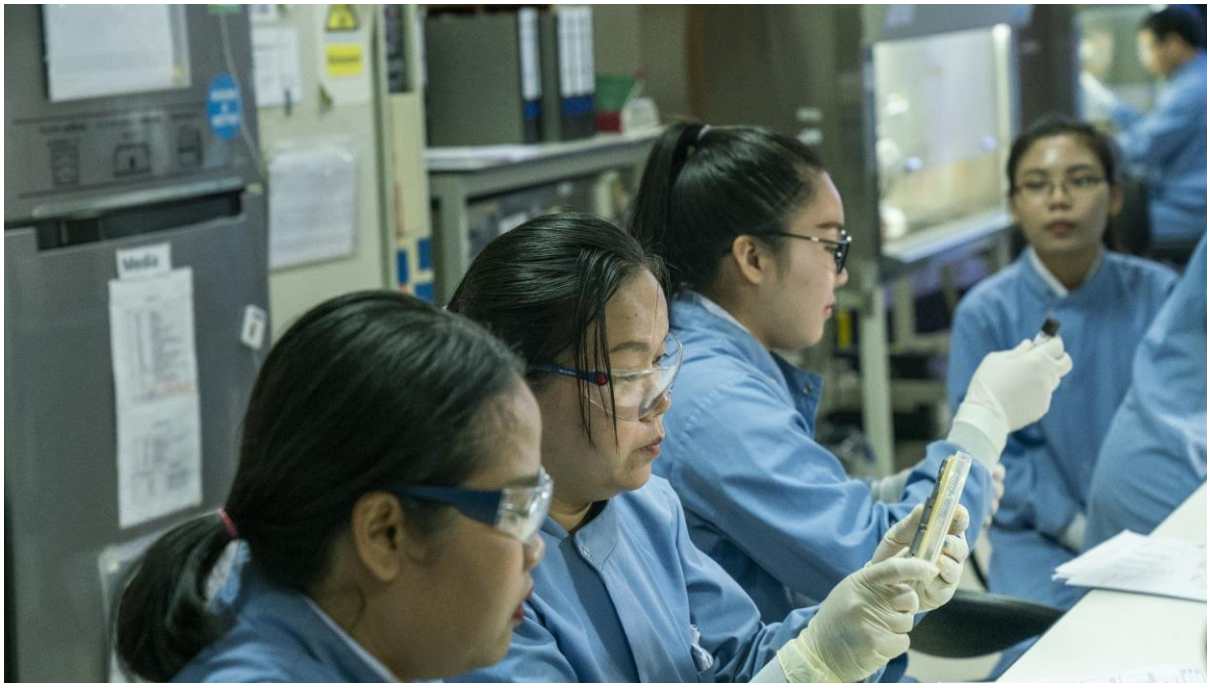
LOMWRU

MORU Tropical Health Network



# ANNUAL REPORT

## 2019

*Activity Report of the Lao-Oxford-Mahosot Hospital-Wellcome Trust Research Unit (LOMWRU)*

IDDO INFECTIOUS DISEASES DATA OBSERVATORY

Aix Marseille université IRD Inserm EFS ÉTABLISSEMENT FRANÇAIS DU SANG IRBA MÉDITERRANÉE INFECTION

# ກ່ຽວກັບໜ່ວຍງານຄົ້ນຄວ້າຂອງພວກເຮົາ

ໂຄງການຄົ້ນຄວ້າພະຍາດເຂດຮ້ອນລະຫວ່າງໂຮງໝໍມະໂຫສົດ - ແອວຄຳຫຼັສ - ມະຫາວິທະຍາໄລອ໋ອກຟອດ ຫຼື The **Lao-Oxford-Mahosot Hospital-Wellcome Trust Research Unit** (LOMWRU) ແມ່ນ ໜ່ວຍງານຄົ້ນຄວ້າທີ່ມີການ ຮ່ວມມືລະຫວ່າງມະຫາວິທະຍາໄລອ໋ອກຟອດ ແລະ ໂຮງໝໍມະໂຫສົດ, ນະຄອນຫຼວງວຽງຈັນ, ສປປ ລາວ ໂດຍໄດ້ຮັບທຶນຊ່ວຍເຫຼືອຫຼັກ ຈາກແອວຄຳຫຼັສ ປະເທດອັງກິດ. ພວກເຮົາຍັງ ແມ່ນສ່ວນໜຶ່ງຂອງເຄືອຄ່າຍໜ່ວຍງານຄົ້ນຄວ້າພະຍາດເຂດຮ້ອນ MORU Tropical Health Network ທີ່ມີ ສູນຄົ້ນຄ້ວາ ຕັ້ງຢູ່ ປະເທດໄທ, ກຳປູເຈຍ, ລາວ, ພະມ້າ ແລະ ສາທາລະນະລັດ ປະຊາທິປະໄຕ ຄອງໂກ.

ປະຈຸບັນ ພວກເຮົາມີພະນັກງານທັງໝົດ 80 ຄົນ ຊຶ່ງລວມມີ ພະນັກງານທີ່ເຮັດວຽກປະຈຳຢູ່ນະຄອນຫຼວງວຽງຈັນ ແລະ ຕ່າງແຂວງ ທີ່ເປັນໜຶ່ງໃນວຽກງານການຮ່ວມມືຄົ້ນຄ້ວາ, ແລະ ໃນນັ້ນຍັງມີ ພະນັກງານພາກລັດຈາກພະ ແນກຈຸລິນຊີວິທະຍາ ຈຳນວນ 23 ຄົນ ໂດຍມີ ດຣ ມະນີວັນ ວົງສຸວັດ ເປັນຫົວໜ້າພະແນກ. ໜ່ວຍງານຄົ້ນຄວ້າ LOMWRU ມີ ຫ້ອງວິເຄາະທາງພັນທຸກຳ, ຫ້ອງວິເຄາະເຊໂຣໂລຊີ ແລະ ຫ້ອງວິເຄາະລະດັບ3 (BSL3) ສຳລັບ ປູກເຊື້ອ rickettsial, *Mycobacterium* spp., *B. pseudomallei* ແລະ ເຊື້ອໄວຣັສ. ຣສ ດຣ ມາຍຝອງ ມາຍ ຊາຍ, ຮອງອະທິການບໍດີ ມະຫາວິທະຍາໄລ ວິທະຍາສາດສຸຂະພາບ ຊ່ວຍຊີ້ນຳວຽກງານຮ່ວມມືຄົ້ນຄ້ວາກັບບັນດາ ແຂວງ ແລະ ວຽກງານຄົ້ນຄ້ວາພາກສະໜາມ.

ໂຄງການຄົ້ນຄວ້າພະຍາດເຂດຮ້ອນລະຫວ່າງໂຮງໝໍມະໂຫສົດ-ແອວຄຳຫຼັສ-ມະຫາວິທະຍາໄລອ໋ອກຟອດ (LOMWRU) ໄດ້ຂະຫຍາຍວຽກງານຄົ້ນຄວ້າພະຍາດຊຶມເຊື້ອທັງພາຍໃນນະຄອນຫຼວງ ແລະ ບັນດາໂຮງໝໍ ແຂວງຕ່າງໆ ໃນຂອບເຂດຊົນນະບົດ ຂອງ ສປປ ລາວ, ນອກນັ້ນ ພວກເຮົາຍັງມີການຮ່ວມມືໃນຫລາຍໆວຽກ ງານການຄົ້ນຄວ້າ ກັບໜ່ວຍງານ MORU Tropical Health Network ກັບ ບັນດາປະເທດອື່ນໆອີກດ້ວຍ.

## 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 80 research and support staff in the capital and the provinces working on projects as part of the collaboration, including 23 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., *B. pseudomallei* and viral culture. The head of field research and Engagement is Associate Professor Mayfong Mayxay, who is Vice President of the University of Health Sciences in Vientiane

LOMWRU conducts research on a wide range of infectious diseases in Vientiane and at a number of provincial hospitals and field sites in rural Laos and participates in multicentre studies across the MORU Network and beyond.

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# MESSAGE FROM THE DIRECTOR

## ຄຳເຫັນຂອງທ່ານ Dr Elizabeth Ashley

ປີຜ່ານມາ ຖືເປັນປີທີ່ມີການປ່ຽນແປງຢ່າງໃຫ່ຍຫລວງ ສຳລັບໂຄງການຮ່ວມມືຄົ້ນຄ້ວາດ້ານພະຍາດເຂດຮ້ອນ ລະຫວ່າງໂຮງຫມໍ ມະໂຫສົດ-ມະຫາວິທະຍາໄລອ໋ອກຟອດ-ແວວຄຳຕູ້ສ (LOMWRU) ເນື່ອງຈາກວ່າ Prof. Paul Newton ເຊິ່ງເປັນຜູ້ກໍ່ຕັ້ງໂຄງການ, ແລະ Prof. David Dance ເຊິ່ງເປັນຊ່ຽວຊານທາງດ້ານຈຸລິນຊີ ທາງຄລີນິກ ໄດ້ກັບຄືນປະເທດອັງກິດ ພາຍຫລັງທີ່ໄດ້ມາປະຈຳການຢູ່ ສປປ ລາວ ເກືອບ 20 ປີ ແລະ 9 ປີ ຕາມລຳດັບ. ທັງສອງທ່ານຍັງເປັນທີ່ຄິດຮອດ ແລະ ຄິດເຖິງສຳລັບທຸກຄົນຢູ່ທີ່ນີ້. ຂ້າພະເຈົ້າເອງ ໄດ້ເຂົ້າມາປະຈຳການ ແທນ ຕັ້ງແຕ່ເດືອນ ພຶດສະພາ 2019, ໂດຍໄດ້ຍ້າຍມາຈາກຫນ່ວຍງານຄົ້ນຄ້ວາດ້ານຄລີນິກ ລະຫວ່າງມະຫາວິທະຍາໄລອ໋ອກຟອດ-ພະມ້າ ເຊິ່ງຕັ້ງຢູ່ນະຄອນຫລວງຢ່າງກຸ້ງ, ປະເທດພະມ້າ (Myanmar Oxford Clinical Research Unit ຫຼື MOCRU). ຫຼັງຈາກທີ່ຂ້າພະເຈົ້າ ມາເຮັດວຽກໄດ້ໜຶ່ງອາທິດ, ທ່ານ Dr Andrew Simpson ກໍ່ໄດ້ຍ້າຍເຂົ້າມາເຮັດວຽກຢູ່ LOMWRU ໂດຍຍ້າຍມາຈາກຫ້ອງວິເຄາະ ຂອງ ສາທາລະນະສຸກ ອັງກິດ ເຊິ່ງມີທີ່ຕັ້ງຢູ່ Porton Down ປະເທດອັງກິດ ເຊິ່ງທ່ານເຄີຍເຮັດການວິໄຈກ່ຽວກັບ ພະຍາດທີ່ບໍ່ຄ່ອຍພົບເຫັນ ແລະ ພະຍາດທີ່ນຳເຂົ້າມາຈາກປະເທດອື່ນ (the Rare and Imported Pathogens Laboratory at Public Health England, Porton Down in the UK). ທ່ານ Dr Andrew Simpson ແມ່ນມາແທນ Prof. David Dance, ທັງສອງ ທ່ານ ແມ່ນມີຄວາມສົນໃຈໃນພະຍາດ melioidosis ເຊັ່ນດຽວກັນ. ຂ້າພະເຈົ້າ ແລະ Dr Andrew Simpson ຈະພະຍາຍາມສຸດຂີດ ເພື່ອບັນລຸເປົ້າ ໝາຍຄືດັ່ງທີ່ສອງທ່ານໄດ້ເຮັດໄວ້ຜ່ານມາ. ໃນປີ 2019, ຫນ່ວຍງານຄົ້ນຄ້ວາພະຍາດເຂດຮ້ອນລະຫວ່າງ ມະຫາວິທະຍາໄລ ມະຫິດົນ-ອ໋ອກຟອດ (Mahidol Oxford Tropical Medicine Research Unit ຫຼື MORU) ເຊິ່ງເປັນສຳນັກງານໃຫຍ່ ກໍ່ໄດ້ ສະເຫລີມສະຫລອງຄົບຮອບ 40 ປີ ແຫ່ງການກໍ່ຕັ້ງຫນ່ວຍງານດັ່ງ ກ່າວທີ່ປະເທດໄທ. ການລະບາດຂອງພະຍາດໄຂ້ຍຸງລາຍໃນປີ 2019 ແລະ ການລະບາດຂອງພະຍາດ COVID-19 ທີ່ກຳລັງລະບາດລະບາດໄປທົ່ວ ໂລກ ເຊິ່ງຊີ້ໃຫ້ເຫັນວ່າ ການຄົ້ນຄ້ວາດ້ານພະຍາດຊຶມເຊື້ອເປັນສິ່ງທີ່ສຳຄັນທີ່ ສຸດ. ສະມາຄົມແພດພະຍາດຊຶມເຊື້ອລາວ ໄດ້ຖືກກໍ່ຕັ້ງຂຶ້ນໃນປີ 2019, ເຊິ່ງປະທານສະມາຄົມແມ່ນ ທ່ານ ສາດສະດາຈານ ດຣ. ມາຍຝອງ ມາຍຊາຍ, ຫົວໜ້າຄົ້ນຄ້ວາວິໄຈພາກສະໜາມ, ຮອງອະທິການບໍດີ ມະຫາວິທະຍາໄລ ວິທະຍາສາດສຸຂະພາບ. ກອງປະຊຸມວິທະຍາສາດຄັ້ງປະຖົມມະເລີກຂອງສະມາຄົມກໍ່ໄດ້ຖືກຈັດ ຂຶ້ນ ໃນລະຫວ່າງວັນທີ 7-8 ເດືອນພະຈິກ ປີ 2019. ທາງການຂອງລາວກໍ່ຮັບຮູ້ ແລະ ຕີລາຄາສູງຕໍ່ຜົນງານ

# MESSAGE FROM THE DIRECTOR

ການຄົ້ນຄວ້າຂອງທີມງານ LOMWRU ເຊິ່ງ ໃນປີທີ່ຜ່ານມາ ທ່ານສາດສະດາຈານ ດຣ. ມາຍຝອງ ມາຍຊາຍ ແລະ ທ່ານ Professor Paul Newton ແມ່ນໄດ້ຮັບຫລຽນໄຊແຮງງານ ຈາກ ລັດຖະບານ ຈາກຜົນງານທີ່ໄດ້ປະກອບສ່ວນໃນວຽກງານການຄົ້ນຄ້ວາວິໄຈ, ແລະ ການສ້າງບຸກຄະລາກອນດ້ານພະຍາດຈຸລິນຊີວິທະຍາ ແລະ ພະຍາດຈຸລະໂລກວິທະຍາ.

## ຜົນການຄົ້ນຄ້ວາທີ່ພົ້ນເດັ່ນໃນປີທີ່ຜ່ານມາ

ໃນປີຜ່ານມາ ນັກຄົ້ນຄວ້າໃນໜ່ວຍງານຄົ້ນຄວ້າ LOMWRU ໄດ້ຕີພິມເຜີຍແຜ່ຜົນການຄົ້ນຄວ້າຂອງຕົນ ຫລື ມີຜົນງານຕີພິມ ເຜີຍແຜ່ຜົນການຄົ້ນຄວ້າຮ່ວມກັບພາກສ່ວນອື່ນ ໃນວາລະສານການແພດສາກົນ ຈຳນວນ 69 ບົດ ເຊິ່ງບົດຄົ້ນຄ້ວາຈຳນວນຫນຶ່ງຈະໄດ້ນຳ ສະເໜີຢູ່ພາກ “ຜົນການຄົ້ນຄວ້າທີ່ພົ້ນເດັ່ນໃນປີຜ່ານມາ” ໃນບົດລາຍງານສະບັບນີ້. ໃນຊຸມປີຜ່ານມາ, ຄົນເຈັບໄດ້ຍິນຍອມເຂົ້າຮ່ວມການ ຄົ້ນຄ້ວາກ່ຽວກັບສາເຫດຂອງໄຂ້ ຢູ່ ສປປ ລາວ ເຮັດໃຫ້ພວກເຮົາມີຂໍ້ມູນກ່ຽວກັບສາເຫດຂອງໄຂ້ຢ່າງຫລວງຫລາຍ ແລະ ເຮັດໃຫ້ພວກ ເຮົາຮູ້ວ່າ ພະຍາດຊຶມເຊື້ອໃດທີ່ພົບຫລາຍ ແລະ ເປັນບັນຫາໃນ ສປປ ລາວ ພ້ອມທັງຮັບຮູ້ເຖິງແນວໂນ້ມ ຂອງເຊື້ອທີ່ຕ້ານຕ່ຢາຕ້ານເຊື້ອ ຢູ່ ໃນນະຄອນຫຼວງວຽງຈັນ ແລະ ບາງແຂວງ ຂອງ ສປປ ລາວ. ໃນປີ 2019 Dr. Audrey Dubot-Pérès ພ້ອມດ້ວຍທີມງານ ໄດ້ຕີພິມເຜີຍ ແຜ່ຜົນຂອງການຄົ້ນຄວ້າກ່ຽວກັບສາເຫດຂອງການຊຶມເຊື້ອ ລະບົບປະສາດສູນກາງໃນຄົນເຈັບທີ່ມານອນປິ່ນປົວຢູ່ໂຮງໝໍມະໂຫສົດ. ການ ສຶກສາຄົ້ນຄວ້ານີ້ ກໍຄືຫຼາຍໆການ ສຶກສາທີ່ຜ່ານມາ ຖືເປັນຜົນສຳເລັດຈາກການເຮັດຄົ້ນຄວ້າຢ່າງມີຈຸດສຸມໃນຫຼາຍປີຜ່ານມາ ຂອງທ່ານໝໍ ປິ່ນປົວ ແລະ ທີມງານຫ້ອງວິເຄາະຈຸລິນຊີວິທະຍາ ໂຮງໝໍມະໂຫສົດ.

## ວຽກງານຝຶກອົບຮົມທີ່ພົ້ນເດັ່ນໃນປີຜ່ານມາ

ໜຶ່ງໃນພາລະບົດບາດ ຂອງ LOMWRU ໄດ້ແກ່ການຝຶກອົບຮົມນັກຄົ້ນຄ້ວາວິໄຈລາວ ແລະ ຕ່າງປະເທດ. ໃນປີ 2019 ມີນັກ ສຶກສາ 4 ຄົນ ທີ່ໄດ້ມາເຮັດການສຶກສາຄົ້ນຄວ້າທັງໝົດ ຫຼື ບາງສ່ວນ ນຳພວກເຮົາ ແລະ ໄດ້ຈົບ ການສຶກສາໄປແລ້ວ, ໃນນັ້ນ 2 ທ່ານ ຈົບ ປະລິນຍາເອກ ແລະ 2 ທ່ານຈົບປະລິນຍາໂທ. Dr Rebecca Inglis, ນັກສຶກສາປະລິນຍາເອກ ຂອງມະຫາວິທະຍາໄລອ໋ອກຟອດ, ໄດ້ພັດທະນາ ແລະ ປະເມີນຫຼັກສູດການຮຽນ-ການ ສອນ ຂອງພະຍາບານ ແລະ ທ່ານໝໍລາວ ຜູ້ທີ່ໃຫ້ການປິ່ນປົວຄົນເຈັບມໍລະສຸມ ເປັນເວລາ 3 ປີ ຮ່ວມກັບ ດຣ. ຄຳໃສ ເດດລືໄຊ, ອາດີດຫົວໜ້າພະແນກຟື້ນຟູຊີບຜູ້ໃຫຍ່, ໂຮງໝໍມະໂຫສົດ, ປັດຈຸບັນດຳລົງຕຳແໜ່ງຮອງ ອຳນວຍການ ໂຮງໝໍມະໂຫສົດ ເຊິ່ງທ່ານແມ່ນໜຶ່ງໃນຜູ້ໃຫ້ຄຳປຶກສາຫຼັກແກ່ Dr Rebecca Inglis. ນອກນີ້

# MESSAGE FROM THE DIRECTOR

ພວກເຮົາມີຄວາມຍິນດີ ທີ່ໄດ້ປະກອບ ສ່ວນໃນການເພີ່ມທະວີຄວາມຮັບຮູ້ກ່ຽວກັບພະຍາດ melioidosis ໃຫ້ແກ່ພະນັກງານແພດໝໍໃນ ປີ 2019 ທີ່ຜ່ານມາ ໂດຍໄດ້ເປັນສ່ວນ ໜຶ່ງຂອງທີມງານ L-TEAM.

## ແຜນວຽກໃນອະນາຄົດ

ເປັນສິ່ງທີ່ເຫັນໄດ້ຢ່າງຊັດເຈນວ່າ ປີ 2020 ເປັນປີທີ່ບໍ່ຄືກັບປີທີ່ຜ່ານມາ ກໍ່ ຄືວ່າ: ທັງ ສປປ ລາວ ແລະ ປະເທດ

ຕ່າງໆໃນທົ່ວໂລກ ກຳລັງຕໍ່ສູ້ກັບພະຍາດ COVID-19 ເຊິ່ງໄດ້ເຮັດ ໃຫ້ວິຖີການດຳລົງຊີວິດຂອງພວກເຮົາມີການປ່ຽນແປງ. ຢູ່ໂຮງໝໍ ມະໂຫສົດ, ພວກເຮົາຍັງລໍຖ້າການສຳເລັດຂອງການປຸກສ້າງອາຄານ ຫຼັງໃໝ່ ແລະ ລໍ ຄອຍການຍ້າຍເຂົ້າຫ້ອງວິເຄາະຫຼັງໃໝ່. ທ່ານ ດຣ. ມະນີວັນ ວົງສຸວັດ, ຫົວໜ້າຫ້ອງ ວິເຄາະຈຸລິນຊີໄດ້ໄປຕິດຕາມ ສະຖານທີ່ປຸກສ້າງ ດັ່ງຢູ່ໃນຮູບ (ຜູ້ທີ່ຢູ່ດ້ານຂວາຂອງຮູບ).

ພວກເຮົາກຳລັງສືບຕໍ່ເຮັດວຽກຮ່ວມກັບເພື່ອນຮ່ວມງານ ຢູ່ໂຮງໝໍ ແຂວງ ຊຽງຂວາງ, ຫຼວງນ້ຳທາ, ສາລະວັນ, ໂຮງໝໍແຂວງວຽງຈັນ. ນອກນັ້ນ ພວກເຮົາກໍ່ມີແຜນ ຮ່ວມມືກັບທີມງານແຂວງສະຫວັນນະ ເຂດ ໃນໂຄງການສຶກສາສາເຫດຂອງໄຂ້ ຢູ່ເຂດ ຫ່າງໄກສອກຫຼີກຢູ່ຂັ້ນສຸກສາລາ ເຊິ່ງເປັນການສຶກສາຄົ້ນຄວ້າທີ່ ເຮັດຢູ່ຫຼາຍປະເທດ ອາຊຽນ ໂດຍມີ Professor Yoel Lubell ຈາກ MORU ເປັນຫົວໜ້າໂຄງການ. ທ່ານ ສາດສະດາຈານ ດຣ. ມາຍຝອງ ມາຍຊາຍ ກຳລັງກໍ່ຕັ້ງໜ່ວຍງານສຳຫຼັບ ຫຼັກຖານ ແລະ ນະໂຍບາຍດ້ານ ສາທາລະນະສຸກ ຢູ່ທີ່ ມະຫາວິທະຍາໄລ ວິທະຍາສາດສຸຂະພາບ. ໃນຕໍ່ໜ້າ ພວກເຮົາຫວັງວ່າ ຈະໃຫ້ໂອກາດ ໃຫ້ແກ່ພະນັກງານ ວິຊາການ ແລະ ອາຈານ ໄດ້ສຶກສາຕໍ່ ໃນລະດັບຫຼັງມະຫາເພີ່ມຂຶ້ນ.

ຂ້າພະເຈົ້າ ຂໍຖືໂອກາດນີ້ ສະແດງຄວາມຂອບໃຈ ເພື່ອນຮ່ວມງານທຸກໆທ່ານໃນລາວ ທີ່ໄດ້ໃຫ້ການຕ້ອນຮັບທີ່ ອົບອຸ່ນ, ໂດຍ ສະເພາະ ດຣ. ພິສິດ ພຸດສະຫວັດ, ພ້ອມດ້ວຍຄະນະອຳນວຍການ ແລະ ພະນັກງານໂຮງໝໍ ມະໂຫສົດທຸກທ່ານ ທີ່ໄດ້ໃຫ້ການສະໜັບ ສະໜູນຢ່າງຕໍ່ເນື່ອງ. ຕາງໜ້າທີມງານ, ຂ້າພະເຈົ້າຂໍອວຍໄຊໃຫ້ພອນ ແກ່ເພື່ອນຮ່ວມງານທຸກທ່ານຈົ່ງມີສຸຂະພາບເຂັ້ມແຂງ, ປາສະຈາກໂລກ ໄພໄຂ້ເຈັບຕ່າງໆ ແລະ ຂ້າພະເຈົ້າຫວັງວ່າ ການຮ່ວມມືຂອງພວກເຮົາ ຈະເກີດດອກອອກຜົນ ແລະ ຈະເລີນກ້າວໜ້າຂຶ້ນໄປເລື້ອຍໆ.

# MESSAGE FROM THE DIRECTOR

ດ້ວຍຄວາມເຄົາລົບ ແລະ ນັບຖື,

ນະຄອນຫຼວງວຽງຈັນ, ວັນທີ 20 ເດືອນ ມິຖຸນາ ປີ 2020

Dr Elizabeth A Ashley
ຜູ້ອຳນວຍການ **LOMWRU**

# MESSAGE FROM THE DIRECTOR

## Message from Dr Elizabeth Ashley

Last year saw big changes at LOMWRU as Professor Paul Newton, the founding Director, and Professor David Dance, Senior Clinical Microbiologist both returned to the UK after almost 20 years and 9 years in Laos respectively. They are both very much missed. I joined in May last year from our sister Unit (Myanmar Oxford Clinical Research Unit) in Yangon. A week earlier Dr Andrew Simpson had joined LOMWRU from the Rare and Imported Pathogens Laboratory at Public Health England, Porton Down in the UK, taking over from David with whom he shares a common interest in melioidosis. We will both try and live up to their achievements. 2019 was also a big year for our parent organization- the Mahidol Oxford Tropical Medicine Research Unit (MORU) which celebrated its 40th anniversary.

The dengue epidemic in the country in 2019 and the current COVID-19 pandemic underscore the fact that infectious diseases research in Laos is as important as ever. The Lao Infectious Disease Society was created in 2019, chaired by LOMWRU Head of Field Research and Vice President of the University of Health Sciences, Professor Mayfong Mayxay. Their inaugural scientific conference was held on 7-8 November 2019. The Lao government recognized the contributions of several LOMWRU team members last year. Professor Mayfong Mayxay and Professor Paul Newton were each awarded the Medal of Labour for their contributions to the health sector of the Lao PDR. Dr Audrey Dubot-Pérès (Head of Virology at LOMWRU) and Professor David Dance were awarded the Cross of Labour for their research and capacity building in virology and microbiology respectively.

### RESEARCH HIGHLIGHTS

LOMWRU team members led or were co-authors on 69 publications last year. Some of these are highlighted in the "Research Highlights" section of this report. By including consenting patients into prospective studies which describe the causes of febrile illness in Laos, we have generated a very rich dataset over the years. This has revealed the leading infectious diseases in the country as well as trends in antimicrobial resistance in Vientiane and some of the provinces. In 2019 a description of the causes of central nervous system infections of 1065 patients in Mahosot Hospital between January 2003–August 2011, was published by Audrey Dubot-Pérès and colleagues. This, like several other projects, was the culmination of years of work in collaboration with Mahosot Hospital clinicians and laboratory staff.

### TRAINING HIGHLIGHTS

A key part of LOMWRU's mission is to provide training to Lao and international researchers. In 2019 four students who did all or part of their studies with us graduated, two with PhDs and two MScs. Dr Rebecca Inglis, a DPhil student, has spent the last three years developing and evaluating a training course for Lao doctors and nurses caring for critically ill patients

with Dr Khamsay Detleuxay, Former Head of Mahosot Hospital Adult Intensive Care Ward (now as a Deputy-Director of Mahosot Hospital) as one of her key advisors. We were also very pleased to contribute to a national training programme to increase awareness about melioidosis in 2019 called L-TEAM.

## LOOKING AHEAD

It is clear that 2020 is not going to be a typical year as Laos and the rest of the world wrestle with COVID-19 which has changed all aspects of life as we knew it. At Mahosot Hospital we await the completion of the new buildings and are looking forward to moving into new laboratories. Dr Manivanh Vongsouvath, Head of the Mahosot Microbiology Laboratory is shown (right of photo) inspecting the building site.

We continue to work with our close partners in Xieng Khouang, Luang Namtha, Salavan and Vientiane provincial hospitals in Phonhong. We also plan to collaborate with colleagues in Savannakhet province on a new multi-centre rural fever project at primary care level, led by Professor Yoel Lubell in MORU. Professor Mayfong Mayxay is creating a Unit for Health Evidence and Policy at the University of Health Sciences. We hope to increase the number of postgraduate training opportunities we can provide to technical and academic staff.

I would like to take this opportunity to thank all of my new colleagues and partners in Laos for their very warm welcome, in particular Dr Phisith Phouthsavath and everyone at Mahosot Hospital, our host institution, for their continued support. On behalf of the whole team I wish all our friends, colleagues and collaborators a safe and healthy year ahead and look forward to our continued collaboration.

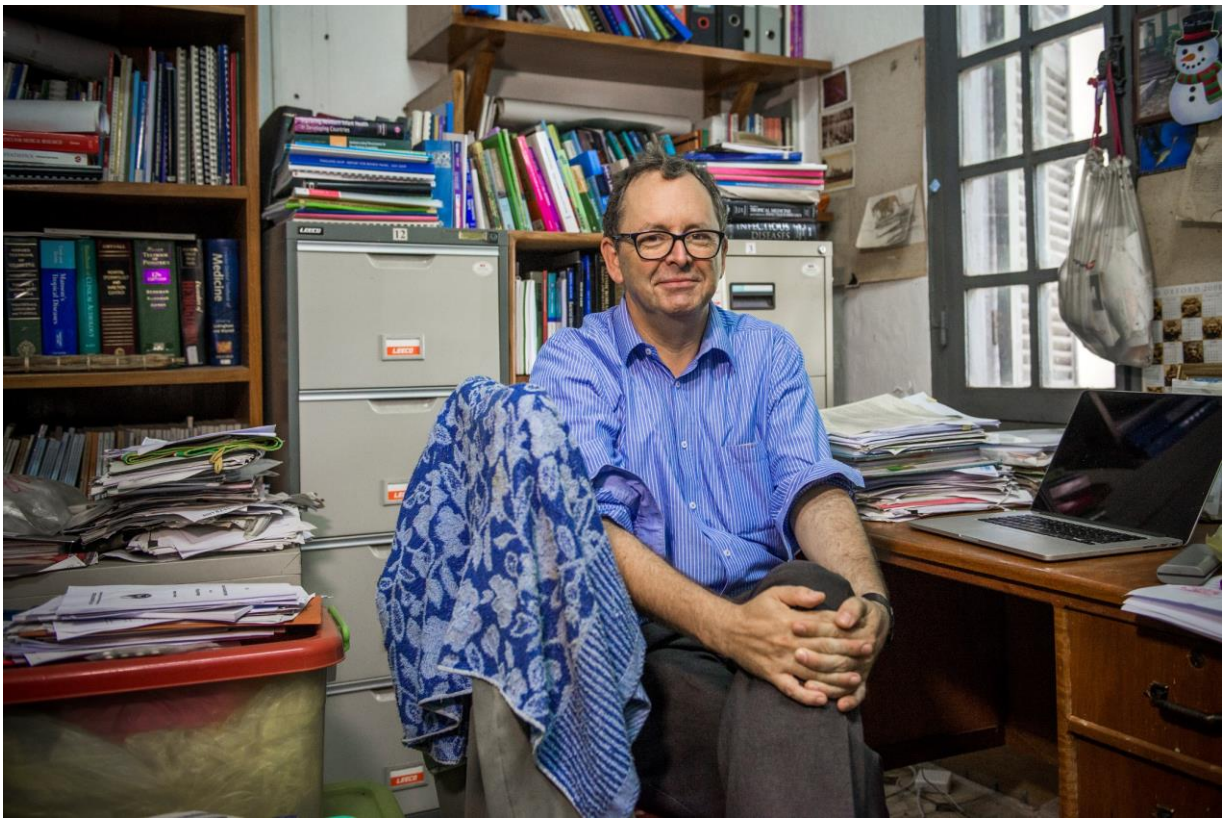
# MESSAGE FROM THE DIRECTOR

Best wishes,

Dr Elizabeth A Ashley
Director
June 3, 2020

## In appreciation of Professor Paul Newton

Professor Paul Newton, founding Director of LOMWRU, moved to Oxford in May 2019, having spent the last 19 years carrying out ground-breaking tropical medicine research in Laos.



Gerhard Joren ©

The collaboration between Mahosot Hospital and Oxford University began in 1999 when Paul started work with the former Head of the Microbiology Laboratory, the late Dr Rattanaphone Phetsouvanh, and a small team of five researchers, including Associate Professor Mayfong Mayxay who is now Vice President of the University of Health Sciences.

