Punchana, 23 de diciembre del 2025

Oficio N°3835 -2025–GRL–GRS–L /30.50

M.C.

DULIO FUENTES
DIRECTOR DE INVESTIGACIÓN E INNOVACIÓN EN SALUD DEL INSTITUTO NACIONAL DE SALUD

Presente

ASUNTO **INFORME FINAL DE ACTIVIDADES, FICHA 48 – 2025 - FORTALECIMIENTO DE LAS ACCIONES DE FOMENTO DE LA INVESTIGACIÓN EN SALUD**

ATENCIÓN **SUB DIRECCIÓN DE INVESTIGACIÓN – SUDIV-INS**

****

Tengo el agrado de dirigirme a usted, para saludarle cordialmente y al mismo tiempo informarle que en el marco de cumplimiento del compromiso de mejora establecido en el **DS N° 022-2024-SA, Ficha N° 48 "Fortalecimiento de las acciones de fomento de la investigación en salud"**, se remite a su despacho el Informe final de actividades, que incluye el **ANEXO 01, 02, 03 y 04**, del Hospital Regional de Loreto 2025, enviados electrónicamente a la REDcap:

https://redcap.ins.gob.pe/surveys/?s=L7XTLTC94M4CP3HA

La misma que se publicará en la Web Institucional del Hospital Regional de Loreto, http://www.hrloreto.gob.pe.

Sin otro particular, me suscribo de usted no sin antes reiterarle las muestras de mi consideración y estima personal.

Atentamente,

Gerencia Regional de Salud Loreto
Hospital Regional de Loreto
"Felipe Arriola Iglesias"
Dr. Jehoshua Rafael López López
C.M.P: 59534
DIRECTOR GENERAL

Cc.
Archivo
JRMLL/RCHH/ HAC/flori

Punchana, 23 de diciembre del 2025

Oficio N°3836-2025–GRL–GRS–L /30.50

GOBIERNO REGIONAL DE LORETO
GERENCIA REGIONAL DE SALUD LORETO
TRAMITE DOCUMENTARIO
23 DIC 2025
Exp. N°: 18831
Folios: Hora:
Fecha: Firma:

Señor

M.C. Guillermo ANGULO AREVALO
Gerente Regional de Salud de Loreto

Presente

ASUNTO **INFORME FINAL DE ACTIVIDADES, FICHA 48 – 2025 - FORTALECIMIENTO DE LAS ACCIONES DE FOMENTO DE LA INVESTIGACIÓN EN SALUD**

ATENCIÓN **ÁREA DE INVESTIGACIÓN EN SALUD - GERESA**

****

Tengo el agrado de dirigirme a usted, para saludarle cordialmente y al mismo tiempo informarle que en el marco de cumplimiento del compromiso de mejora establecido en el **DS N° 022-2024-SA, Ficha N° 48 "Fortalecimiento de las acciones de fomento de la investigación en salud"**, se remite a su despacho el Informe final de actividades, que incluye el **ANEXO 01, 02, 03 y 04**, del Hospital Regional de Loreto 2025, enviados electrónicamente a la REDcap:

https://redcap.ins.gob.pe/surveys/?s=L7XTLTC94M4CP3HA

La misma que se publicará en la Web Institucional del Hospital Regional de Loreto, http://www.hrloreto.gob.pe.

Así mismo, solicitarle por su intermedio hacer llegar este documento a la sub dirección de investigación – SUDIV – de la Dirección de Investigación e Innovación en Salud del INS.

Sin otro particular, me suscribo de usted no sin antes reiterarle las muestras de mi consideración y estima personal.

Atentamente,

Gerencia Regional de Salud Loreto
Hospital Regional de Loreto
"Felipe Arriola Iglesias"
Dr. Jehoshua Rafael López López
CMP: 50534
DIRECTOR GENERAL

Gerencia Regional de Salud - Loreto
Hospital Regional de Loreto
Dirección General

Cc.
Archivo
JRMLL/RCHH/ HAC/fion

Punchana, 23 de diciembre del 2025

HOSPITAL REGIONAL DE LORETO
MESA DE PARTES
RECIBIDO
15 DIC 2025
FIRMA HORA N° EXP

OFICIO N° 246 -2025–GRL–GRS–L /30.50.06

Señor

M.C. Jehoshua Rafael Michelangelo LOPEZ LOPEZ
Director General del Hospital Regional de Loreto

Presente

ASUNTO **INFORME FINAL DE ACTIVIDADES, FICHA 48 – 2025 - FORTALECIMIENTO DE LAS ACCIONES DE FOMENTO DE LA INVESTIGACIÓN EN SALUD**

****

Tengo el agrado de dirigirme a usted, para saludarle cordialmente y al mismo tiempo informarle que en el marco de cumplimiento del compromiso de mejora establecido en el **DS N° 022-2024-SA, Ficha N° 48 "Fortalecimiento de las acciones de fomento de la investigación en salud"**, se remite a su despacho el Informe final de actividades, que incluye el **ANEXO 01, 02, 03 y 04**, del Hospital Regional de Loreto 2025, enviados electrónicamente a la REDcap:

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La misma que se publicará en la Web Institucional del Hospital Regional de Loreto, http://www.hrloreto.gob.pe.

Sin otro particular, me suscribo de usted no sin antes reiterarle las muestras de mi consideración y estima personal.

Atentamente,

GERENCIA REGIONAL DE SALUD-LORETO
HOSPITAL REGIONAL DE LORETO
"FELIPE ARRIOLA IGLESIAS"
Dra. HAYDEE ALVARADO CORA
Jefa de la Oficina de Gestión de la Calidad
C.E.P. 17203

Cc.
Archivo
HAC

ANEXO 01

INFORME CUMPLIMIENTO DE ACTIVIDADES

ANEXO 01: Informe Cumplimiento Actividades (1-2 páginas máximo)

- **Antecedentes**

  El conocimiento generado a partir de la investigación científica debe ser gestionado de forma eficiente por aquellos que lo administran, producen, así como por quienes lo exigen, garantizando que entre otras cosas que el cumplimiento de las metas sea el adecuado. El sistema de gestión de la investigación, requiere de un proceso de control en el cumplimiento de los plazos y entregables en los diferentes procesos a través de los cuales pasa la revisión de una investigación.

  En ese sentido el Hospital Regional de Loreto, con categoría de atención III-1, responsable de satisfacer las necesidades de la población de su ámbito referencial, con atención integral ambulatoria y hospitalaria altamente especializada, con énfasis en la recuperación y rehabilitación de problemas de salud, a través de unidades productoras de servicios de salud medico quirúrgicos de alta complejidad.
  Cuenta con una Oficina de Apoyo a la Docencia e Investigación, así como la conformación de sus comités, siendo uno de ellos en Comité de Investigación, la misma que cuenta con un plan de trabajo que incluye actividades de monitoreo continuo y visitas a los proyectos de investigación en ejecución.
  Dentro del marco de sus funciones consolida y propone a la Dirección, a través de la Oficina de Apoyo a la Docencia e Investigación, la autorización de las investigaciones que se llevan a cabo en el Hospital Regional de Loreto, manteniendo un registro de las mismas, en el marco de la política y normas sectoriales vigentes.

  Los procesos de presentación y revisión de los protocolos de investigación son continuos y permanentes, debiendo cumplirse los requisitos administrativos y técnicos, así como, también las normadas por el comité Institucional de Investigación (Comité de Evaluación Metodológica) y el Comité Institucional de Ética en Investigación, aprobados con RD.

- **Resumen de logros y dificultades para el cumplimiento de cada indicador**

  (protocolos, publicaciones)

  Logros

  La Unidad de Investigación, cuenta con un plan de actividades aprobado.
  Cuenta con un comité institucional de investigación y un comité institucional de ética en investigación.

Se coordinan y se realizan reuniones de revisión de protocolos de investigación mínimo dos veces al mes.
Se trata de crear una cultura de respeto a los derechos humanos de las personas en las investigaciones científicas en proceso.
Las entidades públicas y privadas solicitan constancias del comité institucional de ética CIEI HRL para el desarrollo de sus investigaciones.
Se cuenta con profesionales investigadores quienes gestionan su publicación en revistas indizadas.

