIVES:** The aim of this study was to document common allergens in paediatric patients with atopic dermatitis attending the allergy clinic in the capital, Vientiane. **PATIENTS/MATERIALS/METHODS:** Fifty paediatric patients with atopic dermatitis were patch tested using TRUE Test(R) panels 1 to 3 (35 allergens). Readings were taken at Days 2 and 4. **RESULTS:** Twenty-six positive patch tests were recorded on Day 4 in 15 children (30%). The most common allergens were: gold (18%), nickel (10%), formaldehyde (6%) and p-Phenylenediamine (6%). Other positive allergens were potassium dichromate (2%), cobalt dichloride (2%), Bronopol (2%), paraben mix (2%), fragrance mix 1 (2%) and neomycin (2%). The majority of the patients with positive reactions were female. **CONCLUSIONS:** This study represents the first documented patch test results in the Lao population. It is hoped that these findings will help clinicians to advise the families of children with atopic dermatitis on common allergens to avoid and inform future work on contact dermatitis in this population.

Patch testing in Lao medical students. Wootton CI, Soukavong M, Kidoikhammouan S, Samountry B, English JSC, Mayxay M. *PLoS One* 2020; 15(1): e0217192. Epub 2020/01/17. doi: 10.1371/journal.pone.0217192.
The first study of patch testing in Lao adults provides a background to inform future investigations.
BACKGROUND: Dermatological services in Laos, South East Asia are limited to the capital and patch testing is currently not available, so no data exists regarding the common cutaneous allergens in this population. OBJECTIVES: The aim of this study was to document positive patch tests in medical students without evidence of contact dermatitis in Laos. **PATIENTS/MATERIALS/METHODS:** One hundred and fifty medical students were patch tested using TRUE Test(R) panels 1 to 3 (35 allergens). Readings were taken at Days 2 and 4. **RESULTS:** Thirty-eight students (25.3%) had a positive reaction to at least one allergen, accounting for 52 reactions in total. The proportion of the students with positive patch test reading was significantly higher in the female [33/96 (34%)] than in the male [5/54 (9%)], p<0.001. The most common allergens were: nickel (10%), gold (6.6%), thiomersal (6.6%), cobalt dichloride (2%) and p-tert-Butylphenol formaldehyde resin (2%). Balsam of Peru (0.66%), black rubber mix (0.66%), Cl+Me-Isothiazolinone (0.66%), fragrance mix 1 (0.66%), quinolone mix (0.66%), methyldibromo glutaronitrile (0.66%), mercapto mix (0.66%), epoxy resin (0.66%), paraben mix (0.66%), thiuram (0.66%) and wool alcohols (0.66%) accounted for all of the other positive reactions. CONCLUSION: This study represents the first documented patch test results in Lao medical students and in the adult Lao population. The results of this study will inform any future research into contact allergy in Laos and give an insight into the background level of contact sensitivity in this population.

MONOGRAPHS

LOMWRU staff contributed to two World Health Organization Monographs, both published as part of the fourth edition of the WHO Laboratory Biosafety Manual.

Biosafety programme management. Geneva: World Health Organization; 2020 (Laboratory biosafety manual, fourth edition and associated monographs). Scientific Contributors: Caminiti K, Dance D, Dragon D, Ghariani N, Heisz M, McKinney M, Robertson C, Starr A, Whistler T. https://apps.who.int/iris/handle/10665/337963

Outbreak preparedness and resilience. Geneva: World Health Organization; 2020 (Laboratory biosafety manual, fourth edition and associated monographs). Scientific contributors: Gabriel M, Kurth A, Makison Booth C, Shallcross J, Simpson A. https://apps.who.int/iris/handle/10665/337959

Conference and Meeting Presentations in 2020

Due to the COVID-19 Pandemic, there were very few opportunities to attend scientific conferences or meetings during 2020. Listed below are those where LOMWRU staff were able to participate.

FIEBRE Network Meeting. Vientiane, 11-13 February 2020.

Manophab Luangraj and Somvai Singhaxayaseng. **Laos Site Update. (Oral Presentation).**

MORU Rickettsia Coordination Meeting. Virtual Meeting, 19 May 2020.