Over the past two decades the Unit has gone from strength to strength under Paul's leadership. Paul developed a highly productive programme of research that is recognized internationally and, at its core, has the goal of improving the health of people in Laos and beyond. The development of the diagnostic capability at Mahosot Hospital and the outputs from the research unit have raised awareness of leading infectious diseases in the country, such as melioidosis and scrub typhus, and informed policy decisions made by the Ministry of Health. LOMWRU has provided training opportunities for many talented young Lao researchers who have gone on to get postgraduate degrees at international universities. In recognition of the work he led at LOMWRU Paul was awarded the Medal of Labour by the

# PROFESSOR PAUL NEWTON

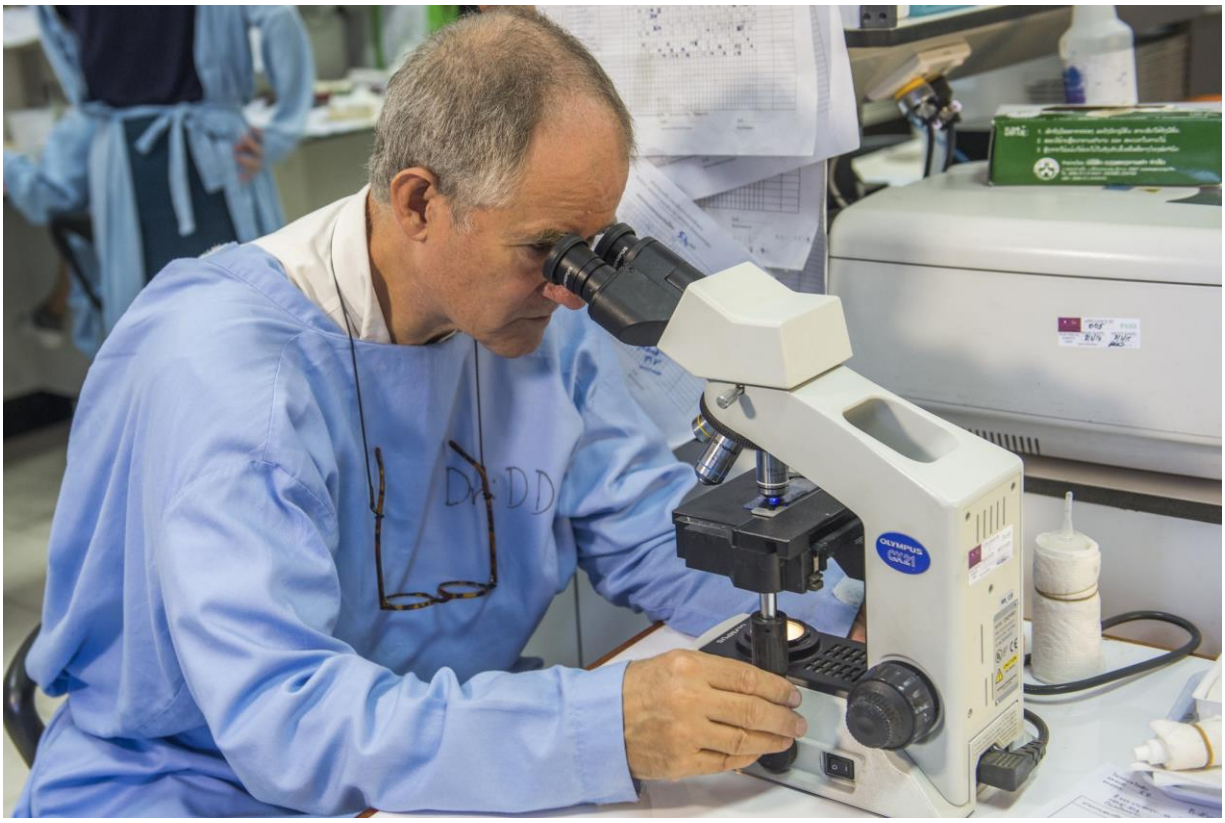
Government of the Lao PDR which was presented by His Excellency Assoc. Professor Bounkong Syhavong, Minister of Health.

As well as his work in the Lao PDR, Professor Newton is a world leader in research into the problem of falsified and substandard medicines, and since his return to the UK on May 13th, 2019, he has continued this work. He still has strong links to LOMWRU and the region as part of the MORU Tropical Health Network.

Gerhard Joren ©

**Professor Paul Newton (pictured seated, front row 5th from left) with the team in front of the Microbiology Laboratory in 2018**

## In appreciation of Professor David Dance



Gerhard Joren ©

Prof David Dance left LOMWRU in 2019 after a 9-year stay as a Clinical Microbiologist and Research Physician. David had originally planned to come to Laos for 5 years but he and his wife Rachel enjoyed living in the country so much that they decided to stay for longer. David has now returned to the UK and claims to be retired.

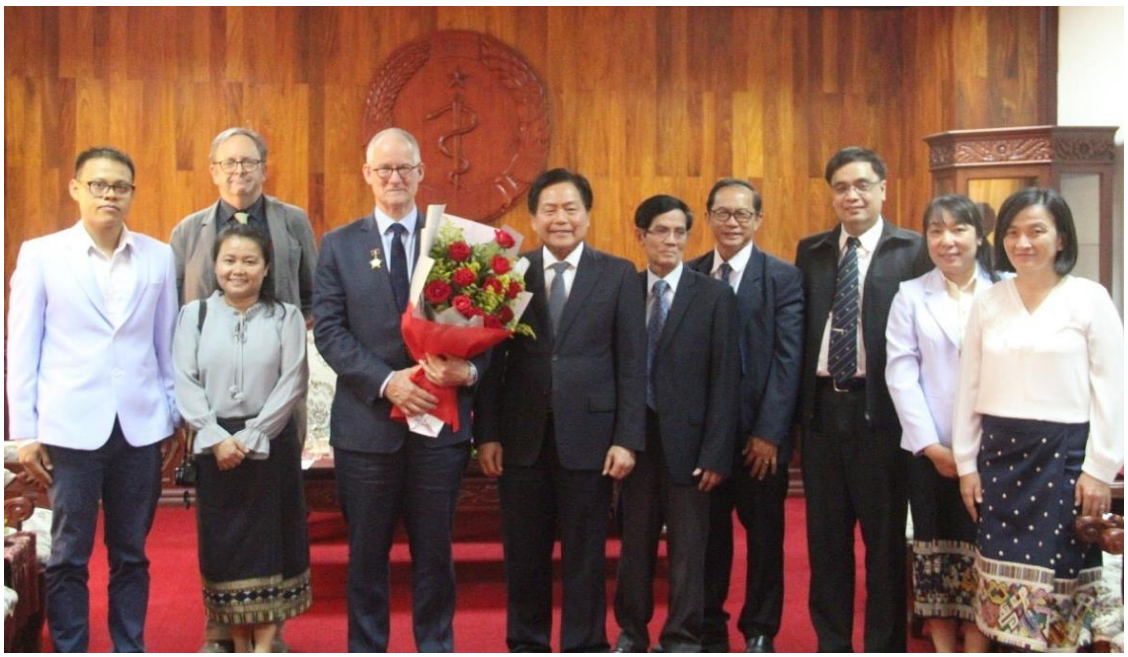
David was already a renowned expert on melioidosis before he joined LOMWRU, having spent several years working in Bangkok and Ubon Ratchathani in Thailand in the 1980s. He had maintained his interest in this disease after he left Thailand and returned to the UK, where he initially worked at the London School of Hygiene and Tropical Medicine. He subsequently moved to Plymouth in the south west of England as a Consultant Microbiologist, to run the microbiology laboratory at Derriford Hospital, before taking on the role of Regional Microbiologist with the Health Protection Agency for several years.

David had a very significant impact on the improvement of microbiology capability at Mahosot during his time in Vientiane, in addition to his research role. He continued to publish on many aspects of melioidosis, including diagnostic testing, laboratory isolation and environmental issues, as well as authoring several papers on epidemiology of the disease and

the causative organism, *Burkholderia pseudomallei*. David also published widely on many other infectious diseases of relevance to Laos, such as typhoid, leptospirosis, respiratory tract infections in children and central nervous system infections, as well as antimicrobial resistance.

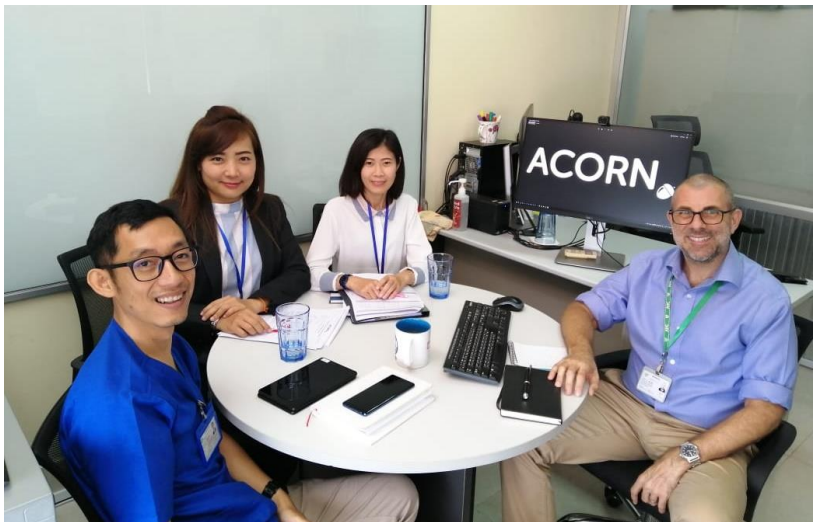
In recognition of his work at LOMWRU, David was awarded the Cross of Labour by the Government of the Lao PDR in 2019. This was presented to David by His Excellency Associate Professor Bounkong Syhavong, Minister of Health. David is seen below at the ceremony, along with His Excellency and colleagues from Mahosot Hospital and LOMWRU.

Although David has left Laos and will be greatly missed, it is expected that he will continue his long-standing interest in researching the history of melioidosis. Hopefully this will be published, when he has the time.



## ຜົນການຄົ້ນຄວ້າທີ່ພົ້ນເດັ່ນໃນປີຜ່ານມາ

ໂຄງການຄົ້ນຄວ້າພະຍາດເຂດຮ້ອນລະຫວ່າງ ມະຫາວິທະຍາໄລອ໊ອກຟອດ-ໂຮງໝໍມະໂຫສົດ-ແວວຄຳຫຼັ້ສ (LOMWRU) ໄດ້ ສືບຕໍ່ໃຫ້ຄວາມສຳຄັນຕໍ່ການຄົ້ນຄວ້າທາງດ້ານລະບາດວິທະຍາ ແລະ ທາງດ້ານຄລີນິກຂອງ ພະຍາດຊຶມເຊື້ອ. ນອກນີ້ ໜ່ວຍງານຄົ້ນຄວ້າ ພວກເຮົາຍັງໄດ້ດຳເນີນການຄົ້ນຄວ້າດ້ານຄຸນນະພາບຂອງຢາໃນ ບັນດາປະເທດທີ່ມີລາຍຮັບນ້ອຍ ຫາ ປານກາງ. ພ້ອມນີ້, ການເພີ້ມຂຶ້ນຂອງ ເຊື້ອຈຸລິນຊີທີ່ຕ້ານຕໍ່ຢາປິ່ນປົວກຳ ລັງເປັນບັນຫາບຸລິມະສິດທີ່ຕ້ອງໄດ້ຮັບການແກ້ໄຂຢ່າງຮີບດວ່ນ ເຊິ່ງທາງພະແນກຈຸລິນຊີວິທະຍາ, ໂຮງ ໝໍ ມະໂຫສົດໄດ້ດຳເນີນການຕິດຕາມເຝົ້າລະວັງການຕ້ານຕໍ່ຢາຕ້ານຂອງເຊື້ອຈຸລິນຊີມາເປັນເວລາເກືອບ 20 ປີ ແລະ ຂໍ້ມູນເຫຼົ່ານີ້ໄດ້ຖືກ ນຳສົ່ງເຂົ້າໃນລະບົບການເຝົ້າລະວັງການຕ້ານຂອງເຊື້ອຕໍ່ຢາຕ້ານເຊື້ອໃນທົ່ວໂລກຂອງ ອົງການອະນາໄມໂລກ (the WHO Global Antimicrobial Surveillance System) ໂດຍຜ່ານກົມຄວບ ຄຸມພະຍາດຕິດຕໍ່ ກະຊວງສາທາລະນະສຸກຂອງລາວ. ໃນປີ 2019 ໂຮງໝໍມະໂຫສົດໄດ້ເຂົ້າຮ່ວມເປັນສ່ວນໜຶ່ງ ໃນເຄືອຄ່າຍການເຝົ້າລະວັງການຕ້ານຕໍ່ຢາຕ້ານເຊື້ອທີ່ເນັ້ນໃສ່ອາການທາງຄລີນິກໄລຍະຫົດລອງ (A Clinically Oriented antimicrobial Resistance Network) ເຊິ່ງນຳໂດຍ Professor Paul Turner, ຜູ້ອຳນວຍ ການໂຄງການຄົ້ນຄວ້າທາງດ້ານການແພດລະຫວ່າງປະເທດກຳປູເຈຍ-ມະຫາວິທະຍາໄລອ໊ອກຟອດ (the Cambodia Oxford Medical Research Unit (COMRU)). ເຄືອຄ່າຍການເຝົ້າລະວັງການຕ້ານຕໍ່ຢາຕ້ານ ເຊື້ອນີ້ ແມ່ນເນັ້ນໃສ່ການຕິດຕາມ ເບິ່ງຜົນກະທົບຂອງເຊື້ອທີ່ຕ້ານຕໍ່ຢາຕ້ານເຊື້ອ, ພ້ອມທັງເກັບກຳຂໍ້ມູນອາການ ທາງຄລີນິກ ແລະ ປັດໄຈທີ່ກ່ຽວຂ້ອງກັບເຊື້ອຕ້ານຕໍ່ຢາ ແລະ ຕິດຕາມຜົນການປິ່ນປົວ.




ໃນຮູບ (ນັບຈາກເບື້ອງຊ້າຍ) Dr Miliya Thyl (Research Microbiologist), Dr Danoy Chommanam (ACORN-Laos Investigator), Dr Anousone Douangnouvong (ACORN-Laos coordinator), Professor Paul Turner (ACORN Principal Investigator) ກຳລັງກະກຽມການສຶກສາຄົ້ນຄວ້າຢູ່ໂຮງໝໍເດັກອັງກໍ, ສຽມຣຽບ ປະເທດກຳປູເຈຍ.

# RESEARCH HIGHLIGHTS

ຕໍ່ໄປນີ້ ພວກເຮົາຂໍນຳສະເໜີຜົນການຄົ້ນຄວ້າທີ່ພົ້ນເດັ່ນຂອງໜ່ວຍງານຄົ້ນຄວ້າ LOMWRU ແລະ ຄູ່ຮ່ວມງານ ທີ່ກ່ຽວຂ້ອງ ເຊິ່ງມີຫລາຍ ຫົວຂໍ້ຄົ້ນຄວ້າທີ່ກ່ຽວຂ້ອງກັບຂົງເຂດພະຍາດຊຶມເຊື້ອ-ເຂດຮ້ອນ ແລະ ຂົງເຂດອື່ນໆ ແລະ ໄດ້ຖືກຕີພິມເຜີຍແຜ່ໃນປີ 2019. ທ່ານ ສາມາດ ເບິ່ງບັນຊີຫົວຂໍ້ຄົ້ນຄວ້າ ແລະ ບົດຄັດຫຍໍ້ ໄດ້ຕື່ມ ໃນ ພາກຕໍ່ໄປຂອງບົດລາຍງານສະບັບນີ້.

### ຢາ AZITHROMYCIN ບໍ່ມີປະສິດພາບດີສຳລັບປິ່ນປົວໄຂ້ໝັດໝູ (MURINE TYPHUS)

ໄຂ້ໝັດໝູ (Murine Typhus), ແມ່ນພະຍາດ rickettsia ທີ່ເກີດມາຈາກເຊື້ອ *Rickettsia typhi*, ເຊິ່ງ ເປັນ

ໜຶ່ງໃນສາເຫດຂອງໄຂ້ທີ່ພົບເຫັນເລື້ອຍໆໃນ ສ.ປ.ປ.ລາວ. ໂຄງການຄົ້ນຄວ້າພະຍາດເຂດຮ້ອນລະຫວ່າງ ມະຫາວິທະຍາໄລອ໋ອກຟອດ-ໂຮງໝໍມະໂຫສົດ-ແວວຄຳຕັ໊ສ (LOMWRU) ໄດ້ສຶກສາຄົ້ນຄວ້າແນວທາງປິ່ນປົວ ພະຍາດໄຂ້ໝັດໝູ ຄື: ຢາ doxycycline ເປັນເວລາ 3 ວັນ ປຽບທຽບກັບ 7 ວັນ ແລະ ທຽບກັບ ຢາ azithromycin ຢ່າງດຽວ 3 ວັນ. ພວກເຮົາພົບວ່າ ປະສິດທິພາບຂອງການປິ່ນປົວດ້ວຍຢາ azithromycin ແມ່ນດ້ອຍກວ່າ ຖ້າທຽບກັບການປິ່ນປົວດ້ວຍຢາ doxycycline ເຊິ່ງພົບອັດຕາປິ່ນປົວຫຼົ້ມເຫຼວ ປະມານ 22.5% ໃນກຸ່ມທີ່ໃຊ້ຢາ azithromycin. ຜົນຂອງການສຶກສານີ້ໄດ້ຖືກຮັບຮອງ ແລະ ຕີພິມເຜີຍແຜ່ໃນ ວາລະສານການແພດ ສາກົນ Clinical Infectious Diseases. (Newton PN, Keolouangkhot V, Lee SJ, et al. A Prospective, Open-label, Randomized Trial of Doxycycline Versus Azithromycin for the Treatment of Uncomplicated Murine Typhus. Clinical Infectious Diseases. 2019; 68(5): 738-47.)

ດຣ ຂັນສຸດາພອນ ພະຄຸນທອງ (ທາງກາງ), ເຊິ່ງເປັນທ່ານໝໍຄົ້ນຄວ້າແຕ່ປີ 2004 ໄດ້ຍ້າຍໄປປະຈຳການຢູ່ກົມຄວບຄຸມພະຍາດຕິດຕໍ່ ສັງກັດກະຊວງສາທາລະນະສຸກ ໃນທ້າຍປີ 2019.

**ຢາ CEFTRIAXONE ສົມທົບກັບຢາ DOXYCYCLINE ແມ່ນຢາຕ້ານເຊື້ອ ທີ່ຄວນໃຊ້ປິ່ນປົວການຊຶມເຊື້ອລະບົບປະສາດສູນກາງ ໃນໄລຍະລໍຖ້າ/ບໍ່ມີຜົນຢັ້ງຢືນທາງຫ້ອງວິເຄາະໃນ ສ.ປ.ປ.ລາວ.**

ໃນໂຮງໝໍມະໂຫສົດ, ລະຫວ່າງປີ 2003 ຫາ 2011 ໄດ້ມີການຄົ້ນຄວ້າສາເຫດຂອງຄົນເຈັບທີ່ເຂົ້າມານອນປິ່ນປົວດ້ວຍອາການທີ່ສົງໃສວ່າເປັນຕິດເຊື້ອທາງລະບົບປະສາດສູນກາງ. ໃນຄົນເຈັບທັງໝົດ 1065 ຄົນ, ມີຄົນເຈັບ ພຽງ 42.3% ທີ່ສາມາດລະບຸສາເຫດໄດ້, ແລະ ພົບວ່າສາເຫດຈາກເຊື້ອຈຸລິນຊີ ກວມເຖິງ 16.4% (ລວມທັງ *Orientia tsutsugamushi* [2.9%] ແລະ *Rickettsia* spp. [2.3%]). ຜົນການຄົ້ນຄວ້ານີ້ ສະແດງໃຫ້ເຫັນວ່າ ຄົນເຈັບທີ່ສົງໃສວ່າ ມີການຊຶມເຊື້ອທາງລະບົບປະສາດສູນກາງຄວນໄດ້ຮັບການປິ່ນປົວດ້ວຍຢາຕ້ານເຊື້ອ ສຳລັບເຊື້ອ rickettsial ແລະ ເຊື້ອຈຸລິນຊີທີ່ພົບເຫັນເລື້ອຍໆໃນໄລຍະລໍຖ້າຜົນກວດ (Dubot-Pérès A, Mayxay M, Phetsouvanh R, et al. Management of Central Nervous System Infections, Vientiane, Laos, 2003-2011. Emerging Infectious Diseases. 2019;25(5):898-910.)

### "ຕະຫຼາດຂາຍຊີ້ນສັດ "ຄວາມສ່ຽງທາງດ້ານສາທາລະນະສຸກ ໃນ ສ.ປ.ປ ລາວ

ການຄ້າຂາຍຊີ້ນສັດ ແລະ ຊີ້ນສັດປ່າ ເພື່ອການບໍລິໂພກຢູ່ຕາມຕະຫລາດສົດຕ່າງໆ ເປັນສິ່ງທ້າທາຍອັນໜຶ່ງ ສຳລັບຜູ້ກຳນົດນະໂຍບາຍ. ເນື່ອງຈາກການແຜ່ລະບາດຂອງພະຍາດ SARS-CoV-2 ໃນທົ່ວທຸກມຸມໂລກ ພົບວ່າ ຍັງມີຫຼາຍໆຄວາມສ່ຽງທາງດ້ານສາທາລະນະສຸກທີ່ຍັງສູງ ນອກນັ້ນ, ບັນດາຜູ້ກຳນົດນະໂຍບາຍຈະຕ້ອງພົບພໍ້ ບັນຫາ ຕ່າງໆທີ່ກ່ຽວພັນກັບການຄ້າຂາຍເຊັ່ນ: ການອະນຸລັກສະພາບແວດລ້ອມ, ຄວາມໝັ້ນຄົງ ແລະ ຄວາມ ປອດໄພທາງ ດ້ານອາຫານ, ວັດທະນະທຳ ແລະ ປະເພນີ. ໂຄງການ LACANET study ເຊິ່ງເປັນໂຄງການໜຶ່ງ ທີ່ໄດ້ຮັບທຶນ ຊ່ວຍເຫຼືອຈາກກອງທຶນສະຫະພາບເອີລົບ, ໄດ້ເຮັດການສຳລວດຜູ້ບໍລິໂພກ ແລະ ວິເຄາະພຶດຕິກຳ ຂອງເຂົາເຈົ້າ. ພວກເຮົາໄດ້ພັດທະນາຮູບແບບກອບແນວຄວາມຄິດ ເພື່ອສ້າງຄວາມຮູ້, ຄວາມເຂົ້າໃຈ ແລະ ສາມາດກຳນົດ ບັນດາຄວາມສ່ຽງຈາກການຕິດເຊື້ອພະຍາດທີ່ມາຈາກສັດ ໂດຍການບໍລິໂພກຊີ້ນສັດ. ນີ້ແມ່ນ ໜຶ່ງໃນຫຼາຍໆການ ສຶກສາທີ່ຈະຖືກຕີພິມເຜີຍແຜ່ຈາກໂຄງການດັ່ງກ່າວ ເຊິ່ງເປັນໂຄງການທີ່ຢູ່ພາຍໃຕ້ການຮ່ວມ ມືກັນລະຫວ່າງ ສູນວິໃຈ ສຸຂະພາບສັດແຫ່ງຊາດ (National Animal Health Laboratories) ແລະ ອົງການອະນຸລັກສັດປ່າ ປະຈຳ ສ.ປ.ປ ລາວ. (Pruvot M, Khammavong K, Milavong P, et al. Toward a quantification of risks at the nexus of conservation and health: The case of bushmeat markets in Lao PDR. Science of the Total Environment. 2019;676: 732-745)

### ປາເປັນແຫຼ່ງທີ່ສຳຄັນຂອງການຕິດເຊື້ອ *STREPTOCOCCUS AGALACTIAE* ຮຸນແຮງ ໃນເຂດ ອາຊີຕາເວັນ ອອກ.

ໃນເດືອນມິຖຸນາ ປີ 2019, ດຣ ມະໂນພາບ ຫຼວງຣາຊ ແລະ ດຣ ແອນດຣູ ຊິມຊັນ ໄດ້ເຂົ້າຮ່ວມກິດຈະກຳ ເຄືອ ຄ່າຍກຸ່ມ Group B *Streptococcus* ພາກພື້ນອາຊີຕາເວັນອອກ (the South-East Asian group B Streptococcus ຫຼື SEA-BeaSt) ຄັ້ງທີ 2 ທີ່ບາງກອກ ເຊິ່ງສືບເນື່ອງຈາກກິດຈະກຳຄັ້ງທຳອິດ ທີ່ຈັດຂຶ້ນທີ່ ປະເທດສິງກະໂປ ໃນປີ 2018, ເພື່ອເປັນການປຶກສາຫາລື ໃນລະດັບພູມມິພາກ ກ່ຽວກັບການປະສານງານ ແລະ ການຄົ້ນຄວ້າຮ່ວມກັນ ໃນເລື່ອງການລະບາດຂອງເຊື້ອ Group B *Streptococcus* (GBS) ໃນອາຫານ ທີ່ ປະເທດສິງກະໂປ.

ການກ່ຽວຂ້ອງກັນຂອງເຊື້ອ GBS ໃນປາ ແລະ ພະຍາດໃນຄົນ, ຖືກກ່າວເຖິງເປັນຄັ້ງທຳອິດ ເມື່ອມີການລະບາດ ຂອງການຕິດເຊື້ອຮຸນແຮງຈາກເຊື້ອດັ່ງກ່າວໃນຜູ້ໃຫຍ່ທີ່ມີສຸຂະພາບແຂງແຮງ ທີ່ປະເທດ ສິງກະໂປ. ການສືບຄົ້ນຫາສາເຫດອຸບັດການດັ່ງກ່າວ ໄດ້ເປີດເຜີຍເຖິງການກ່ຽວເນື່ອງກັນ ກັບການບໍລິໂພກປາ ນ້ຳຈືດດິບ ໂດຍສະເພາະໃນອາຫານຈີນຊະນິດ Yusheng ທີ່ປຸງແຕ່ງໂດຍມີ ປາເກັບແລັບ (ປາກິນຫຍ້າ) (Asian bighead carp) ແລະ ປາຄໍ່ (Snakehead) ເປັນວັດຖຸດິບຫຼັກ. ການວິເຄາະດ້ວຍ ການແຍກ ຄຸນລັກສະນະ ທາງສາຍພັນ ແລະ ການສຶກສາດ້ານກຳມະພັນຈາກເຊື້ອທີ່ໄດ້ຈາກຄົນເຈັບ ໄດ້ຊີ້ໃຫ້ເຫັນວ່າ: ມີສາຍພັນ

Serotype III, sequence type 283 ໜຶ່ງດຽວເທົ່ານັ້ນ ທີ່ມີການພົວພັນກັນການລະບາດ. ສາຍພັນດັ່ງກ່າວ ຖືກພົບວ່າເປັນສາຍພັນດຽວກັນກັບ GBS ST283 ທີ່ພົບໃນປາ.

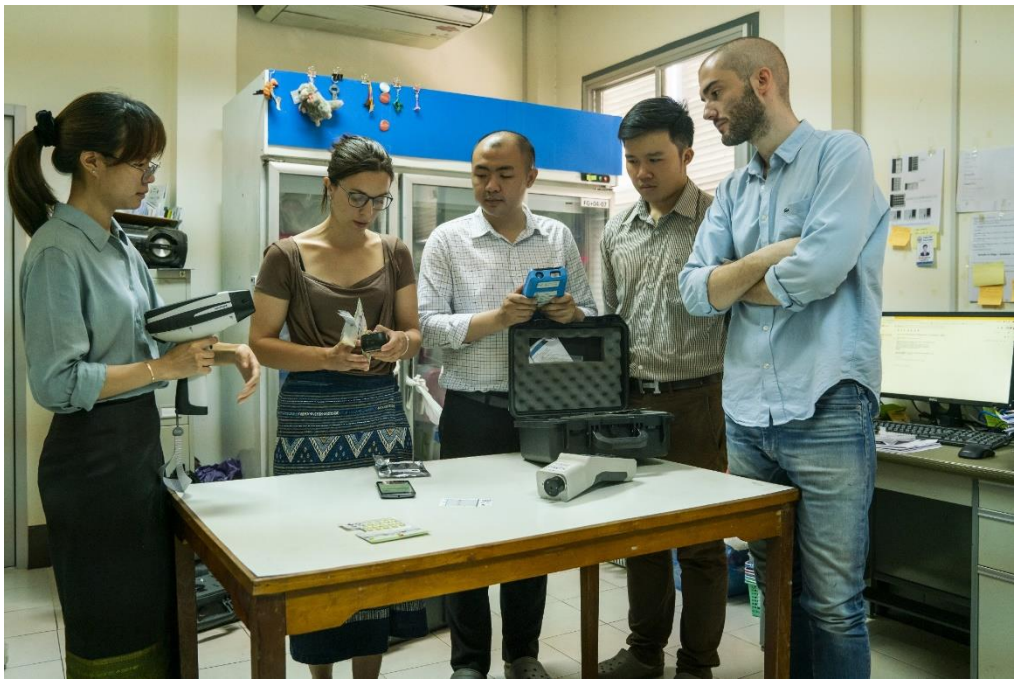
ຈາກການວິເຄາະຍ້ອນຫຼັງຂອງຂໍ້ມູນການສຶກສາ ສາເຫດຂອງໄຂ້ໃນ ສ.ປ.ປ.ລາວ ລະຫວ່າງປີ 2000 ຫາປີ 2017, ພົບເຊື້ອ GBS ຈຳນວນ 38 ເຊື້ອ ຈາກການປູກຕົວຢ່າງເລືອດ ແລະ ນ້ຳໄຂສັນຫຼັງຂອງຄົນເຈັບ. ເຊື້ອດັ່ງກ່າວ ຖືກສົ່ງໄປໄຈ້ແຍກຄຸນລັກສະນະດ້ານສາຍພັນ ແລະ ສຶກສາປຽບທຽບກຳມະພັນ ທີ່ສະຖາບັນດ້ານກຳມະພັນ ຂອງປະເທດສິງກະໂປ (the Genome Institute of Singapore), ແລະ ພົບວ່າ 76% ຂອງໂຕເຊື້ອ ແມ່ນສາຍພັນ Sequence type 283 (ST283). ການຄົ້ນພົບດັ່ງກ່າວ ໄດ້ຍົກບັນຫາຄວາມເປັນໄປຂອງການກ່ຽວພັນກັນ ລະຫວ່າງພະຍາດໃນຄົນ ແລະ ການກິນປາດິບຢູ່ໃນລາວ, ເຖິງຢ່າງໃດກໍຕາມ, ສົມມຸດຖານດັ່ງກ່າວ ຍັງບໍ່ໄດ້ຮັບການຢັ້ງຢືນ ແລະ ຍັງຂາດຫຼັກຖານທີ່ໜັກແໜ້ນພຽງພໍໃນການປະກົດຕົວຂອງ GBS ສາຍພັນ ST283 ທີ່ຢູ່ໃນປາໃນປະເທດນີ້. ພວກເຮົາມີແຜນທີ່ຈະເຮັດການສຶກສານີ້ເພີ່ມຕື່ມໃນອະນາຄົດ. (Barkham T, Zadoks RN, Azmai MNA, et al. One hypervirulent clone, sequence type 283, accounts for a large proportion of invasive *Streptococcus agalactiae* isolated from humans and diseased tilapia in Southeast Asia. PLoS Neglected Tropical Diseases. 2019;13(6): e0007421).

### ການກິນຢາທົ່ວປວງຊົນ ອາດເປັນເຄື່ອງມືໜຶ່ງທີ່ໃຊ້ໃນການລົບລ້າງພະຍາດໄຂ້ມາລາເລຍ

ການແຜ່ກະຈາຍຂອງເຊື້ອຕ້ານຕໍ່ຢາກຸ່ມ artemisinin, piperaquine ແລະ mefloquine ຢູ່ໃນບັນດາປະເທດເຂດລຸ່ມແມ່ນ້ຳຂອງ ເຮັດໃຫ້ການລົບລ້າງໄຂ້ມາລາເລຍ ກາຍເປັນເປົ້າໝາຍອັນຮີບດ່ວນທາງດ້ານສາທາລະນະສຸກ. ສປປ ລາວ ຕັ້ງເປົ້າໝາຍລົບລ້າງໄຂ້ມາລາເລຍ ພາຍໃນ ປີ 2030. ສປປ ລາວ ຈຶ່ງໄດ້ສຶກສາທົດລອງການກິນຢາທົ່ວປວງຊົນ ດ້ວຍຢາ dihydroartemisinin-piperaquine ຢູ່ເມືອງນອງ, ແຂວງສະຫວັນນະເຂດ ເພື່ອເລັ່ງການລົບລ້າງໄຂ້ມາລາເລຍ ຊະນິດ *falciparum*. ການສຶກສາດັ່ງກ່າວນີ້ ແມ່ນໄດ້ເຮັດໄປພ້ອມໆກັບ ປະເທດກຳປູເຈຍ, ພະມ້າ ແລະ ຫວຽດນາມ. ຜົນກະທົບຂອງການກິນຢາທົ່ວປ່ວງຊົນຕໍ່ກັບອັດຕາຊຸກຊຸມ ແລະ ອຸບັດການເກີດການຕິດເຊື້ອໄຂ້ມາລາເລຍຊະນິດ *falciparum* ແມ່ນແຕກຕ່າງກັນໃນແຕ່ລະປະເທດ. ຜົນກະທົບ ທີ່ພົບຫຼາຍທີ່ສຸດແມ່ນຢູ່ລາວ, ຕໍ່ມາແມ່ນກຳປູເຈຍ, ແລະ ມີຜົນກະທົບພຽງເລັກນ້ອຍຢູ່ຫວຽດນາມ. ຜົນຂອງການ ຄົ້ນຄ້ວາແມ່ນຕີພິມຢູ່ PLOS Medicine. (von Seidlein L, Peto TJ, Landier J, Nguyen TN, Tripura R, Phommasone, K., et al. The impact of targeted malaria elimination with mass drug administrations on falciparum malaria in Southeast Asia: A cluster randomised trial. PLoS Medicine. 2019;16(2):e1002745.)