Dificultades
La disponibilidad de RRHH, en la unidad de investigación es muy limitado, por lo que el sistema de monitoreo y control de las investigaciones no llega al 100% de los protocolos en ejecución y aquellos en publicación.

Avances
En el primer semestre del 2025, se otorgaron 57 constancias del comité de ética, 15 de ellos fueron extra institucional.
En el segundo semestre 2025, se otorgaron 72 constancias del comité de ética, 16 fueron extra institucional.
La Unidad de Investigación, cuenta con dos comités: Comité Institucional de Investigación y Comité Institucional de Ética en la Investigación, conformados con RD.
Existe muy buena disposición de la Dirección del Hospital Regional de Loreto para fortalecer la Oficina de Apoyo a la Docencia e Investigación.

Conclusiones
La Oficina de Apoyo a la Docencia e Investigación, forma parte de la estructura orgánica del Hospital Regional de Loreto, por lo tanto, es una fortaleza, con el apoyo de los integrantes de los comités se gestiona todo el proceso de la investigación científica.

Si bien el Hospital Regional de Loreto, tiene muchas carencias existe la motivación para seguir adelante.

Recomendaciones
Fortalecer capacidades del personal que dirige la Unidad de Investigación y de los miembros de los comités, que dan el respaldo a la unidad.

Establecer coordinación muy estrecha con las diferentes áreas del INS, para conducir adecuadamente las actividades de investigación en el Hospital Regional de Loreto.