Oral presentations:
Matthew T Robinson. **LOMWRU Round-Up.**
Weerawat Phuklia. **Optimizing conditions for Rickettsia typhi isolation using cell culture.**

American Society of Tropical Medicine & Hygiene 2020 (69th) Annual Meeting. Virtual Meeting, 15-19 November 2020.

Mullins KE, Canal E, Ouch P, Prasetyo D, Tagoe J, Robinson M, Simons M, Newton P, Richards A, Faris C. ***Bartonella* species in Cambodia, Ghana, Laos and Peru: Results from sero- and vector-surveys'. (Poster).**
Abstract Book,
Abstract 576. Am J Trop Med Hyg 2020; 103 (5 Supplement): 162. https://www.astmh.org/getmedia/71a0e5e6-7c06-48a4-ab47-d50c4ec870a2/ASTMH-2020-Abstract-Book.pdf
Swe MMM, Win MM, Cohen J, Phyo AP, Parker D, Dance D, Ashley E, Smithuis F. **Mapping and Geographic distribution of Burkholderia pseudomallei in Myanmar. (Oral Presentation).**
Abstract Book, Abstract 946. Am J Trop Med Hyg 2020; 103 (5 Supplement): 267. https://www.astmh.org/getmedia/71a0e5e6-7c06-48a4-ab47-d50c4ec870a2/ASTMH-2020-Abstract-Book.pdf

The Lao Infectious Diseases Society Conference, 2020 was held in the University of Health Sciences.
ຮູບພາບ ກອງປະຊຸມສະມາຄົມພະຍາດຊຶມເຊື້ອປີ 2020 ເຊິ່ງໄດ້ຈັດຂຶ້ນທີ່ ມະຫາວິທະຍາໄລ ວິທະຍາສາດ ສຸຂະພາບ

2nd Annual Scientific Meeting of the Lao Infectious Disease Society (LIDS). Vientiane, 10-11 December 2020.

Oral presentations:
Elizabeth Ashley. AMR in Laos: **The increasing challenge of ESBL-producing *Enterobacterales*.**
Mayfong Mayxay. **Dengue: not easy to diagnose.**
Tamalee Roberts. **Evidence for *Leishmania* in Laos.**
Andrew Simpson. **Methicillin-resistant Staphylococcus aureus (MRSA) in Laos.**
Lee Youn and Matthew Robinson. **Angiostrongylus: Case presentation & laboratory diagnosis.**
Danoy Chommanam. **Interesting Infectious Disease Case Presentation.**
Souphaphone Vannachone. **Interesting Infectious Disease Case Presentation.**

Joint International Tropical Medicine Meeting 2020 (JITMM Virtual 2020). 15-16 December 2020.

Simpson A. **Melioidosis in the Lao PDR.** Program Book, page 212. https://www.jitmm.com/scientific-program/

University of Health Sciences Annual Scientific Meeting 2020. Vientiane, 16 December 2020.

Oral presentations:
Vilada Chansamouth. **Methicillin Resistant *Staphylococcus aureus* (MRSA)** ໃນລາວ. **(Methicillin Resistant *Staphylococcus aureus* (MRSA) in Laos.)**
Manophab Luangraj. ເຊື້ອຈຸລິນຊີທີ່ຕ້ານຕໍ່ຢາຕ້ານເຊື້ອກຸ່ມ **Carbapenem** ໃນ ສປປ ລາວ. **(Carbapenem resistance in the Lao PDR.)**
Mayfong Mayxay. **(AMR in Laos: An Increasing Challenge with ESBL)**

OTHER ACTIVITIES IN 2020

PUBLIC ENGAGEMENT

Led by Professor Mayfong Mayxay, Head of Field Research and Engagement, LOMWRU has continued its programme of community, public and policy engagement activities.

Dr Manivanh Vongsouvath gives an interview on COVID-19 testing on Lao television
Early in the pandemic Dr Manivanh Vongsouvath, Head of the Microbiology laboratory in Mahosot Hospital, gave a long television interview on COVID-19 and the testing service.