**ການເຂົ້າເຖິງຜະລິດຕະພັນຢາທີ່ໄດ້ຄຸນນະພາບ: ມະຕິຂອງກອງປະຊຸມທີ່ OXFORD ແລະ ການຮຽກຮ້ອງໃຫ້ມີການຈັດຕັ້ງປະຕິບັດທີ່ເຂັ້ມງວດ.**

ປະຊຸມໃນຫົວຂໍ້ 'ຄຸນນະພາບຢາ ແລະ ສາທາລະນະສຸກ - Medicine Quality & Public Health ໄດ້ຈັດຂຶ້ນເປັນຄັ້ງທຳອິດ ໃນເດືອນກັນຍາ 2018 ທີ່ເມືອງ Oxford ປະເທດອັງກິດ ເຊິ່ງມີຜູ້ເຂົ້າຮ່ວມເປັນຈຳນວນ 200 ກວ່າຄົນຈາກ 50 ປະເທດ. ກອງປະຊຸມດັ່ງກ່າວໄດ້ປຶກສາຫາລື ກ່ຽວກັບຫຼັກຖານດ້ານລະບາດວິທະຍາຂອງ ຜະລິດຕະພັນ ຢາຕ້ານມາດຕະຖານ ແລະ ຢາປອມ; ຜົນກະທົບຈາກຢາບໍ່ໄດ້ຄຸນນະພາບເຫຼົ່ານີ້ຕໍ່ສຸຂະພາບ, ເສດຖະກິດ, ສັງຄົມ ພ້ອມທັງດ້ານກົດໝາຍ ແລະ ຈັນຍາທຳ. ນອກນັ້ນ



**ສະມະຊິກໃນທີມງານ LOMWRU Medicine Quality Team. ຈາກຊ້າຍ ຫາ ຂວາ: ວາຍລີ ວິດາມາລີ, Céline Caillet, ພອນປະສິດ ບຸບຜາ, ເກມ ບຸດສະໄໝ, ແລະ Guillermo Alonso ພ້ອມກັບເຄື່ອງກວດຄຸນນະພາບຢາ ແບບມືຖື**

ຍັງໄດ້ມີການໂອ້ລົມກັບພາກສ່ວນກ່ຽວຂ້ອງ ເພື່ອຮັບປະກັນໃຫ້ປະຊາຊົນທົ່ວໂລກສາມາດເຂົ້າເຖິງຜະລິດຕະພັນຢາທີ່ມີຄຸນນະ ພາບດີ. ຜູ້ເຂົ້າຮ່ວມຈຳນວນ 159 ຄົນ ໄດ້ເຮັດໜັງສືຍິນຍອມຮ່ວມກັນ ເພື່ອສົ່ງສານເຖິງທຸກໆ ພາກສ່ວນທີ່ກ່ຽວຂ້ອງ ແລະ ຮຽກຮ້ອງໃຫ້ທຸກຄົນຊ່ວຍກັນກຳຈັດຜະລິດຕະພັນຢາທີ່ຕ້ານມາດຕະຖານ ແລະ ຢາ ປອມຢ່າງຮີບດ່ວນ ເຊິ່ງເປັນບັນຫາໜຶ່ງໃນ ລະບົບສາທາລະນະສຸກ ແລະ ເປັນການທຳລາຍຊັບພະຍາກອນທີ່ມີຄ່າ ຂອງມະນຸດ. ມະຕິຈາກກອງປະຊຸມທີ່ Oxford ຄັ້ງນີ້ ໄດ້ກະຕຸ້ນການມີສ່ວນຮ່ວມຂອງສະມາຄົມສຸຂະພາບໂລກ

ເພື່ອຍົກລະດັບຄຸນນະພາບຜະລິດຕະພັນຢາໃຫ້ທຸກຄົນທົ່ວປວງຊົນ ສາມາດເຂົ້າເຖິງໄດ້. ວຽກງານດັ່ງກ່າວ ຕ້ອງໄດ້ອາໄສການພັດທະນາປັບປຸງຂໍ້ມູນໃຫ້ໄດ້ມາດຕະຖານ, ການເກັບຂໍ້ມູນ ແລະ ການເຜີຍແຜ່ຂໍ້ມູນ ແລະ ສຸມໃສ່ການສຶກສາຄົ້ນຄວ້າທາງດ້ານວິທະຍາສາດທີ່ກວ້າງຂວາງ ແລະ ຫຼາກຫຼາຍສາຂາ ເພື່ອສ້າງ ເປັນຫຼັກຖານພື້ນຖານ ແລະ ນຳໃຊ້ຂໍ້ມູນດັ່ງກ່າວໃຫ້ເກີດມີການປັບປຸງ, ປ່ຽນແປງນະໂຍບາຍເພື່ອຮັບປະກັນວ່າ ທຸກໆຄົນ ສາມາດເຂົ້າເຖິງຜະລິດຕະພັນຢາທີ່ມີຄຸນນະພາບດີ.

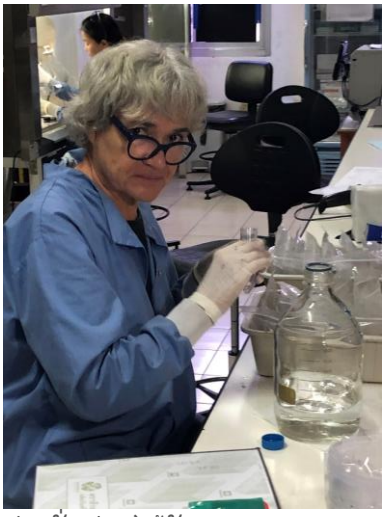
## ການຮ່ວມມືດ້ານການຄົ້ນຄ້ວາວິທະຍາສາດ

ການຄົ້ນຄວ້າວິທະຍາສາດທັງໝົດ ຂອງໂຄງການຄົ້ນຄ້ວາພະຍາດເຂດຮ້ອນລະຫວ່າງແວວຄຳຕັ໊ສ-ໂຮງໝໍມະໂຫສົດ-ມະຫາວິທະຍາໄລອ໋ອກຟອດ, ປະເທດອັງກິດ ແມ່ນຢູ່ໃນເງື່ອນໄຂຂອງການຮ່ວມມືກັນຂອງທັງສອງຝ່າຍ ເຊິ່ງໂຄງການເອງ ແມ່ນຢູ່ພາຍໃຕ້ການຮ່ວມມືກັນລະຫວ່າງ ມະຫາວິທະຍາໄລ ອ໋ອກຟອດ ແລະ ໂຮງໝໍມະໂຫສົດ, ໂດຍໄດ້ຮັບເງິນສະໜັບສະໜຸນຫຼັກຈາກແວວຄຳຕັ໊ສ. ໂຄງການຄົ້ນຄ້ວາພະຍາດເຂດຮ້ອນລະຫວ່າງແວວຄຳຕັ໊ສ-ໂຮງໝໍມະໂຫສົດ-ມະຫາວິທະຍາໄລອ໋ອກຟອດ ຫຼື LOMWRU ນີ້ ແມ່ນໜຶ່ງໃນຫ້າຂອງສູນຄົ້ນຄ້ວາພະຍາດເຂດ ຮ້ອນຂອງ the MORU Tropical Health Network, ໂດຍມີ ທ່ານສາດສະດາຈານ ນິກເດ ເປັນຜູ້ອຳນວຍການ ແລະ ມີຫ້ອງການປະຈຳຢູ່ໂຄງການຄົ້ນຄ້ວາພະຍາດເຂດຮ້ອນມະຫິດົນ-ອ໋ອກຟອດ, ຄະນະເວດຊະສາດເຂດຮ້ອນ, ມະຫາ ວິທະຍາໄລມະຫິດົນ, ປະເທດໄທ.

ໂຄງການຄົ້ນຄ້ວາພະຍາດເຂດຮ້ອນລະຫວ່າງ ແວວຄຳຕັ໊ສ-ໂຮງໝໍມະໂຫສົດ-ມະຫາວິທະຍາໄລອ໋ອກຟອດ ໄດ້ຮ່ວມມືກັບເຄືອຄ່າຍໂຄງການຄົ້ນຄ້ວາພະຍາດເຂດຮ້ອນມະຫິດົນ-ອ໋ອກຟອດ, ມະຫາວິທະຍາໄລມະຫິດົນ ໃນ ຫຼາຍໆການຄົ້ນຄ້ວາວິທະຍາສາດ ພ້ອມທັງໄດ້ຮັບການສະໜັບສະໜຸນທາງດ້ານວິຊາການ ແລະ ການ

ບໍລິຫານງານ ໃນຫຼາຍໆດ້ານ. ຍົກຕົວຢ່າງ 2 ການຄົ້ນຄ້ວາທີ່ພົ້ນເດັ່ນ ພາຍໃຕ້ການຮ່ວມມືດັ່ງກ່າວ ແມ່ນ ໂຄງການ GenRe ແລະ END-GAME ໂດຍເປັນການຮ່ວມມືກັນລະຫວ່າງ ສູນໄຂ້ຍຸງ ,ແມ່ກາຝາກ ແລະ ແມງໄມ້ ແລະ ໂຄງການຄົ້ນຄ້ວາພະຍາດ ເຂດຮ້ອນລະຫວ່າງແວວຄຳຕັ໊ສ-ໂຮງໝໍມະໂຫສົດ-ມະຫາວິທະຍາໄລອ໋ອກຟອດ .ນອກນັ້ນຍັງມີການຮ່ວມມືກັບ ສະຖາບັນຄົ້ນຄວ້າ

ເພື່ອການພັດທະນາ ຝຣັ່ງປະຈຳລາວ Institut de recherche pour le développement (IRD) ນັບແຕ່ ປີ 2006 ເປັນຕົ້ນມາ .ທ່ານ ປອ ນາງ ໂອເດຣ ດູໂບ-ເປແລສ ປະຈຸບັນ ແມ່ນ ຫົວໜ້າໜ່ວຍງານ ຄົ້ນຄ້ວາຈຸ ລະໂລກປະຈຳໂຄງການ ແຕ່ມີຫ້ອງການປະຈຳຢູ່ the Unité des Virus Émergents (UVE), ມາກຊາຍສ , ປະເທດຝຣັ່ງ .



ເຊິ່ງໜ່ວຍງານດັ່ງກ່າວເປັນປະທານໂດຍທ່ານສາດສະດາຈານ ຊາວິເອ ເດີ ລໍາ ບານເລີຣີ) ຮູບດ້ານເທິງ (ເຊິ່ງທ່ານໄດ້ມາຢ້ຽມຢາມວຽງຈັນ ແລະ ໄດ້ປຶກສາ ໂຄງການຄົ້ນຄ້ວາວິທະຍາສາດຫຼາຍໆໂຄງການ .ໃນຫວ່າງບໍ່ດົນ ມານີ້ ຍັງມີ ໂຄງການຮ່ວມມືກັບສະຖາບັນຄົ້ນຄ້ວາເພື່ອການພັດທະນາຝຣັ່ງ ,ໂດຍ ແມ່ນ ທ່ານ ປອ ອາແລັນ ເປແລັສ ແລະ ທ່ານ ປອ ນາງ ແອນ ແພນໂດ (ຮູບດ້ານ ຂວາມື) ເຊິ່ງທັງສອງທ່ານມີຄວາມສົນໃຈກ່ຽວກັບລະບົບນິເວດວິທະຍາ ຂອງ ດິນ ແລະ ເຊື້ອ *B. pseudomallei*.

ໃນໄລຍະ 2 ປີ ຜ່ານມານີ້, ໂຄງການດັ່ງກ່າວໄດ້ເກັບຕົວຢ່າງດິນຈຳນວນທັງ ໝົດ 300 ຕົວຢ່າງ ຢູ່ທີ່ບ້ານ ນາບອນ, ເມືອງ ໂພນໂຮງ, ແຂວງວຽງຈັນ ເຊິ່ງຕົວຢ່າງດັ່ງກ່າວໄດ້ຮັບການກວດ ຊອກຫາເຊື້ອ *B. pseudomallei* ຢູ່ທີ່ພະແນກຈຸລິນຊີວິທະຍາ, ໂຮງໝໍມະໂຫສົດ ພ້ອມນັ້ນຍັງຖືກສົ່ງໄປກວດ ວິເຄາະຄຸນລັກຊະນະທາງດ້ານຟີຊິກ ແລະ ເຄມີຂອງດິນເຊັ່ນ: dissolved organic carbon, major cations, major nutrients ແລະ major anions. ໃນນັ້ນຍັງພົບວ່າມີ 130 ຕົວຢ່າງທີ່ໃຫ້ຜົນກວດພົບ ເຊື້ອ *B. pseudomallei* ດ້ວຍເຕັກນິກທາງດ້ານພັນທຸກໍາ (qPCR).

ຍິ່ງໄປກວ່ານັ້ນ, ຍັງມີຕົວຢ່າງດິນອີກ 370 ຕົວຢ່າງທີ່ຖືກເກັບມາຈາກຊັ້ນດິນຕ່າງໆທີ່ຄວາມເລິກຈົນ ເຖິງ 3 ແມັດ ເຊິ່ງໄດ້ນໍາມາປູກເພື່ອຊອກຫາເຊື້ອ *B. pseudomallei* ພ້ອມທັງວັດ ແທກຄຸນລັກຊະນະທາງ ດ້ານຟີຊິກເຊັ່ນ: soil chemistry and mineralogy, magnetic susceptibility. ການຄົ້ນຄ້ວາຄັ້ງນີ້ພົບ ວ່າ ເຮົາສາມາດພົບເຊື້ອ *B. pseudomallei* ທີ່ມີຄວາມໜາແໜ້ນສູງ ທີ່ຄວາມເລິກ 1 ແມັດ (ຄວາມໜາແໜ້ ນຫຼາຍກວ່າ 1000 CFU/g ລະຫວ່າງຄວາມເລິກ 130 ແລະ 215 ຊັງຕິແມັດ, ສົມທຽບຄວາມໜາ ແໜ້ນສູງ ສຸດໃນລະດູແລ້ງ ປີ 2018 ພົບມີຄວາມໜາແໜ້ນພຽງແຕ່ 30 CFU/g ລະຫວ່າງຄວາມເລິກ 10 ແລະ 30 ຊັງຕິແມັດ). ນອກນັ້ນ, ເຊື້ອ *B. pseudomallei* ທີ່ຢູ່ໃນຊັ້ນດິນຕ່າງໆຈົນຮອດລະດັບຄວາມເລິກ 3 ແມັດໄດ້ ເອົາມາສຶກສາຄຸນລັກຊະນະທາງດ້ານກໍາມະພັນຂອງເຊື້ອ ແລະ ຄຸນລັກຊະນະຂອງຊັ້ນດິນຕ່າງໆ ເພື່ອພິສູດ ສົມມຸດຖານທີ່ວ່າ ເຊື້ອດັ່ງກ່າວມີການສົ່ງຜ່ານສາຍກໍາມະພັນທາງກົງຕາມລະດູການທີ່ມີການປ່ຽນແປງຫຼືບໍ່ .ປະຈຸ

# RESEARCH HIGHLIGHTS

ບັນ ພວກເຮົາກຳລັງດຳເນີນການວິເຄາະຂໍ້ມູນທີ່ໄດ້ຢູ່ໂຄງການຄົ້ນຄ້ວາພະຍາດເຂດຮ້ອນມະຫິດົນ-ອ໋ອກຝອດ, ຄະນະເວດ ຊະສາດເຂດຮ້ອນ, ມະຫາວິທະຍາໄລມະຫິດົນ, ປະເທດໄທ.

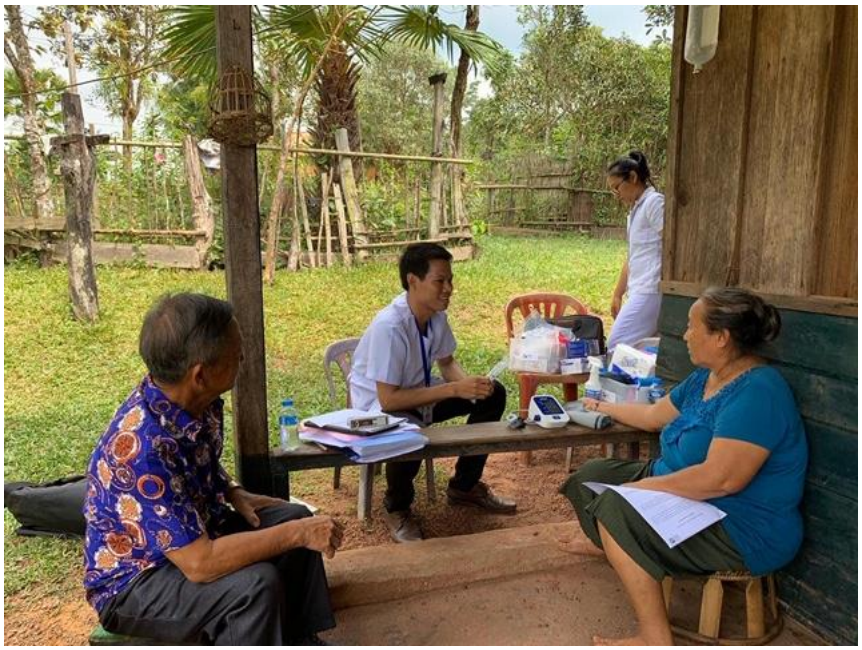
ນອກນັ້ນ, ບາງຂໍ້ມູນຈາກໂຄງການສຶກສານີ້ໄດ້ຖືກນຳສະເໜີຢູ່ກອງປະຊຸມສາກົນ The 9th World Melioidosis Congress ທີ່ຮ່າໂນ້ຍ, ປະເທດຫວຽດນາມ, ໃນເດືອນຕຸລາ ປີ 2019 ໂດຍ ທ່ານ ນາງ ເຂັມ ເງິນ ຜົງມາລາ, ນັກສຶກສາປະລິນຍາເອກ ຈາກສະຖາບັນຄົ້ນຄ້ວາເພື່ອການພັດທະນາຝຣັ່ງ. ການນຳສະເໜີບົດ ຜົນການສຶກສາດັ່ງກ່າວ ຂອງ ທ່ານ ນາງ ເຂັມເງິນ ແມ່ນ ໄດ້ຮັບລາງວັນບົດສະເໜີດີເດັ່ນອັນດັບ 2 ຈາກກອງ ປະຊຸມ (Pongmala K, Pierret A, Pando A, Silvera N, Oliva P, Boithias L, Xayyathip K, Macouin M, Rochelle-Newall, Rattanavong, S., Luangraj, M., Ribolzi O. Occurrence of *Burkholderia pseudomallei* along a 3 m deep soil profile in a paddy field of central Laos. 9th WMC, Programme & Abstract Book, Page 91).

ທີມງານການສຶກສາຄຸນນະພາບຂອງຢາ ໄດ້ດຳເນີນການຄົ້ນຄ້ວາຮ່ວມກັນກັບ The Infectious Disease Data Observatory (IDDO: https://www.iddo.org/medicine-quality) ແລະ ໄດ້ເພີ່ມທະວີການ ການຮ່ວມມືໃນຫຼາຍດ້ານຕື່ມ ໂດຍສະເພາະພາຍຫຼັງທີ່ທ່ານສາດສະດາຈານ ໂປນ ນິວຕັນ ໄດ້ຍົກຍ້າຍໜ້າທີ່ຕຳແ ໜ່ງ ມາເປັນຫົວໜ້າຄະນະຄົ້ນຄ້ວາຄຸນນະພາບຢາທີ່ມະຫາວິທະຍາໄລອ໋ອກຝອດ, ປະເທດອັງກິດ. ນອກນັ້ນ, ທ່ານ ປອ ນາງ ເຊລີນ ກາຍເຢ ຍັງໄດ້ເຂົ້າຮ່ວມນຳຄະນະຄົ້ນຄ້ວາຄຸນນະພາບຢາດັ່ງກ່າວໃນປີ 2020 ນີ້.

ໂຄງການຮ່ວມມືຄົ້ນຄ້ວາດ້ານການເຝົ້າລະວັງພະຍາດ ລະຫວ່າງ NAMRU-2 ແລະ ໂຄງການຄົ້ນຄ້ວາຂອງ ພວກ ເຮົາ ແມ່ນຍັງໄດ້ສືບຕໍ່ຈົນເຖິງປີ 2019 ເຊິ່ງແມ່ນໂຄງການຄົ້ນຄ້ວາໄລຍະຍາວອັນໜຶ່ງທີ່ໄດ້ຮ່ວມມືກັບບັນດາ ໂຮງໝໍແຂວງຕ່າງໆໃນລາວເຊັ່ນ: ໂຮງໝໍແຂວງ ຊຽງຂວາງ, ແຂວງ ຫຼວງນ້ຳທາ ແລະ ແຂວງ ສາລະວັນ. ຜົນ ໄດ້ຮັບຈາກໂຄງການສຶກສານີ້ ຊີ້ໃຫ້ເຫັນຄວາມຫຼາກຫຼາຍຂອງພະຍາດຊຶມເຊື້ອທີ່ແຈກຢາຍຢູ່ໃນລາວ ເຊິ່ງເປັນຂໍ້ ມູນທີ່ສຳຄັນສຳລັບຂໍ້ແນະນຳໃນການປິ່ນປົວ ຕົວຢ່າງເຊັ່ນ ພະຍາດ ເມລິອອຍໂດສິດ ທີ່ພົບໄດ້ຢູ່ ແຂວງ ຊຽງ ຂວາງ ແລະ ແຂວງ ສາລະວັນ ແຕ່ບໍ່ເຄີຍພົບຢູ່ແຂວງຫຼວງນ້ຳທາເລີຍ.

*ນັບຕັ້ງແຕ່ປີ 2018 ເປັນຕົ້ນມາ ,ໂຄງການຄົ້ນຄວ້າພະຍາດເຂດຮ້ອນລະຫວ່າງ ມະຫາວິທະຍາໄລອ໋ອກຝອດ-ໂຮງຫມໍມະໂຫສິດ-ແອວຳຕ໌ສ (LOMWRU) ໄດ້ຮ່ວມມືກັບ London School of Hygiene and Tropical Medicine, ປະເທດອັງກິດ ຈັດຕັ້ງປະຕິບັດໂຄງການສຶກສາຄົ້ນຄວ້າໃນຫົວຂໍ້ “ການສຶກສາຊອກຫາ ເຫດຂອງໄຂ້ໃນເຂດພື້ນທີ່ເຊິ່ງມີພະຍາດ ບິ່ມຊ້ອນຕ່າງກັນ ຫຼື Febrile Illness Epidemiology in a Broad Range of Endemicities (FIEBRE). ການສຶກສານີ້ໄດ້ນຳໃຊ້ວິທີວິທະຍາການສຶກສາແບບດຽວ

ກັນໃນ 5 ປະເທດ (ລາວ ,ໂມຊັມບິ ,ຊິມບັບເວ ,ມາລາວີ ແລະ ບັງກະລາເດຊ) .ສະຖານທີ່ດຳເນີນການສຶກສາ ໃນປະເທດລາວ ແມ່ນ ຕັ້ງຢູ່ທີ່ໂຮງໝໍແຂວງວຽງຈັນ ຫຼື ໂຮງໝໍມາເຣຍເຕເຣຊາ ,ເມືອງ ວຽງຄຳ ,ແຂວງ ວຽງຈັນ. ນັບແຕ່ເລີ່ມການສຶກສາຈົນເຖິງໄລຍະທ້າຍຂອງປີ 2019 ພົບວ່າ :ມີຜູ້ເຂົ້າຮ່ວມການຄົ້ນຄ້ວາທັງໝົດ 1379 ຄົນ. ການສຶກສານີ້ ແມ່ນ ແນ່ໃສ່ເພື່ອສ້າງໃຫ້ມີຄວາມຮູ້, ຄວາມເຂົ້າໃຈກ່ຽວກັບຄວາມ



ສຳພັນກັນຂອງຜົນກວດວິເຄາະຕ່າງໆຂອງການສຶກສາ. ສະນັ້ນ, ຈຶ່ງໄດ້ມີການເກັບກຳຂໍ້ມູນໃນຄົນເຈັບກຸ່ມສົມທຽບທີ່ອາໄສຢູ່ຂອບເຂດອ້ອມແອ້ມບໍລິເວນຂອງໂຮງຫມໍແຂວງເຂົ້າຮ່ວມການຄົ້ນຄ້ວານຳ .ຮູບພາບສະແດງໃຫ້ເຫັນການເດີນທາງໄປບ້ານຕ່າງໆເພື່ອເກັບກຳຂໍ້ມູນກຸ່ມສົມທຽບຂອງດຣ ຄຳຟອງ ກັນລະຍາ ເຊິ່ງແມ່ນໜຶ່ງໃນທີມງານຂອງໂຄງການຄົ້ນຄ້ວາຂອງພວກເຮົາ .ການຈັດຕັ້ງປະຕິບັດໂຄງການນີ້ ຈະສືບຕໍ່ໄປຈົນເຖິງທ້າຍປີ 2020 ແລະ ບັນດາຕົວຢ່າງຈະຖືກສົ່ງໄປຫ້ອງວິເຄາະອ້າງອີງຫຼາຍໆແຫ່ງເພື່ອຮັບປະກັນ ໃຫ້ຜົນກວດຕ່າງໆ ອອກມາຖືກຕ້ອງທີ່ສຸດສຳລັບໃນແຕ່ລະບ່ອນທີ່ເຮັດການສຶກສາ.

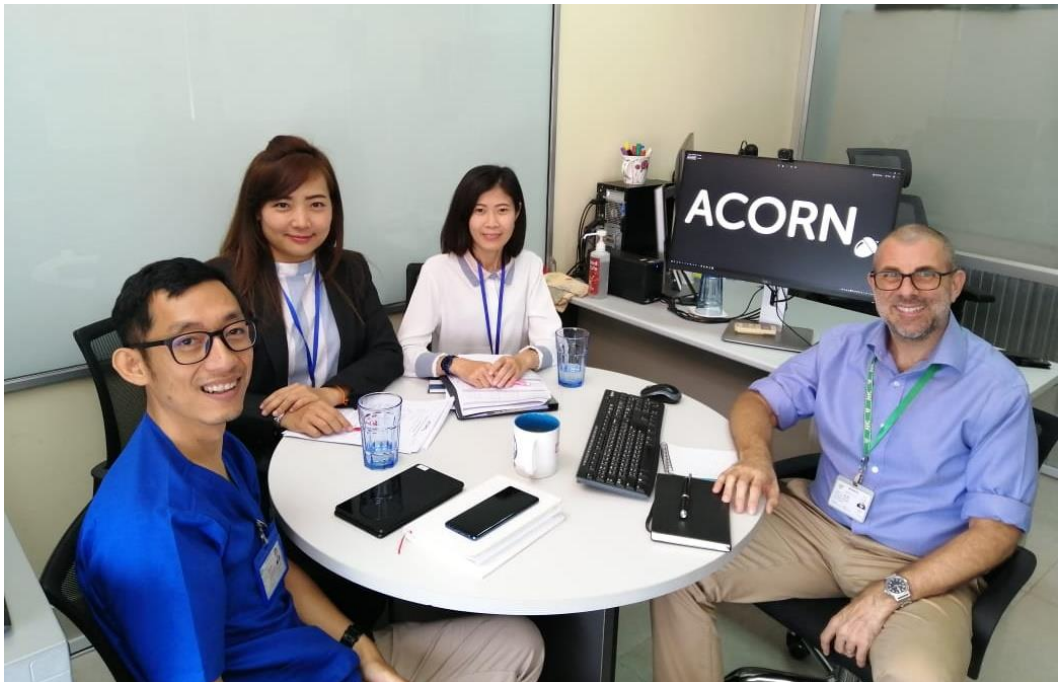
### ການຫຼຸດລົງຂອງຜູ້ທີ່ຖືເຊື້ອ ນິວໂມກອກັສໃນເສັ້ນທາງເດີນຫາຍໃຈ ຂອງເດັກນ້ອຍກຸ່ມອາຍຸ 12-23 ເດືອນ ພາຍຫຼັງທີ່ມີການນຳໃຊ້ ວັກຊີນປ້ອງກັນອັກເສບປອດຊະນິດ 13.

ນັບຕັ້ງແຕ່ປີ 2015, ໂຄງການຄົ້ນຄວ້າພະຍາດເຂດຮ້ອນລະຫວ່າງໂຮງໝໍມະໂຫສົດ - ແວວຄຳຕັ໊ສ - ອ໋ອກ ຝອດ (LOMWRU) ໄດ້ຮ່ວມມືກັບ ສະຖາບັນຄົ້ນຄວ້າວິໄຈພະຍາດເດັກນ້ອຍເມິດອກ (MCRI) ປະເທດອອສ ເຕຣເລຍ ຈັດຕັ້ງດຳເນີນການສຶກສາ ກ່ຽວກັບຜົນກະທົບຂອງວັກຊີນປ້ອງກັນອັກເສບປອດຊະນິດທີ 13 (PCV-13) ທີ່ໄດ້ນຳໃຊ້ໃນ ສ.ປ.ປ ລາວ, ນຳພາໂດຍ ທ່ານ ສາສະດາຈານ Fiona Russell. ໂດຍໄດ້ເຮັດການສຶກສາ ແບບຕັດຂວາງນະຈຸດເວລາໃດໜຶ່ງ (cross-sectional study) ເພື່ອສຶກສາເບິ່ງ ການຖືເຊື້ອນິວໂມກອກັສ ໃນເສັ້ນທາງເດີນຫາຍໃຈ ດ້ວຍວິທີການກວດຫາເຊື້ອແບບ qPCR ແລະ ຈຳແນກ ຊະນິດສາຍພັນໂມເລກຸນ

ດ້ວຍການເຮັດ DNA microarray. ພາຍຫຼັງທີ່ໄດ້ນຳໃຊ້ວັກຊີນ PCV-13, ມີການຫຼຸດລົງ 23% ຂອງຜູ້ທີ່ຖືເຊື້ອດັ່ງກ່າວ ໃນເດັກນ້ອຍກຸ່ມອາຍຸ 12-23 ເດືອນ (ຄ່າອັດຕາສ່ວນປ່ຽນແປງຄວາມຊຸກຊຸມ [aPR] ຢູ່ທີ່ 0.77 [0.61-0.96]). ທ່ານ ສາສະດາຈານ Russell, ດຣ Shereen Labib ພ້ອມດ້ວຍສະມາຊິກທີມງານ ໄດ້ຈັດການປະຊຸມ ສະເໜີແນະເຖິງຜົນກະທົບຂອງວັກຊີນປ້ອງກັນອັກເສບປອດ ເຊິ່ງເປັນພາກສ່ວນໜຶ່ງຂອງ ກອງປະຊຸມນານາຊາດ ຄັ້ງທີ 11 ເລື່ອງສາທາລະນະສຸກສາດໃນບັນດາກຸ່ມປະເທດລຸ່ມແມ່ນ້ຳຂອງ, ນະຄອນຫຼວງວຽງຈັນ, ວັນທີ 18 ຕຸລາ 2019. ຜົນໄດ້ຮັບສ່ວນ ຫຼາຍແມ່ນຖືກເຜີຍແຜ່ໃນວາລະສານວັກຊີນ. (Satzke C, Dunne EM, Choummanivong M, Ortika BD, Neal EFG, Pell CL, et al. ການຖືເຊື້ອນິວໂມກອກັສໃນເດັກທີ່ໄດ້ຮັບວັກຊີນ ແລະ ເດັກອ່ອນທີ່ບໍ່ໄດ້ຮັບວັກຊີນ ໃນ ສ.ປ.ປ ລາວ 2 ປີ ຫຼັງ ຈາກທີ່ໄດ້ນຳໃຊ້ ວັກຊີນປ້ອງກັນອັກເສບປອດຊະນິດທີ 13. Vaccine. 2019;37(2):296-305.)

# Research Highlights

LOMWRU continues to focus on epidemiological and clinical research on infectious diseases. Our active programme of research on the quality of medicines is one of very few based in low- and middle- income countries. Tackling the rise of antimicrobial resistance (AMR) is becoming an increasing priority. The Microbiology Laboratory of Mahosot Hospital has been conducting pathogen-based antimicrobial resistance surveillance for almost 20 years and data are submitted to the WHO Global Antimicrobial Surveillance System by the Laos Ministry of Health Department for Communicable Disease Control. In 2019 Mahosot Hospital joined as a site for the ACORN study (A Clinically Oriented antimicrobial Resistance Network), a pilot project led by Professor Paul Turner of the Cambodia Oxford Medical Research Unit (COMRU). ACORN looks at the impact of AMR on patients, collecting data on risk factors for drug-resistant infections and clinical outcomes.




**Pictured (from left) Dr Miliya Thyl (Research Microbiologist), Dr Danoy Chommanam (ACORN-Laos Investigator), Dr Anousone Douangnouvong (ACORN-Laos Coordinator), Professor Paul Turner (ACORN Principal Investigator) preparing for the study in the Angkor Hospital for Children, Siem Reap, Cambodia.**

Here we highlight a selection of research outputs of LOMWRU and partner organisations published in 2019 covering a range of topics and disciplines. The complete list with abstracts is found in the following section of the report.

## AZITHROMYCIN IS NOT A GOOD TREATMENT FOR MURINE TYPHUS

Murine typhus, a rickettsial disease caused by *Rickettsia typhi*, is a common cause of fever in Laos. LOMWRU investigated different treatment options for murine typhus including three- and seven-day courses of oral doxycycline and a three-day course of azithromycin. They found that azithromycin treatment was inferior to doxycycline with a treatment failure rate of 22.5%. The results were published in Clinical Infectious Diseases. (Newton PN, Keolouangkhot V, Lee SJ, et al. A Prospective, Open-label, Randomized Trial of Doxycycline Versus Azithromycin for the Treatment of Uncomplicated Murine Typhus. *Clinical Infectious Diseases.* 2019;68(5):738-47.)

**Dr Khansoudaphone Phakhounthong (centre), Research Physician since 2014 who left at the end of 2019 to continue to work for the Lao Government in the Department for Communicable Disease Control.**

pathogen was detected in 42.3% of cases, of whom 16.4% had a bacterial cause (including *Orientia tsutsugamushi* [2.9%] and *Rickettsia* spp. [2.3%]). These findings suggest that all patients suspected of having CNS infections should receive empirical treatment for rickettsial infections as well as other typical bacterial pathogens, pending the results of investigations.

(Dubot-Pérès A, Mayxay M, Phetsouvanh R, et al. Management of Central Nervous System Infections, Vientiane, Laos, 2003-2011. Emerging Infectious Diseases. 2019;25(5):898-910.)

### PUBLIC HEALTH RISKS OF BUSHMEAT MARKETS IN LAOS

Trade of bushmeat and other wildlife for human consumption at wet markets presents a unique set of challenges to policymakers. As we have seen with the recent SARS-CoV-2 pandemic, the risks to public health are high, yet policymakers are confronted with multiple trade-offs between conservation, food security, food safety, culture and tradition. As part of the large EU-funded LACANET study, using consumer surveys and behavioural analysis we developed a conceptual model to be able to understand and quantify the risks of transmission of zoonotic diseases through bushmeat consumption.

This is the first of a series of papers that will be published from the LACANET project, which involved collaborations with the National Animal Health Laboratories and Wildlife Conservation Society Laos. (Pruvot M, Khammavong K, Milavong P, et al. Toward a quantification of risks at the nexus of conservation and health: The case of bushmeat markets in Lao PDR. Science of the Total Environment. 2019. 676:732-745.)

### FISH ARE AN IMPORTANT SOURCE OF INVASIVE STREPTOCOCCUS AGALACTIAE INFECTION IN SOUTHEAST ASIA

In June 2019, Dr Manophab Luangraj and Dr Andrew Simpson attended the South-East Asian group B Streptococcus (SEA-BeaSt) 2nd Networking Event in Bangkok. This was a follow-on to a previous meeting held in Singapore in 2018, held to discuss regional co-ordination and collaborative research following a food-borne outbreak of Group B streptococcal (GBS) infection in Singapore.

This link between GBS in fish and human disease was first described when there was an outbreak of invasive GBS infection in healthy adults in Singapore in 2015. Investigations revealed that this occurrence was related to raw freshwater fish consumption, particularly Yusheng, a Chinese-style raw fish dish made with either the Asian bighead carp or the Snakehead fish. Characterisation and whole genome sequencing analysis from human isolates demonstrated that a single GBS strain (serotype III, sequence type 283) was associated with the outbreak. This strain was found to be the same GBS strain as that found in fish.