ANEXO 02

LISTA DE PROTOCOLOS APROBADOS EN EL 2025

#	Título de Protocolo	Autor (investigador principal)	Co-autores	Tipo de Estudio (Pregrado*, Posgrado, Institucional, Colaborativo)	Diseño de Estudio: Análisis de Datos Secundarios, Estudios Primarios, Ensayo Clinico, Revisiones Sistemáticas, Reportes de Casos, Otro)	Es un protocolo de innovación? Si/No	Fondos (Autofinanciado, Institucional, Otros-especificar)	Nombre el Comité de Etica que aprobó el protocolo	Código Comité (ejem: RCEI-8)	Constancia/ Certificado de CEI	Fecha de Aprobación	Código del Protocolo (si aplica)	Departamento / Área / Servicio donde se va desarrollar
1	OROPUCHE VIRUS IN LORETO,PERU-CLINIC AL CHARACTERISRICAS AND PCR POSITIVITY TIMING: A CASE SERIES	EDGAR ANTONIO RAMIREZ GARCIA		POST-GRADO	REPORTE DE CASOS	SI	AUTOFINANCIADO	C.I.E.I.	C.E.I.-HRL	001-CIEI-HRL-2025	1/6/2025		INFECTOLOGIA
2	PRUEBA DE NUEVOS DISPOSITIVOS PARA ENFERMEDADES FEBRILES	ISABEL BAZAN ARISTA		EXTRA-INSTITUCIONAL	REPORTE DE CASOS	SI	SI	C.I.E.I.	C.E.I.-HRL	002-CIEI-HRL-2025	1/6/2025		INFECTOLOGIA
3	FACTORES ASOCIADOS A MACROSOMIA FETAL EN DOS HOSPITALES DE LA CIUDAD DE IQUITOS 2022-2023	DANISSA JAHIMAR FLORES DIAZ. JOSE LUIS BARCIA PEZO		PRE-GRADO	OTROS	SI	SI	C.I.E.I.	C.E.I.-HRL	003-CIEI-HRL-2025	1/23/2025		DPTO DE GINECOLOGIA
4	CARACTERISTICAS ASOCIADAS A MORTALIDAD POR NEUMONIA EXTRA HOSPITALARIA EN ADULTOS MAYORES HOSPITAL REGION AL DE LORETO 2022-2026	TAMARA SOLANGE VILLENA RENGIFO		PRE-GRADO	OTROS	SI	SI	C.I.E.I.	C.E.I.-HRL	004-CIEI-HRL-2025	1/23/2025		DPTO DE ESTADISTICA
5	KT/V UREA Y MORTALIDAD EN PACIENRES EN HEMODIALISIS DEL HOSPITAL REGIONAL DE LORETO 2023-2024	MILAGROS FLORES VELA		PRE-GRADO	OTROS	SI	SI	C.I.E.I.	C.E.I.-HRL	005-CIEI-HRL-2025	1/23/2025		DPTO. ESTADISTICA
6	FACTORES DE RIESGO MATERNOS ASOCIADOS A MUERTE FETAL INTRAUTERINA EN UN HOSPITAL MINSA DE LA PROVINCIA MAYNAS 2021 AL 2023	PAOLA ALEXANDRA ARMAS ZAMORA		PRE-GRADO	OTROS	SI	SI	C.I.E.I.	C.E.I.-HRL	006-CIEI-HRL-2025	2/3/2025		DPTO. ESTADISTICA
7	FACTORES DE RIESGO ASOCIADOS A REACCIONES ADVERSOS A MEDICAMENTOS Y SUBNOTIFICACION EN PACIENTES DE ESTRATEGIAS SANITARIAS EN EL HOSPITAL REGIONAL DE LORETO 2025	JACQUELINE MARGOT GONZALES DIAZ DE MORA		POST-GRADO	OTROS	SI	SI	C.I.E.I.	C.E.I.-HRL	007-CIEI-HRL-2025	03/02/20254		DPTO. ESTADISTICA
8	FACTORES ASOCIADOISA TRANSTORNOS MUSCULOESQUELETICOS EN PERSONAL ADMINISTRATIVOS DE UN HOSPITAL DE IQUITOS 2024	LAURA CAMILA RUIZ SALDAÑA - DIANA NICOLE AREVALO FLORES		PRE-GRADO	OTROS	SI	SI	C.I.E.I.	C.E.I.-HRL	008-CIEI-HRL-2025	2/12/2025		OFC. ADMINISTRATIVAS
9	DIVERSIDAD GENETICA EN LAS COMUNIDADES MATSES Y UROS: FUNDAMENTOS PARA UNA MEDICINA GENOMICA EQUITATIVA EN EL PERU	HEINNER GUIO		EXTRA-INSTITUCIONAL	REPORTE DE CASOS	SI	SI	C.I.E.I.	C.E.I.-HRL	009-CIEI-HRL-2025	2/19/2025		HOSPITAL REGIONAL DE LORETO
10	SEGUIMIENTO FARMACOTERAPEUTICO A PACIENTES ONCOLOGICOS AMBULATORIOS QUE RECIBEN QUIMIOTERAPIA EN UN HOSPITAL DE IQUITOS PERIODO AGOSTO-DICIEMBRE 2024	IVONNE NAVARRO DEL AGUILA		POST-GRADO	OTROS	SI	SI	C.I.E.I.	C.E.I.-HRL	010-CIEI-HRL-2025	2/25/2025		ONCOLOGIA
11	FACTORES CONDICIONANTES EN LA ETAPA PRENATAL PARA EL DESARROLLO DEL TRANSTORNO DEL ESPACIO AUTISTA	JOSE MARIA HERRERA ROSAS		EXTRA-INSTITUCIONAL	REPORTE DE CASOS	SI	SI	C.I.E.I.	C.E.I.-HRL	011-CIEI-HRL-2025	3/4/2025		EE.UU(FLORIDA) IQUITOS
12	DESCIFRANDO LA ARQUITECTURA GENETICA DE LAS ENFERMEDADES AUTOINMUNES EN POBLACIONES INDIGENAS DEL PERU	WILFREDO MARTIN CASAPIA MORALES		EXTRA-INSTITUCIONAL	REPORTE DE CASOS	SI	SI	C.I.E.I.	C E.I.-HRL	012-CIEI-HRL-2025	3/4/2025		LIMA-IQUITOS-SAN MARTIN-PIURA
13	FACOPRES DE RIESGO ASOCIADOS A PARTO PRETERMINO EN PRIMIGESTA HOSPITAL REGIONAL DE LORETO ENERO 2021 A DICIEMBRE 2022	JENNY CORINA VARELA RODRIGUEZ-CINDY LIZETH TORRES MESIA		POST-GRADO	OTROS	SI	SI	C.I.E.I.	C.E.I.-HRL	013-CIEI-HRL-2025	3/17/2025		
14	CARACTERISTICAS CLINICAS Y EPIDEMIOLOGICAS DE HIDROCEFALIA EN PACIENTES DE UN HOSPITAL II-1 DE LA AMAZONIA PERUANA 2025	WILLIAN JUNIOR LOEZ ISUIZA		PRE-GRADO	REPORTE DE CASOS	SI	SI	C.I.E.I.	C.E.I.-HRL	014-CIEI-HRL-2025	19/032025		DPTTO ESTADISTICA