Lao Youth Radio Weekly slot with Dr Vatthanaphone Latthaphasavang

LOMWRU has been collaborating with Dr Vatthanaphone Latthaphasavang, who hosts a live radio show weekly on Lao Youth Radio. Professor Mayfong Mayxay and other health experts in Laos have been interviewed on a range of topics such as research in Laos, protecting patients/ethics in research, AMR, melioidosis and childhood diseases.

From *left*: Dr Vatthanaphone Latthaphasavang (host), Dr Danoy Chommanam, Dr Anousone Douangnouvong and Dr Vilada Chansamouth, who was interviewed about antimicrobial resistance on Lao Youth Radio.

ຮູບພາບລຽນຈາກຊ້າຍຫາຂວາ, ດຣ ວັດທະນາພອນ ລັດທະພາສະຫວ່າງ (ໂຄສິກ), ດຣ ດານ້ອຍ ຈອມມະນາມ, ດຣ ອານຸສອນ ດວງມຸວົງ ແລະ ດຣ ວິລະດາ ຈັນສະມຸດ ທີ່ໄດ້ໃຫ້ສຳພາດກ່ຽວກັບການຕ້ານຕໍ່ຢາຕ້ານເຊື້ອ ຜ່ານສະຖານີວິທະຍຸຊາວໜຸ່ມລາວ.

World Antimicrobial Awareness Week Event at Mahosot Hospital

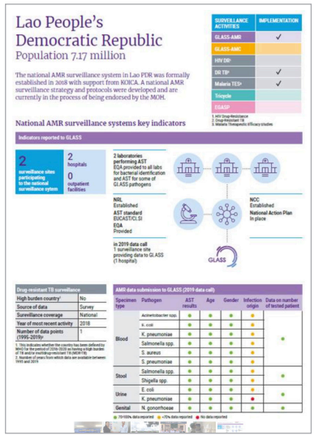
In November 2020 Dr Vilada Chansamouth continued to raise awareness about antibiotic use and antimicrobial resistance to mark World Antimicrobial Awareness Week (WAAW) with a special event and slogan competition at Mahosot Hospital presided over by the Hospital Director, Dr Phisith Phouthsavath.

Dr Bandith Soumphonphakdy, Paediatric Infectious Diseases physician at Mahosot Hospital, shown wearing the winning T-shirt of a slogan competition for the World Antibiotic Awareness Week, 2020.

ຮູບພາບ ດຣ ບັນດິດ ຊຸມພົນພັກດີ, ຊ່ຽວຊານພະຍາດຊຶມເຊື້ອເດັກນ້ອຍ ທີ່ໂຮງໝໍມະໂຫສົດ, ໄດ້ນຸ່ງເສື້ອຍືດທີ່ມີຄຳຂວັນຂອງຜູ້ທີ່ໄດ້ຮັບລາງວັນຊະນະເລີດໃນການແຂ່ງຂັນການແຕ່ງຄຳຂວັນໃນງານ ສັບປະດາສັບປະດາສາກົນແຫ່ງການປຸກຈິດສຳນຶກໃນການນຳໃຊ້ຢາຕ້ານເຊື້ອຈຸລະຊີບ ປະຈຳປີ 2020

AMR dictionary translated into Lao

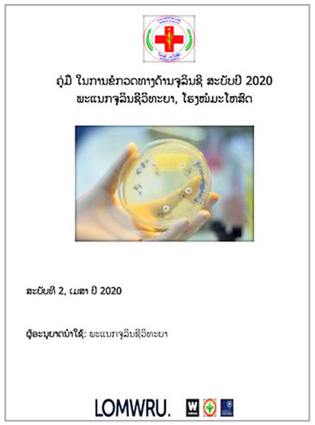
This AMR dictionary is based upon an idea by Associate Professor Direk Limmathurotsakul, Mahidol-Oxford Tropical Medicine Research Unit and Department of Tropical Hygiene, Faculty of Tropical Medicine, Mahidol University, Thailand. AMR Dictionary uses content generated from multiple sources and translated by researchers, healthcare workers and networks in each country. The AMR dictionary was funded by The Wellcome Trust Provision for Public Engagement Award and supported by many collaborators and institutions. Dr Vilada Chansamouth led the Lao translation with support from Prof Mayfong Mayxay, Dr Sayaphet Rattanavong, Dr Souphaphone Vannachone, Mr Kem Boutsamay and Ms Vayouly Vidhamaly.