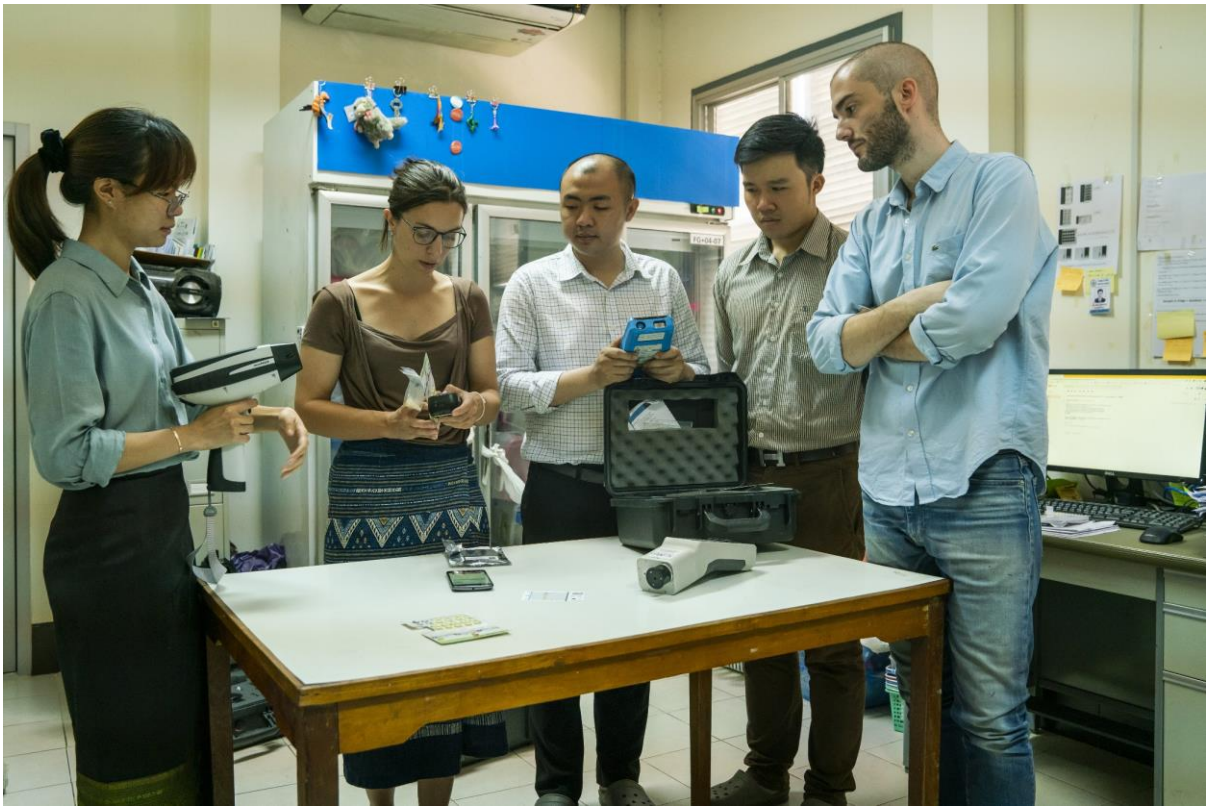
From retrospective analysis of data from fever aetiology studies conducted in Laos between 2000 and 2017, 38 GBS isolates from human blood and CSF culture were identified. Stored isolates were sent for characterisation and whole genome sequencing at The Genome Institute in Singapore, and 76% were identified as sequence type 283. This raises the possibility of a link between human disease and raw fish consumption in Laos, although this has not yet been confirmed, and there is a lack of evidence of the presence of GBS strain ST283 in fish in this country. We plan to study this further. (Barkham T, Zadoks RN, Azmai

MNA, et al. One hypervirulent clone, sequence type 283, accounts for a large proportion of invasive *Streptococcus agalactiae* isolated from humans and diseased tilapia in Southeast Asia. PLoS Neglected Tropical Diseases. 2019;13(6): e0007421.)

### TARGETED MASS DRUG ADMINISTRATION CAN BE A USEFUL TOOL TO ELIMINATE MALARIA

The continued spread and emergence of artemisinin, piperaquine and mefloquine resistance in the Greater Mekong Subregion makes elimination of malaria an urgent public health goal. Laos aims to eliminate malaria by 2030 and, together with Cambodia and Myanmar, piloted targeted mass drug administration with dihydroartemisinin-piperaquine in Nong district, Savannakhet Province as a means of accelerating elimination of falciparum malaria. The impact of MDA on falciparum malaria varied by country. The greatest impact was in Laos, followed by Cambodia and Myanmar, and there was little effect in Vietnam. The findings were published in PLOS Medicine. (von Seidlein L, Peto TJ, Landier J, Nguyen TN, Tripura R, Phommasone, K., et al. The impact of targeted malaria elimination with mass drug administrations on falciparum malaria in Southeast Asia: A cluster randomised trial. PLoS Medicine. 2019;16(2):e1002745.)

## GLOBAL ACCESS TO QUALITY-ASSURED MEDICAL PRODUCTS: THE OXFORD STATEMENT AND CALL TO ACTION



**Members of the LOMWRU Medicine Quality Team. Left to right: Vayouly Vidhamaly, Céline Caillet, Phonepasith Boupha, Kem Boutsamay and Guillermo Alonso with a portable medicine screening device.**

In September 2018 the first Medicine Quality & Public Health Conference was held in Oxford, United Kingdom [https://www.tropicalmedicine.ox.ac.uk/medicinequality2018/]. The conference was attended by over 200 delegates from over 50 countries - they discussed the latest evidence on the epidemiology of substandard and falsified medical products, their health, economic, social, legal and ethical implications, and debated interventions to ensure that all the world's population have access to affordable and quality-assured medical products. One hundred and fifty-nine of those attending wrote a consensus statement and declaration calling for urgent attention to eliminate substandard and falsified medical products that undermine public health and waste precious resources. This Oxford Statement urges the global health community to step up their efforts to make quality medical products affordable and accessible to all. It calls for improvements in data quality, collection and data sharing and underlines the urgent need for wider, multidisciplinary research to build the evidence base globally and to use these data for informing interventions and policy to ensure that we all have access to good quality medical products. [Newton, P. N., Bond KC; Oxford

Statement signatories. Global access to quality-assured medical products: the Oxford Statement and call to action. Lancet Glob Health. 2019 Dec;7(12).]

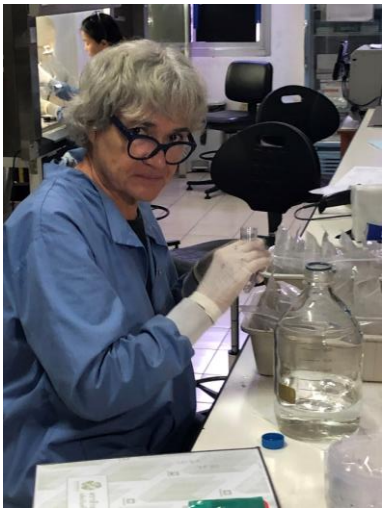
## RESEARCH COLLABORATIONS

All of LOMWRU's research is collaborative. LOMWRU itself is a collaboration between Oxford University and Mahosot Hospital, receiving core funding from the Wellcome Trust. LOMWRU is one of the five research units of the MORU Tropical Health Network, directed by Professor Nick Day who is based in the Mahidol Oxford Tropical Medicine Research Unit in the Faculty of Tropical Medicine, Mahidol University, Bangkok, Thailand. LOMWRU collaborates on several MORU network research projects and receives strong scientific and administrative support from the Bangkok Unit. Two examples of research coordinated from MORU are the GenRe and ENDGAME malaria projects with the Laos Centre of Malariology, Parasitology and Entomology (CMPE). The collaboration between LOMWRU and the Institut de recherche pour le développement (IRD) dates back to 2006. Dr Audrey Dubot-Pérès is the Head of Virology at

LOMWRU but now based in the Unité des Virus Émergents (UVE), Marseille, France. UVE Director, Professor Xavier de Lamballerie (shown above, left, between Dr Manivanh Vongsouvath and Dr Audrey Dubot-Pérès in the old Microbiology Laboratory) visited Vientiane this year after a long absence to discuss collaborative projects. A more recent collaboration with IRD dates back to 2011, and involves Dr Alain Pierret and Dr Anne Pando (shown overleaf), who are interested in soil ecology, and *B. pseudomallei* in particular.

Over the course of the last two years, over 300 water samples have been collected at the IRD'S Ban Nabone field site, Vientiane province. Each of these samples was tested for the presence of *B. pseudomallei* at the Mahosot microbiology lab, as well as being submitted to various

physico-chemical analyses (dissolved organic carbon (DOC), major cations, major nutrients and traces by Q-ICPMS multi-elemental analyzes and major anions by ion chromatography). Following cultures, a batch of 130 determinations of *B. pseudomallei* by qPCR was also carried out.



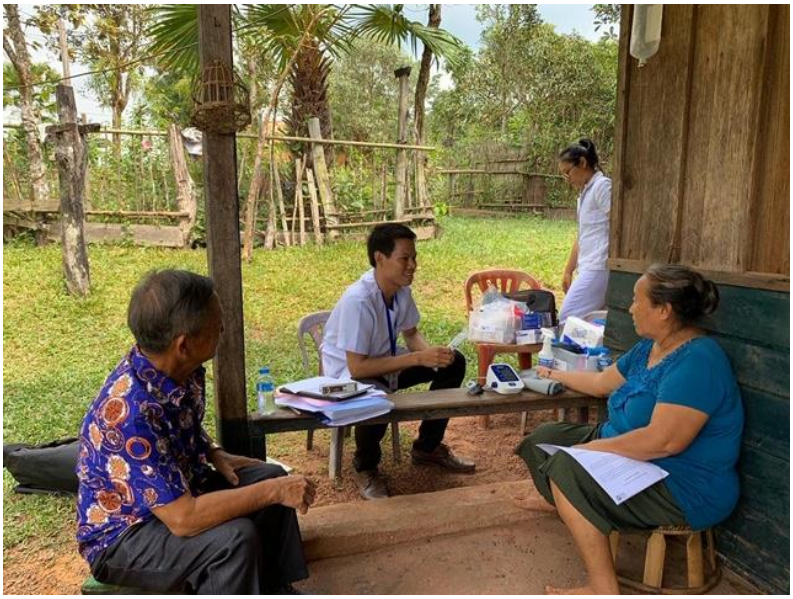
More than 370 soil samples corresponding to sequential cores to a depth of 3 m were also taken in order to carry out cultures for the detection of *B. pseudomallei* as well as physical measurements (soil chemistry and mineralogy, magnetic susceptibility). These core samples revealed very high concentrations of *B. pseudomallei* at depths of more than 1 m (concentrations >1000 CFU/g between 130 and 215 cm, compared to a maximum of 30 CFU/g between 10 and 30 cm in the 2018 late dry season). Additionally, strains of *B. pseudomallei* isolated from sequential 3 m core samples are being studied to try to characterize the possible genetic variability of *B. pseudomallei* as a function of soil depth and to test the hypothesis of vertical transfer of these strains during seasonal cycles. These analyses are currently underway at MORU in Bangkok.

Some of this work was presented at the 9th World Melioidosis Congress in Hanoi in October 2019, by Khemngeun Pongmala, a PhD student with IRD. Khemngeun was awarded the second prize for best presentation at the Congress (Pongmala K, Pierret A, Pando A, Silvera N, Oliva P, Boithias L, Xayyathip K, Macouin M, Rochelle-Newall, Rattanavong, S., Luangraj, M., Ribolzi O. Occurrence of *Burkholderia pseudomallei* along a 3 m deep soil profile in a paddy field of central Laos. 9th WMC, Programme & Abstract Book, Page 91).

The Medicine Quality team is linked to the Infectious Disease Data Observatory (IDDO) and this link has been strengthened with Professor Paul Newton's move to Oxford. Dr Céline Caillet plans to join the Medicine Quality Research Group there in 2020.

Our collaborative disease surveillance with NAMRU-2 continued throughout 2019 with our longstanding provincial hospital collaborators in three locations (Xieng Khuang, Luang Namtha and Salavan). This work has shown variations in infectious disease incidence around Laos, useful information for making empirical treatment recommendations, for example patients present with melioidosis in Xieng Khuang and Salavan regularly but almost never in Luang Namtha.

Since 2018 LOMWRU has been collaborating with the London School of Hygiene and Tropical Medicine on the **FIEBRE** project (Febrile Illness Epidemiology in a Broad Range of Endemicities). The same protocol is being followed in five countries (Laos, Mozambique, Zimbabwe, Malawi and Bangladesh). The Lao site is in the Maria Teresa Hospital, Viengkham District, Vientiane Province and the team had included 1379 participants at the end of 2019. To understand the relevance of many of the test results in the study, matched controls are recruited from villages close to the hospital. Dr Khamfong Kunlaya, one of the FIEBRE study doctors is shown recruiting a volunteer in one of the villages. Recruitment should end in 2020 and the specimens will be sent to different reference laboratories to ensure consistency between the sites.



## REDUCTION IN PCV13-TYPE CARRIAGE IN LAO CHILDREN AGED 12-23 MONTHS AFTER VACCINE INTRODUCTION

Since 2015, LOMWRU has been collaborating with the Murdoch Children's Research Institute, Melbourne, Australia on studies looking at the impact of introducing PCV-13 vaccine in Laos, led by Professor Fiona Russell. Using a cross-sectional survey approach to study pneumococcal carriage in the nasopharynx by quantitative real-time PCR, with molecular serotyping performed using DNA microarray. Post PCV13, there was a 23% relative reduction in PCV13-type carriage in children aged 12-23 months (adjusted prevalence ratio [aPR] 0.77 [0.61-0.96]). Professor Russell, Project Manager Dr Shereen Labib and other team members organized a PCV impact feedback session as part of the 11th International Conference on Public Health among Greater Mekong Sub-Regional countries, Vientiane, on 18th October 2019. The main results have been published in Vaccine. (Satzke C, Dunne EM, Choummanivong M, Ortika BD, Neal EFG, Pell CL, et al. Pneumococcal carriage in vaccine-eligible children and unvaccinated infants in Lao PDR two years following the introduction of the 13-valent pneumococcal conjugate vaccine. Vaccine. 2019;37(2):296-305.)

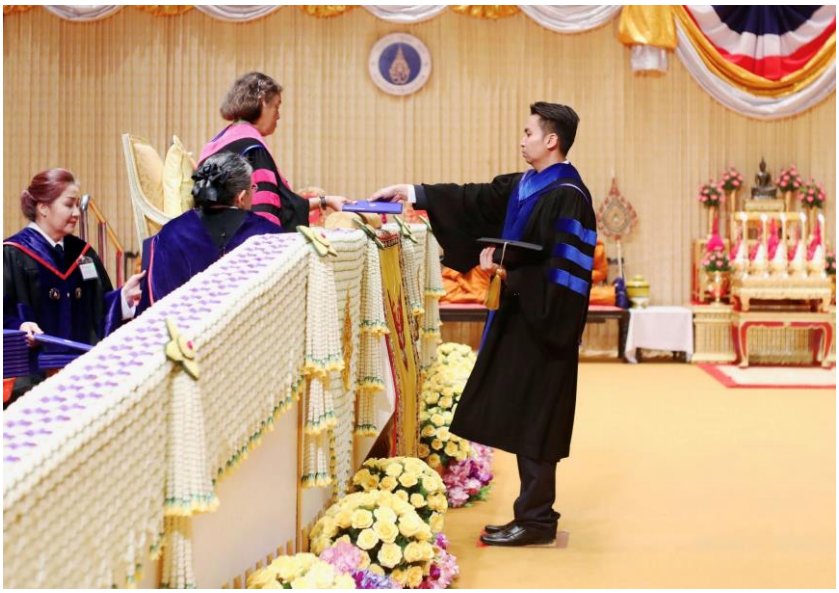
# Training Highlights

LOMWRU has an active PhD and Master's programme for Lao and international students. In addition, LOMWRU and MORU provide other training courses such as Good Clinical Practice and Research Ethics.

## DOCTORAL STUDENTS

### Dr WEERAWAT PHUKLIA GRADUATES FROM MAHIDOL UNIVERSITY

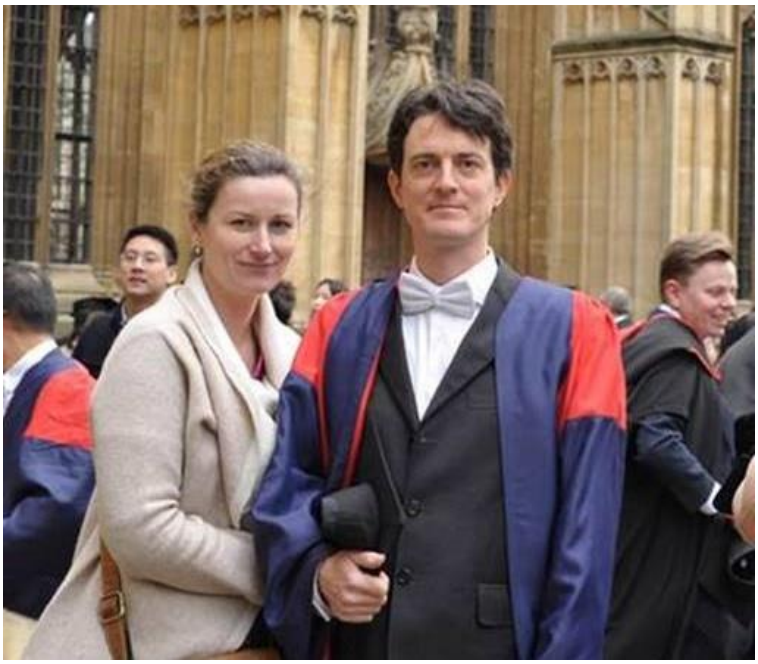
Dr Weerawat Phuklia, a scientist in the Molecular Bacteriology Laboratory received his PhD in Tropical Medicine from Mahidol University in 2019, in a ceremony presided over by Her Royal Highness, Princess Maha Chakri Sirindhorn (*see photograph below*). The subject of Dr Phuklia's PhD was "Antibiotic susceptibilities of *Orientia* spp. from clinical isolates in Laos and Thailand." Dr Phuklia was supervised by Assistant Professor Piengchan Sonthayanon, Professor Paul Newton, Professor Nick Day, Dr Jeanne Salje and Associate Professor Daniel Paris. Dr Phuklia developed a method to enable the screening of antimicrobial susceptibility of clinical isolates and investigated known antibiotic target genes. No evidence of reduced susceptibility of *O.tsutsugamushi* to doxycycline or azithromycin was demonstrated. Some of this work has already been published. (Phuklia W, Panyanivong P, Sengdetka D, Sonthayanon P, Newton, P. N., Paris DH, et al. Novel high-throughput screening method using quantitative PCR to determine the antimicrobial susceptibility of *Orientia tsutsugamushi* clinical isolates. The Journal of Antimicrobial Chemotherapy. 2019;74(1):74-81.)



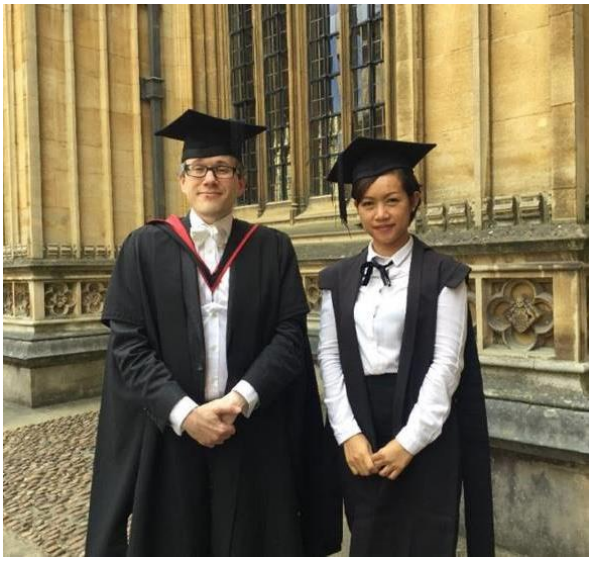
# TRAINING HIGHLIGHTS

## DR IVO ELLIOTT PASSED HIS DPHIL EXAMINATION AT THE UNIVERSITY OF OXFORD

On 16 Oct, 2019, Wellcome Trust Research Training Fellow, Dr Ivo Elliott was informed by the University of Oxford in the UK that he had successfully passed his DPhil. Entitled: *The Clinical Epidemiology of Scrub Typhus in Humans, Chiggers and Rodents*, Ivo did his fieldwork in Laos and Thailand and was supervised by Professors Paul Newton, Rory Bowden, Daniel Paris and Nick Day. Ivo has returned to Oxford and is working in the Oxford University NHS Foundation Trust as a Consultant in Infectious Diseases and Microbiology. Ivo is pictured (*left*) at his 2020 Graduation ceremony at the Sheldonian Theatre in Oxford with his wife Dr Catriona Wootton who is a Consultant Dermatologist.



## DR VILADA CHANSAMOUTH'S DPHIL MATRICULATION AT THE UNIVERSITY OF OXFORD, UK



Dr Vilada Chansamouth is in the first year of her DPhil at the University of Oxford and attended her Matriculation Ceremony on 21st June, 2019. Dr Vilada is funded by the Wellcome Trust, having been awarded a prestigious International Training Fellowship in 2019. The subject of her research is antimicrobial resistance in Laos. She plans the evaluate 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. Dr Vilada's achievements were recognised by the British Embassy in Laos at the Queen's Birthday Celebrations in Vientiane in June 2019.

# TRAINING HIGHLIGHTS

### DR KOUKEO PHOMMASONE ENTERED THE FINAL YEAR OF HIS PHD STUDIES IN 2019

Dr Koukeo has been studying for a PhD at the University of Amsterdam since 2016, on the subject of Targeted Malaria Elimination. He is due to graduate in the last quarter of 2020.

## MASTER'S STUDENTS

Two Master's students graduated this year.

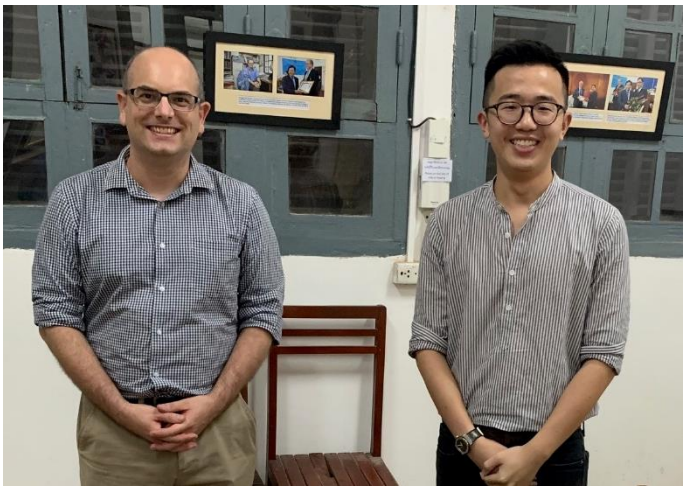
### Ms Ngan Thi Do


Ms Ngan Thi Do (pictured L, centre between Ms Vayouly Vidhamaly and Dr Céline Caillet), from the Medicine Quality Team, attended her Masters' Graduation Ceremony in Hanoi in December. She was based in Vientiane working on the quality of cardiovascular medicines and has now returned to Vietnam.

# TRAINING HIGHLIGHTS

### Mr Soo Kai Ter

Mr Soo Kai Ter, from the London School of Hygiene and Tropical Medicine, completed his MSc thesis at LOMWRU with the Molecular Bacteriology Group. He looked at methods of detecting pathogens in culture negative haemoculture fluids.



Matthew Robinson and Soo Kai Ter (right)

### DR TOM CUSACK, MICROBIOLOGY TRAINEE SPONSORED BY PUBLIC HEALTH ENGLAND RETURNED TO SOUTHAMPTON IN UK TO COMPLETE HIS SPECIALIST TRAINING

LOMWRU has been very lucky over the years to have hosted a number of excellent Microbiology Trainees from the UK, sponsored by Public Health England (PHE). Dr Tomas-Paul Cusack, a microbiologist/ infectious diseases trainee, was on secondment from Public Health England from August 2017 to February 2019. Whilst here, as well as participating in board rounds and running tutorials with the clinical team, he worked on several different projects including the development of EUCAST epidemiological cut-off values for *B. pseudomallei,* the impact of changing from CLSI to EUCAST antibiotic testing guidelines, the molecular characterization of carbapenem resistant *Acinetobacter* spp. and *E. coli* and whole genome sequencing of regional *Neisseria meningitidis* isolates.

# TRAINING HIGHLIGHTS

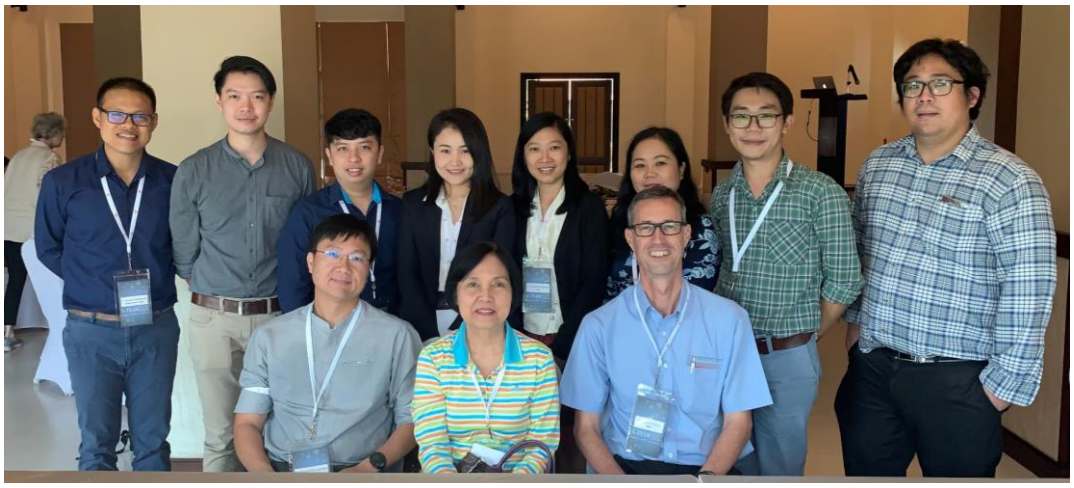
## L-TEAM

Several members of the Mahosot Hospital Microbiology Laboratory, the Adult Infectious Diseases Ward team and LOMWRU, together with colleagues from MORU, Bangkok, joined a series of education workshops on Melioidosis in 2019. These Building National Awareness events were termed L-TEAM – **L**ao **T**raining **E**vent for the **A**wareness of **M**elioidosis. These workshops were funded by the US Government Defense Threat Reduction Agency's (DTRA) Biological Threat Reduction Program (BTRP), in partnership with the Laos Ministry of Health,

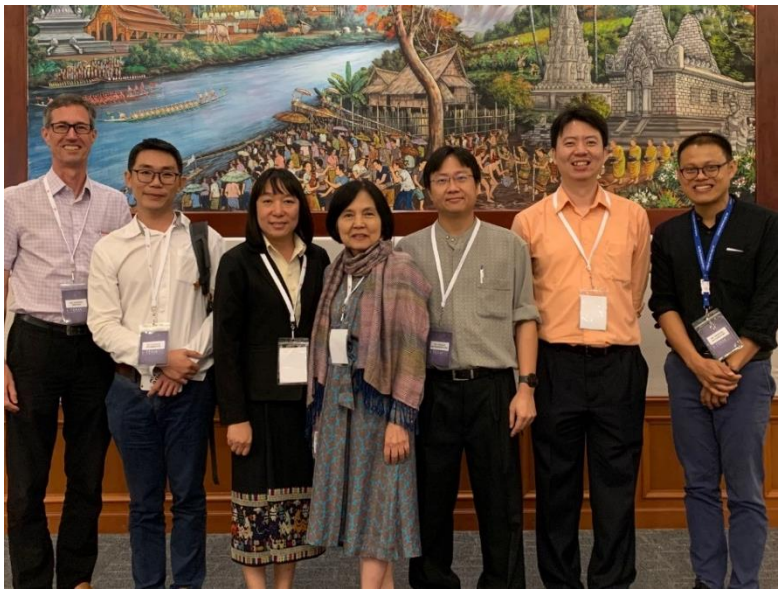
Department of Communicable Disease Control, and Department of Curative and Rehabilitation. Two 3-day workshops were held in Vang Vieng (October 2019, shown below) and Pakse (November), and were aimed principally at clinicians and hospital laboratory staff, as well as veterinary officers and epidemiologists. A third workshop was to be held in Luang Prabang in January 2020.

In addition, two week-long L-TEAM Laboratory training events were conducted at the National Center for Laboratory and Epidemiology (NCLE) in Vientiane, in October 2019. Mahosot Microbiology Laboratory staff also contributed to these events.

# TRAINING HIGHLIGHTS



**LOMWRU, Mahosot and MORU contributors and participants, Vang Vieng (*above)* and Pakse (*below)***



# TRAINING HIGHLIGHTS

## TRAINING OF TRAINERS IN CRITICAL CARE UNITS IN LAOS

Dr Rebecca Inglis is studying for a DPhil degree with the University of Oxford and has spent the last three years developing and evaluating a training course for Lao doctors and nurses caring for critically ill patients. Dr Khamsay Detleuxay, Head of Mahosot Hospital Adult Intensive Care Ward, was one of her key advisors. She spent her first year collecting baseline data from three intensive care units (ICUs) in Laos (Mahosot Hospital, Mittaphab Hospital and Luang Prabang Provincial Hospital) and conducted her first Training-of-Trainers in June 2019. She trained 13 trainers who went on to train over 90% of the staff working on Mahosot and Mittaphab ICUs. The five-day training course was delivered in Lao language and used interactive training techniques, including medical simulation and video case discussions that proved popular among learners. She will train more trainers in Luang Prabang in 2020 and hopes to support the Lao Critical Care Society to disseminate this bespoke training course more widely in the future.

## GOOD CLINICAL PRACTICE REFRESHER TRAINING IN VIENTIANE

Dr Vimalay Souvong (far left), LOMWRU's Clinical Research Coordinator organized a successful GCP training on 26-27 September 2019, with support from Mr Prayoon Yuentrakul from the Clinical Trials Support Group in MORU, Bangkok. There were 30 participants from

Mahosot, Mittaphab and National Children hospitals, the Lao Blood Bank Center, National ethics committees and LOMWRU.

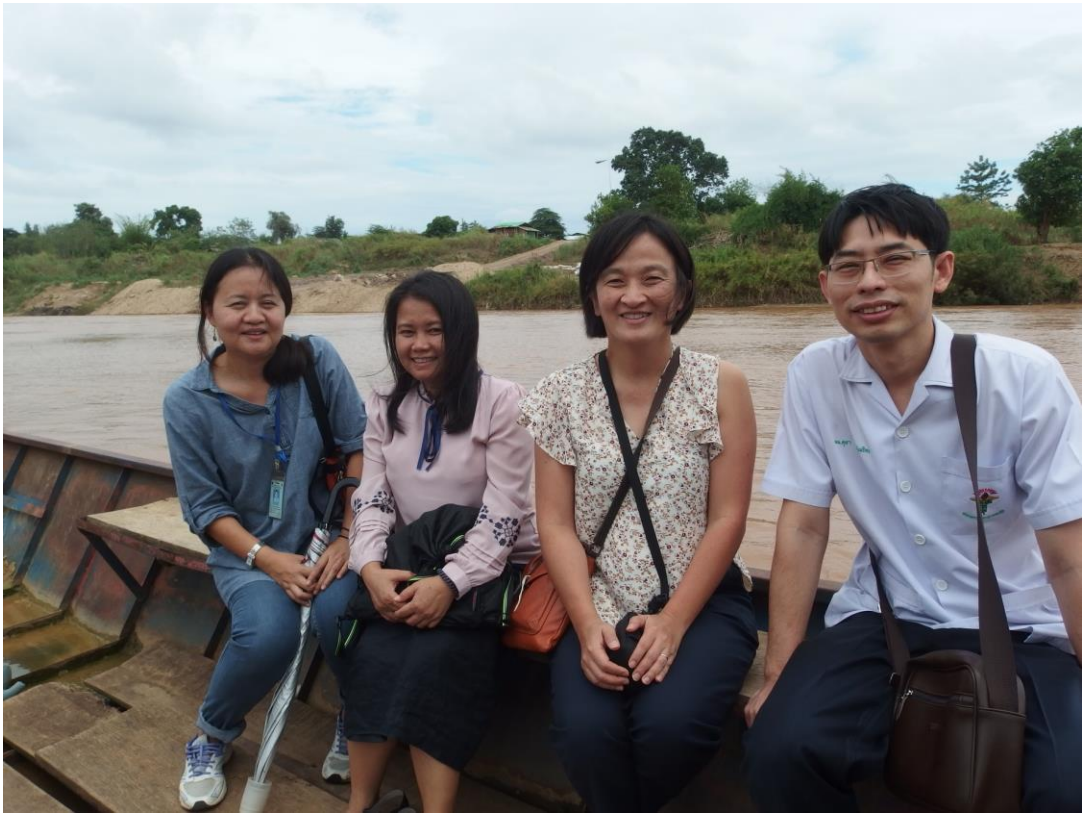
**Good Clinical Practice in Research Training held at the University of Health Sciences.**

## MS SENGMANY SYMANIVONG MAKING A DIFFERENCE

Ms Sengmany Symanivong, LOMWRU Administrator spent a month in Oxford with the Nuffield Department of Medicine Grants and Administration team. She was also one of a few people in the MORU Network to be nominated to join the "Make a Difference" personal development programme facilitated by an Executive Performance coach. The programme runs over 2 years and uses a mixture of group work and one-to -one sessions aiming to enable participants to be more effective in the workplace.

Sengmany and Mrs Athirat Black (LOMWRU Operations Manager) also spent a few days with the finance team at our sister organization, the Shoklo Malaria Research Unit based in Mae Sot, Tak Province in Thailand to exchange experiences.

# TRAINING HIGHLIGHTS



***From L to R*; Ms Wannee Riwongsakul (SMRU Administrator), Ms Sengmany Symanivong, Mrs Athirat Black and the Director of Mae Ramat Hospital in Thailand, shown on the Moei river which is the natural border between Thailand and Myanmar.**

# LOMWRU publications in 2019

In 2019 LOMWRU published 69 articles or letters in peer-reviewed journals and had 66 conference abstracts accepted. Abstracts are reproduced below with articles grouped by theme.