15	DESARROLLANDO Y MEJORANDO ESTRATEGIAS PARA LA PREVENCION DEL CANCER DE CUELLO UTERINO EN EL PERU	VALERIE PAZ SOLDAN		EXTRA-INSTITUCIONAL	REPORTE DE CASOS	SI	SI	C.I.E.I.	C.E.I.-HRL	015-CIEI-HRL-2025	3/20/2025		HRL-HAI-CERITSS
16	MEJORANDO LA IDENTIFICACION DEL TRANSTORNO NEUROCOGNITIVO ASOCIADO A VIH (TNAV) EN LATINOAMERICA EN ENFOQUE MULTIMODAL EN PERU	MONICCA MARIA DIAZ-CESAR RAMAL ASAYAG-MARTIN CASAPIA MORALES	ADRIAN ZEGARRA VALDIVIA-SHEILA CASTRO SUAREZ-NOELIA RAFFO MORON	EXTRA-INSTITUCIONAL	REPORTE DE CASOS	SI	SI	C.I.E.I.	C.E.I.-HRL	016-CIEI-HRL-2025	3/27/2024		HOSPITAL CAYETANO HEREEDIA/CENTRO SALUD LAURA CALLER-HOSPITAL REGIONAL DE LORETO
17	EVALUACION DE DOS TECNICAS DIAGNOSTICAS PARA LA DETECCION DE HIPLASMOSIS EN UNA REGION CON ELEVADO RIESGO DE ADQUISISICION	JUAN CARLOS CELIS SALINAS-EDGAR ANTONIO RAMIREZ GARCIA-WILFREDO MARTIN CASAPIA MORALES		EXTRA-INSTITUCIONAL	REPORTE DE CASOS	SI	SI	C.I.E.I.	C.E.I.-HRL	017-CIEI-HRL-2025	4/3/2025		INFECTOLOGIA
18	ANALISIS GENOMICO DE BACTERIAS KAPEc RESISTENTES A ANTIBIOTICOS DE DIFERENTES REGIONES DE PERU PARA ELUCIDAR RUTAS DE TRANSMISION MEDIANTE EL ENFOQUE ONE HEALTH	LUCIANO AUGUSTO PALOMINO KOBAYASHI	RUTH HORTENSIA GARCIA DE LA GUARDA-MARIA JESUS PONS CASELLAS	EXTRA-INSTITUCIONAL	REPORTE DE CASOS	SI	SI	C.I.E.I.	C.E.I.-HRL	018-CIEI-HRL-2025	4/7/2025		HOSPITALES MINSA
19	INTERVENCION EDUCATIVA NUTRICIONAL EN HABITOS ALIMENTARIOS INDICADORES ANTROPOMETRICOS Y RIESGO DE PRECLAMPSIA EN GESTANTES DEL HOSPITAL REGIONAL DE LORETO, IQUITOS 2025	GILMA VIRGINIA MORI PROKOPUIK-CYNDI ELAYNE SILVA MESTANZA		POST-GRADO	OTROS	SI	SI	C.I.E.I.	C.E.I.-HRL	019-CIEI-HRL-2025	4/9/2025		DPTO. GINECO OBSTETRICIA
20	RECOLECCION DE MUESTRAS CLINICAS DE ENFERMEDADES TROPICALES E INFECCIOSAS, ENFERMEDADES AUTOINMUNE Y DONANTES SANOS,VERSION 3.5 FECHA 26/02/2024 PROTOCOLO: CRSPTL-00001(bb-ID-061)	JUAN CARLOS HINOJOSA BOYER		EXTRA-INSTITUCIONAL	REPORTE DE CASOS	SI	SI	C.I.E.I.	C.E.I.-HRL	020-CIEI-HRL-2025	4/8/2025		ASOCIACION CIVIL SELVA AMAZONICA
21	COLECCION DE MUESTRAS CLINICAS VOLUNTARIOS PEDIATRICOS SALUDABLES VERSION 2.0-PROTOCOLO CRSPTL-00072	JUAN CARLOS HINOJOSA BOYER		EXTRA-INSTITUCIONAL	REPORTE DE CASOS	SI	SI	C.I.E.I.	C.E.I.-HRL	021-CIEI-HRL-2025	4/8/2025		ASOCIACION CIVIL SELVA AMAZONICA
22	COLECCION DE MUESTRAS CLINICAS VOLUNTARIOS PEDIATRICOS SALUDABLES VERSION 2.0	JUAN CARLOS HINOJOSA BOYER		EXTRA-INSTITUCIONAL	REPORTE DE CASOS	SI	SI	C.I.E.I.	C.E.I.-HRL	022-CIEI-HRL-2025	4/8/2025		ASOCIACION CIVIL SELVA AMAZONICA
23	COLECCION DE MUESTRAS CLINICAS VOLUNTARIOS PEDIATRICOS SALUDABLES VERSION 2.0-PROTOCOLO CRSPTL-00072	JUAN CARLOS HINOJOSA BOYER		EXTRA-INSTITUCIONAL	REPORTE DE CASOS	SI	SI	C.I.E.I.	C.E.I.-HRL	023-CIEI-HRL-2025	4/8/2025		ASOCIACION CIVIL SELVA AMAZONICA
24	RECOLECCION DE MUESTRAS CLINICAS DE ENFERMEDADES TROPICALES E INFECCIOSAS, ENFERMEDADES AUTOINMUNE Y DONANTES SANOS,VERSION 3.5 FECHA 26/02/2024 PROTOCOLO: CRSPTL-00001(bb-ID-061)	JUAN CARLOS HINOJOSA BOYER		EXTRA-INSTITUCIONAL	REPORTE DE CASOS	SI	SI	C.I.E.I.	C.E.I.-HRL	0024-CIEI-HRL-2025	4/8/2025		ASOCIACION CIVIL SELVA AMAZONICA
25	RELACION ENTRE LA ESCALA DIAGNOSTICA DE MORENO Y EL DIAGNOSTICO CLINICO DE NEUMONIA EN PACIENTES PEDIATRICOS HOSPITALIZADOS,LORETO 2024	LUCIA FERNANDA SARITA RODRIGUEZ RIVERA		PRE-GRADO	OTROS	SI	SI	C.I.E.I.	C.E.I.-HRL	025-CIEI-HRL-2025	4/15/2025		DPTO-ESTADISTICA-RECOJO DE INFORMACION
26	MODELO DEL SISTEMA DE CONTROL INTERNO PARA GESTION DE INVENTARIOS DE MEDICAMENTOS EN EL HOSPITAL REGIONAL DE LORETO 2025	ENZO JOSE MANUEL SIFUENTES OLIVEIRA-ANTHONY MARTION MARQUEZ CALVO		POST-GRADO	REPORTE DE CASOS	SI	SI	C.I.E.I.	C.E.I.-HRL	026-CIEI-HRL-2025	4/15/2025		DPTO. DE FARMACIA
27	ESTUDIO COMPARATIVO SOBRE EL PAPEL DE LOS PROFESIONALES DE ATENCION PRIMARIA DE SALUD EN BRASIL,ANGOLA,ARGENTINA,CHILE,COLOMBIA,GUINEA -B ISSAU-MEXICO, PERU,MOZOMBIQUE Y PORTUGAL, EN LA PREVENCION DE LA DESINFORMACION EN SALUD.	MARITZA EVANGELINA VILLANUEVA BENITES	RUTH VICHEZ RAMIREZ-GRESY CURICO HUANSI-ELBA FLORES TORRES-JESUS J.MAGALLANES CASTILLA-HAYDEE ALV ARADO CORA-PATRICIA PINCHEZ TORRES-ROXANA CARDOZO GONZALES-ANA VALERIA MACHADO MENDONCA	EXTRA-INSTITUCIONAL	REPORTE DE CASOS	SI	SI	C.I.E.I.	C.E.I.-HRL	027-CIEI-HRL-2025	4/28/2025		UNAP-UNIVERSIDAD DE BRASSILIA-UNIVERSIDAD DE GOIANA BRASIL-GERESA LORETO