WHO GLASS 2020 Report published with Mahosot Microbiology Laboratory representing Laos

WHO published a new report of the Global Antimicrobial Resistance Surveillance System (GLASS) in 2020. The report described the status of development of GLASS and summarises the results of the call for 2018 AMR surveillance data from participating countries, territories and areas.

ພະແນກຈຸລິນຊີ, ໂຮງໝໍມະໂຫສົດ ໄດ້ເປັນຕົວແທນຈາກ ສປປ ລາວ ໃນການຕອບສະໜອງຂໍ້ມູນສຳລັບການເຜີຍແຜ່ບົດລາຍງານ WHO GLASS ປີ 2020. ອົງການອະນາໄມໂລກ ໄດ້ຕີພິມບົດລາຍງານສະບັບໃໝ່ຂອງລະບົບການເຝົ້າລະວັງການຕ້ານຕ່ຍາຕ້ານເຊື້ອທົ່ວໂລກ (GLASS) ໃນປີ 2020. ບົດລາຍງານໄດ້ອະທິບາຍສະຖານະພາບການພັດທະນາຂອງ GLASS GLASS ແລະ ໄດ້ສະຫຼຸບຜົນການເຝົ້າລະວັງການຕ້ານຕ່ຍາຕ້ານເຊື້ອຈຸລະຊີບ ໃນປີ 2018 ຈາກປະເທດ ແລະ ຂົງເຂດທີ່ເຂົ້າຮ່ວມ.



Mahosot microbiology laboratory launches the new laboratory user manual

After an extended incubation the Mahosot Microbiology Laboratory User Manual completed its first Lao language print run and was launched in a session organised for Users in Mahosot Hospital on Thursday 25th June 2020.

ພະແນກຈຸລິນຊີ ໂຮງໝໍມະໂຫສົດ ໄດ້ເຜີຍແຜ່ຄູ່ມືການປະຕິບັດໃນຫ້ອງແລັບ ສະບັບໃໝ່ ຫຼັງຈາກທີ່ໄດ້ຂະຫຍາຍການປິ່ມເພາະເປັນເວລາດົນ, ໃນວັນທີ 25 ມິຖຸນາ 2020 ພະແນກຈຸລິນຊີ ໂຮງໝໍມະໂຫສົດໄດ້ສຳເລັດການເຜີຍແຜ່ປຶ້ມຄູ່ມືການປະຕິບັດໃນຫ້ອງແລັບພາສາລາວ ສະບັບທຳອິດ ເພື່ອໃຫ້ຜູ້ຊິມໃຊ້ ໃນໂຮງໝໍມະໂຫສົດ.

LAO MEDICAL JOURNAL

LOMWRU continues to support publication of the *Lao Medical Journal*. The latest issue (Volume 11) was published in September 2020.

RICKETTSIA THREAT REDUCTION NETWORK

LOMWRU continued its involvement in the Rickettsia Threat Reduction Network, supported by the Defense Threat Reduction Agency (DTRA; Department of Defense, USA). The network provides a forum to collaborate and standardize research and diagnostics on all rickettsial organisms in the region, with the aim of highlighting their importance in febrile illness. LOMWRU is one of the active contributing centres to the network, providing diagnostics, *Rickettsia* identification, isolate biobanking, and biosafety guidance. The global rickettsia mapping database (www.rickettsia.net), to which LOMWRU contributes to, will be officially opened in 2021.

MELIOIDOSIS THREAT REDUCTION NETWORK

LOMWRU also continued its involvement with the Melioidosis Threat Reduction Network, which is supported by DTRA. The Network provides a forum to facilitate collaboration on research into many aspects of melioidosis in the region, including clinical management, diagnostics and biosafety. Due to the COVID-19 pandemic, Network activity was very limited during 2020. A planning and update meeting was held after the L-TEAM Meeting in Luang Prabang in January, but a larger planned meeting at the 6th World One Health Congress in Edinburgh was cancelled after the Congress was postponed. DTRA remain committed to funding melioidosis projects in Laos and the wider Mekong region, particularly on development of clinical and diagnostic capacity. Discussions about next steps are continuing.