## MICROBIOLOGY

**Ashton, P. M., Thanh, L. T., Trieu, P. H., Van Anh, D., Trinh, N. M., Beardsley, J., Kibengo, F., Chierakul, W., Dance, D. A. B., Rattanavong, S., Davong, V., Hung, L. Q., Chau, N. V. V., Tung, N. L. N., Chan, A. K., Thwaites, G. E., Lalloo, D. G., Anscombe, C., Nhat, L. T. H., Perfect, J., Dougan, G., Baker, S., Harris, S., Day, J. N. (2019). "Three phylogenetic groups have driven the recent population expansion of *Cryptococcus neoformans*." Nat Commun 10(1): 2035.** doi: 10.1038/s41467-019-10092-5

***This paper includes results of whole genome-sequencing of 73 invasive isolates of Cryptococcus spp. from Laos***

*Cryptococcus neoformans* (*C. neoformans* var. grubii) is an environmentally acquired pathogen causing 181,000 HIV-associated deaths each year. We sequenced 699 isolates, primarily *C. neoformans* from HIV-infected patients, from 5 countries in Asia and Africa. The phylogeny of *C. neoformans* reveals a recent exponential population expansion, consistent with the increase in the number of susceptible hosts. In our study population, this expansion has been driven by three sub-clades of the *C. neoformans* VNIa lineage; VNIa-4, VNIa-5 and VNIa-93. These three sub-clades account for 91% of clinical isolates sequenced in our study. Combining the genome data with clinical information, we find that the VNIa-93 sub-clade, the most common sub-clade in Uganda and Malawi, was associated with better outcomes than VNIa-4 and VNIa-5, which predominate in Southeast Asia. This study lays the foundation for further work investigating the dominance of VNIa-4, VNIa-5 and VNIa-93 and the association between lineage and clinical phenotype.

**Barkham, T., Zadoks, R. N., Azmai, M. N. A., Baker, S., Bich, V. T. N., Chalker, V., Chau, M. L., Dance, D., Deepak, R.N., van Doorn, H. R., Gutierrez, R. A., Holmes, M. A., Huong, L. N. P., Koh, T. H., Martins, E., Mehershahi, K., Newton, P., Ng, L. C., Phuoc, N. N., Sangwichian, O., Sawatwong, P., Surin, U., Tan, T. Y., Tang, W. Y., Thuy, N. V., Turner, P., Vongsouvath, M., Zhang, D., Whistler, T., Chen, S. L. (2019). "One hypervirulent clone, sequence type 283, accounts for a large proportion of invasive *Streptococcus agalactiae* isolated from humans and diseased tilapia in Southeast Asia." PLoS Negl Trop Dis 13(6): e0007421.** doi: 10.1371/journal.pntd.0007421

***This paper demonstrates the existence of food (fish)-borne Streptococcus agalactiae (Group B Streptococcus) infection in Laos***

BACKGROUND: In 2015, Singapore had the first and only reported foodborne outbreak of invasive disease caused by the group B *Streptococcus* (GBS; *Streptococcus agalactiae*). Disease, predominantly septic arthritis and meningitis, was associated with sequence type (ST)283, acquired from eating raw farmed freshwater fish. Although GBS sepsis is well-described in neonates and older adults with co-morbidities, this outbreak affected non-pregnant and younger adults with fewer co-morbidities, suggesting greater virulence. Before 2015 ST283 had only been reported from twenty humans in Hong Kong and two in France, and from one fish in Thailand. We hypothesised that ST283 was causing region-wide infection in Southeast Asia. METHODOLOGY/PRINCIPAL FINDINGS: We performed a literature review, whole genome sequencing on 145 GBS isolates collected from six Southeast Asian countries, and phylogenetic analysis on 7,468 GBS sequences including 227 variants of ST283 from humans and animals. Although almost absent outside Asia, ST283 was found in all invasive Asian collections analysed, from 1995 to 2017. It accounted for 29/38 (76%) human isolates in Lao PDR, 102/139 (73%) in Thailand, 4/13 (31%) in Vietnam, and 167/739 (23%) in Singapore. ST283 and its variants were found in 62/62 (100%) tilapia from 14 outbreak sites in Malaysia and Vietnam, in seven fish species in Singapore markets, and a diseased frog in China. CONCLUSIONS: GBS ST283 is widespread in Southeast Asia, where it accounts for a large proportion of bacteraemic GBS, and causes disease and economic loss in aquaculture. If human ST283 is fishborne, as in the Singapore outbreak, then GBS sepsis in Thailand and Lao PDR is predominantly a foodborne disease. However, whether transmission is from aquaculture to humans, or vice versa, or involves an unidentified reservoir remains unknown. Creation of cross-border collaborations in human and animal health are needed to complete the epidemiological picture.

**Birnie, E., Virk, H. S., Savelkoel, J., Spijker, R., Bertherat, E., Dance, D. A. B., Limmathurotsakul, D., Devleesschauwer, B., Haagsma, J. A., Wiersinga, W. J. (2019). "Global burden of melioidosis in 2015: a systematic review and data synthesis." Lancet Infect Dis 19(8): 892-902.** doi: 10.1016/S1473-3099(19)30157-4

***This paper estimated the global burden of melioidosis in disability-adjusted-life-years (DALYs) and included country-specific estimates for Laos***

BACKGROUND: Melioidosis is an infectious disease caused by the environmental bacterium *Burkholderia pseudomallei.* It is often fatal, with a high prevalence in tropical areas. Clinical presentation can vary from abscess formation to pneumonia and sepsis. We assessed the global burden of melioidosis, expressed in disability-adjusted life-years (DALYs), for 2015. METHODS: We did a systematic review of the peer-reviewed literature for human melioidosis cases between Jan 1, 1990, and Dec 31, 2015. Quantitative data for cases of melioidosis were extracted, including mortality, age, sex, infectious and post-infectious sequelae, antibiotic treatment, and symptom duration. These data were combined with established disability

weights and expert panel discussions to construct an incidence-based disease model. The disease model was integrated with established global incidence and mortality estimates to calculate global melioidosis DALYs. The study is registered with PROSPERO, number CRD42018106372. FINDINGS: 2888 articles were screened, of which 475 eligible studies containing quantitative data were retained. Pneumonia, intra-abdominal abscess, and sepsis were the most common outcomes, with pneumonia occurring in 3633 (35.7%, 95% uncertainty interval [UI] 34.8-36.6) of 10 175 patients, intra-abdominal abscess in 1619 (18.3%, 17.5-19.1) of 8830 patients, and sepsis in 1526 (18.0%, 17.2-18.8) of 8469 patients. We estimate that in 2015, the global burden of melioidosis was 4.6 million DALYs (UI 3.2-6.6) or 84.3 per 100 000 people (57.5-120.0). Years of life lost accounted for 98.9% (UI 97.7-99.5) of the total DALYs, and years lived with disability accounted for 1.1% (0.5-2.3). INTERPRETATION: Melioidosis causes a larger disease burden than many other tropical diseases that are recognised as neglected, and so it should be reconsidered as a major neglected tropical disease. FUNDING: European Society of Clinical Microbiology and Infectious Diseases (ESCMID) Research Grant 2018, AMC PhD Scholarship, The Netherlands Organisation for Scientific Research (NWO), H2020 Marie Sklodowska-Curie Innovative Training Network European Sepsis Academy.

**Blacksell, S. D., Robinson, M. T., Newton, P. N., Day, N. P. J. (2019). "Laboratory-acquired Scrub Typhus and Murine Typhus Infections: The Argument for a Risk-based Approach to Biosafety Requirements for *Orientia tsutsugamushi* and *Rickettsia typhi* Laboratory Activities." Clin Infect Dis 68(8): 1413-1419.** doi: 10.1093/cid/ciy675

***This paper gives practical recommendations regarding safe handling of rickettsial pathogens in laboratories in low resource settings***

This study examined the literature on laboratory-acquired infections (LAIs) associated with scrub typhus (*Orientia tsutsugamushi*) and murine typhus (*Rickettsia typhi*) research to provide an evidence base for biosafety and biocontainment. Scrub typhus LAIs were documented in 25 individuals, from 1931 to 2000 with 8 (32%) deaths during the preantibiotic era. There were 35 murine typhus LAI reports and no deaths. Results indicated that the highest-risk activities were working with infectious laboratory animals involving significant aerosol exposures, accidental self-inoculation, or bite-related infections. A risk-based biosafety approach for in vitro and in vivo culture of *O. tsutsugamushi* and *R. typhi* would require that only high-risk activities (animal work or large culture volumes) be performed in high-containment biosafety level (BSL) 3 laboratories. We argue that relatively low-risk activities including inoculation of cell cultures or the early stages of in vitro growth using low volumes/low concentrations of infectious materials can be performed safely in BSL-2 laboratories within a biological safety cabinet.

**Blacksell, S. D., Robinson, M. T., Newton, P. N., Ruanchaimun, S., Salje, J., Wangrangsimakul, T., Wegner, M. D., Abdad, M. Y., Bennett, A. M., Richards, A. L., Stenos,**

**J., Day, N. P. J. (2019). "Biosafety and biosecurity requirements for *Orientia* spp. diagnosis and research: recommendations for risk-based biocontainment, work practices and the case for reclassification to risk group 2." BMC Infect Dis 19(1): 1044.** doi: 10.1186/s12879-019-4653-4

***This paper outlines the case for lowering the Risk Group assigned to Orientia spp. (the causative agent of scrub typhus) from 3 to 2. This would facilitate research in low resource settings***

Scrub typhus is an important arthropod-borne disease causing significant acute febrile illness by infection with *Orientia* spp. Using a risk-based approach, this review examines current practice, the evidence base and regulatory requirements regarding matters of biosafety and biosecurity, and presents the case for reclassification from Risk Group 3 to Risk Group 2 along with recommendations for safe working practices of risk-based activities during the manipulation of *Orientia* spp. in the laboratory. We recommend to reclassify *Orientia* spp. to Risk Group 2 based on the classification for RG2 pathogens as being moderate individual risk, low community risk. We recommend that low risk activities, can be performed within a biological safety cabinet located in a Biosafety Level (BSL) 2 core laboratory using standard personal protective equipment. But when the risk assessment indicates, such as high concentration and volume, or aerosol generation, then a higher biocontainment level is warranted. For, the majority of animal activities involving *Orientia* spp., Animal BSL 2 (ABSL2) is recommended however where high risk activities are performed including necropsies, Animal BSL (ABSL3) is recommended.

**Boss, J., Dance, D. A. B., Chanthongthip, A., Newton, P. N., Wuthiekanun, V., Robinson, M. T. (2019). "Antimicrobial Susceptibility Testing of *Leptospira* spp. in the Lao People's Democratic Republic Using Disk Diffusion." Am J Trop Med Hyg 100(5): 1073-1078.** doi: 10.4269/ajtmh.18-0955

***Leptospirosis is a common cause of febrile illness in Laos. This paper proposes a novel method to assess antimicrobial susceptibility of Leptospira spp. The isolates tested came from Mahosot Hospital and Friendship Hospital in Vientiane, Luang Namtha Provincial Hospital, and Salavan Provincial Hospital***

Leptospirosis is a global zoonotic disease caused by pathogenic bacteria of the *Leptospira* genus, which are fastidious, slow-growing organisms. Antimicrobial susceptibility data are limited; traditionally, the organisms have not been culturable on solid media. The recent development of *Leptospira* Vanaporn Wuthiekanun (LVW) agar, which facilitates rapid growth of *Leptospira* spp., provides the opportunity for antimicrobial susceptibility testing. Eighty-three *Leptospira* spp. clinical isolates originating from patients in Laos between 2006 and 2016 were tested against six antimicrobials (azithromycin, ceftriaxone, ciprofloxacin, doxycycline, gentamicin, and penicillin G) using disk diffusion on LVW agar. Quality control was undertaken using American Type Culture Collection (ATCC) reference strains with known susceptibilities on both standard media and LVW agar. All *Leptospira* spp. isolates produced

large zones of inhibition around each of the six antimicrobials. All zones were greater than 25 mm: gentamicin produced the smallest zones (median 35 mm; interquartile range 30 mm-37 mm) and azithromycin produced the largest zones (median 85 mm; interquartile range 85 mm-85 mm). Zones produced by non-leptospiral ATCC reference strains on LVW agar were within 2 mm of accepted strain-specific quality control range on standard media. Antimicrobial activity on LVW agar appears to be similar to that on standard media. As there are no published susceptibility guidelines for the *Leptospira* genus, zone interpretation was subjective. *Leptospira* Vanaporn Wuthiekanun agar enabled antimicrobial susceptibility testing of multiple *Leptospira* isolates on solid media; the large zone sizes observed suggest that resistance has not emerged to these six antimicrobials in Lao *Leptospira* spp.

**Cusack, T.-P., Ashley, E. A., Ling, C. L., Rattanavong, S., Roberts, T., Turner, P., Wangrangsimakul, T., Dance, D. A. B. (2019). "Impact of CLSI and EUCAST breakpoint discrepancies on reporting of antimicrobial susceptibility and AMR surveillance." Clin Microbiol Infect 25(7): 910-911.** doi: 10.1016/j.cmi.2019.03.007

Letter.

**Cusack, T.-P., Ashley, E. A., Ling, C. L., Roberts, T., Turner, P., Wangrangsimakul, T., Dance, D. A. B. (2019). "Time to switch from CLSI to EUCAST? A Southeast Asian perspective." Clin Microbiol Infect 25(7): 782-785.** doi: 10.1016/j.cmi.2019.03.016

***Microbiology laboratories across Laos are changing the method of antimicrobial susceptibility testing from CLSI to EUCAST this year. Using data collected at Mahosot Hospital as a case study these two papers discussed the impact of this change***

Commentary.

**Cusack, T.-P., Phimolsarnnousith, V., Duangmala, K., Phoumin, P., Turton, J., Hopkins, K. L., Woodford, N., Shetty, N., Stoesser, N., Phan, H. T. T., Dance, D. A. B. (2019). "Molecular characterization of carbapenem-resistant *Escherichia coli* and *Acinetobacter baumannii* in the Lao People's Democratic Republic." J Antimicrob Chemother 74(9): 2810-2821.** doi: 10.1093/jac/dkz234

***Antimicrobial resistance is a growing problem worldwide and emergence of carbapenem-resistance Enterobacteriales is a major concern. This paper reported the discovery of carbapenem resistance in Laos***

Letter.

**Dailey, P. J., Osborn, J., Ashley, E. A., Baron, E. J., Dance, D. A. B., Fusco, D., Fanello, C., Manabe, Y. C., Mokomane, M., Newton, P. N., Tessema, B., Isaacs, C., Dittrich, S. (2019). "Defining System Requirements for Simplified Blood Culture to Enable Widespread Use in Resource-Limited Settings." Diagnostics (Basel) 9(1): 10.** doi: 10.3390/diagnostics9010010

***This paper outlines the characteristics of a simplified blood culture system which could improve access to this investigation in low-resource settings***

Bacterial blood stream infections (BSI) are a common cause of mortality and morbidity globally. As the causative agents and the resulting treatment decisions vary, near-patient testing and surveillance tools are necessary to monitor bacterial causes and resistance to antimicrobial agents. The gold standard to identify BSIs is blood culture (BC), a methodology not widely available in resource-limited settings. The aim of the study was to map out a target product profile of a simplified BC system (SBCS) to inform product development efforts. To identify the desired characteristics of a SBCS, we enlisted a small group of specialists working in Africa and Asia. Questions were used to understand challenges and how these constraints inform system requirements. The specialists were infectious disease physicians, public health/clinical microbiologists, clinical researchers, and technology experts with different geographical backgrounds. All suggested that BC should ideally be available at the district hospital level. Many of the same operational challenges, such as limited availability of culture bottles, electricity and internet connectivity, profuse dust, the lack of ambient temperature control, and human capacity constraints were identified across the different regions. BCs, although the accepted gold standard for diagnosis of BSIs, are not widely available outside of reference/research centers in Africa and Asia. To extend the reach of this important tool, it is crucial to engage product developers and academic research partners to develop accessible alternatives.

**Dance, D. A., Wuthiekanun, V., Sarovich, D., Price, E. P., Limmathurotsakul, D., Currie, B. J., Trung, T. T. (2019). "Pan-drug-resistant and biofilm-producing strain of *Burkholderia pseudomallei*: first report of melioidosis from a diabetic patient in Yogyakarta, Indonesia." Int Med Case Rep J 12: 117-118.** doi: 10.2147/IMCRJ.S205245.

Letter.

**Dance, D. A. B., Sihalath, S., Rith, K., Sengdouangphachanh, A., Luangraj, M., Vongsouvath, M., Newton, P. N., Lubell, Y., Turner, P. (2019). "The cost-effectiveness of the use of selective media for the diagnosis of melioidosis in different settings." PLoS Negl Trop Dis 13(7): e0007598.** doi: 10.1371/journal.pntd.0007598

***Laboratory diagnosis of melioidosis can be challenging and to improve the yield testing of additional specimens is recommended from patients suspected of having the disease, ie throat swab and urine specimens which are cultured on selective media. This analysis which included a review of testing for melioidosis in Mahosot Hospital in 2017 confirmed that this approach is cost-effective***

BACKGROUND: Melioidosis is a frequently fatal disease requiring specific treatment. The yield of *Burkholderia pseudomallei* from sites with a normal flora is increased by culture using selective, differential media such as Ashdown's agar and selective broth. However, since

melioidosis mainly affects people in resource-poor countries, the cost effectiveness of selective culture has been questioned. We therefore retrospectively evaluated this in two laboratories in southeast Asia. METHODOLOGY/PRINCIPAL FINDINGS: The results of all cultures in the microbiology laboratories of Mahosot Hospital, Vientiane, Laos and Angkor Hospital for Children, Siem Reap, Cambodia, in 2017 were reviewed. We identified patients with melioidosis who were only diagnosed as a result of culture of non-sterile sites and established the total number of such samples cultured using selective media and the associated costs in each laboratory. We then conducted a rudimentary cost-effectiveness analysis by determining the incremental cost-effectiveness ratio (ICER) per DALY averted and compared this against the 2017 GDP per capita in each country. Overall, 29 patients in Vientiane and 9 in Siem Reap (20% and 16.9% of all culture-positive patients respectively) would not have been diagnosed without the use of selective media, the majority of whom (18 and 8 respectively) were diagnosed by throat swab culture. The cost per additional patient detected by selective culture was approximately $100 in Vientiane and $39 in Siem Reap. Despite the different patient populations (all ages in Vientiane vs. only children in Siem Reap) and testing strategies (all samples in Vientiane vs. based on clinical suspicion in Siem Reap), selective *B. pseudomallei* culture proved highly cost effective in both settings, with an ICER of ~$170 and ~$28 in Vientiane and Siem Reap, respectively. CONCLUSIONS/SIGNIFICANCE: Selective culture for *B. pseudomallei* should be considered by all laboratories in melioidosis-endemic areas. However, the appropriate strategy for implementation should be decided locally.

**Dubot-Pérès, A., Mayxay, M., Phetsouvanh, R., Lee, S. J., Rattanavong, S., Vongsouvath, M., Davong, V., Chansamouth, V., Phommasone, K., Moore, C., Dittrich, S., Lattana, O., Sirisouk, J., Phoumin, P., Panyanivong, P., Sengduangphachanh, A., Sibounheuang, B., Chanthongthip, A., Simmalavong, M., Sengdatka, D., Seubsanith, A., Keoluangkot, V., Phimmasone, P., Sisout, K., Detleuxay, K., Luangxay, K., Phouangsouvanh, I., Craig, S. B., Tulsiani, S. M., Burns, M. A., Dance, D. A. B., Blacksell, S .D., de Lamballerie, X., Newton, P. N. (2019). "Management of Central Nervous System Infections, Vientiane, Laos, 2003-2011." Emerg Infect Dis 25(5): 898-910.** doi: 10.3201/eid2505.180914

***This paper describes the leading causes of CNS infection in patients admitted to Mahosot Hospital, leading to the recommendation that all patients suspected of having meningitis should receive empiric treatment with ceftriaxone and doxycycline, in view of the number of patients with rickettsial infections diagnosed in Laos***

During 2003-2011, we recruited 1,065 patients of all ages admitted to Mahosot Hospital (Vientiane, Laos) with suspected central nervous system (CNS) infection. Etiologies were laboratory confirmed for 42.3% of patients, who mostly had infections with emerging pathogens: viruses in 16.2% (mainly Japanese encephalitis virus [8.8%]); bacteria in 16.4% (including *Orientia tsutsugamushi* [2.9%], *Leptospira* spp. [2.3%], and *Rickettsia* spp. [2.3%]); and *Cryptococcus* spp. fungi in 6.6%. We observed no significant differences in distribution of

clinical encephalitis and meningitis by bacterial or viral etiology. However, patients with bacterial CNS infection were more likely to have a history of diabetes than others. Death (26.3%) was associated with low Glasgow Coma Scale score, and the mortality rate was higher for patients with bacterial than viral infections. No clinical or laboratory variables could guide antibiotic selection. We conclude that high-dependency units and first-line treatment with ceftriaxone and doxycycline for suspected CNS infections could improve patient survival in Laos.

**Elliott, I., Batty, E. M., Ming, D., Robinson, M. T., Nawtaisong, P., de Cesare, M., Newton, P. N., Bowden R. (2020). "Oxford Nanopore MinION Sequencing Enables Rapid Whole Genome Assembly of *Rickettsia typhi* in a Resource-Limited Setting." Am J Trop Med Hyg 102(2): 408-414. Published online: 09 Dec 2019**. doi: 10.4269/ajtmh.19-0383

***This paper describes genome sequencing of an isolate of Rickettsia typhi in Vientiane, Laos for the first time***

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.

**Elliott, I., Pearson, I., Dahal, P., Thomas, N. V., Roberts, T., Newton, P. N. (2019). "Scrub typhus ecology: a systematic review of *Orientia* in vectors and hosts." Parasit Vectors 12(1): 513.** doi: 10.1186/s13071-019-3751-x

***This systematic review synthesises what is know about the ecology of O. tsutsugamushi, the causative agent of scrub typhus***

Scrub typhus, caused by *Orientia tsutsugamushi*, is an important and neglected vector-borne zoonotic disease with an expanding known distribution. The ecology of the disease is complex and poorly understood, impairing discussion of public health interventions. To highlight what we know and the themes of our ignorance, we conducted a systematic review of all studies investigating the pathogen in vectors and non-human hosts. A total of 276 articles in 7 languages were included, with 793 study sites across 30 countries. There was no time restriction for article inclusion, with the oldest published in 1924. Seventy-six potential vector species and 234 vertebrate host species were tested, accounting for over one million trombiculid mites ('chiggers') and 83,000 vertebrates. The proportion of *O. tsutsugamushi* positivity was recorded for different categories of laboratory test and host species. Vector and host collection sites were geocoded and mapped. Ecological data associated with these sites were summarised. A further 145 articles encompassing general themes of scrub typhus ecology were reviewed. These topics range from the life-cycle to transmission, habitats, seasonality and human risks. Important gaps in our understanding are highlighted together with possible tools to begin to unravel these. Many of the data reported are highly variable and inconsistent and minimum data reporting standards are proposed. With more recent reports of human *Orientia* spp. infection in the Middle East and South America and enormous advances in research technology over recent decades, this comprehensive review provides a detailed summary of work investigating this pathogen in vectors and non-human hosts and updates current understanding of the complex ecology of scrub typhus. A better understanding of scrub typhus ecology has important relevance to ongoing research into improving diagnostics, developing vaccines and identifying useful public health interventions to reduce the burden of the disease.

**Greer, R. C., Wangrangsimakul, T., Amornchai, P., Wuthiekanun, V., Laongnualpanich, A., Dance, D. A. B., Limmathurotsakul, D. (2019). "Misidentification of *Burkholderia pseudomallei* as *Acinetobacter* species in northern Thailand." Trans R Soc Trop Med Hyg 113(1): 48-51.** doi: 10.1093/trstmh/try108

***This is a short report from Thailand highlighting the difficulties routine laboratories encounter in the identification of Burkholderia pseudomallei, the causative agent of melioidosis. This is likely to lead to delays in diagnosis and worse patient outcomes***

Background: *Burkholderia pseudomallei* is the causative agent of melioidosis, a disease endemic throughout the tropics. Methods: A study of reported *Acinetobacter* spp. bacteraemia was performed at Chiang Rai provincial hospital from 2014 to 2015. Isolates were collected and tested for confirmation. Results: A total of 419 putative *Acinetobacter* spp. isolates from 412 patients were re-identified and 5/419 (1.2%) were identified as *B. pseudomallei*. Four of the five patients with melioidosis died. An estimated 88/419 (21%) isolates were correctly

identified as *Acinetobacter* spp. Conclusions: Misidentification of *Acinetobacter* spp. as *B. pseudomallei* or other bacteria is not uncommon and programmes to address these shortfalls are urgently required.

**Houlihan, C. F., Bharucha, T., Breuer, J. (2019). "Advances in molecular diagnostic testing for central nervous system infections." Curr Opin Infect Dis 32(3): 244-250.** doi: 10.1097/QCO.0000000000000548.

*This review presents an update on molecular technologies for the diagnosis of CNS infections*

Purpose of review: Central nervous system (CNS) infections present an ongoing diagnostic challenge for clinicians, with an aetiological agent remaining unidentified in the majority of cases even in high-income settings. This review summarizes developments in a range of diagnostic methods published in the past 18 months. Recent findings: Several commercial assays exist for the detection of viral, bacterial and fungal pathogens using single multiplex PCR. Multicentre validation of the Biofire FilmArray panel illustrated high sensitivity for bacterial and fungal pathogens, but poor results for Cryptococcus species detection. The development of microarray cards for bacterial CNS pathogens shows promise but requires further validation. Few developments have been made in proteomics and transcriptomics, contrasted with significant increase in the use of metagenomic (or unbiased) sequencing. Novel viruses causing CNS infection have been described using this technique but contamination, cost, expertise and turnaround time requirements remain restrictive. Finally, the development of Gene Xpert and Ultra has revolutionized tuberculosis meningitis diagnostics with newly released recommendations for their use from the WHO. Summary: Progress has been made in the clinical validation and international recommendation of PCR-based tests for CNS infections. Sequencing techniques present the most dynamic field, although significant ongoing challenges persist.

**Limmathurotsakul, D., Daily, F., Bory, S., Khim, G., Wiersinga, W. J., Torres, A. G., Dance, D. A. B., Currie, B. J. (2019). "Melioidosis: The hazards of incomplete peer-review." PLoS Negl Trop Dis 13(3): e0007123.** doi: 10.1371/journal.pntd.0007123

Letter.

**Luangasanatip, N., Flasche, S., Dance, D. A. B., Limmathurotsakul, D., Currie, B. J., Mukhopadhyay, C., Atkins, T., Titball, R., Jit, M. (2019). "The global impact and cost-effectiveness of a melioidosis vaccine." BMC Med 17(1): 129.** doi: 10.1186/s12916-019-1358-x

*This study estimated the potential impact, cost-effectiveness and market size for melioidosis vaccines*

BACKGROUND: Every year, 90,000 people may die from melioidosis. Vaccine candidates have not proceeded past animal studies, partly due to uncertainty around the potential market size.

This study aims to estimate the potential impact, cost-effectiveness and market size for melioidosis vaccines. METHODS: Age-structured decision tree models with country-specific inputs were used to estimate net costs and health benefits of vaccination, with health measured in quality-adjusted life years (QALYs). Four target groups of people living in endemic regions were considered: (i) people aged over 45 years with chronic renal disease, (ii) people aged over 45 years with diabetes, (iii) people aged over 45 years with diabetes and/or chronic renal disease, (iv) everyone aged over 45 years. Melioidosis risk was estimated using Bayesian evidence synthesis of 12 observational studies. In the base case, vaccines were assumed to have 80% efficacy, to have 5-year mean protective duration and to cost USD10.20-338.20 per vaccine. RESULTS: Vaccination could be cost-effective (with incremental cost-effectiveness ratio below GDP per capita) in 61/83 countries/territories with local melioidosis transmission. In these 61 countries/territories, vaccination could avert 68,000 lost QALYs, 8300 cases and 4400 deaths per vaccinated age cohort, at an incremental cost of USD59.6 million. Strategy (ii) was optimal in most regions. The vaccine market may be worth USD268 million per year at its threshold cost-effective price in each country/territory. CONCLUSIONS: There is a viable melioidosis vaccine market, with cost-effective vaccine strategies in most countries/territories with local transmission.

**Miller, A.K., Ghionea, S., Vongsouvath, M., Davong, V., Mayxay, M., Somoskovi, A., Newton, P. N., Bell, D., Friend, M. (2019). "A robust incubator to improve access to microbiological culture in low resource environments." J Med Devices 13(4): 045001.** doi: 10.1115/1.4042206

***This report describes the results of testing prototype incubators designed to work in places with unstable power supply***

To help address the limitations of operating conventional microbiological culture incubators in low resource environments, a new incubator design was developed and tested to meet the requirements of operation in laboratories without reliable power (power outages up to 12 contiguous hours) or climate control (ambient indoor temperatures from 5 °C to 45 °C). The device is designed to enable adherence to incubation temperatures recommended for growth detection, identification, and drug susceptibility testing (DST) of human pathogenic bacteria. During power outages, stable temperatures are maintained in the device's internal sample compartment by employing phase change material (PCM) as a bi-directional thermal battery to maintain incubation temperature. Five prototypes were tested in a laboratory setting using environmental test chambers and programmable power supplies, and three were field tested in the Lao PDR in situations of intended use. The prototypes successfully held their temperature to within ±1 °C in both laboratory environmental chamber testing as well as during the field test. The results indicate that the device will maintain stable culture temperatures across periods of intermittent power supply, while enabling normal workflow of this could greatly increase the availability of microbiological culture for diagnosis and antimicrobial resistance (AMR) monitoring.

**Muthumbi, E. M., Gordon, N. C., Mochamah, G., Nyongesa, S., Odipo, E., Mwarumba, S., Mturi, N., Etyang, A. O., Dance, D. A. B., Scott, J. A. G., Morpeth, S. C. (2019). "Population-Based Estimate of Melioidosis, Kenya." Emerg Infect Dis 25(5): 984-987.** doi: 10.3201/eid2505.180545

***Experience from Laos and the rest of Southeast Asia has led to cases of melioidosis being uncovered in countries where it was not thought to exist previously***

Melioidosis is thought to be endemic, although underdiagnosed, in Africa. We identified 5 autochthonous cases of *Burkholderia pseudomallei* infection in a case series in Kenya. Incidence of *B. pseudomallei* bacteremia in Kenya's Kilifi County is low, at 1.5 cases per million person-years, but this result might be an underestimate.

**Newton, P. N., Keolouangkhot, V., Lee, S. J., Choumlivong, K., Sisouphone, S., Choumlivong, K., Vongsouvath, M., Mayxay, M., Chansamouth, V., Davong, V., Phommasone, K., Sirisouk, J., Blacksell, S .D., Nawtaisong, P., Moore, C. E., Castonguay-Vanier, J., Dittrich, S., Rattanavong, S., Chang, K., Darasavath, C., Rattanavong, O., Paris, D. H., Phetsouvanh, R. (2019). "A Prospective, Open-label, Randomized Trial of Doxycycline Versus Azithromycin for the Treatment of Uncomplicated Murine Typhus." Clin Infect Dis 68(5): 738-747.** doi: 10.1093/cid/ciy563

***See Research Highlights***

BACKGROUND: Murine typhus, or infection with *Rickettsia typhi*, is a global but neglected disease without randomized clinical trials to guide antibiotic therapy. METHODS: A prospective, open, randomized trial was conducted in nonpregnant, consenting inpatient adults with rapid diagnostic test evidence of uncomplicated murine typhus at 2 hospitals in Vientiane, Laos. Patients were randomized to 7 days (D7) or 3 days (D3) of oral doxycycline or 3 days of oral azithromycin (A3). Primary outcome measures were fever clearance time and frequencies of treatment failure and relapse. RESULTS: Between 2004 and 2009, the study enrolled 216 patients (72 per arm); 158 (73.2%) had serology/polymerase chain reaction (PCR)-confirmed murine typhus, and 52 (24.1%) were *R. typhi* PCR positive. The risk of treatment failure was greater for regimen A3 (22.5%; 16 of 71 patients) than for D3 (4.2%; 3 of 71) or D7 (1.4%; 1 of 71) (P < .001). Among *R. typhi* PCR-positive patients, the area under the time-temperature curve and the fever clearance time were significantly higher for A3 than for D3 (1.8- and 1.9-fold higher, respectively; P = .005) and D7 (1.5- and 1.6-fold higher; P = .02). No patients returned with PCR-confirmed *R. typhi* relapse. CONCLUSION: In Lao adults, azithromycin is inferior to doxycycline as oral therapy for uncomplicated murine typhus. For doxycycline, 3- and 7-day regimens have similar efficacy. Azithromycin use in murine typhus should be reconsidered. Investigation of genomic and phenotypic markers of *R. typhi* azithromycin resistance is needed. CLINICAL TRIAL REGISTRATION: ISRCTN47812566.

**Phakhounthong, K., Mukaka, M., Dittrich, S., Tanganuchitcharnchai, A., Day, N. P. J., White, L. J., Newton, P. N., Blacksell, S .D. The temporal dynamics of humoral immunity to *Rickettsia typhi* infection in murine typhus patients. Clin Microbiol Infect. Published online 30 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.

**Phuklia, W., Panyanivong, P., Sengdetka, D., Sonthayanon, P., Newton, P. N., Paris, D. H., Day, N. P. J., Dittrich, S. (2019). "Novel high-throughput screening method using quantitative PCR to determine the antimicrobial susceptibility of *Orientia tsutsugamushi* clinical isolates." J Antimicrob Chemother 74(1): 74-81.** doi: 10.1093/jac/dky402

***This laboratory-based study demonstrated a new method for qPCR-based assessment of antimicrobial susceptibility of Orientia tsutsugamushi clinical isolates***

Objectives: To develop a method to enable the large-scale antimicrobial susceptibility screening of *Orientia tsutsugamushi* clinical isolates, using one timepoint and one concentration of antibiotics to considerably speed up the time to result. Methods: Growth, harvesting, multiplicity of infection (moi) and the day to determine the MICs were optimized

using five *O. tsutsugamushi* reference strains [susceptible (Karp, Kato and Gilliam) and putatively resistant (AFC-3 and AFSC-4)], one clinical isolate (UT76) and one rodent isolate (TA763). Subsequently, the MICs of azithromycin, chloramphenicol and doxycycline for these strains and 51 clinical isolates including AFSC-7 were determined. An optimal concentration was calculated using the epidemiological cut-off value. Results: The conditions for *O. tsutsugamushi* infection, growth and harvesting were determined to be an moi of 100:1 and trypsinization with the peak growth on day 10. The resulting MICs were in line with previously published susceptibility data for all reference strains, except for Karp and AFSC-4, which showed azithromycin MICs of 0.0156 and 0.0313 mg/L, compared with 0.0078 and 0.0156 mg/L, respectively, in previous reports. The MIC of doxycycline for AFC-3 was 0.125 mg/L compared with >4 mg/L in earlier reports. The final single screening concentrations were identified as: azithromycin, 0.125 mg/L; chloramphenicol, 8 mg/L; and doxycycline, 1 mg/L. Conclusions: This simplified procedure facilitates the simultaneous screening of 48 isolates for actively monitoring potential resistance of this important fever pathogen, with an 8-fold throughput improvement over early methods. The data do not support the existence of doxycycline- and chloramphenicol-resistant scrub typhus.