16

28	EFECTOS ADVERSOS DE FARMACOS ANTITUBERCULOSOS EN EL PROGRAMA DE CONTROL DE TUBERCULOSIS-PROVINCIA DE MAYNAS, ABRIL-JUNIO, 2025	JORGE IGNACIO CARRASCO CELI	ANGULO QUINTANILLA RITA JACKRLIN-CABANILLAS TUIRO ISAIS JOSUE-CENEPO YAHUARCANI ABNER-CHACAYAN VELA MATHIAS DAVIS-CHILCO MACEDO ALFRED	PRE-GRADO	OTROS	SI	SI	C.I.E.I.	C.E.I.-HRL	028-CIEI-HRL-2025	4/28/2025		UN IOVERSIDAD NACIONAL DE LA AMAZONIA PERUANA
29	EVALUACION DE LA RESPUESTA TEMPRANA A UNA SOLA DOSIS DE ARTESUNATO INTRAVENOSO EN MALARIA GRAVE, UN ESTUDIO PROSPECTIVOS UN ENTORNO CON RECYRSOS LIMITADOS	LIVIA BRESCIANE		EXTRA-INSTITUCIONAL	REPORTE DE CASOS	SI	SI	C.I.E.I.	C.E.I.-HRL	029-CIEI-HRL-2025	5/12/2025		UNIVERSIDAD LA SAPIENZA DE ROMA
30	EVALUACION RETROSPECTIVA DEL ACLARAMIENTO DE PARASITEMIA TRAS UNA DOSIS UNICA DE AFRTESUZANTO INTRAVENOSO PARA MLARIA GREAVE :EVALUACION DEL POTENCIAL DE TRANSICION TEMPRANA A TRATAMIENTO OREAL EN CONTEXTOS CON RECURSOS LIMITADOS	LIVIA BRESCIANE		EXTRA-INSTITUCIONAL	REPORTE DE CASOS	SI	SI	C.I.E.I.	C.E.I.-HRL	030-CIEI-HRL-2025	5/12/2025		UNIVERSIDAD LA SAPIENZA DE ROMA
31	USO DE ANTIBIOTICO EN PACIENTES CON COVID 19 INTERNADOS EN LA PRIMERA OLA EN ELÑ HOSPITAL REGIONAL DE LORETO 2020	GUILLERMO MAXCIMILIANO DONAYRE VASQUEZ		POST-GRADO	OTROS	SI	SI	C.I.E.I.	C.E.I.-HRL	031-CIEI-HRL-2025	5/12/2025		DPTO.ESTADISTICA
32	MEDIDAS ANTROPOMETRICAS DE DIAGNOSTICO DE OBESIDAD Y SU APROXIMACION CON LA BIA EN ESTUDIANTES DEL CUARTO AÑO DE MEDICINA DE UNA UNIVERSIDAD PUBLICA DE LORETO	BARBARA ISABEL RODRIGUEZ	RAMIREZ GONZALES FERNANDO BALTAZAR-RIOS ALAVA YOKI NUR-PEREZ PINEDO TEDDY- ROMERO LOPOEZ CHASKA ARIADNA-HUCOBA PEZO CLAUDIA CAROLINA	PRE-GRADO	OTROS	SI	SI	C.I.E.I.	C.E.I.-HRL	032-CIEI-HRL-2025	5/12/2025		UNAP
33	SALUD MENTAL Y ADHERENCIA AL TRATAMIENTO DE HEMODIALISIS EN PACIENTES DEL HOSPITAL REGIONASL DE LORETO, 2025	ADRIANA GERALDINE FLORES VILLAVERDE	CONDORI VILCA JEYDY SOLYBEL, UBALDO RENGIFO CARLOS HILDEBRANDO- VAQUEZ ALVARADO SAIRA FERNANDA-ZORILLA DE LA CRUZ DAENE	PRE-GRADO	OTROS	SI	SI	C.I.E.I.	C.E.I.-HRL	033-CIEI-HRL-2025	5/15/2025		UNAP
34	PREVALENCIA DEL USO NO PRESCRITO DE ANSIOLITICOS EN INTERNOS DEL AREA DE LA SALUD HOSPITAL REGIONAL DE LORETO 2025	ANGELES GUERRA FLORES	BANIO GUEVATRA NATHALY GERALDINE-CCAPCHA QUISPE IDANIA VICTORIA-MORI AGUILAR JESSY MADELEINE	PRE-GRADO	REPORTE DE CASOS	SI	SI	C.I.E.I.	C.E.I.-HRL	034-CIEI-HRL-2025	5/15/2025		UNAP
35	FACTORES DE RIESGO PARA MALA ADHERENCIA AL TRATAMIENTO FARMACOLOGICO DE HIPERTENSION ARTERIAL EN PACIENTES ATENDIDOS EN CONSULTORIO DE CARDIOLOGIA DEL HOSPITAL REGIONAL DE LORETO ENTGRE ABRIL A JULIO 2025	LEYDI KARINA NUÑEZ CIEZA	CHACON MAYURI PERCY FABRIZIO-HUANCAPAZA ROJAS SHEILA MARYORI-RUIZ RUIZ DAVID MARTIN	PRE-GRADO	OTROS	SI	SI	C.I.E.I.	C.E.I.-HRL	035-CIEI-HRL-2025	5/15/2025		CONSULTORIO DE CARDIOLOGIA-HOSPITAL REGIONAL DE LORETO
36	NIVEL DE CONOCIMIENTOS EN DIAGNOSTICOS Y TRATAMIENTO DEL DENGUE EN MEDICOS GENERALES DEL SERVICIO DE EMERGENCIA DE LOS HOSPITALES DEL MINSA DE IQUITOS LORETO 2025	ARANA RAMIREZ AMY	GASTELU YALTA ALISSA GALIANA-IÑAPE DONAYRE JOSE SEBASTIAN-MONDRAGON RIOSS DEMI BARESSI-VASQUEZ QUIROZ PATRICK	PRE-GRADO	OTROS	SI	SI	C.I.E.I.	C.E.I.-HRL	036-CIEI-HRL-2025	5/15/2025		SERVICIODE EMERGENCIA DEL HOSPITAL REGIONAL DE LORETO- MINSA
37	FACTORES SOCIODEMOGRAFICOS Y USO DE ANTI BIOTICOS EN LOS CUIDADORES DE PACIENTES PEDIATRICOS EN LOS ESTABLECIMIENTO DE SALUD DE IQUITOS 2025	ANA MILAGROS MANTILLA RENGIFO		PRE-GRADO	OTROS	SI	SI	C.I.E.I.	C.E.I.-HRL	037-CIEI-HRL-2025	5/15/2025		DPTO ENFERMERIA-CONSULTPORIO EXTERNO DE PEDIATRIA
38	CONOCIMIENTOS SOBRE DIABETES MELLITUS TIPO 2 Y ADHERENCIA AL TRATAMIENTO EN PACIENTES DEL HOSPITAL REGIONAL DE LORETO MAYO -JUNIO 2025	SOTO DEL CASTILLO VALERIA	VALDIVIA RUIZ ENZO FABIO MIGUEL ORBE SATALAY KEVIN DAVID	PRE-GRADO	OTROS	SI	SI	C.I.E.I.	C.E.I.-HRL	038CIEI-HRL-2025	5/15/2025		CONSULTORIO DE ENDOCRINOLOGIA HOSPITAL REGIONAL DE LORETO