Dr Tamalee Roberts volunteers in Lebanon

In December 2019- February 2020, Dr Tamalee Roberts (shown *left* with Lebanon MoH laboratory staff) volunteered with Médecins Sans Frontières in Lebanon where she helped to install and train staff on the use of the BacT/ALERT blood culture machine as well as writing and training staff on microbiology laboratory procedures for the MSF paediatric hospital.

ໃນເດືອນທັນວາ ປີ 2019 ຫາ ເດືອນກຸມພາ ປີ 2020, Dr Tamalee Roberts (ທາງດ້ານຊ້າຍ ແລະ ພະນັກງານຫ້ອງວິເຄາະວິທະຍາ, ກະຊວງສາທາລະນະສຸກ ຈາກປະເທດ Lebanon) ໄດ້ອາສາສະໝັກເຮັດວຽກຮ່ວມກັບ Médecins Sans Frontières ຢູ່ໃນປະເທດ Lebanon ເພື່ອຊ່ວຍໃນການຕິດຕັ້ງ ແລະ ໃຫ້ການເຝິກອົບຮົມການນຳໃຊ້ເຄື່ອງ BacT/ALERT blood culture, ພ້ອມດຽວກັນນີ້ ກໍ່ໄດ້ຊ່ວຍໃນການຂຽນ ແລະ ໃຫ້ການເຝິກອົບຮົມພະນັກງານຫ້ອງວິເຄາະກ່ຽວກັບຂັ້ນຕອນການປະຕິບັດການທາງດ້ານຈຸລິນຊີວິທະຍາ ໃນ MSF paediatric hospital.

Chiggers revival

The Chiggers were finally back in action in 2020 when they travelled to Vientiane province on Saturday 26 September to play against the FIEBRE team who narrowly beat them 6-5.

ໃນທີ່ສຸດ ທີມ Chiggers ກໍ່ກັບມາອີກຄັ້ງໃນປີ 2020. ທີມ Chiggers ໄດ້ເດີນທາງໄປແຂວງວຽງຈັນໃນວັນເສົາທີ 26 ເດືອນກັນຍາ ເພື່ອທຳການແຂ່ງຂັນກັບທີມ FIEBRE, ໂດຍທີມ Chiggers ຍາດຊິງເອົາໄຊຊະນະມາໄດ້ຈຸດວິດດ້ວຍຄະແນນ 6 ຕໍ່ 5.

FAREWELLS

Céline Caillet, Martial Battain and their son Raphaël left Laos in 2020. Céline is continuing her work on Medicine Quality at the University of Oxford.

ຮູບພາບ ນາງ Céline Caillet, ທ້າວ Martial Battain ແລະ ລູກຊາຍ Raphaël, ໄດ້ອຳລາປະເທດລາວໃນປີ 2020. ເຖິງຢ່າງໃດກໍຕາມ ນາງ Céline ຍັງຄົງສືບຕໍ່ເຮັດວຽກງານກວດກາຄຸນນະພາບຢາ ທີ່ ມະຫາວິທະຍາໄລ Oxford.

Mr. Chanthala Vilayhong, LOMWRU laboratory technician and field researcher, left LOMWRU in 2020.

ທ່ານ ຈັນທະລາ ວິໄລຫົງ, ພະນັກງານວິເຄາະ ແລະ ນັກຄົ້ນຄ້ວາພາກສະໜາມ ຂອງ LOMWRU, ໄດ້ອອກຮັບເບ້ຍບຳນານໃນທ້າຍປີ 2020.

Dr Sayaphet Rattanavong, Deputy Head of the Microbiology Laboratory, transferred to Savannakhet Provincial Hospital in 2020.

ຮູບພາບ ດຣ ໄຊຍະເພັດ ຣັດຕະນະວົງ, ຄະນະພະແນກຈຸລິນຊີ, ທີ່ໄດ້ຍົກຍ້າຍໄປປະຈຳການຢູ່ທີ່ໂຮງໝໍແຂວງສະຫວັນນະເຂດ, ໃນປີ 2020

THANK YOU TO OUR FUNDERS

Project funders in 2020

We would like to thank all of our funders for their very generous support of projects in 2020