**Rizzi, M., Rattanavong, S., Bouthasavong, L., Seubsanith, A., Vongsouvath, M., Davong, V., De Silvestri, A., Manciulli, T., Newton, P. N., Dance, D. A. B. (2019). "Evaluation of the Active Melioidosis Detect™ test as a point-of-care tool for the early diagnosis of melioidosis: a comparison with culture in Laos." Trans R Soc Trop Med Hyg 113(12): 757-763.** doi: 10.1093/trstmh/trz092

***Reliable point-of-care tests (POCT) are needed to expedite the diagnosis of melioidosis. This report presents the results of an evaluation of a new rapid diagnostic test***

BACKGROUND: Melioidosis is difficult to diagnose clinically and culture of *Burkholderia pseudomallei* is the current, imperfect gold standard. However, a reliable point-of-care test (POCT) could enable earlier treatment and improve outcomes. METHODS: We evaluated the sensitivity and specificity of the Active Melioidosis Detect™ (AMD) rapid test as a POCT and determined how much it reduced the time to diagnosis compared with culture. RESULTS: We tested 106 whole blood, plasma and buffy coat samples, 96 urine, 28 sputum and 20 pus samples from 112 patients, of whom 26 (23.2%) were culture-positive for *B. pseudomallei*. AMD sensitivity and specificity were 65.4 and 87.2%, respectively, the latter related to 10 weak positive reactions on urine samples, considered likely false positives. The positive predictive value was 60.7%, negative predictive value was 89.3% and concordance rate between operators reading the test was 95.7%; time to diagnosis decreased by a median of 23 h. CONCLUSIONS: Our findings confirm that a strongly positive AMD result can reduce the time to diagnosis of melioidosis. However, the AMD currently has a disappointing overall sensitivity, especially with blood fractions, and specificity problems when testing urine samples.

**Roberts, T., Limmathurotsakul, D., Turner, P., Day, N. P. J., Vandepitte, W. P., Cooper, B. S. (2019). "Antimicrobial-resistant Gram-negative colonization in infants from a neonatal intensive care unit in Thailand." J Hosp Infect 103(2): 151-155**. doi: 10.1016/j.jhin.2019.04.004

***This study from a neonatal intensive care unit in Thailand shows high rates of acquisition of antimicrobial resistant bacteria among admitted neonates***

Antimicrobial-resistant Gram-negative bacteria are a major cause of morbidity and mortality in hospitalized neonates in South and South-East Asia. This study aimed to determine the dynamics of colonization with antimicrobial-resistant Gram-negative bacteria amongst patients in a neonatal intensive care unit (NICU) in Thailand. From 97 enrolled patients, 52% were colonized by an extended-spectrum beta-lactamase (ESBL) organism at some point during their stay and 64% were colonized by a carbapenem-resistant organism. Rapid acquisition of ESBL-positive and carbapenem-resistant organisms was found. Once colonized with an antibiotic-resistant organism, patients remained colonized for the remainder of their NICU stay.

**Robinson, M. T., Satjanadumrong, J., Hughes, T., Stenos, J., Blacksell, S .D. (2019). "Diagnosis of Spotted Fever Group Rickettsia infections: The Asian perspective." Epidemiol Infect 147: e286**. doi: 10.1017/S0950268819001390

***This review describes challenges in the diagnosis of Spotted Fever Group Rickettsia infections***

Spotted fever group rickettsiae (SFG) are a neglected group of bacteria, belonging to the genus Rickettsia, that represent a large number of new and emerging infectious diseases with a worldwide distribution. The diseases are zoonotic and are transmitted by arthropod vectors, mainly ticks, fleas and mites, to hosts such as wild animals. Domesticated animals and humans are accidental hosts. In Asia, local people in endemic areas as well as travellers to these regions are at high risk of infection. In this review we compare SFG molecular and serological diagnostic methods and discuss their limitations. While there is a large range of molecular diagnostics and serological assays, both approaches have limitations and a positive result is dependent on the timing of sample collection. There is an increasing need for less expensive and easy-to-use diagnostic tests. However, despite many tests being available, their lack of suitability for use in resource-limited regions is of concern, as many require technical expertise, expensive equipment and reagents. In addition, many existing diagnostic tests still require rigorous validation in the regions and populations where these tests may be used, in particular to establish coherent and worthwhile cut-offs. It is likely that the best strategy is to use a real-time quantitative polymerase chain reaction (qPCR) and immunofluorescence assay in tandem. If the specimen is collected early enough in the infection there will be no antibodies but there will be a greater chance of a PCR positive result. Conversely, when there are detectable antibodies it is less likely that there will be a positive PCR result. It is therefore extremely important that a complete medical history is provided especially the number of

days of fever prior to sample collection. More effort is required to develop and validate SFG diagnostics and those of other rickettsial infections.

**Satjanadumrong, J., Robinson, M. T., Hughes, T., Blacksell, S .D. (2019). "Distribution and Ecological Drivers of Spotted Fever Group Rickettsia in Asia." Ecohealth 16(4): 611-626.** doi: 10.1007/s10393-019-01409-3

*This article provides an overview of ecological factors on Spotted Fever Group Rickettsia in Asia*

Spotted fever group and related rickettsia (SFGR) are a neglected group of pathogens that belong to the genus *Rickettsia*. SFGR are zoonotic and are transmitted by arthropod vectors, primarily ticks, fleas and mites to accidental hosts. These emerging and re-emerging infections are widely distributed throughout the world. Land-use change and increasing human-wildlife conflict compound the risk of SFGR infection to local people in endemic areas and travelers to these regions. In this article, we discuss the rickettsial organisms causing spotted fever and related diseases, their arthropod vectors in Asia and the impact of land-use change on their spread.

**Satzke, C., Dunne, E. M., Choummanivong, M., Ortika, B. D., Neal, E. F. G., Pell, C. L., Nation, M. L., Fox, K. K., Nguyen, C. D., Gould, K. A., Hinds, J., Chanthongthip, A., Xeuatvongsa, A., Mulholland, E. K., Sychareun, V., Russell, F. M. (2019). "Pneumococcal carriage in vaccine-eligible children and unvaccinated infants in Lao PDR two years following the introduction of the 13-valent pneumococcal conjugate vaccine." Vaccine 37(2): 296-305.** doi: 10.1016/j.vaccine.2018.10.077

*This reports the impact of introduction of pneumococcal conjugate vaccine (PCV13) in Laos on rates of pneumococcal carriage in children*

Pneumococcal carriage is a prerequisite for disease, and underpins herd protection provided by pneumococcal conjugate vaccines (PCVs). There are few data on the impact of PCVs in lower income settings, particularly in Asia. In 2013, the Lao People's Democratic Republic (Lao PDR) introduced 13-valent PCV (PCV13) as a 3+0 schedule (doses at 6, 10 and 14 weeks of age) with limited catch-up vaccination. We conducted two cross-sectional carriage surveys (pre- and two years post-PCV) to assess the impact of PCV13 on nasopharyngeal pneumococcal carriage in 5-8 week old infants (n=1000) and 12-23 month old children (n=1010). Pneumococci were detected by quantitative real-time PCR, and molecular serotyping was performed using DNA microarray. Post PCV13, there was a 23% relative reduction in PCV13-type carriage in children aged 12-23 months (adjusted prevalence ratio [aPR] 0.77 [0.61-0.96]), and no significant change in non-PCV13 serotype carriage (aPR 1.11 [0.89-1.38]). In infants too young to be vaccinated, there was no significant change in carriage of PCV13 serotypes (aPR 0.74 [0.43-1.27]) or non-PCV13 serotypes (aPR 1.29 [0.85-1.96]), although trends were suggestive of indirect effects. Over 70% of pneumococcal-positive samples contained at least one antimicrobial resistance gene, which were more common in

PCV13 serotypes (p<0.001). In 12-23month old children, pneumococcal density of both PCV13 serotypes and non-PCV13 serotypes was higher in PCV13-vaccinated compared with undervaccinated children (p=0.004 and p<0.001, respectively). This study provides evidence of PCV13 impact on carriage in a population without prior PCV7 utilisation, and provides important data from a lower-middle income setting in Asia. The reductions in PCV13 serotype carriage in vaccine-eligible children are likely to result in reductions in pneumococcal transmission and disease in Lao PDR.

**Sonthayanon, S., Jaresitthikunchai, J., Mangmee, S., Thiangtrongjit, T., Wuthiekanun, V., Amornchai, P., Newton, P., Phetsouvanh, R., Day, N. P. J., Roytrakul, S. (2019). "Whole cell matrix assisted laser desorption/ionization time-of-flight mass spectrometry (MALDI-TOF MS) for identification of *Leptospira* spp. in Thailand and Lao PDR." PloS Negl Trop Dis 13(4): e0007232.** doi: 10.1371/journal.pntd.0007232

***This study used matrix assisted laser desorption/ionization time-of-flight mass spectrometry (MALDI-TOF MS) as a rapid and accurate tool for the identification of leptospires***

Leptospirosis is a zoonosis with a worldwide distribution, caused by pathogenic spirochetes of the genus *Leptospira*. The classification and identification of leptospires can be conducted by both genotyping and serotyping which are time-consuming and established in few reference laboratories. This study used matrix assisted laser desorption/ionization time-of-flight mass spectrometry (MALDI-TOF MS) as rapid and accurate tool for the identification of leptospires. The whole cell protein spectra of 116 *Leptospira* isolates including 15 references *Leptospira* spp. (pathogenic, n = 8; intermediate, n = 2; non-pathogenic, n = 5) and 101 *Leptospira* spp. clinical isolates was created as an in-house MALDI-TOF MS database. Ninety-seven clinical isolates from Thailand and Laos was validated with these protein spectra and revealed 98.9% correct identification when compared with 16S rRNA gene sequences method. Moreover, MALDI-TOF MS could identify spiked leptospires whole cell in urine. Biomarkers for differentiation of leptospires phylogeny and specific protein spectra for most found *Leptospira* spp. in this area (*L. interrogans, L. kirschneri, L. borgpetersenii*) based on MALDI-MS algorithm were demonstrated.

**Turner, P., Ashley, E. A. (2019). "Standardising the reporting of microbiology and antimicrobial susceptibility data." Lancet Infect Dis 19(11): 1163-1164.** doi: 10.1016/S1473-3099(19)30561-4

Comment.

**Turner, P., Fox-Lewis, A., Shrestha, P., Dance, D. A. B., Wangrangsimakul, T., Cusack, T.-P., Ling, C. L., Hopkins, J., Roberts, T., Limmathurotsakul, D., Cooper, B. S., Dunachie, S., Moore, C. E., Dolecek, C., van Doorn, H. R., Guerin, P. J., Day, N. P. J., Ashley, E. A. (2019). "Microbiology Investigation Criteria for Reporting Objectively (MICRO): a framework**

**for the reporting and interpretation of clinical microbiology data." BMC Med 17(1): 70.** doi: 10.1186/s12916-019-1301-1

*This article proposes a framework for reporting Microbiology data in research articles*

BACKGROUND: There is a pressing need to understand better the extent and distribution of antimicrobial resistance on a global scale, to inform development of effective interventions. Collation of datasets for meta-analysis, mathematical modelling and temporo-spatial analysis is hampered by the considerable variability in clinical sampling, variable quality in laboratory practice and inconsistencies in antimicrobial susceptibility testing and reporting. METHODS: The Microbiology Investigation Criteria for Reporting Objectively (MICRO) checklist was developed by an international working group of clinical and laboratory microbiologists, infectious disease physicians, epidemiologists and mathematical modellers. RESULTS: In keeping with the STROBE checklist, but applicable to all study designs, MICRO defines items to be included in reports of studies involving human clinical microbiology data. It provides a concise and comprehensive reference for clinicians, researchers, reviewers and journals working on, critically appraising, and publishing clinical microbiology datasets. CONCLUSIONS: Implementation of the MICRO checklist will enhance the quality and scientific reporting of clinical microbiology data, increasing data utility and comparability to improve surveillance, grade data quality, facilitate meta-analyses and inform policy and interventions from local to global levels.

**Wangrangsimakul, T., Phuklia, W., Newton, P. N., Richards, A. L., Day, N. P. J. (2020). "Scrub typhus and the misconception of doxycycline resistance." Clin Infect Dis 70(11): 2444-2449. 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 over a billion people at risk. Treatment with antibiotics such as doxycycline or chloramphenicol are 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.

**Wangrangsimakul, T., Phuklia, W., Newton, P. N., Richards, A. L., Day, N. P. J. "Drug-resistant scrub typhus." Clin Infect Dis: ciz1192. Published Online: 14 December 2019.** doi: 10.1093/cid/ciz1192

Letter.

**Win, M. M., Hla, T., Phyu, K. P., Aung, W. W., Win, K. K. N., Aye, S. N., Wah, T. T., Aye, K. M., Htwe, T. T., Htay, M. T., San, K. K., Dance, D. A. B. (2019). "A Study of *Burkholderia pseudomallei* in the Environment of Farms in Thanlyin and Hmawbi Townships, Myanmar." Am J Trop Med Hyg 100(5): 1082-1084.** doi: 10.4269/ajtmh.18-0678

***This study and the one below confirmed the existence of Burkholderia pseudomallei in the environment in Myanmar.***

Melioidosis is a tropical infection, first described in Myanmar but now rarely diagnosed there, which is widespread in Southeast Asia. The infection is predominantly acquired by people and animals through contact with soil or water. This study aimed to detect the causative organism, *Burkholderia pseudomallei*, in environmental samples from farms in Thanlyin and Hmawbi townships near Yangon, Myanmar. One hundred and twenty soil samples and 12 water samples were collected and processed using standard microbiological methods. *Burkholderia* species were isolated from 50 of the 120 (42%) soil samples but none of the water samples. Arabinose assimilation was tested to differentiate between *B. pseudomallei* and the nonpathogenic *Burkholderia thailandensis*, and seven of 50 isolates (14%) were negative. These were all confirmed as *B. pseudomallei* by a species-specific multiplex polymerase chain reaction (PCR). This is the first study to detect environmental *B. pseudomallei* in Myanmar and confirms that melioidosis is still endemic in the Yangon area.

**Win, T. T., Su, K, K., Than, A. M., Htut, Z. M., Pyar, K. P., Ashley, E. A., Dance, D. A. B., Tun, K. M. (2019). "Presence of *Burkholderia pseudomallei* in the 'Granary of Myanmar'." Trop Med Infect Dis 4(1): 8.** doi: 10.3390/tropicalmed4010008

Melioidosis is a frequently fatal infectious disease caused by the Gram negative bacillus *Burkholderia pseudomallei*. Although it was originally discovered in Myanmar, the disease disappeared from sight for many decades. This study focuses on detection of *B. pseudomallei* in soil in selected sampling sites in an attempt to start to fill the gaps in the current status of our knowledge of the geographical distribution of *B. pseudomallei* in soil in Myanmar. This cross-sectional study consists of 400 soil samples from 10 selected study townships from two major paddy growing regions. Bacterial isolation was done using a simplified method for the isolation of *Burkholderia pseudomallei* from soil. In this study, only 1% (4/400) of soil samples were found to be positive; two of four were found at 90 cm depth and another two positive samples were found at 30 cm and 60 cm. This survey has confirmed the presence of environmental *B. pseudomallei* in Myanmar indicating that the conditions are in place for melioidosis acquisition.

## MALARIA

**Duanguppama, J., Mathema, V. B., Tripura, R., Day, N. P. J., Mayxay, M., Nguon, C., von Seidlein, L., Dhorda, M., Peto, T. J., Nosten, F., White, N. J., Dondorp, A. M., Imwong, M. (2019). "Polymorphisms in Pvkelch12 and gene amplification of Pvplasmepsin4 in *Plasmodium vivax* from Thailand, Lao PDR and Cambodia." Malar J 18(1): 114.** doi: 10.1186/s12936-019-2749-3.

***This paper looked for molecular markers of artemisinin or piperaquine resistance in Plasmodium vivax in Laos and neighbouring countries and concluded that resistance was unlikely***

Background: Mutations in Pfkelch13 and Pfplasmepsin2/3 gene amplification are well-established markers for artemisinin and piperaquine resistance in *Plasmodium falciparum*, a widespread problem in the Greater Mekong Subregion (GMS). The *Plasmodium vivax* parasite population has experienced varying drug pressure dependent on local drug policies. We investigated the correlation between drug pressure from artemisinins and piperaquine and mutations in the P. vivax orthologous genes Pvkelch12 and Pvplasmepsin4 (Pvpm4), as candidate resistance markers. Methods: Blood samples from 734 *P. vivax* patients were obtained from Thailand (n = 399), Lao PDR (n = 296) and Cambodia (n = 39) between 2007 and 2017. Pvkelch12 and Pvpm4 was amplified and sequenced to assess gene mutations. To assess PvPM4 gene amplification, a Taqman® Real-Time PCR method was developed and validated. Selection of non-synonymous mutations was assessed by its ratio with synonymous mutations (Ka/Ks ratios). Mutation rates were compared to the estimated local drug pressure. Results: Polymorphisms in Pvkelch12 were rare. Pvkelch12 mutations V552I, K151Q and M124I were observed in 1.0% (7/734) of P. vivax samples. V552I was the most common mutation with a frequency of 0.7% (5/734), most of which (4/5) observed in Ubon Ratchathani, Thailand. Polymorphisms in Pvpm4 were more common, with a frequency of 40.3% (123/305) in 305 samples from Thailand, Lao PDR and Cambodia, but this was not related to the estimated piperaquine drug pressure in these areas (Pearson's $\chi^2$ test, p = 0.50). Pvpm4 mutation V165I was most frequent in Tak, Thailand (40.2%, 43/107) followed by Pailin, Cambodia (43.5%, 37/85), Champasak, Lao PDR (40.4%, 23/57) and Ubon Ratchathani, Thailand (35.7%, 20/56). Pvpm4 amplification was not observed in 141 samples from Thailand and Cambodia. For both Pvkelch12 and Pvpm4, in all areas and at all time points, the Ka/Ks values were < 1, suggesting no purifying selection. Conclusions: A novel real-time PCR-based method to assess P. vivax Pvpm4 gene amplification was developed. Drug pressure with artemisinins and piperaquine in the GMS was not clearly related to signatures of selection for mutations in the *P. vivax* orthologous resistance genes Pvkelch12 and Pvpm4 in areas under investigation. Current resistance of P. vivax to these drugs is unlikely and additional observations including analysis of associated clinical data from these regions could further clarify current findings.

**Hamilton, W. L., Amato, R., van der Pluijm, R. W., Jacob, C. G., Quang, H. H., Thuy-Nhien, N. T., Hien, T. T., Hongvanthong, B., Chindavongsa, K., Mayxay, M., Huy, R., Leang, R., Huch,**

**C., Dysoley, L., Amaratunga, C., Suon, S., Fairhurst, R. M., Tripura, R., Peto, T. J., Sovann, Y., Jittamala, P., Hanboonkunupakarn, B., Pukrittayakamee, S., Chau, N. H., Imwong, M., Dhorda, M., Vongpromek, R., Chan, X. H. S., Maude, R. J., Pearson, R. D., Nguyen, T., Rockett, K., Drury, E., Gonçalves, S., White, N. J., Day, N. P., Kwiatkowski, D. P., Dondorp, A. M., Miotto, O. (2019). "Evolution and expansion of multidrug-resistant malaria in southeast Asia: a genomic epidemiology study." Lancet Infect Dis 19(9): 943-951.** doi: 10.1016/S1473-3099(19)30392-5

***This paper presents the results of a genomic epidemiology study describing the spread of Plasmodium falciparum resistant to artemisinin and piperaquine from Cambodia into Laos and other countries in the Greater Mekong SubRegion***

BACKGROUND: A multidrug-resistant co-lineage of *Plasmodium falciparum* malaria, named KEL1/PLA1, spread across Cambodia in 2008-13, causing high rates of treatment failure with the frontline combination therapy dihydroartemisinin-piperaquine. Here, we report on the evolution and spread of KEL1/PLA1 in subsequent years. METHODS: For this genomic epidemiology study, we analysed whole genome sequencing data from *P falciparum* clinical samples collected from patients with malaria between 2007 and 2018 from Cambodia, Laos, northeastern Thailand, and Vietnam, through the MalariaGEN *P falciparum* Community Project. Previously unpublished samples were provided by two large-scale multisite projects: the Tracking Artemisinin Resistance Collaboration II (TRAC2) and the Genetic Reconnaissance in the Greater Mekong Subregion (GenRe-Mekong) project. By investigating genome-wide relatedness between parasites, we inferred patterns of shared ancestry in the KEL1/PLA1 population. FINDINGS: We analysed 1673 whole genome sequences that passed quality filters, and determined KEL1/PLA1 status in 1615. Before 2009, KEL1/PLA1 was only found in western Cambodia; by 2016-17 its prevalence had risen to higher than 50% in all of the surveyed countries except for Laos. In northeastern Thailand and Vietnam, KEL1/PLA1 exceeded 80% of the most recent *P falciparum* parasites. KEL1/PLA1 parasites maintained high genetic relatedness and low diversity, reflecting a recent common origin. Several subgroups of highly related parasites have recently emerged within this co-lineage, with diverse geographical distributions. The three largest of these subgroups (n=84, n=79, and n=47) mostly emerged since 2016 and were all present in Cambodia, Laos, and Vietnam. These expanding subgroups carried new mutations in the crt gene, which arose on a specific genetic background comprising multiple genomic regions. Four newly emerging crt mutations were rare in the early period and became more prevalent by 2016-17 (Thr93Ser, rising to 19.8%; His97Tyr to 11.2%; Phe145Ile to 5.5%; and Ile218Phe to 11.1%). INTERPRETATION: After emerging and circulating for several years within Cambodia, the *P falciparum* KEL1/PLA1 co-lineage diversified into multiple subgroups and acquired new genetic features, including novel crt mutations. These subgroups have rapidly spread into neighbouring countries, suggesting enhanced fitness. These findings highlight the urgent need for elimination of this increasingly drug-resistant parasite co-lineage, and the importance of

genetic surveillance in accelerating malaria elimination efforts. FUNDING: Wellcome Trust, Bill & Melinda Gates Foundation, UK Medical Research Council, and UK Department for International Development.

**O'Flaherty, K., Ataíde, R., Zaloumis, S. G., Ashley, E. A., Powell, R., Feng, G., Reiling, L., Dondorp, A. M., Day, N. P., Dhorda, M., Fairhurst, R. M., Lim, P., Amaratunga, C., Pukrittayakamee, S., Hien, T. T., Htut, Y., Mayxay, M., Faiz, M. A., Beeson, J. G., Nosten, F., Simpson, J. A., White, N. J., Fowkes, F. J. I. (2019). "Contribution of functional antimalarial immunity to measures of parasite clearance in therapeutic efficacy studies of artemisinin derivatives." J Infect Dis 220(7): 1178-1187.** doi:10.1093/infdis/jiz247

***This sub-study of TRAC (Tracking Resistance to Artemisinin Collaboration) a malaria project that took place in 10 countries in Africa and Asia, including Laos, described the role of malarial immunity in clearing drug resistant malaria parasites from the circulation***

BACKGROUND: Antibodies to the blood-stages of malaria enhance parasite-clearance and antimalarial efficacy. The antibody subclass and functions that contribute to parasite-clearance during anti-malarial treatment and their relationship with malaria transmission intensity have not been characterised. METHODS: IgG subclasses and C1q-fixation in response to *P. falciparum* merozoite antigens (EBA-175RIII-V, MSP-2 and MSP-142), and opsonic-phagocytosis of merozoites were measured in a multinational trial assessing the efficacy of artesunate across 11 South-East Asian sites. Regression analyses assessed the effects of antibody seropositivity on parasite-clearance half-life (hours)(PC(1/2)), PC(1/2)>/=5 hours, and day-3 parasitemia. RESULTS: IgG3, followed by IgG1, was the predominant IgG subclass detected (seroprevalence range IgG1: 5%-35% and IgG3: 27%-41%), varied across study-sites, and was lowest in study-sites with the lowest transmission intensity, and slowest mean PC(1/2). IgG3, C1q-fixation and opsonic-phagocytosis seropositivity were associated with faster PC(1/2) (mean reduction in PC(1/2) range 0.47-1.16 (hours), p-range: 0.001-0.03) and reduced odds of PC(1/2)>/=5 hours and day-3 parasitemia. CONCLUSIONS: Prevalence of IgG3, complement-fixing antibodies and merozoite phagocytosis vary according to transmission intensity, are associated with faster parasite-clearance and may be a sensitive surrogate of augmented clearance capacity of infected-erythrocytes. Determining the functional immune mechanisms associated with parasite-clearance will improve characterisation of artemisinin resistance.

**Peerawaranun, P., Landier, J., Nosten, F. H., Nguyen, T. N., Hien, T. T., Tripura, R., Peto, T. J., Phommasone, K., Mayxay, M., Day, N. P. J., Dondorp, A., White, N., von Seidlein, L., Mukaka, M. (2019). "Intracluster correlation coefficients in the Greater Mekong Subregion for sample size calculations of cluster randomized malaria trials." Malar J 18(1): 428.** doi: 10.1186/s12936-019-3062-x

***This statistical methodology paper used data from a cluster-randomized trial in Laos, Myanmar, Vietnam and Cambodia to make recommendations for sample size calculations for future similar studies***

BACKGROUND: Sample size calculations for cluster randomized trials are a recognized methodological challenge for malaria research in pre-elimination settings. Positively correlated responses from the participants in the same cluster are a key feature in the estimated sample size required for a cluster randomized trial. The degree of correlation is measured by the intracluster correlation coefficient (ICC) where a higher coefficient suggests a closer correlation hence less heterogeneity within clusters but more heterogeneity between clusters. METHODS: Data on uPCR-detected *Plasmodium falciparum* and *Plasmodium vivax* infections from a recent cluster randomized trial which aimed at interrupting malaria transmission through mass drug administrations were used to calculate the ICCs for prevalence and incidence of *Plasmodium* infections. The trial was conducted in four countries in the Greater Mekong Subregion, Laos, Myanmar, Vietnam and Cambodia. Exact and simulation approaches were used to estimate ICC values for both the prevalence and the incidence of parasitaemia. In addition, the latent variable approach to estimate ICCs for the prevalence was utilized. RESULTS: The ICCs for prevalence ranged between 0.001 and 0.082 for all countries. The ICC from the combined 16 villages in the Greater Mekong Subregion were 0.26 and 0.21 for *P. falciparum* and *P. vivax* respectively. The ICCs for incidence of parasitaemia ranged between 0.002 and 0.075 for Myanmar, Cambodia and Vietnam. There were very high ICCs for incidence in the range of 0.701 to 0.806 in Laos during follow-up. CONCLUSION: ICC estimates can help researchers when designing malaria cluster randomized trials. A high variability in ICCs and hence sample size requirements between study sites was observed. Realistic sample size estimates for cluster randomized malaria trials in the Greater Mekong Subregion have to assume high between cluster heterogeneity and ICCs. This work focused on uPCR-detected infections; there remains a need to develop more ICC references for trials designed around prevalence and incidence of clinical outcomes. Adequately powered trials are critical to estimate the benefit of interventions to malaria in a reliable and reproducible fashion. TRIAL REGISTRATION: ClinicalTrials.govNCT01872702. Registered 7 June 2013. Retrospectively registered. https://clinicaltrials.gov/ct2/show/NCT01872702.

**von Seidlein, L., Peerawaranun, P., Mukaka, M., Nosten, F. H., Nguyen, T. N., Hien, T. T., Tripura, R., Peto, T. J., Pongvongsa, T., Phommasone, K., Mayxay, M., Imwong, M., Watson, J., Pukrittayakamee, S., Day, N. P. J., Dondorp, A. M. (2019). "The probability of a sequential *Plasmodium vivax* infection following asymptomatic *Plasmodium falciparum* and *P. vivax* infections in Myanmar, Vietnam, Cambodia, and Laos." Malar J 18(1): 449.** doi: 10.1186/s12936-019-3087-1

***This paper explores the relationship between asymptomatic P.falciparum infection and subsequent P.vivax infection in Laos and other countries in the GMS and discusses whether radical cure should be given after falciparum malaria to reduce the size of the P.vivax reservoir***

BACKGROUND: Adding 8-aminoquinoline to the treatment of falciparum, in addition to vivax malaria, in locations where infections with both species are prevalent could prevent vivax reactivation. The potential risk of haemolysis under a universal radical cure policy using 8-aminoquinoline needs to be weighed against the benefit of preventing repeated vivax episodes. Estimating the frequency of sequential *Plasmodium vivax* infections following either falciparum or vivax malaria episodes is needed for such an assessment. METHODS: Quarterly surveillance data collected during a mass drug administration trial in the Greater Mekong Subregion in 2013-17 was used to estimate the probability of asymptomatic sequential infections by the same and different *Plasmodium* species. Asymptomatic *Plasmodium* infections were detected by high-volume ultrasensitive qPCR. Quarterly surveys of asymptomatic *Plasmodium* prevalence were used to estimate the probability of a *P. vivax* infection following *Plasmodium falciparum* and P. vivax infections. RESULTS: 16,959 valid sequential paired test results were available for analysis. Of these, 534 (3%) had an initial *P. falciparum* monoinfection, 1169 (7%) a *P. vivax* monoinfection, 217 (1%) had mixed (*P. falciparum* + *P. vivax*) infections, and 15,039 (89%) had no *Plasmodium* detected in the initial survey. Participants who had no evidence of a *Plasmodium* infection had a 4% probability to be found infected with *P. vivax* during the subsequent survey. Following an asymptomatic *P. falciparum* monoinfection participants had a 9% probability of having a subsequent *P. vivax* infection (RR 2.4; 95% CI 1.8 to 3.2). Following an asymptomatic *P. vivax* monoinfection, the participants had a 45% probability of having a subsequent P. vivax infection. The radical cure of 12 asymptomatic *P. falciparum* monoinfections would have prevented one subsequent *P. vivax* infection, whereas treatment of 2 *P. vivax* monoinfections may suffice to prevent one *P. vivax* relapse. CONCLUSION: Universal radical cure could play a role in the elimination of vivax malaria. The decision whether to implement universal radical cure for *P. falciparum* as well as for *P. vivax* depends on the prevalence of *P. falciparum* and *P. vivax* infections, the prevalence and severity of G6PD deficiency in the population and the feasibility to administer 8-aminoquinoline regimens safely. Trial registration ClinicalTrials.gov Identifier: NCT01872702, first posted June 7th 2013, https://clinicaltrials.gov/ct2/show/NCT01872702. This study was registered with ClinicalTrials.gov under NCT02802813 on 16th June 2016. https://clinicaltrials.gov/ct2/show/NCT02802813.

**von Seidlein, L., Peto, T. J., Landier, J., Nguyen, T. N., Tripura, R., Phommasone, K., Pongvongsa, T., Lwin, K. M., Keereecharoen, L., Kajeechiwa, L., Thwin, M. M., Parker, D. M., Wiladphaingern, J., Nosten, S., Proux, S., Corbel, V., Tuong-Vy, N., Phuc-Nhi, T. L., Son, D. H., Huong-Thu, P. N., Tuyen, N. T. K., Tien, N. T., Dong, L. T., Hue, D. V., Quang, H. H., Nguon, C., Davoeung, C., Rekol, H., Adhikari, B., Henriques, G., Phongmany, P., Suangkanarat, P., Jeeyapant, A., Vihokhern, B., van der Pluijm, R. W., Lubell, Y., White, L.**

**J., Aguas, R., Promnarate, C., Sirithiranont, P., Malleret, B., Rénia, L., Onsjö, C., Chan, X. H., Chalk, J., Miotto, O., Patumrat, K., Chotivanich, K., Hanboonkunupakarn, B., Jittmala, P., Kaehler, N., Cheah, P. Y., Pell, C., Dhorda, M., Imwong, M., Snounou, G., Mukaka, M., Peerawaranun, P., Lee, S. J., Simpson, J. A., Pukrittayakamee, S., Singhasivanon, P., Grobusch, M. P., Cobelens, F., Smithuis, F., Newton, P. N., Thwaites, G. E., Day, N. P. J., Mayxay, M., Hien, T. T., Nosten, F. H., Dondorp, A. M., White, N. J. (2019). "The impact of targeted malaria elimination with mass drug administrations on falciparum malaria in Southeast Asia: A cluster randomised trial." PLoS Med 16(2): e1002745.** doi: 10.1371/journal.pmed.1002745

***This paper described pilot evaluations of mass drug administration (MDA) in Laos and neighbouring countries as a tool to eliminate malaria, particularly in contexts where multidrug resistance is widespread***

BACKGROUND: The emergence and spread of multidrug-resistant *Plasmodium falciparum* in the Greater Mekong Subregion (GMS) threatens global malaria elimination efforts. Mass drug administration (MDA), the presumptive antimalarial treatment of an entire population to clear the subclinical parasite reservoir, is a strategy to accelerate malaria elimination. We report a cluster randomised trial to assess the effectiveness of dihydroartemisinin-piperaquine (DP) MDA in reducing falciparum malaria incidence and prevalence in 16 remote village populations in Myanmar, Vietnam, Cambodia, and the Lao People's Democratic Republic, where artemisinin resistance is prevalent. METHODS AND FINDINGS: After establishing vector control and community-based case management and following intensive community engagement, we used restricted randomisation within village pairs to select 8 villages to receive early DP MDA and 8 villages as controls for 12 months, after which the control villages received deferred DP MDA. The MDA comprised 3 monthly rounds of 3 daily doses of DP and, except in Cambodia, a single low dose of primaquine. We conducted exhaustive cross-sectional surveys of the entire population of each village at quarterly intervals using ultrasensitive quantitative PCR to detect *Plasmodium* infections. The study was conducted between May 2013 and July 2017. The investigators randomised 16 villages that had a total of 8,445 residents at the start of the study. Of these 8,445 residents, 4,135 (49%) residents living in 8 villages, plus an additional 288 newcomers to the villages, were randomised to receive early MDA; 3,790 out of the 4,423 (86%) participated in at least 1 MDA round, and 2,520 out of the 4,423 (57%) participated in all 3 rounds. The primary outcome, *P. falciparum* prevalence by month 3 (M3), fell by 92% (from 5.1% [171/3,340] to 0.4% [12/2,828]) in early MDA villages and by 29% (from 7.2% [246/3,405] to 5.1% [155/3,057]) in control villages. Over the following 9 months, the *P. falciparum* prevalence increased to 3.3% (96/2,881) in early MDA villages and to 6.1% (128/2,101) in control villages (adjusted incidence rate ratio 0.41 [95% CI 0.20 to 0.84]; p = 0.015). Individual protection was proportional to the number of completed MDA rounds. Of 221 participants with subclinical *P. falciparum* infections who participated in MDA and could be followed up, 207 (94%) cleared

their infections, including 9 of 10 with artemisinin- and piperaquine-resistant infections. The DP MDAs were well tolerated; 6 severe adverse events were detected during the follow-up period, but none was attributable to the intervention. CONCLUSIONS: Added to community-based basic malaria control measures, 3 monthly rounds of DP MDA reduced the incidence and prevalence of falciparum malaria over a 1-year period in areas affected by artemisinin resistance. *P. falciparum* infections returned during the follow-up period as the remaining infections spread and malaria was reintroduced from surrounding areas. Limitations of this study include a relatively small sample of villages, heterogeneity between villages, and mobility of villagers that may have limited the impact of the intervention. These results suggest that, if used as part of a comprehensive, well-organised, and well-resourced elimination programme, DP MDA can be a useful additional tool to accelerate malaria elimination. TRIAL REGISTRATION: ClinicalTrials.gov NCT01872702.