39	USO DE ANALGESICOS EN PACIENTES ONCOLOGICOS DEL HOSPITAL REGIONAL DE LORETO EN EL PRIMER TRIMESTRE, IQUITOS 2025	BRAVO CUBAS ELMER PEPE	DIAZ RODRIGUEZ CATHERINE ALEXA- MARIN VASQUEZ MELITA NATALY- RAMIREZ SAAVEDRA ISIS GEARELLY-TUESTA ALVARADO ANA MARIA ADELEINE	PRE-GRADO	OTROS	SI	SI	C.I.E.I.	C.E.I.-HRL	039-CIEI-HRL-2025	5/15/2025		DPTO. ESTADISTICA
40	RELACION ENTRE EL PORTCENTAJE DE GRASA CORPORAL Y EL INDICE DE MASA CORPORAL EN LA EVALUACION SOBREPESO Y OBESIDAD EN ADULTOS ATENDIDOS EN EL HOSPITAL REGIONAL REGIONAL 2025	JUAN DIEGO AGUSTIN VASQUEZ		PRE-GRADO	OTROS	SI	SI	C.I.E.I.	C.E I.-HRL	040-CIEI-HRL-2025	5/20/2025		DPTO ENFERMERIA-CONSULTORIO DE MEDICINA
41	CARACTERISTICAS CLINICAS Y EPIDEMIOLOGICAS DE LA EPIDEMIA DE VIRUS OROPOUCHE EN LA REGION LORETO, PERU	MIGUEL ANGEL ROJO PEREZ	JARA LLENAS-GARCIA-EDGAR RAMIREZ-JOSE MANUEL RAMOS	EXTRA-INSTITUCIONAL	REPORTE DE CASOS	SI	SI	C.I.E.I.	C.E.I.-HRL	041-CIEI-HRL-2025	8/21/2025		REGION LORET-PERU
42	CARACTERISTICAS CLINICAS Y GRADO DE DISCAPACIDAD EN PACIENTES CON DOLOR LUMBAR CRONICO EN CONSULTORIO DE NEUROCIRUGIA DEL HOSPITAL REGIONAL DE LORETO ABRIL - MAYO 2025	CESAR ALEXANDER MORALES GUZMAN		PRE-GRADO	OTROS	SI	SI	C.I.E.I.	C.E.I.-HRL	042-CIEI-HRL-2025	5/22/2025		CONSULTORIO DE NEUROICIRUGIA-HOSPITAL REGIONAL DE LORETO
43	ASOCIACION DEL NIVEL DE AUTOCUIADDO Y LAA CALIDAD DE VIDA EN PACIENTES EN HEMIDIALISIS DEL HOSPITAL EGIONAL DE LORETO 2025	SIXTO JUNIOR FLORES OLANO		PRE-GRADO	OTROS	SI	SI	C.I.E.I.	C.E.I.-HRL	043-CIEI-HRL-2025	5/22/2025		SERVICIO DE HEMODIALIS-
44	INFLUENCIA DE LOS RASGOS DE PERSONALIAD EN LA ADHERENCIA AL TRATAMIENTO DE PACIENTES CON DIABETES MELLITUS TIPO 2 EN UN HOSPITAL PUBLICO DE IQUITOS,2025	MILAGROS IDROGO HERRERA		PRE-GRADO	OTROS	SI	SI	C.I.E.I.	C.E.I.-HRL	044-CIEI-HRL-2025	5/22/2025		SERVICIO DE EMERGENCIA-HOSPITAL REGIONAL DE LORETO
45	NIVEL DE SATISFACCIO DEL USUARIO EN LOS CONSULTORIO EXTERNOS DEL SERVICIO DE GINECOLOGIA Y OBSTERICIA DEL HOSPITAL REGIONJAL DE LORETO MAYO-JULIO 2025	DIAZ RAMIREZ DALIA BRIGITTE	FLORES DAVILA PIERO FRABCESCO- MESONES RAMIREZ LUIS VICENTE - SANDOVAL REATEGUI MILAGROS ISABEL-SIFUENTES VIDIGAL SAMAR SARAI-VARELA MEZA ELIANA ESPERANZA-VELARDE MERA MIGUEL ANGEL	PRE-GRADO	OTROS	SI	SI	C.I.E.I.	C.E.I.-HRL	045-CIEI-HRL-2025	5/23/2025		CONSULTORIO DE GINEGOLOGIA
46	FACTORES ASOCIADOS A HIPEREMESIS GRAVIDICA EN PACIENTES DEL HOSPITAL REGIONAL DE LORETO DEL 2022-2025	PEDRO ALEJANDRO LADERA URPAY		PRE-GRADO	OTROS	SI	SI	C.I.E.I.	C.E.I.-HRL	046-CIEI-HRL-2025	5/23/2025		DPTO DE ESTADISTICA
47	VARIACION DEL VOLUMEN INTRAVENTRICULAR CON 3D SLICER Y COMPLICACIONES EN PACIENTES PEDIATRICOS POSTOPERADOS POR HIDROCEFALIA EN LORETO 2023-20258	ANDREA VFALENTINA MURRIETA RUIZ		PRE-GRADO	OTROS	SI	SI	C.I.E.I.	C.E.I.-HRL	047-CIEI-HRL-2025	28/05/205		DPTO DE ESTADISTICA
48	CALIDAD DE SUEÑO Y CONTROL GLUCEMICO EN PACIENTES DIABETICOS DE UN HOSPITAL DEL TERCER NIVEL EN LA AMAZONIA PERUANA 2025	ABDUL JHAREY SUNCION CALDERON		PRE-GRADO	OTROS	SI	SI	C.I.E.I.	C.E.I.-HRL	048-CIEI-HRL-2025	5/28/2025		CONSULTORIO DE ENDOCRINOLOGIA HOSPITAL REGIONAL DE LORETO
49	ESTUDIO OBSERVACIONAL DE SEPSIS EN IQUITOS-PERU	CAROLINA GUEVARA		EXTRA-INSTITUCIONAL	REPORTE DE CASOS	SI	SI	C.I.E.I.	C.E.I.-HRL	049-CIEI-HRL-2025	5/29/2025		REGION LORETO 2025
50	CALIDAD DE ATENCION DEL SERVICIO DE NUTRICION Y SATISFACCION DEL PERSONAL ASISTENCIAL DEL HOSPITAL REGIONAL DE LORETO,IQUITOS,	GLADIS CHAVARRI TELLO		POST-GRADO	OTROS	SI	SI	C.I.E.I.	C.E.I.-HRL	050-CIEI-HRL-2025	6/10/2025		SERVICIO DE NUTRICION Y DIETETICA DEL HOSPITAL REGIONAL DE LORETO
51	ASOCIACION ENTRE EL RETRAZO DEL INTERVALO DIAGNOSTICO Y ESTADIOS AVANZADOS DEL CANCER DE MAMA EN PACIENTES ATENDIDAS EN EL HOSPITAL REGIONAL DE LORETO,2018-2025	THAYA CATACORA VALENCIA		POST-GRADO	OTROS	SI	SI	C.I.E.I.	C.E.I.-HRL	051-CIEI-HRL-2025	6/10/2025		DPTO.ONCOLOGIA-DPTO.DE PATOLOGIA CLINICA-DPTO ESTADISTICA
52	COMPLICACIONES MATERNAS Y NEONATALES POR EL VIRUS DEL DENGUE EN GESTANTES DEL HOSPITAL REGIONAL DE LORETO"FELIPE SANTIAGO ARRIOLA IGLESIAS" ENERO-DICIEMBRE 2023-2024	ANGULO PINEDO ESTHEFANY NICOLE-TAPIA MURO GRISELDA FABIANA		PRE-GRADO	OTROS	SI	SI	C.I.E.I.	C.E.I.-HRL	052-CIEI-HRL-2025	6/11/2025		DPTO ESTADISTICA