**WorldWide Antimalarial Resistance Network Methodology Study Group. (2019). Competing risk events in antimalarial drug trials in uncomplicated *Plasmodium falciparum* malaria: a WorldWide Antimalarial Resistance Network individual participant data meta-analysis. Malar J 18(1): 225.** doi: 10.1186/s12936-019-2837-4

***This statistical methodological paper analysed data from more than 30 000 patients included into malaria trials (including studies in Laos) and made recommendations to improve approaches to analysing efficacy data from antimalarial trials***

BACKGROUND: Therapeutic efficacy studies in uncomplicated *Plasmodium falciparum* malaria are confounded by new infections, which constitute competing risk events since they can potentially preclude/pre-empt the detection of subsequent recrudescence of persistent, sub-microscopic primary infections. METHODS: Antimalarial studies typically report the risk of recrudescence derived using the Kaplan-Meier (K-M) method, which considers new infections acquired during the follow-up period as censored. Cumulative Incidence Function (CIF) provides an alternative approach for handling new infections, which accounts for them as a competing risk event. The complement of the estimate derived using the K-M method (1 minus K-M), and the CIF were used to derive the risk of recrudescence at the end of the follow-up period using data from studies collated in the WorldWide Antimalarial Resistance Network data repository. Absolute differences in the failure estimates derived using these two methods were quantified. In comparative studies, the equality of two K-M curves was assessed using the log-rank test, and the equality of CIFs using Gray's k-sample test (both at 5% level of significance). Two different regression modelling strategies for recrudescence were considered: cause-specific Cox model and Fine and Gray's sub-distributional hazard model. RESULTS: Data were available from 92 studies (233 treatment arms, 31,379 patients) conducted between 1996 and 2014. At the end of follow-up, the median absolute overestimation in the estimated risk of cumulative recrudescence by using 1 minus K-M approach was 0.04% (interquartile range (IQR): 0.00-0.27%, Range: 0.00-3.60%). The overestimation was correlated positively with the proportion of patients with recrudescence

[Pearson's correlation coefficient (ρ): 0.38, 95% Confidence Interval (CI) 0.30-0.46] or new infection [ρ: 0.43; 95% CI 0.35-0.54]. In three study arms, the point estimates of failure were greater than 10% (the WHO threshold for withdrawing antimalarials) when the K-M method was used, but remained below 10% when using the CIF approach, but the 95% confidence interval included this threshold. CONCLUSIONS: The 1 minus K-M method resulted in a marginal overestimation of recrudescence that became increasingly pronounced as antimalarial efficacy declined, particularly when the observed proportion of new infection was high. The CIF approach provides an alternative approach for derivation of failure estimates in antimalarial trials, particularly in high transmission settings.

## MEDICINE QUALITY

**Assemat, G., Balayssac, S., Gerdova, A., Gilard, V., Caillet, C., Williamson, D., Malet-Martino, M. (2019). "Benchtop low-field (1)H Nuclear Magnetic Resonance for detecting falsified medicines." Talanta 196: 163-173.** doi: 10.1016/j.talanta.2018.12.005

***Laos has played a leading role in medicine quality research globally. This paper assessed a new NMR-based method of assessing the quality of medicines***

Falsified medicines represent a serious threat to public health. Among the different measures to effectively combat this scourge, analytical methods play a key role in their detection and removal from the market before they reach patients. The present study evaluates for the first time the potential of a benchtop low-field (LF) Nuclear Magnetic Resonance (NMR) spectrometer for uncovering drug falsification by focusing on the analysis of fifteen erectile dysfunction and nine antimalarial medicines, the most commonly reported falsified medicines in developed and developing countries respectively. After a simple and rapid sample preparation and approximately 5min of spectrum recording, LF (1)H NMR allows to conclude on the quality of the medicine: presence or absence of the expected active pharmaceutical ingredient (API), presence of unexpected API, absence of any API. Some 2D experiments are also described but although conclusive they are hampered by the duration of the experiments. The LF (1)H NMR assay, based on the internal standard method, is validated by the determination of its accuracy, repeatability, limits of detection (LOD) and quantification (LOQ), and by comparison of the data obtained on some medicines after 45min of spectrum recording to those measured with high-field (1)H NMR. Because of its saving capabilities (cost, space, user experience), LF (1)H NMR spectroscopy might become a routine screening tool in laboratories in charge of detecting falsified medicines.

**Newton, P. N., Bond, K. C.; Oxford Statement signatories. (2019). Global access to quality-assured medical products: the Oxford Statement and call to action. Lancet Glob Health 7(12): e1609-e1611.** doi: 10.1016/S2214-109X(19)30426-7

***See Research Highlights section***

Comment.

**Saraswati, K., Sichanh, C., Newton, P. N., Caillet, C. (2019). "Quality of medical products for diabetes management: a systematic review." BMJ Glob Health 4(5): e001636.** doi: 10.1136/bmjgh-2019-001636

*Diabetes is a growing problem in Laos. This review examined the evidence for the existence of poor quality medical products to treat diabetes worldwide*

Background: The global prevalence of diabetes mellitus is increasing alarmingly. However, the quality of vital medicines and medical products used to treat and monitor diabetes remains uncertain but of potential great public health significance. Here, we review the available evidence on the quality of antidiabetic medicines and supplies for self-monitoring of blood glucose (SMBG) and discuss their potential impact for the patients and society. Methods: Searches were conducted in PubMed, Embase, Google Scholar, Google and relevant websites in English and French. The Medicine Quality Assessment Reporting Guideline (MEDQUARG) was used to assess the quality of medicine quality surveys. Results: 52 publications on the quality of antidiabetic medicines, including 5 medicine quality prevalence surveys and 20 equivalence studies, were analysed. The prevalence surveys and equivalence studies included 674 samples of which 73 (10.8%) were of poor quality. The median (Q1-Q3) concordance with MEDQUARG items was 30.8% (19.2%-42.3%). No prevalence surveys on SMBG supplies' quality were found, but 29 publications, including falsified products and incorrect results due to strip degradation or contamination, were identified. Conclusion: There is little accessible evidence on the quality of antidiabetic medicines and SMBG supplies. Surveys were poorly designed and reported, making data aggregation and interpretation problematic. Despite these caveats, these results suggest that there are important issues with the quality of medical products for diabetes that need focused monitoring. There is an urgent need to achieve consensus protocols for designing, conducting and reporting medical product quality surveys. PROSPERO registration number: CRD42016039841.

**Tabernero, P., Swamidoss, I., Mayxay, M., Khanthavong, M., Phonlavong, C., Vilayhong, C., Yeuchaixiong, S., Sichanh, C., Sengaloundeth, S., Green, M. D., Newton, P. N. (2019). "A random survey of the prevalence of falsified and substandard antibiotics in the Lao PDR." J Antimicrob Chemother 74(8): 2417-2425.** doi: 10.1093/jac/dkz164

*This survey reported evidence for substandard antibiotics circulating in Laos*

OBJECTIVES: In 2012, a stratified random survey, using mystery shoppers, was conducted to investigate the availability and quality of antibiotics sold to patients in the private sector in five southern provinces of the Lao People's Democratic Republic (Laos). METHODS: A total of 147 outlets were sampled in 10 districts. The active pharmaceutical ingredient (API) content measurements for 909 samples, including nine APIs (amoxicillin, ampicillin, ceftriaxone, ciprofloxacin, doxycycline, ofloxacin, sulfamethoxazole, tetracycline and trimethoprim), were determined using HPLC. RESULTS: All the analysed samples contained the stated API and we found no evidence for falsification. All except one sample had all the units tested with %API

values between 75% and 125% of the content stated on the label. However, we identified the presence of substandard antibiotics: 19.6% (201/1025) of samples had their units outside the 90%-110% content of the label claim and 60.2% (617/1025) of the samples had units outside of the International Pharmacopoeia uniformity of content limit range. Amoxicillin had a high number of samples [67.1% (151)] with units above the limit range, followed by ciprofloxacin [58.8% (10)] and ofloxacin [57.4% (39)]. Ceftriaxone, trimethoprim and sulfamethoxazole had the highest number of samples with low API content: 57.1% (4), 51.6% (64) and 34.7% (43), respectively. Significant differences in %API were found between stated countries of manufacture and stated manufacturers. CONCLUSIONS: With the global threat of antimicrobial resistance to patient outcomes, greater understanding of the role of poor-quality antibiotics is needed. Substandard antibiotics will have reduced therapeutic efficacy, impacting public health and control of bacterial infections.

## VIROLOGY

**Bharucha, T., Gangadharan, B., Kumar, A., de Lamballerie, X., Newton, P. N., Winterberg, M., Dubot-Pérès, A., Zitzmann, N. (2019). "Mass spectrometry-based proteomic techniques to identify cerebrospinal fluid biomarkers for diagnosing suspected central nervous system infections. A systematic review." J Infect 79(5): 407-418.** doi: 10.1016/j.jinf.2019.08.005

***Proteomics is a promising approach to improve diagnostics of CNS infections such as Japanese encephalitis, an important childhood infection in Laos. This systematic review summarised existing knowledge on promising biomarkers detected in cerebrospinal fluid***

OBJECTIVES: Central nervous system (CNS) infections account for considerable death and disability every year. An urgent research priority is scaling up diagnostic capacity, and introduction of point-of-care tests. We set out to assess current evidence for the application of mass spectrometry (MS) peptide sequencing in identification of diagnostic biomarkers for CNS infections. METHODS: We performed a systematic review (PROSPEROCRD42018104257) using PRISMA guidelines on use of MS to identify cerebrospinal fluid (CSF) biomarkers for diagnosing CNS infections. We searched PubMed, Embase, Web of Science, and Cochrane for articles published from 1 January 2000 to 1 February 2019, and contacted experts. Inclusion criteria involved primary research except case reports, on the diagnosis of infectious diseases except HIV, applying MS to human CSF samples, and English language. RESULTS: 4,620 papers were identified, of which 11 were included, largely confined to pre-clinical biomarker discovery, and eight (73%) published in the last five years. 6 studies performed further work termed verification or validation. In 2 of these studies, it was possible to extract data on sensitivity and specificity of the biomarkers detected by ELISA, ranging from 89-94% and 58-92% respectively. CONCLUSIONS: The findings demonstrate feasibility and potential of the

methods in a variety of infectious diseases, but emphasise the need for strong interdisciplinary collaborations to ensure appropriate study design and biomarker validation.

**Bharucha, T., Sengvilaipaseuth, O., Seephonelee, M., Vongsouvath, M., Vongsouvath, M., Rattanavong, S., Piorkowski, G., Lecuit, M., Gorman, C., Pommier, J. D., Garson, J. A., Newton, P. N., de Lamballerie, X., Dubot-Pérès, A. (2019). "Viral RNA Degradation Makes Urine a Challenging Specimen for Detection of Japanese Encephalitis Virus in Patients With Suspected CNS Infection." Open Forum Infect Dis 6(3): ofz048.** doi: 10.1093/ofid/ofz048

***This study in Laos patients evaluated whether urine could be an alternative specimen to improve the diagnosis of Japanese Encephalitis***

Background: Japanese encephalitis virus (JEV) is a leading cause of central nervous system (CNS) infections in Asia and results in significant morbidity and mortality. JEV RNA is rarely detected in serum or cerebrospinal fluid (CSF), and diagnosis of JEV infection is usually based on serological tests that are frequently difficult to interpret. Unlike serum or CSF, urine is relatively easy to obtain, but, to date, there has been minimal work on the feasibility of testing urine for JEV RNA. Methods: We investigated the use of lysis buffer and a Microsep device to optimize urine storage for detection of JEV RNA by reverse transcription real-time polymerase chain reaction (RT-qPCR). The best of the studied methods was then evaluated in consecutive patients admitted to the hospital with suspected CNS infections in Laos. Results: We demonstrated degradation of JEV RNA in urine after even short storage periods at 4 degrees C or -80 degrees C. Although there was no advantage in using a Microsep concentration device alone, immediate addition of lysis buffer to fresh urine improved the detection of JEV RNA at the limit of detection. Conclusions: In 2 studies of 41 patients with acute encephalitis syndrome, 11 (27%) were positive for JEV IgM in CSF and/or serum, and 2 (4.9%) were JEV RT-qPCR positive from throat swabs. JEV RNA was not detected in any of these patients' urine samples. However, lysis buffer was only used during a prospective study, that is, for only 17/41 (41%) patient urine samples. Our findings suggest a need for larger studies testing urine for JEV RNA, with urine collected at different times from symptom onset, and using lysis buffer, which stabilizes RNA, for storage.

**Cassidy-Seyoum, S., Vongsouvath, M., Sengvilaipaseuth, O., Seephonelee, M., Bharucha, T., de Lamballerie, X., Newton, P. N., Dubot-Pérès, A. (2019). "Rapid Diagnostic Tests as a Source of Dengue Virus RNA for Envelope Gene Amplification: A Proof of Concept." Am J Trop Med Hyg 101(2): 451-455**. doi: 10.4269/ajtmh.18-0831

***Performing dengue molecular surveillance in remote areas is challenging. This study showed that it is possible to extract dengue RNA from rapid diagnostic tests in Laos***

Molecular epidemiological data are key for dengue outbreak characterization and preparedness. However, sparse Dengue virus (DENV) molecular information is available in

Laos because of limited resources. In this proof-of-concept study, we evaluated whether DENV1 RNA extracted from rapid diagnostic tests (RDTs) could be amplified and sequenced. The protocol for envelope gene amplification from RNA purified from RDTs was first assessed using viral isolate dilutions then conducted using 14 dengue patient sera. Envelope gene amplification was successful from patient sera with high virus titer, as was sequencing but with lower efficiency. Hence, based on our results, RDTs can be a source of DENV1 RNA for subsequent envelope gene amplification and sequencing. This is a promising tool for collecting molecular epidemiology data from rural dengue-endemic areas. However, further investigations are needed to improve assay efficiency and to assess this tool's level of efficacy on a larger scale in the field.

**Lu, Y., Sengvilaipaseuth, O., Chanthongthip, A., Phonemixay, O., Vongsouvath, M., Phouminh, P., Blacksell, S. D., Newton, P. N., Dubot-Pérès, A. (2019). "Comparison of Two Commercial ELISA Kits for the Detection of Anti-Dengue IgM for Routine Dengue Diagnosis in Laos." Trop Med Infect Dis 4(3): 111.** doi: 10.3390/tropicalmed4030111

***This study reports an evaluation of two commercially available ELISAs for the diagnosis of dengue, a leading cause of febrile illness in Laos***

The endemicity of Dengue virus (DENV) infection remains a major public health problem in Lao PDR. In this study, we compared two commercial anti-dengue IgM ELISA kits, Panbio((R)) Dengue IgM Capture ELISA (Panbio Kit, Alere, Waltham, MA, USA) and DEN Detect(TM) MAC-ELISA (InBios kit, InBios International, Inc., Seattle, WA, USA), in the context of diagnosis of patients admitted to hospital with clinical dengue presentation. Two panels of paired blood samples were tested. Panel A was composed of 54 dengue confirmed patients (by DENV real-time RT-PCR) and 11 non-dengue dengue patients (other infections confirmed by corresponding PCR results). Panel B included 74 patients randomly selected from consecutive patients admitted to Mahosot Hospital in 2008 with suspicion of dengue fever according to WHO criteria. Results from panel A showed significantly better sensitivity for Panbio kit (64.8%; 95%CI: 50.6-77.3%) than for InBios kit (18.5%; 95%CI: 9.3-31.4%) when testing admission sera. Sensitivity was increased for both kits when combining results from admission and convalescent sera. Concordant results were obtained from panel B with fair agreement (kappa = 0.29) between both kits when testing single admission samples, and moderate agreement (kappa = 0.5) when combining results from admission and convalescent sera.

**Nguyen, V. H., Russell, F. M., Dance D. A. B., Vilivong, K., Phommachan, S., Syladeth, C., Lai, J., Lim, R., Morpeth, M., Mayxay, M., Newton, P. N., De Lamballerie, X., Dubot-Pérès, A. (2019). "Nasal or throat sampling is adequate for the detection of the human**

**respiratory syncytial virus in children with acute respiratory infections." J Med Virol 91(9): 1602-1607.** doi: 10.1002/jmv.25496

*Nasopharyngeal aspirates or swabs are often used in young children to test for respiratory syncytial virus (RSV) if bronchiolitis is suspected. This study showed that nose and throat swabs provide similar results*

Human respiratory syncytial virus (HRSV) is one of the most important causes of acute respiratory infections (ARI) in young children. HRSV diagnosis is based on the detection of the virus in respiratory specimens. Nasopharyngeal swabbing is considered the preferred method of sampling, although there is limited evidence of the superiority of nasopharyngeal swabs (NPS) over the less invasive nasal (NS) and throat (TS) swabs for virus detection by real-time reverse transcription quantitative polymerase chain reaction (RT-qPCR). In the current study, we compared the three swabbing methods for the detection of HRSV by RT-qPCR in children hospitalized with ARI at Mahosot Hospital, Vientiane, Laos. In 2014, NS, NPS, and TS were collected from 288 children. All three samples were tested for HRSV by RT-qPCR; 141 patients were found positive for at least one sample. Almost perfect agreements (kappa > 0.8) between the swabs, compared two by two, were observed. Detection rates for the three swabs (between 93% and 95%) were not significantly different, regardless of the clinical presentation. Our findings suggest that the uncomfortable and technically more demanding NPS method is not mandatory for HRSV detection by RT-qPCR.

**Pastorino, B., Sengvilaipaseuth, O., Chanthongthip, A., Vongsouvath, M., Souksakhone, C., Mayxay, M., Thirion, L., Newton, P. N., de Lamballerie, X., Dubot-Pérès, A. (2019). "Low Zika Virus Seroprevalence in Vientiane, Laos, 2003-2015." Am J Trop Med Hyg 100(3): 639-642.** doi: 10.4269/ajtmh.18-0439

*Increased transmission of Zika virus (ZIKV), transmitted by mosquitos, was reported from the Americas from 2015 onwards and was associated with increased numbers of congenital malformations. This study of blood donors in Laos found low ZIKV seroprevalence*

Zika virus (ZIKV) has been presumed to be endemic in Southeast Asia (SEA), with a low rate of human infections. Although the first ZIKV evidence was obtained in the 1950s through serosurveys, the first laboratory-confirmed case was only detected in 2010 in Cambodia. The epidemiology of ZIKV in SEA remains uncertain because of the scarcity of available data. From 2016, subsequent to the large outbreaks in the Pacific and Latin America, several Asian countries started reporting increasing numbers of confirmed ZIKV patients, but no global epidemiological assessment is available to date. Here, with the aim of providing information on ZIKV circulation and population immunity, we conducted a seroprevalence study among blood donors in Vientiane, Laos. Sera from 359 asymptomatic consenting adult donors in 2003-2004 and 687 in 2015 were screened for anti-ZIKV IgG using NS1 ELISA assay (Euroimmun, Luebeck, Germany). Positive and equivocal samples were confirmed for anti-ZIKV-neutralizing antibodies by virus neutralization tests. Our findings suggest that ZIKV has

been circulating in Vientiane over at least the last decade. Zika virus seroprevalence observed in the studied blood donors was low, 4.5% in 2003-2004 with an increase in 2015 to 9.9% (P = 0.002), possibly reflecting the increase of ZIKV incident cases reported over this period. We did not observe any significant difference in seroprevalence according to gender. With a low herd immunity in the Vientiane population, ZIKV represents a risk for future large-scale outbreaks. Implementation of a nationwide ZIKV surveillance network and epidemiological studies throughout the country is needed.

**Pettersson, J. H.-O., Piorkowski, G., Mayxay, M., Rattanavong, S., Vongsouvath, M., Davong, V., Alfsnes, K., Eldholm, V., de Lamballerie, X., Holmes, E. C., Newton, P. N., Dubot-Pérès, A. (2019). "Meta-transcriptomic identification of hepatitis B virus in cerebrospinal fluid in patients with central nervous system disease." Diagn Microbiol Infect Dis 95(4): 114878.** doi: 10.1016/j.diagmicrobio.2019.114878

***This paper reports the identification of hepatitis B virus in cerebrospinal fluid in Lao patients, of uncertain clinical significance***

Determining the etiological basis of central nervous system (CNS) infections is inherently challenging, primarily due to the multi-etiological nature. Using RNA sequencing, we aimed to identify microbes present in cerebrospinal fluid (CSF) of two patients suffering CNS infection, previously diagnosed with *Cryptococcus* spp. and *Streptococcus pneumoniae* infection, respectively. After meta-transcriptomic analysis, and confirmation with real-time PCR, hepatitis B virus (HBV) was detected in the CSF of two patients diagnosed with CNS syndrome. Phylogenetic analysis of the partial HBV genomes from these patients showed that they belonged to genotypes B and C and clustered with other viruses of Asian origin. In countries with high levels of HBV endemicity, the virus is likely to be found in patients diagnosed with CNS infections, although whether it contributes to symptoms and pathology, or is simply a coincidental infection, is unknown and merits further investigation.

**Rudge, J. W., Inthalaphone, N., Pavlicek, R., Paboriboune, P., Flaissier, B., Monidarin, C., Steenkeste, N., Davong, V., Vongsouvath, M., Bonath, K. A., Messaoudi, M., Saadatian-Elahi, M., Newton, P., Endtz, H., Dance, D., Paranhos Baccala, G., Sanchez Picot, V. (2019). ""Epidemiology and aetiology of influenza-like illness among households in metropolitan Vientiane, Lao PDR": A prospective, community-based cohort study." PLoS One 14(4): e0214207**. doi: 10.1371/journal.pone.0214207

***This paper reports results of a cohort study in Vientiane which investigated episodes of acute respiratory illness in households over one year***

Respiratory diseases are a major contributor to morbidity and mortality in many tropical countries, including Lao PDR. However, little has been published regarding viral or bacterial pathogens that can contribute to influenza-like illness (ILI) in a community setting. We report on the results of a community-based surveillance that prospectively monitored the incidence

of ILI and its causative pathogens in Vientiane capital in Lao PDR. A cohort of 995 households, including 4885 study participants, were followed-up between May 2015 and May 2016. Nasopharyngeal swabs, throat swabs, and sputum specimens were collected from ILI cases identified through active case-finding. Real-Time PCR was used to test nasopharyngeal swabs for 21 respiratory pathogens, while throat and sputum samples were subjected to bacterial culture. Generalized linear mixed models were used to assess potential risk factors for associations with ILI. In total, 548 episodes of ILI were reported among 476 (9.7%) of the study participants and 330 (33.2%) of the study households. The adjusted estimated incidence of ILI within the study area was 10.7 (95%CI: 9.4-11.9) episodes per 100 person-years. ILI was significantly associated with age group ($p<0.001$), sex ($p<0.001$), and number of bedrooms ($p = 0.04$) in multivariate analysis. In 548 nasopharyngeal swabs, the most commonly detected potential pathogens were *Streptococcus pneumoniae* (17.0%), *Staphylococcus aureus* (11.3%), influenza A (11.1%; mostly subtype H3N2), rhinovirus (7.5%), and influenza B (8.0%). Streptococci were isolated from 42 (8.6%) of 536 throat swabs, most (27) of which were Lancefield Group G. Co-infections were observed in 132 (24.1%) of the 548 ILI episodes. Our study generated valuable data on respiratory disease burden and patterns of etiologies associated with community-acquired acute respiratory illness Laos. Establishment of a surveillance strategy in Laos to monitor trends in the epidemiology and burden of acute respiratory infections is required to minimize their impact on human health.

## SOCIAL SCIENCE

**Adhikari, B., Phommasone, K., Pongvongsa, T., Koummarasy, P., Soundala, X., Henriques, G., Sirithiranont, P., Parker, D. M., von Seidlein, L., White, N. J., Day, N. P. J., Dondorp, A. M., Newton, P. N., Cheah, P. Y., Pell, C., Mayxay, M. (2019). "Treatment-seeking behaviour for febrile illnesses and its implications for malaria control and elimination in Savannakhet Province, Lao PDR (Laos): a mixed method study." BMC Health Serv Res 19(1): 252.** doi: 10.1186/s12913-019-4070-9

***This qualitative study investigated health care utilisation behaviour of people experiencing febrile illnesses in Savannakhet, Southern Laos with implications for how malaria test-and treat services could be offered when aiming for malaria elimination from the country***

BACKGROUND: How people respond to febrile illness is critical to malaria prevention, control, and ultimately elimination. This article explores factors affecting treatment-seeking behaviour for febrile illnesses in a remote area of Lao PDR. METHODS: Household heads or their representatives (n = 281) were interviewed using a structured questionnaire. A total of twelve focus group discussions (FGDs) each with eight to ten participants were conducted in four villages. In addition, observations were recorded as field notes (n = 130) and were used to collect information on the local context, including the treatment seeking behaviour and the health services. RESULTS: Almost three-quarters (201/281) of respondents reported fever in

past two months. Most (92%, 185/201) sought treatment of which 80% (149/185) sought treatment at a health centre. Geographic proximity to a health centre (AOR = 6.5; CI = 1.74-24.25; for those < 3.5 km versus those > 3.6 km) and previous experience of attending a health centre (AOR = 4.7; CI = 1.2-19.1) were strong predictors of visiting a health centre for febrile symptoms. During FGDs, respondents described seeking treatment from traditional healers and at health centre for mild to moderate illnesses. Respondents also explained how if symptoms, including fever, were severe or persisted after receiving treatment elsewhere, they sought assistance at health centres. Access to local health centres/hospitals was often constrained by a lack of transportation and an ability to meet the direct and indirect costs of a visit. CONCLUSION: In Nong District, a rural area bordering Vietnam, people seek care from health centres offering allopathic medicine and from spiritual healers. Decisions about where and when to attend health care depended on their economic status, mobility (distance to the health centre, road conditions, availability of transport), symptoms severity and illness recognition. Current and future malaria control/elimination programmes could benefit from greater collaboration with the locally accessible sources of treatments, such as health volunteers and traditional healers.

**Haenssgen, M.J., Charoenboon, N., Zanello, G., Mayxay, M., Reed-Tsochas, F., Lubell, Y., Wertheim, H., Lienert, J., Xayavong, T., Khine Zaw, Y., Thepkhamkong, A., Sithongdeng, N., Khamsoukthavong, N., Phanthavong, C., Boualaiseng, S., Vongsavang, S., Wibunjak, K., Chai-In, P., Thavethanutthanawin, P., Althaus, T., Greer, R. C., Nedsuwan, S., Wangrangsimakul, T., Limmathurotsakul, D., Elliott, E., Ariana, P. (2019). "Antibiotic knowledge, attitudes and practices: new insights from cross-sectional rural health behaviour surveys in low-income and middle-income South-East Asia." BMJ Open 9(8): e028224.** doi: 10.1136/bmjopen-2018-028224

***This qualitative study investigated awareness of antibiotics and patterns of antibiotic use in Salavan in southern Laos***

INTRODUCTION: Low-income and middle-income countries (LMICs) are crucial in the global response to antimicrobial resistance (AMR), but diverse health systems, healthcare practices and cultural conceptions of medicine can complicate global education and awareness-raising campaigns. Social research can help understand LMIC contexts but remains under-represented in AMR research. OBJECTIVE: To (1) Describe antibiotic-related knowledge, attitudes and practices of the general population in two LMICs. (2) Assess the role of antibiotic-related knowledge and attitudes on antibiotic access from different types of healthcare providers. DESIGN: Observational study: cross-sectional rural health behaviour survey, representative of the population level. SETTING: General rural population in Chiang Rai (Thailand) and Salavan (Lao PDR), surveyed between November 2017 and May 2018. PARTICIPANTS: 2141 adult members (>/=18 years) of the general rural population, representing 712 000 villagers. OUTCOME MEASURES: Antibiotic-related knowledge, attitudes and practices across sites and healthcare access channels. FINDINGS: Villagers were

aware of antibiotics (Chiang Rai: 95.7%; Salavan: 86.4%; p<0.001) and drug resistance (Chiang Rai: 74.8%; Salavan: 62.5%; p<0.001), but the usage of technical concepts for antibiotics was dwarfed by local expressions like 'anti-inflammatory medicine' in Chiang Rai (87.6%; 95% CI 84.9% to 90.0%) and 'ampi' in Salavan (75.6%; 95% CI 71.4% to 79.4%). Multivariate linear regression suggested that attitudes against over-the-counter antibiotics were linked to 0.12 additional antibiotic use episodes from public healthcare providers in Chiang Rai (95% CI 0.01 to 0.23) and 0.53 in Salavan (95% CI 0.16 to 0.90). CONCLUSIONS: Locally specific conceptions and counterintuitive practices around antimicrobials can complicate AMR communication efforts and entail unforeseen consequences. Overcoming 'knowledge deficits' alone will therefore be insufficient for global AMR behaviour change. We call for an expansion of behavioural AMR strategies towards 'AMR-sensitive interventions' that address context-specific upstream drivers of antimicrobial use (eg, unemployment insurance) and complement education and awareness campaigns. TRIAL REGISTRATION NUMBER: Clinicaltrials.gov identifier NCT03241316.

**Pell, C. L., Adhikari, B., Myo Thwin, M., Kajeechiwa, L., Nosten, S., Nosten, F. H., Sahan, K. M., Smithuis, F. M., Nguyen, T. N., Hien, T. T., Tripura, R., Peto, T. J., Sanann, N., Nguon, C., Pongvongsa, T., Phommasone, K., Mayxay, M., Mukaka, M., Peerawaranun, P., Kaehler, N., Cheah, P. Y., Day, N. P. J., White, N. J., Dondorp, A.M., von Seidlein, L. (2019). "Community engagement, social context and coverage of mass anti-malarial administration: Comparative findings from multi-site research in the Greater Mekong sub-Region." PLoS One 14(3): e0214280.** doi: 10.1371/journal.pone.0214280

***This mixed-methods study explored factors determining coverage of mass drug administration for malaria in Laos and other countries in the Greater Mekong sub-Region***

BACKGROUND: Between 2013 and 2017, targeted malaria elimination (TME), a package of interventions that includes mass drug administration (MDA)-was piloted in communities with reservoirs of asymptomatic *P. falciparum* across the Greater Mekong sub-Region (GMS). Coverage in target communities is a key determinant of the effectiveness of MDA. Drawing on mixed methods research conducted alongside TME pilot studies, this article examines the impact of the community engagement, local social context and study design on MDA coverage. METHODS AND FINDINGS: Qualitative and quantitative data were collected using questionnaire-based surveys, semi-structured and in-depth interviews, focus group discussions, informal conversations, and observations of study activities. Over 1500 respondents were interviewed in Myanmar, Vietnam, Cambodia and Laos. Interview topics included attitudes to malaria and experiences of MDA. Overall coverage of mass anti-malarial administration was high, particularly participation in at least a single round (85%). Familiarity with and concern about malaria prompted participation in MDA; as did awareness of MDA and familiarity with the aim of eliminating malaria. Fear of adverse events and blood

draws discouraged people. Hence, community engagement activities sought to address these concerns but their impact was mediated by the trust relationships that study staff could engender in communities. In contexts of weak healthcare infrastructure and (cash) poverty, communities valued the study's ancillary care and the financial compensation. However, coverage did not necessarily decrease in the absence of cash compensation. Community dynamics, affected by politics, village conformity, and household decision-making also affected coverage. CONCLUSIONS: The experimental nature of TME presented particular challenges to achieving high coverage. Nonetheless, the findings reflect those from studies of MDA under implementation conditions and offer useful guidance for potential regional roll-out of MDA: it is key to understand target communities and provide appropriate information in tailored ways, using community engagement that engenders trust.

**Phommachanh, S., Essink, D. R., Wright, E. P., Broerse, J. E. W., Mayxay, M. (2019). "Do health care providers give sufficient information and good counseling during ante-natal care in Lao PDR?: an observational study." BMC Health Serv Res 19(1): 449**. doi: 10.1186/s12913-019-4258-z

***This qualitative study showed poor communication skills, behaviour and attitudes of antenatal healthcare providers in Laos and made recommendations for improvement***

BACKGROUND: It is increasingly recognized that improving the quality of maternal health care delivery is of utmost importance in many countries. In Laos, the quality of antenatal care (ANC) service remains inadequate, but it has never been assessed thoroughly. This study aims to determine the ANC quality at the urban and rural public health facilities in Laos and provides suggestions to improve health education and counseling in addition to other routine care in public ANC services. METHODS: This health-facility based, cross-sectional observation study included both health providers (n = 77) and pregnant women (n = 421) from purposively selected health facilities (n = 16). Information on the mothers' current pregnancies, previous visits and their last children was collected. The time spent for each ANC session as well as ANC services provided were recorded. Descriptive and inferential statistics were applied to analyze the data. RESULTS: Overall performance of ANC services by health care providers was poor in both urban and rural areas. Insufficient provision of information on danger signs during pregnancy, nutrition, breast feeding and iron supplements was revealed. Generally the communication skills, behavior and attitude of health providers were very poor. Less than a quarter of pregnant women were treated with kindness and respect. Only 4% of the observed ANC session took privacy into consideration. Less than 10% of available information materials were used during each ANC session. None of the health providers in both rural and urban areas performed specific counselling. Overall mean (SD) time-spent for each ANC session was 16.21 (4.28) minutes. A positive correlation was identified between the length of working experience of health providers and their physical performance scores (adjusted R square = 0.017). CONCLUSIONS: The overall performance of ANC services by health care providers was inadequate in both urban and rural areas.

Insufficient provision of health education and poor communication skills of health care providers were revealed. Existing IEC materials were scarcely used. Taking action to improve the quality of ANC services by training and providing specific guidelines, creating dedicated rooms, and providing sufficient and effective materials for counseling are all greatly needed in public health facilities in Laos.

## OTHER

**Adhikari, B., Hlaing, P. H., Robinson, M. T., Ruecker, A., Tan, N. H., Jatupornpimol, N., Chanviriyavuth, R., Cheah, P. Y. (2019). "Evaluation of the Pint of Science festival in Thailand." PLoS One 14(7): e0219983**. doi: 10.1371/journal.pone.0219983

***Public engagement with science is increasing. This paper describes introduction of an international public engagement activity to Thailand***

BACKGROUND: The Pint of Science festival is the biggest annual international science festival. In May 2017, we coordinated the first Pint of Science festival in Thailand and reported our initial reflections. Building on this work, we set out to evaluate more systematically events conducted in 2018. METHODS: In 2018, we conducted Pint of Science events at four different locations in Bangkok. Overall, there were 18 talks held over six event-days in 2018. We administered 180 self-reported questionnaires as well as conducted 11semi-structured interviews and a focus group discussion with audience members and speakers. RESULTS: Of the 180 questionnaires handed out, 125 attendees completed the questionnaire. The majority of attendees came because they were interested in science (68.0%), to learn something new (46.4%) and to enjoy themselves (44.8%). Our qualitative results confirm the quantitative findings. In addition, speakers viewed that they benefited by improving their communication skills and having the opportunity to network with scientists and non-scientists. Speakers also mentioned that such events were a good means to engage with the public, can improve the visibility of their work and potentially attract more funding. To improve the Pint of Science activities, audience members suggested to include a more diverse range of topics, more collaborations with other local research institutions and to hold the event at larger venues. CONCLUSIONS: We conclude that Pint of Science was well received in Bangkok with recommendations to improve minor issues related to practicalities and logistics.

**Bancone, G., Menard, D., Khim, N., Kim, S., Canier, L., Nguong, C., Phommasone, K., Mayxay, M., Dittrich, S., Vongsouvath, M., Fievet, N., Le Hesran, J. Y., Briand, V., Keomany, S., Newton, P. N., Gorsawun, G., Tardy, K., Chu, C. S., Rattanapalroj, O., Dong, L. T., Quang, H. H., Tam-Uyen, N., Thuy-Nhien, N., Hien, T. T., Kalnoky, M., Nosten, F. (2019). "Molecular characterization and mapping of glucose-6-phosphate dehydrogenase (G6PD)**

**mutations in the Greater Mekong Subregion." Malar J 18(1): 20.** doi: 10.1186/s12936-019-2652-y

***Glucose-6-phosphate-dehydrogenase is one of the most important human enzymopathies and is common in Laos, affecting more than 8% of survey participants in this study. This suggests that G6PD testing should be performed before administering oxidant drugs such as primaquine (recommended to eradicate P.vivax hypnozoites)***

BACKGROUND: *Plasmodium vivax* malaria elimination can only be achieved by the deployment of 8-aminoquinolines (primaquine and tafenoquine) in combination with ACT to kill both blood and liver-stage parasites. However, primaquine and the other 8-aminoquinolines cause dose-dependent haemolysis in subjects with G6PD deficiency, an X-linked disorder of red blood cells that is very common in populations living in tropical and subtropical areas. In order to inform safer use of 8-aminoquinolines in the Greater Mekong Subregion, a multi-centre study was carried out to assess the prevalence of G6PD deficiency and to identify the main G6PD variants in samples collected in Cambodia, Lao PDR, Myanmar, Thailand and Vietnam. METHODS: Blood samples were collected in the five countries during National Malaria Surveys or during Population Surveys. During Population Surveys samples were characterized for G6PD phenotype using the Fluorescent Spot Test. Samples were then genotyped for a panel of G6PD mutations. RESULTS: G6PD deficiency was found to be common in the region with an overall mean prevalence of deficient or mutated hemizygous males of 14.0%, ranging from a mean 7.3% in Thailand, 8.1% in Lao PDR, 8.9% in Vietnam, 15.8% in Myanmar and 18.8% in Cambodia. Mahidol and Viangchan mutations were the most common and widespread variants found among the nine investigated. CONCLUSIONS: Owing to the high prevalence of G6PD deficiency in the Greater Mekong Subregion, strategies for vivax malaria elimination should include point-of-care G6PD testing (both qualitative and quantitative) to allow safe and wide treatment with 8-aminoquinolines.

**Burns, R. J. L., Douangngeun, B., Theppangna, W., Mukaka, M., Wegner, M. D., Windsor, P. A., Blacksell S. D. (2019). "Peste des Petits Ruminants (PPR) virus serological surveillance in goats in Lao PDR: Issues for disease eradication in a low-resource disease-free setting." Transbound Emerg Dis 66(2): 939-947.** doi: 10.1111/tbed.13109.

***This study showed that the Lao goat population is highly likely to be naïve to Peste des Petits Ruminants (PPR) virus and therefore at risk of an outbreak***

Peste des Petits ruminants (PPR) is an economically important transboundary viral disease of goats. This study aimed to determine a baseline of serological evidence for Peste des petits ruminants virus (PPRV) in Lao goats. A total of 1,072 serum samples were collected by convenience sampling across five provinces in Laos and tested for antibody response to PPRV using a commercially available competitive ELISA. Positive antibody responses were found in 2.2% (95% CI 1.4, 3.2) of the samples. True prevalence calculations indicated a total overall sample prevalence of 1.7% (95% CI 0.9, 2.8). The highest provincial seroprevalences were

Xiangkhouang (3.5%, 95% CI 1.6, 6.9) and Xayaboury (2.9% (95% CI 1.3, 5.7). There was no association between antibody response and each of the following factors: location, breed, gender or age. Considering the apparent absence of disease manifestation of PPR in Laos, likely explanations for the antibody positivity could include cross reaction to other Morbilliviruses such as Measles or Canine Distemper, importation of pre-vaccinated goats, need for test cut-off re-evaluation to be region specific, or a subclinical and a less virulent circulating virus. This study highlights that the sampled Lao goat population is highly likely to be naïve to PPRV and therefore at risk of an outbreak, possibly by transboundary incursion of livestock from PPR endemic China. Further work is required in the testing of small ruminants in Laos that may eventually provide evidence for a status of freedom from disease, particularly in support of programs aimed at global PPR eradication.

**Chandna, A., White, L. J., Pongvongsa, T., Mayxay, M., Newton, P. N., Day, N. P. J., Lubell, Y. (2019). "Accounting for aetiology: can regional surveillance data alongside host biomarker-guided antibiotic therapy improve treatment of febrile illness in remote settings?" Wellcome Open Res 4: 1.** doi: 10.12688/wellcomeopenres.14976.2

***This mathematical modelling study simulated whether management of patients in Savannakhet could be improved by combining data on aetiology of febrile illness with biomarker results when choosing whether or not to prescribe antibiotics***

Background: Across Southeast Asia, declining malaria incidence poses a challenge for healthcare providers, in how best to manage the vast majority of patients with febrile illnesses who have a negative malaria test. In rural regions, where the majority of the population reside, empirical treatment guidelines derived from central urban hospitals are often of limited relevance. In these settings, relatively untrained health workers deliver care, often without any laboratory diagnostic support. In this paper, our aim was to model the impact on mortality from febrile illness of using point-of-care C-reactive protein testing to inform the decision to prescribe antibiotics and regional surveillance data to inform antibiotic selection, rooted in the real-world context of rural Savannakhet province, southern Laos. Methods: Our model simulates 100 scenarios with varying quarterly incidence of six key pathogens known to be prevalent in rural Laos. In the simulations, community health workers either prescribe antibiotics in-line with current practice as documented in health facilities in rural Laos, or with the aid of the two interventions. We provide cost-effectiveness estimates for each strategy alone and then for an integrated approach using both interventions. Results: We find that each strategy alone is predicted to be highly cost-effective, and that the combined approach is predicted to result in the biggest reduction in mortality (averting a predicted 510 deaths per year in rural Savannakhet, a 28% reduction compared to standard practice) and is highly cost-effective, with an incremental cost-effectiveness ratio of just $66 per disability-adjusted life year averted. Conclusions: Substantial seasonal variation in the predicted optimal empirical antibiotic treatment for febrile illness highlights the benefits of up-to-date information on regional causes of fever. In this modelling analysis, an integrated system

incorporating point-of-care host biomarker testing and regional surveillance data appears highly cost-effective, and may warrant piloting in a real-life setting.

**Holt, H. R., Inthavong, P., Blaszak, K., Keokamphe, C., Phongmany, A., Blacksell, S. D., Durr, P. A., Graham, K., Allen, J., Donnelly, B., Newberry, K., Grace, D., Alonso, S., Gilbert, J., Unger, F. (2019). "Production diseases in smallholder pig systems in rural Lao PDR." Prev Vet Med 162: 110-116.** doi: 10.1016/j.prevetmed.2018.11.012.

***This serological survey found that pigs in smallholder farming systems in Laos had variable antibody levels to common pig production diseases and that vaccination coverage for foot and mouth disease and Classical Swine Fever was low***

Pigs in Lao People's Democratic Republic are important for income and food security, particularly in rural households. The majority of pigs are reared in smallholder systems, which may challenge the implementation of any disease control strategies. To investigate risk factors for pig production diseases in such farming systems in the country a serological survey was conducted during 2011. A total of 647 pigs were sampled, accounting for 294 households in Luang Prabang and 353 in Savannakhet province representing upland and lowland, respectively. The results demonstrated that pigs in Lao PDR had antibodies against erysipelas (45.2%), CSF (11.2%), PRRS (8.6%), FMD O (17.2%) and FMD Asia 1, (3.5%). Differences in the housing systems influenced disease risk, for example, penned pigs had reduced odds of FMD and CSF, compared to those in scavenger systems. Pigs owned by farms using a sanaam (a communal area where pigs are kept for some time of the year) had 3.93 (95% confidence interval (CI): 1.09-14.7) times the odds of having pigs seropositive for FMD. Farms on which sudden piglet deaths had been experienced were more likely to have pigs seropositive for FMD O and erysipelas. These diseases constrain the development of village farming and the wider livestock industry due to their impact on productivity and trade. Vaccination coverage for FMD and CSF was low and there was a lack of national funding for livestock disease control at the time of the study. Further investigation into sustainable low-cost control strategies for these pathogens is warranted.

**Inglis, R., Ayebale, E., Schultz, M. J. (2019). "Optimizing respiratory management in resource-limited settings." Curr Opin Crit Care 25(1): 45-53.** doi: 10.1097/MCC.0000000000000568

***This paper reports on the high mortality associated with mechanical ventilation in critical care in some low-and middle- income countries and proposes alternative strategies to give respiratory support***

PURPOSE OF REVIEW: This review focuses on the emerging body of literature regarding the management of acute respiratory failure in low- and middle-income countries (LMICs). The aim is to abstract management principles that are of relevance across a variety of settings where resources are severely limited. RECENT FINDINGS: Mechanical ventilation is an

expensive intervention associated with considerable mortality and a high rate of iatrogenic complications in many LMICs. Recent case series report crude mortality rates for ventilated patients of between 36 and 72%. Measures to avert the need for invasive mechanical ventilation in LMICs are showing promise: bubble continuous positive airway pressure has been demonstrated to decrease mortality in children with acute respiratory failure and trials suggest that noninvasive ventilation can be conducted safely in settings where resources are low. SUMMARY: The management of patients with acute respiratory failure in LMICs should focus on avoiding intubation where possible, improving the safety of mechanical ventilation and expediting weaning. Future directions should involve the development and trialing of robust and context-appropriate respiratory support technology.

**Nakahara, S., Hoang, B. H., Mayxay, M., Pattanarattanamolee, R., Jayatilleke, A. U., Ichikawa, M., Sakamoto, T. (2019). "Development of an emergency medical system model for resource-constrained settings." Trop Med Int Health 24(10): 1140-1150.** doi: 10.1111/tmi.13301

***This Delphi survey proposed a comprehensive emergency care system model, which could provide a basis to evaluate emergency care systems in resource-constrained LMICs***

OBJECTIVES: An emergency care system is an important aspect for healthcare organisations in low- and middle-income countries (LMICs) with a growing burden from emergency disease conditions. Evaluations of emergency care systems in LMICs in broader contexts are lacking. Thus, this study aimed to develop a comprehensive emergency medical system model appropriate for resource-constrained settings, based on expert opinions. METHODS: We used the Delphi method, in which questionnaire surveys were administered three times to an expert panel (both emergency medical care providers and healthcare service researchers), from which opinions on the model's components were compiled. The panel members were mostly from Asian countries. In the first round, the questionnaire drew a list of model components developed through a literature review; the panel members then proposed new components to create a more comprehensive list. In the second and third rounds, the panel members rated the listed components to achieve consensus, as well as to remove components with low ratings. Finally, we rearranged the list to improve its usability. RESULTS: In total, 32 experts from 12 countries participated. The final model totalled 177 components, categorised into 8 domains (leadership, community-based actions, emergency medical services, upward referral, definitive care, rehabilitation, downward referral, and evaluation and research). No components needed removal. CONCLUSIONS: We developed a comprehensive emergency care system model, which could provide a basis to evaluate emergency care systems in resource-constrained LMICs; however, field-testing and validation of this system model remain to be done.

**Phommachanh, S., Essink, D. R., Jansen, M., Broerse, J. E. W., Wright, P., Mayxay, M. (2019). "Improvement of Quality of Antenatal Care (ANC) Service Provision at the**

**Public Health Facilities in Lao PDR: Perspective and Experiences of Supply and Demand Sides." BMC Pregnancy Childbirth 19(1): 255.** doi: 10.1186/s12884-019-2345-0

***This qualitative study of different stakeholder groups involved in antenatal care service provision in Laos identified challenges to providing high quality ANC care and proposed solutions to improve the quality of care***

BACKGROUND: The maternal mortality rate in Lao PDR (Laos) is still the highest in Southeast Asia, at 197 per 100,000 live births. Antenatal care (ANC) could contribute to maternal and child mortality reduction. The quality of ANC service remains inadequate and little information is available on the quality of health education and counseling services of health providers in Laos. This study aims to gain insight into the perceptions of stakeholders on both supply and demand sides of public ANC services in Laos and evidence for recommendations to improve the quality of ANC services. METHODS: Semi-structured interviews were conducted with 50 participants from different stakeholder groups; on the demand side, couples with a currently pregnant woman and mothers with children under one year of age and a family member; and on the supply side, health providers, managers, policy makers of the Ministry of Health, and development partners. The interviews were voice recorded and transcribed verbatim for analysis by open and thematic coding, using the MAXQDA software program. RESULTS: All respondents reported that the number of pregnant women who visit ANC services has increased. However, an analysis of the supply side identified issues related to the quality of ANC that need to be improved in the areas of facilities, human resources, privacy and confidentiality, providers' behavior, attitudes, and ineffective communication skills when it comes to providing health education and counseling to pregnant women and their family members. The analysis of the demand side mainly emphasized the issues of providers' behavior, attitude, communication and unequal treatment, and the lack of privacy. Both sides also suggested solutions to the problems, such as training, effective materials, rewarding good role models, and building a feedback system. CONCLUSION: The number of public ANC services has increased, but both supply and demand sides experienced challenges with the quality of ANC. All respondents proposed possible solutions to improve quality of ANC service in public health facilities in Laos.

**Pruvot, M., Khammavong, K., Milavong, P., Philavong, C., Reinharz, D., Mayxay, M., Rattanavong, S., Horwood, P., Dussart, P., Douangngeun, B., Theppangna, W., Fine, A. E., Olson, S. H., Robinson, M., Newton, P. (2019). "Toward a quantification of risks at the nexus of conservation and health: The case of bushmeat markets in Lao PDR." Sci Total Environ 676: 732-745**. doi: 10.1016/j.scitotenv.2019.04.266

***The bushmeat trade in Laos poses risks to human health. This qualitative study of wildlife consumers and vendors gathered information in order to better understand these risks and proposed a conceptual model for disease transmission risk analysis***

Trade of bushmeat and other wildlife for human consumption presents a unique set of challenges to policy-makers who are confronted with multiple trade-offs between conservation, food security, food safety, culture and tradition. In the face of these complex issues, risk assessments supported by quantitative information would facilitate evidence-based decision making. We propose a conceptual model for disease transmission risk analysis, inclusive of these multiple other facets. To quantify several processes included in this conceptual model we conducted questionnaire surveys with wildlife consumers and vendors in semi-urban centers in Lao People's Democratic Republic (Lao PDR, Laos) and direct observations of consumer behaviors. Direct observation of market stalls indicated an estimated average of 10kg bushmeat biomass per stall per hour. The socio-demographic data suggested that consumption of bushmeat in urban areas was not for subsistence but rather driven by dietary preference and tradition. Consumer behavioral observations indicated that each animal receives an average of 7 contacts per hour. We provide other key parameters to estimate the risk of disease transmission from bushmeat consumption and illustrate their use in assessing the total public health and socio-economic impact of bushmeat consumption. Pursuing integrative approaches to the study of bushmeat consumption is essential to develop effective and balanced policies that support conservation, public health, and rural development goals.

## CONFERENCE AND MEETING PRESENTATIONS

**AAAS Annual Meeting, Washington, D.C., USA. 14-17th Feb 2019.**

Newton, P. N., Caillet, C., Roberts, T., Ashley, E. A. AMR & Medicine Quality - Ecology of Pathogen-Antimicrobial High Risk Pairs & Antimicrobial Quality. (Oral Presentation).

**National Symposium on Melioidosis, Kaohsiung, Taiwan. March 2019.**

Dance, D. A. B. Melioidosis and the Clinical Microbiology Laboratory. (Invited Oral Presentation).

**Consortium of Universities for Global Health Conference, Chicago, USA. March 2019.**

Chan, J., Nguyen, C. D., Lai, J. Y. R., Dunne, E. M., Blyth, C., Datta, S., Fox, K., Ford, R., Hinds, J., La Vincente, S., Lehmann, D., Lim, R., Mungun, T., Nation, M., Newton, P. N., Phetsouvanh, R., Pomat, W., Xeuatvongsa, A., von Mollendorf, C., Dance, D. A. B., Satzke, C., Mulholland, E. K., Russell, F. M. Determining the Pneumococcal Conjugate Vaccine Coverage Required for Indirect Protection within Asia and the Pacific. (Oral Presentation).

**29th European Congress of Clinical Microbiology and Infectious Diseases (ECCMID), Amsterdam, The Netherlands. April 2019.**

Karatuna, O., Dance, D., Matuschek, E., Åhman, J., Turner, P., Hopkins, J., Amornchai, P., Wuthiekanun, V., Cusack, T.-P., Baird, R., Norton, R., Armstrong, M., Zange, S., Zoeller, L., Wahab, T., Jacob, D., Grunow, R., Kahlmeter, G. Multi-centre Study to Establish MIC and Zone Diameter Epidemiological Cut-off (ECOFF) Values for *Burkholderia pseudomallei*. (Poster).

**Greater Mekong SubRegion Antimicrobial Resistance Meeting, Yangon, Myanmar. May 2019**

Chansamouth, V. Antimicrobial resistance (AMR) in Laos. (Oral presentation).

**The UK Hepacivirus and Flavivirus Meeting, Cumbria, U.K. 17-18 May 2019.**

Bharucha, T., Gangadharan, B., Kumar, A., de Lamballerie, X., Newton, P., Dubot-Pérès, A., Zitzmann, N. Protein biomarkers for detection of Japanese encephalitis virus infection. (Oral Presentation).

**29th HUPO Human Brain Proteome Project meeting, Amsterdam, The Netherlands. 27-28 May 2019.**

Bharucha, T., Gangadharan, B., Kumar, A., de Lamballerie, X., Newton, P., Dubot-Pérès, A., Zitzmann, N. Cerebrospinal fluid biomarkers for Japanese encephalitis virus infection. (Oral Presentation).

**8th Annual Global Health Bioethics Network (GHBN) Summer School, Vientiane, Laos. 19-23 August 2019.**

Robinson, M.T. Pandora's Pets: The ethics of bushmeat research. (Invited Oral Presentation).

**Oxford Tropical Network Conference, Oxford, U.K. 8-11 September 2019.**

Ashley, E. Priorities for tackling antimicrobial resistance in low-and middle-income countries. (Poster).

Caillet, C. Portable screening devices to assess medicines quality. (Oral Presentation).

Chansamouth, V. Antimicrobial susceptibility patterns of organisms causing bacteraemia and hospital antimicrobial prescriptions in rural Laos. (Poster).

Elliott, I. The clinical epidemiology of scrub typhus. (Oral Presentation).

Dubot-Pérès, A. Using rapid diagnostic tests as a source of viral RNA for combined surveillance of dengue, Zika and chikungunya viruses. (Poster).

Mayxay, M., Ashley, E. A., Newton, P. N., Teerawattananon, Y., Chalkidou, K., White, L., Lubell, Y., Cheah, P. Y., Day, N., White, N. J. The founding of a "Lao NICE" to facilitate translation of evidence into policy and implementation. (Oral Presentation).

Newton, P. Mapping the quality of essential medical products to inform strategy and policy change. (Oral Presentation).

Panapruksachat, S., Pruvot, M., Khammavong, K., Milavong, P., Fine, A. E., Newton, P. N., Robinson, M. T. Detection of *Mycobacterium* spp. in squirrels: a source of clinical infection? (Oral Presentation).

Phommasone, K. 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. (Oral Presentation).

Rattanavong, S. Bacteremia caused by extended spectrum beta-lactamase-producing Enterobacteriaceae in Vientiane, Lao PDR: a 5-year study. (Poster).

Roberts, T., Rattanavong, S., Niehus, R., Davong, V., Vongsouvath, M., Chansamouth, V., Mayxay, M., Dance, D., Newton, P. N., Cooper, B.S. Extended spectrum beta-lactamases in Laos: a spatiotemporal analysis. (Poster).

Roberts, T., Rattanavong, S., Phommasone, K., Chansamouth, V., Davong, V., Hongsakhone, S., Bounsavath, N., Keoluangkhot, V., Mayxay, M., Vongsouvath, M., Dance, D. A. B., Newton, P. N. The burden of typhoid in Laos. (Rapid Oral Presentation).

Robinson, M. Detection of *Mycobacterium* spp. in squirrels: a source of clinical infection? (Rapid Oral Presentation).

Sengduangphachanh, A., Jaksuwan, R., Roberts, T., Phoumin, P., Vongsouvath, M., Davong, V., Rattanavong, S., Dance D. A. B., Cusack, T.-P. Impact of CLSI and EUCAST breakpoint discrepancies on reporting of antimicrobial susceptibility and AMR surveillance. (Poster).

Thongpaseuth, S., Rattanavong, S., Dittrich, S., Moore, C., Sihalath, S., Roberts, T., Dance, D. A. B., Dubot-Pérès, A., Maxay, M., Vongsouvath, M., Newton, P. N., Robinson, M. T. *Cryptococcus* identification and typing at Mahosot Hospital, Vientiane, Lao PDR; 2000-2019. (Poster).

Vongsouvath, M., Bharucha, T., Seephonelee, M., de Lamballerie, X., Newton, P. N., Dubot-Pérès, A. Using rapid diagnostic tests as a source of viral RNA for combined surveillance of dengue, Zika and chikungunya viruses. (Poster).

Watthanaworawit, W., Ling, C., Limmathurotsakul, D., Robinson, M.T., Roberts, T., Hopkins, J., Turner, P., Wuthiekanun, V., Nosten, F. Rapid identification of *Burkholderia pseudomallei* using matrix assisted laser desorption/ionization time-of-flight mass spectrometry (MALDI-TOF MS). (Poster).

# PUBLICATIONS & CONFERENCE ABSTRACTS

Delegates at the Oxford Tropical Network Meeting, September 2019

**'One Health Perspectives on Infection and Immunity', Chiang Mai, Thailand. October 2019.**

Dance, D. A. B. Global epidemiology of infectious diseases and antimicrobial resistance. (Invited Oral Presentation).

**13th National Health Research Forum 2019, Vientiane, Lao P.D.R. 15th-17th October 2019.**

Chansamouth, V. Hospital Antimicrobial Prescription in Laos. (Poster).

Iwagami, M., Khattignavong, P., Mayxay, M., Brey, P. T., Kano, S. Development of new clinical research beyond the SATREPS Project. (Oral Presentation).

Ter, S. K., Rattanavong, S., Roberts, T., Vongsouvath, M., Newton, P. N., Simpson, A., Ashley, E., Robinson, M.T. Detection of pathogens in negative blood culture in Lao People's Democratic Republic. (Poster Presentation).

**9th World Melioidosis Congress (WMC 2019), Hanoi, Vietnam. 15-18 October 2019.**

# PUBLICATIONS & CONFERENCE ABSTRACTS

Birnie, E., Virk, H. S., Savelkoel, J., Spijker, R., Bertherat, E., Dance, D. A. B., Limmathurotsakul, D., Devleesschauwer, B., Haagsma, J. A., Wiersinga, W. J. Global burden of melioidosis in 2015: a systematic review and data synthesis. Programme & Abstract Book, Page 56. (Oral Presentation).

Burtnick, M. N., Dance, D. A. B., Vongsouvath, M., Newton, P. N., Davong, V., Kenna, D., Saiprom, N., Wuthiekanun, V., Limmathurotsakul, D, AuCoin, D. P. , Chantratita, N., Brett, P. J. Identification of *Burkholderia cepacia* strains that express a *Burkholderia pseudomallei*-like capsular polysaccharide.. Programme & Abstract Book, Page 44. (Oral Presentation).

Dance, D. A. B. Whitmore and Krishnaswami Revisited (History Session). Programme & Abstract Book, Page 53. (Oral Presentation).

Green, H. R., Chung, C. C., Sorenson, J. T., Hau, D., Hannah, E. E., DeMers, H. L., Pandit, S. G., Thorkildson, P. N., Gates-Hollingsworth, M. A., Burtnick, M. N., Woods, K., Luangraj, M., Boutthasavong, L., Davong, V., Dance, D. A. B., AuCoin, D. P.  Quantification of capsular polysaccharide in melioidosis samples and the enhancement of the Active Melioidosis *Detect*™ lateral flow assay. Programme & Abstract Book, Page 152. (Poster).

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**The International Research Forum on Sciences, Technology and Innovation for Sustainable Development, National University of Laos, Vientiane, Lao P.D.R. 5-6th November 2019.**

Mayxay, M. Research in health sector in the Lao PDR: How far are we now? (Oral Presentation).

**The First Annual Scientific Conference of the Lao Infectious Disease Society (LIDS), Vientiane, Lao P.D.R. 7 – 8th November 2019.**

Chansamouth, V. Antimicrobial resistance (AMR) in Laos and Hospital Antimicrobial Prescription in Laos. (Oral Presentation).

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Newton, P. N. Update on diagnosis and treatment of rickettsial infection. (Oral Presentation).

**1st International Research Forum on Leishmaniasis, Bangkok, Thailand. 13-14 November 2019.**

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**68th Annual Meeting of the American Society of Tropical Medicine & Hygiene (ASTMH), National Harbor, MD, USA. 20 - 24 November 2019.**

Garcia, J. A., Chansamouth, V., Robinson, M. T., Newton, P. N. Expanded fever surveillance among provincial hospitals in the Lao People's Democratic Republic. Abstract Book, Page 34, Abstract 109. (Poster).

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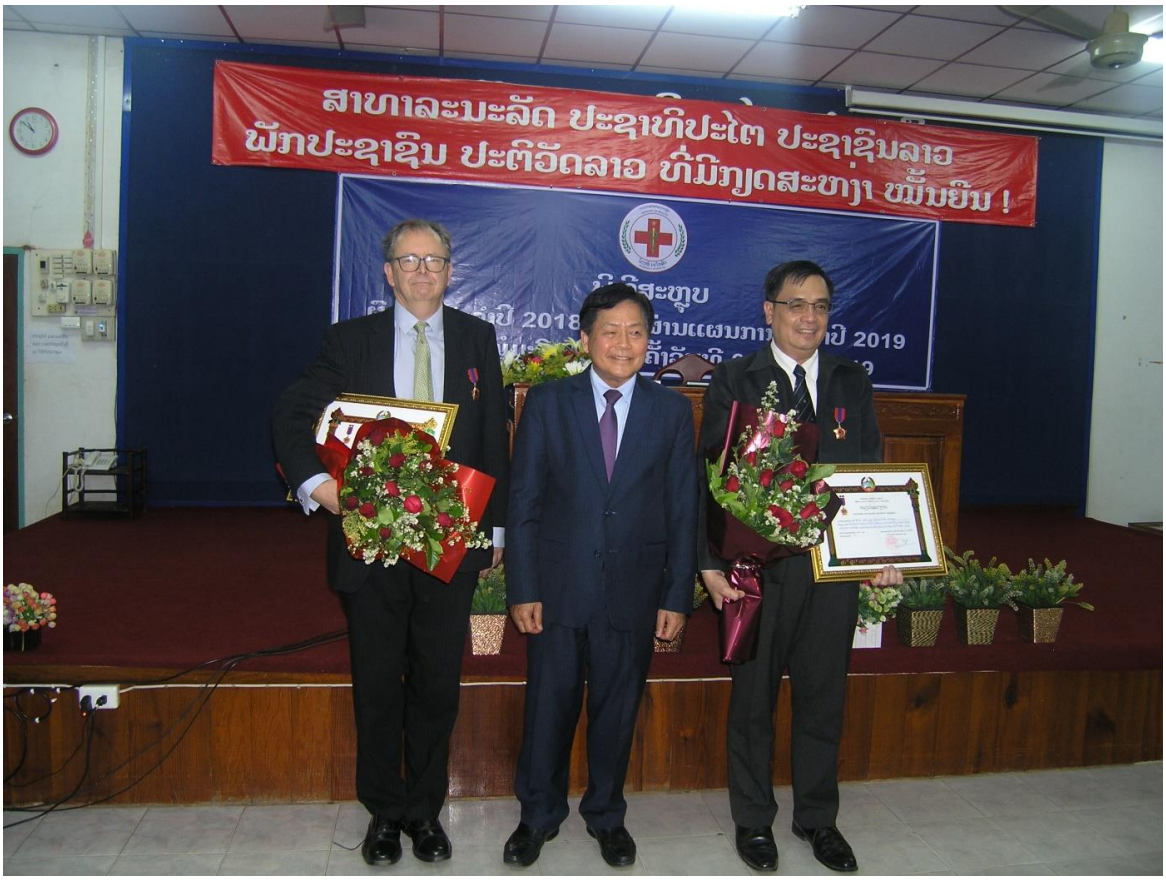
# PUBLICATIONS & CONFERENCE ABSTRACTS




**His Excellency Minister of Health, Professor Bounkong Syhavong (centre) with Professor Paul Newton (left) and Professor Mayfong Mayxay (right) at the Medal of Labour presentation ceremony.**

# Other Activities in 2019

## 8TH ANNUAL GLOBAL HEALTH BIOETHICS NETWORK SUMMER SCHOOL

LOMWRU and MORU co-hosted the 8th Annual Global Health Bioethics Network Summer School in August 2019 at the Lao Plaza Hotel in Vientiane. This annual event provides a friendly, informal environment in which people at the Wellcome Major Overseas Programmes (MOPs) in Kenya, Malawi, South Africa, Thailand-Laos, Vietnam, at the Ethox Centre in the UK and at the Wellcome Trust Brighton and Sussex Centre for Global Health Research, can meet to share ideas, experiences and expertise about ethics and community engagement, learn more about these important areas of practice in low income settings, and develop ideas for future research projects.

## 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.

### Dengue engagement activites in schools during the 2019 epidemic

In response to the dengue outbreak in Laos in 2019 LOMWRU organized some public engagement events in schools in Vientiane to raise awareness about the disease and how to prevent it. Shown here is Dr Vatthanaphone Latthaphasavang from Mahosot Hospital with Dr Phetsavanh Chanthavilay in the background at Sinxay school on 19th July 2019. Approximately 160 students from grade 6 to 12 participated to the event.

# OTHER ACTIVITIES

### What's in your medicines?

On Tues 22 Oct, the art exhibition *What's in your medicines?* (Pharmacide Arts) was relaunched at the Institut Français du Laos in Vientiane, before moving to the University of Health Sciences, having originally toured Southeast Asia in 2012. Featuring the work of 12 artists from Cambodia, Indonesia, Laos, Thailand, and Vietnam, and prepared by the LOMWRU Medicine Quality team, *What's in your medicines* uses art to discuss the problems caused by poor quality (substandard) and fake (falsified) medicines. Dr Bounxou Keohavong Deputy Director General of the Food and Drug Department, opened the exhibition at the Institut Français du Laos in Vientiane and stressed the importance of raising awareness about poor quality medicines. Dr Mayfong Mayxay opened the exhibition at the University of Health Sciences. The exhibitions were funded by a Wellcome Trust Provision for Public Engagement, supported by MORU in Bangkok, Thailand.

## LAO MEDICAL JOURNAL

LOMWRU continues to support publication of the *Lao Medical Journal*. The latest issue was published in April 2019 and includes a diverse number of articles e.g. health impacts of pesticide use in Lao farmers, neonatal sepsis and job satisfaction of nurses working in the Emergency Department of Mahosot Hospital.

## LAO HEALTH WORKERS' DAY CONFERENCE

LOMWRU was pleased to support a scientific conference to mark Lao Health Workers' Day, organized by Professor Mayfong Mayxay and held at the University of Health Sciences on July 5th, 2019.

## ACPR CONFERENCE

The 2nd Asia Pacific Rickettsia Conference was held in Chiang Rai, Thailand in November, 2019. Dr Matthew Robinson (LOMWRU) was part of the Organizing and Scientific Committees of the conference, which was hosted by MORU. Attended by over 150 researchers from more than 20 countries the conference was a great success. Several LOMWRU staff attended, and presentations were given by Professor Paul Newton, Dr Matthew Robinson, Dr Ivo Elliot, Dr Weerawat Phuklia, Mr Vanheuang Phommadeechack, Dr Tamalee Roberts and Dr Siribun Panapruksachat.

## ASTMH SYMPOSIUM: SCRUB TYPHUS, A GLOBAL BUT NEGLECTED DISEASE

Dr Matthew Robinson (LOMWRU) organized a symposium at the American Society of Tropical Medicine and Hygiene annual meeting in National Harbor, USA in November. Although rickettsias are already recognized as the most common treatable cause of febrile illness in rural Southeast Asia, we still know relatively little about them, and this symposium brought

researchers from across the globe to discuss scrub typhus. Dr Weerawat Phuklia was one of the invited speakers, and discussed his work on antimicrobial resistance of *O. tsutsugamushi*.

### RICKETTSIA THREAT REDUCTION NETWORK

LOMWRU continues to be an active member of 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.

### MELIOIDOSIS THREAT REDUCTION NETWORK

LOMWRU staff also contribute to the Melioidosis Threat Reduction Network, 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.

# THANK YOU TO OUR FUNDERS

## Project funders in 2019

We would like to thank all of our funders for their very generous support of projects in 2019

# CONTACT INFORMATION

## Contact Information

If you have any questions about this report please email LOMWRUinfo@tropmedres.ac


**Group photograph of some of the participants at the MORU Tropical Health Network 40th Anniversary celebrations, 2019, Khao Yai, Thailand**