53	ASOCIACION DE HEMOGLOBINA GLICOSILADA E HIGADO GRASO NO ALCOHOLICO EN PACIENTES CON DIABETES MELLITUS TIPO 2 ATENDIDOS EN EL HOSPITAL REGIONAL DE LORETO DURANTE ENERO A DICIEMBRE DEL 2024	ARBILDO LOZAN WHENDI DANAE	COLLI ALAVARDO ANGELO EDUARDO-HUAMAN MAGALLANES ALBERT SEGUNDO-GARCIA PAIMA ANLLELO PIERO-GILABERT DAVILA ALISON SOLANG-VARGAS DEL CASTILLO SERGIO DANIEL	PRE-GRADO	OTROS	SI	SI	C.I.E.I.	C.E.I.-HRL	053-CIEI-HRL-2025	6/12/2025		DPTO ESTADISTICA
54	COMORBILIDADES ASOCIADAS A MORTALIDAD EN PACIENTES DE HEMODIALISIS ATENDIDOS EN UN HOSPITAL DE LORETO PERIODO 2022 A 2024	CONTRERAS RAMIREZ, LINDA BRENDA	LACHI RAMIREZ LINDA BRENDA-ROJAS BARRIENTOS JULIO CESAR-PAREDES OCAAMPO ANGEL GABRIEL-PEREZ SANCHEZ JUAN CARLOS-TORRE JON CADILLO LUIS	PRE-GRADO	OTROS	SI	SI	C.I.E.I.	C.E.I.-HRL	054-CIEI-HRL-2025	6/12/2025		DPTO ESTADISTICA
55	NIVEL DE CONOCIEMIENTOS Y ACTITUDES PREVENTIVAS DE LOS ESTUDIANTES DE MEDICINA HACIA LA INFECCION POR HELICOBACTER PYLORI EN UNA UNIVESIDAD PUBLICA DE IQUITOS DURANTE EL AÑO 2025	SALAZAR PEREZ JHOYNER SANTIAGO-	TARICUARIMA MATOS NATALY CRISTINA-TRUJILLO NARVAJA MONICA LUCIA-VARGAS GONZALES HECTOR-VEGA QUIROZ NADYA-VELA TELLO KARY KCAMILA	PRE-GRADO	OTROS	SI	SI	C.I.E.I.	C.E.I.-HRL	055-CIEI-HRL-2025	6/12/2025		DPTO ESTADISTICA
56	CONTROL INTERNO Y GESTION DE ADQUISICIONES DE INSUMOS MEDICOS DEL HOSPITAL REGIONAL DE LORETO, 2025	DEL AGUILA GUIERREZ ANA PAULA-PARANA TAMANI JIMENA CAROLINA		POST-GRADO	OTROS	SI	SI	C.I.E.I.	C.E.I.-HRL	056-CIEI-HRL-2025	6/18/2025		DPTO.ECONOMIA-ADMINISTRACION-LOGISTICA RR.HH
57	UNA APLICACIÓN DE TELEFONOS INTELIGENTESA BASADA EN UNA RED NEURONAL ARTIFICIALES PARA DIAGNOSTICO EN EL PUNTO DE ATENCION DE LA MALARIA EN LA AMAZONIA PERUANA	MARIN CASAPIA MORALES		EXTRA-INSTITUCIONAL	REPORTE DE CASOS	SI	SI	C.I.E.I.	C.E.I.-HRL	057-CIEI-HRL-2025	6/19/2025		REGION LORETO .
58	TUBERCULOSIS RESISTENTE: FACTORES PREDICTIVOS DE RESULTADOS NO EXITOSOS AL TRATAMIENTO EN LA REGIÓN LORETO, PERÚ, 2015-2023	EVELYN GENTHELL CÓRDOVA PISCO	GEORGE OBREGÓN BOLTAN, KARINE ZEVALLOS VILLEGAS, ESTELA ALEJANDRA HUAMÁN ANGELES, TERY VASQUEZ	EXTRA-INSTITUCIONAL	OTROS	SI	SI	C.I.E.I.	C.E.I.-HRL	058-CIEI-HRL-2025	23-Jun-25		
59	BROTE DE ENFERMEDAD MENINGOCÓCICA INVASIVA EN LA AMAZONÍA PERUANA	JUAN CARLOS CELIS SALINAS		EXTRAINSTITUCIONAL	OTROS	SI	SI	C.I.E.I.	C.E.I.-HRL	059-CIEI-HRL-2025	30-Jun-25		
60	SEGUIMIENTO FARMACOTERAPEUTICO A PACIENTES CON PSORIASIS ATENTIDOS EN UN HOSPITAL PÚBLICO DE LORETO 2024	ROY ALEXANDER ALVAREZ MARREROS		POST - GRADO.	OTROS	SI	SI	C.I.E.I.	C.E.I.-HRL	060-CIEI-HRL-2025	7/1/2025		
61	CARACTERIZACIÓN DE LAS CAUSAS INFECCIOSAS DE LA ENFERMEDAD FEBRIL AGUDA Y EXANTEMÁTICA EN LATINOAMERICA	JULIA SONIA AMPUERO VELA.		EXTRAINSTITUCIONAL	OTROS	SI	SI	C.I.E.I.	C.E.I.-HRL	061-CIEI-HRL-2025	7-Jul-25		
62	CRECIMIENTO Y DESARROLLO NEUROCOGNITIVO DE NIÑOS Y ADOLESCENTES CON INFECCION POR VIH EN LA CIUDAD DE IQUITOS 2025	JESSICA SAMAR ALVÁN MURO		PRE-GRADO	OTROS	SI	SI	C.I.E.I.	C.E.I.-HRL	062-CIEI-HRL-2025	7-Jul-25		
63	LESIÓN ESCAMOSA INTRA EPITELIAL DE ALTO GRADO	ZONITA RUIZ VASQUEZ		POST-GRADO	OTROS	SI	SI	C.I.E.I.	C.E.I.-HRL	063-CIEI-HRL-2025	7-Jul-25		
64	VARIABLES DEMOGRÁFICAS Y REINFECCIÓN POR MALARIA VIVAX EN USUARIOS ATENDIDOS EN EL HOSPITAL REGIONAL DE LORETO AÑOS 2022 AL 2023 IQUITOS 2025	DARA MISHEL LOPEZ DEL AGUILA	CLAUDIA PEREZ SILVA	PRE-GRADO	OTROS	SI	SI	C.I.E.I.	C.E.I.-HRL	064-CIEI-HRL-2025	7-Jul-25		
65	FACTORES ASOCIADOS AL AUTOCUIDADO DEL PIE DIABÉTICO EN PACIENTES QUE ACUDEN A UN HOSPITAL DE LA CIUDAD DE IQUITOS DURANTE EL AÑO 2025	GIOSELYN JHOSIANE MARGIORY CHUQUIZUTA HUANIN.		PRE-GRADO	OTROS	SI	SI	C.I.E.I.	C.E.I.-HRL	065-CIEI-HRL-2025	14-Jul-25		
66	FACTORES ASOCIADOS A FRACTURA DE TIBIA EN ADULTOS EN EL SERVICIO DE TRAUMATOLOGÍA DEL HOSPITAL REGIONAL DE LORETO, 2020-2024	EMERSON URRELO CORDOVA		PRE-GRADO	OTROS	SI	SI	C.I.E.I.	C.E.I.-HRL	066-CIEI-HRL-2025	14-Jul-25		
67	ESTUDIO OBSERVACIONAL DE SEPSIS EN IQUITOS, PERU	CAROLINA GUEVARA		EXTRAINSTITUCIONAL	REPORTE DE CASOS	SI	SI	C.I.E.I.	C.E.I.-HRL	067-CIEI-HRL-2025	21-Jul-25		
68	EVALUACIÓN DE UN SISTEMA INTEGRADO DE MICROSCOPÍA CON FLUORESCENCIA PARA EL DIAGNÓSTICO AUTOMATIZADO DE TUBERCULOSIS EN BACILOSCOPIA DE ZIEHL NEELSEN, HOSPITAL REGIONAL DE LORETO 2025	GREISI ELENA CURICO HUANCI.		POST-GRADO	OTROS	SI	SI	C.I.E.I.	C.E.I.-HRL	068-CIEI-HRL-2025	25-Jul-25		
69	PRESCRIPCIÓN DE MEDICAMENTOS SEGÚN CRITERIOS STOPP Y START EN PACIENTES ADULTOS MAYORES ASISTIDOS EN UN HOSPITAL DE LORETO	KELVY DANIEL TAFUR YAICATE		PRE-GRADO	OTROS	SI	SI	C.I.E.I.	C.E.I.-HRL	069-CIEI-HRL-2025	30-Jul-25		
70	PREVALENCIA Y FACTORES ASOCIADOS A TRANSTORNOS NEUROCOGNITIVOS EN PACIENTES CON VIH EN IQUITOS, PERÚ	WILFREDO MARTIN CASAPIA MORALES		EXTRAINSTITUCIONAL	OTROS	SI	SI	C.I.E.I.	C.E.I.-HRL	070-CIEI-HRL-2025	1-Aug-25		
71	EFECTO DE UNA INTERVENCIÓN EDUCATIVA EN PERSONAL DE SALUD SOBRE SATISFACCIÓN LABORAL Y EL COMPROMISO INSTITUCIONAL EN UN HOSPITAL RURAL II-1 SANTA CLOTILDE, MAYNAS, 2024 Y 2025	LILA YANABEL FERNANDEZ BURGA		EXTRAINSTITUCIONAL	OTROS	SI	SI	C.I.E.I.	C.E.I.-HRL	071-CIEI-HRL-2025	1-Aug-25		
72	RETRASO DE TRATAMIENTO QUIRÚRGICO COMO FACTOR ASOCIADO A APENDICITIS AGUDA COMPLICADA EN PACIENTES DEL HOSPITAL REGIONAL DE LORETO,2024	GIANINA GERALDINE CORNEJO PADILLA		PRE-GRADO	OTROS	SI	SI	C.I.E.I.	C.E.I.-HRL	072-CIEI-HRL-2025	5-Aug-25		
73	RENDIMIENTO PRONÓSTICO DEL ÍNDICE NEUTRÓFILOS/LINFOCITOS Y EL ÍNDICE PLAQUETAS/LINFOCITOS PARA MORTALIDAD EN PACIENTES CON ICTUS AGUDO ATENDIDOS EN UN HOSPITAL DE LORETO 2019-2024	SEBASTIAN VÁSQUEZ INGA		PRE-GRADO	OTROS	SI	SI	C.I.E.I.	C.E.I.-HRL	073-CIEI-HRL-2025	5-Aug-25		
74	DIAGNÓSTICO DE TUBERCULOSIS MAMARIA, ENTIDAD DESATENDIDA EN LA PRÁCTICA CLÍNICA: EVALUACIÓN MULTICÉNTRICA DEL RENDIMIENTO DE GENEXPERT MTB/RIF ULTRA Y STANDARD M10 EN EL PERÚ	LIVIA TUCKER BRESCIANI		EXTRAINSTITUCIONAL	OTROS	SI	SI	C.I.E.I.	C.E.I.-HRL	074-CIEI-HRL-2025	7-Aug-25		
75	SEROVARES IDENTIFICADOS EN CASOS CONFIRMADOS DE LEPTOSPIROSIS HUMANA EN LORETO, 2022 – 2025	Jorge Ignacio CARRASCO CELI		PRE-GRADO	OTROS	SI	SI	C.I.E.I.	C.E.I.-HRL	075-CIEI-HRL-2025	18-Aug-25		
76	ABANDONO FAMILIAR Y DEPRESIÓN EN EL ADULTO MAYOR HOSPITAL REGIONAL DE LORETO IQUITOS 2025	ELIZA LUZ VASQUEZ VANCES	GUILLERMO PORTAL SANDI	PRE-GRADO	OTROS	SI	SI	C.I.E.I.	C.E.I.-HRL	076-CIEI-HRL-2025	20-Aug-25		
77	Miasis oral causada por Cochliomyia hominivorax en paciente en estado vegetativo: reporte de caso en la Amazonía Peruana	MAURO MILKO ECHEVARRIA CHONG		POST-GRADO	OTROS	SI	SI	C.I.E.I.	C.E.I.-HRL	077-CIEI-HRL-2025	25-Aug-25		
78	VARIABLES ASOCIADAS AL NIVEL DE ESTRÉS LABORAL EN EL PERSONAL DE SALUD DEL CENTRO QUIRÚRGICO HOSPITAL REGIONAL DE LORETO IQUITOS 2025	AMALIA IRENE CONCHA OLÓRTEGUI.		POST-GRADO	OTROS	SI	SI	C.I.E.I.	C.E.I.-HRL	078-CIEI-HRL-2025	26-Aug-25		
79	COLECCIÓN DE MUESTRAS CLINICAS VOLUNTARIOS PEDIATRICOS SALUDABLES.PROTOCOLO # CRSPTL – 00072. VERSION 2.0	JUAN CARLOS HINOJOSA BOYER		EXTRAINSTITUCIONAL	OTROS	SI	SI	C.I.E.I.	C.E.I.-HRL	079-CIEI-HRL-2025	8-Sep-25		
80	COLECCIÓN DE MUESTRAS CLINICAS VOLUNTARIOS PEDIATRICOS SALUDABLES PROTOCOLO # CRSPTL – 00072, VERSION 2.0	JUAN CARLOS HINOJOSA BOYER		EXTRAINSTITUCIONAL	OTROS	SI	SI	C.I.E.I.	C.E.I.-HRL	080-CIEI-HRL-2025	2-Sep-25		
81	COLECCIÓN DE MUESTRAS CLINICAS VOLUNTARIOS PEDIATRICOS SALUDABLES PROTOCOLO # CRSPTL – 00072, VERSION 2.0	JUAN CARLOS HINOJOSA BOYER		EXTRAINSTITUCIONAL	OTROS	SI	SI	C.I.E.I.	C.E.I.-HRL	081-CIEI-HRL-2025	2-Sep-25		
82	LACTANCIA MATERNA ASOCIADA A BRONQUIOLITIS AGUDA EN MENORES DE 2 AÑOS EN UN HOSPITAL NIVEL III , 2025 IQUITOS	EVER ANTONIO VASQUEZ VILLANUEVA.		POST-GRADO	OTROS	SI	SI	C.I.E.I.	C.E.I.-HRL	082-CIEI-HRL-2025	8-Sep-25		
83	CONOCIMIENTO Y ESTADO NUTRICIONAL DE MADRES ADOLESCENTES EN LACTANCIA EXCLUSIVA DE TRES CENTROS DE SALUD DEL DISTRITO DE SAN JUAN BAUTISTA, 2025	KEYSI NAYELI MURRIETA RUIZ	OLENKA PATRICIA CHANTA PANDURO	PRE-GRADO	OTROS	SI	SI	C.I.E.I.	C.E.I.-HRL	083-CIEI-HRL-2025	8-Sep-25		

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84	RELACIÓN ENTRE EL ESTADO NUTRICIONAL, CALIDAD DE VIDA Y ESTILO DE VIDA DE PACIENTES EN HEMODIÁLISIS DEL HOSPITAL REGIONAL DE LORETO, IQUITOS 2024	LEIDY GABRIELA QUINTANA RUIZ	GLORIA LUZ MAGNO MERMAO	PRE-GRADO	OTROS	SI	SI	C.I.E.I.	C.E.I.-HRL	084-CIEI-HRL-2025	8-Sep-25		
85	PRIMER CASO DE SINDROME DE CARPENTER EN PERÚ: REPORTE DE UN CASO	RONY GOMEZ RODRIGUEZ	VALENTINA MURRIETA RUIZ	POST-GRADO	OTROS	SI	SI	C.I.E.I.	C.E.I.-HRL	085-CIEI-HRL-2025	15-Sep-25		
86	SATISFACCIÓN LABORAL Y SINDROME DE BURNOUT EN ENFERMERAS ASISTENCIALES DEL HOSPITAL REGIONAL DE LORETO "FELIPE SANTIAGO ARRIOLA IGLESIAS IQUITOS 2025	FRANK JOEL PEREZ RAMIREZ	ALEXIA SHANTAL VELASQUEZ PEREZ	PRE-GRADO	OTROS	SI	SI	C.I.E.I.	C.E.I.-HRL	086-CIEI-HRL-2025	22-Sep-25		
87	ASOCIACIÓN ENTRE COMORBILIDADES Y COMPLICACIONES DEL INFARTO AGUDO DE MIOCARDIO EN PACIENTES DEL HOSPITAL REGIONAL DE LORETO, IQUITOS 2024-2025	CHACAYAN VELA, MATHIAS DAVID	ADRIANA ROCIO LADERA URDAY, MARÍA VICTORIA MONTUFAR LLERENA, ANGEL GABRIEL PAREDES OCAMPO, CHASKA ARIADNA ROMERO LÓPEZ, HÉCTOR	PRE-GRADO	OTROS	SI	SI	C.I.E.I.	C.E.I.-HRL	087-CIEI-HRL-2025	22-Sep-25		
88	CONOCIMIENTO Y ACTITUD HACIA LA DONACIÓN DE SANGRE SEGÚN PROCEDENCIA DE USUARIOS EN INSTITUCIONES PRESTADORAS DE SERVICIOS DE SALUD 1 – 4 MINSA IQUITOS 2025	JORGE RIOS PEZO		POST-GRADO	OTROS	SI	SI	C.I.E.I.	C.E.I.-HRL	088-CIEI-HRL-2025	23-Sep-25		
89						SI	SI	C.I.E.I.	C.E.I.-HRL				
90	FACTORES SOCIODEMOGRÁFICOS, CLÍNICOS Y LABORATORIALES ASOCIADOS CON EL TIPO DE ACCIDENTE CEREBROVASCULAR EN HOSPITAL REGIONAL DE LORETO 2022-2024	ABNER CENEPO YAHUARCANI	PIERO FRANCESCO FLORES DÁVILA, MALDONADO CÓRDOBA RICARDO HERNÁN, JUAN CARLOS PÉREZ SÁNCHEZ, SAMAR SARAÍ SIFUENTES VIDIGAL, LUIS	PREGRADO	OBSERVACIONAL TRANSVERSAL RETROSPECTIVO ANALITICO	SI	SI	C.I.E.I.	C.E.I.-HRL	090– CIEI – HRL – 2025	6-Oct-25		DPTO ESTADISTICA
91	ASOCIACIÓN ENTRE DIABETES MELLITUS TIPO 2 Y MANIFESTACIONES CUTÁNEAS DE PACIENTES ATENDIDOS EN CONSULTORIA EXTERNA DEL HOSPITAL REGIONAL DE LORETO PERIODO ENERO A JULIO 2025	ALFRED DONNY CHILCO MACEDO	ANDREA ALEXANDRA LÓPEZ RÍOS, CLAUDIA CAROLINA RUCOBA PEZO, NADYA VEGA QUIROZ, FILOMENA JANAMPA NINAMPAYTA, VICTOR ANDRES MURRIETA RIOS, YOKINUR	PREGRADO	OBSERVACIONAL TRANSVERSAL RETROSPECTIVO ANALITICO	SI	SI	C.I.E.I.	C.E.I.-HRL	091– CIEI – HRL – 2025	6-Oct-25		DPTO ESTADISTICA
92	MICROBIOME OBSERVATORY OF INDUSTRALIZATION	RAUL YHOSSEF TITO TADEO	GRACIELA ROCIO MEZA SANCHEZ y JEROEN RAES	EXTRAINSTITUCIONAL	OBSERVACIONAL MIXTO (TRANVERSAL + LONGITUDINAL) ANALITICO	SI	SI	C.I.E.I.	C.E.I.-HRL	092– CIEI – HRL – 2025	9-Oct-25		Pueblo Matses, Loreto
93	ASOCIACIÓN ENTRE OBESIDAD Y DIABETES GESTACIONAL EN GESTANTES ATENDIDAS EN EL HOSPITAL REGIONAL DE LORETO DURANTE EL 2024	MÓNICA MILAGROS MORÍ CORAL	GINO ARLEY PEREZ MORI, MILAGROS ISABEL SANDOVAL REÁTEGUI, SAMAR SARAI SIFUENTES VIDIGAL, ANGÉLICA SANDY TACA HINOJOSA, ELIANA	PREGRADO	OBSERVACIONAL TRANSVERSAL RETROSPECTIVO ANALITICO	SI	SI	C.I.E.I.	C.E.I.-HRL	093– CIEI – HRL – 2025	10-Oct-25		DPTO ESTADISTICA
94	PSICOPROFILAXIS OBSTÉTRICA RELACIONADO AL TIPO DE PARTO EN EL HOSPITAL REGIONAL DE LORETO 2023-2024	ANDY CELIKA CAROLINA ALVA REATEGUI		PREGRADO	OBSERVACIONAL TRANSVERSAL RETROSPECTIVO CORRELACIONAL	SI	SI	C.I.E.I.	C.E.I.-HRL	094– CIEI – HRL – 2025	10-Oct-25		DPTO ESTADISTICA
95	PREVALENCIA Y FACTORES ASOCIADOS A HÍGADO GRASO NO ALCOHÓLICO EN PACIENTES CON DIABETES MELLITUS TIPO 2 DEL HOSPITAL REGIONAL DE LORETO 2025	CESIA ONELLY ACHONG CASIMIRO		PREGRADO	OBSERVACIONAL TRANSVERSAL RETROSPECTIVO DESCRIPTIVO Y CORRELACIONAL	SI	SI	C.I.E.I.	C.E.I.-HRL	095– CIEI – HRL – 2025	10-Oct-25		DPTO ESTADISTICA y DPTO ENDOCRINOLOGIA
96	EFECTIVIDAD DEL PROGRAMA DE PSICOPROFILAXIS OBSTÉTRICA EN EL ESTRÉS DE LAS GESTANTES DEL HOSPITAL REGIONAL DE LORETO – 2025	ROCÍO DEL PILAR SEGOVIA SAAVEDRA	KYARA MALÚ PINCHI ORBE	PREGRADO	PRE-EXPERIMENTAL CUANTITATIVO LONGITUDINAL	SI	SI	C.I.E.I.	C.E.I.-HRL	096– CIEI – HRL – 2025	10-Oct-25		DPTO GINECOLOGIA Y OBSTETRICIA
97	NECESIDAD DE TRATAMIENTO PERIODONTAL EN PACIENTES CON ENFERMEDADES SISTÉMICAS MAS FRECUENTES ATENDIDOS EN EL SERVICIO DE MEDICINA DE UN HOSPITAL DE IQUITOS - 2025	CYNTHIA NADINNE MOREY TRUJILLO	PIERO MARTIN PAREDES HIDALGO	PREGRADO	TRANSVERSAL DESCRIPTIVO CORRELACIONAL	SI	SI	C.I.E.I.	C.E.I.-HRL	097– CIEI – HRL – 2025	10-Oct-25		DEPARTAMENTO MEDICINA
98	BIOMARCADORES INFLAMATORIOS Y TIEMPO DE ENFERMEDAD COMO PREDICTORES DE APENDICITIS AGUDA COMPLICADA EN PACIENTES MENORES DE 18 AÑOS ATENDIDOS EN EL HOSPITAL REGIONAL DE LORETO 2023-2024	CRISTHIAN LUIS TULUMBA AVIDON		PREGRADO	OBSERVACIONAL TRANSVERSAL RETROSPECTIVO ANALITICO	SI	SI	C.I.E.I.	C.E.I.-HRL	098– CIEI – HRL – 2025	13-Oct-25		DPTO ESTADISTICA
99	"APROVECHAMIENTO DE LA RESPUESTA DEL HUÉSPED FRENTE A LA LEPTOSPIROSIS PARA EL DIAGNÓSTICO Y PRONÓSTICO" VERSION 1.2	JUAN CARLOS CELIS SALINAS		EXTRAINSTITUCIONAL	CLINICO TRANSVERSAL ESTACIONAL	SI	SI	C.I.E.I.	C.E.I.-HRL	099– CIEI – HRL – 2025	15-Oct-25		DPTO INFECTOLOGIA
100	ASOCIACIÓN ENTRE TRAUMATISMO CRANEOENCEFÁLICO LEVE Y DESARROLLO DE ALTERACIONES COGNITIVAS TEMPRANAS EN PACIENTES DE NEUROCIRUGÍA DE UN HOSPITAL DE LORETO	FRANCIS ALASKA LAVI OLANO		PREGRADO	observacional descriptivo, transversal y analitico	SI	SI	C.I.E.I.	C.E.I.-HRL	100– CIEI – HRL – 2025	28-Oct-25		DPTO CIRUGIA
101	ASOCIACIÓN ENTRE CONOCIMIENTOS, ACTITUDES, Y PRACTICAS SOBRE EL CÁNCER DE CUELLO UTERINO Y DETERMINANTES SOCIODEMOGRÁFICAS, LABORALES Y FORMATIVOS EN PROFESIONALES NO MÉDICOS DE IQUITOS, 2026	JORGE KALEEP MORENO GARCÍA		PREGRADO	observacional descriptivo, transversal y analitico	SI	SI	C.I.E.I.	C.E.I.-HRL	101– CIEI – HRL – 2025	28-Oct-25		DPTO GINECOLOGIA
102	EVALUACIÓN DE LA ADHERENCIA AL TRATAMIENTO ANTIHIPERTENSIVO MEDIANTE LA ESCALA HILL-BONE EN PACIENTES ATENDIDOS EN UN HOSPITAL DE IQUITOS, 2025-2026	OSCAR ALÍ VÁSQUEZ MORA		PREGRADO	observacional descriptivo, transversal y analitico	SI	SI	C.I.E.I.	C.E.I.-HRL	102– CIEI – HRL – 2025	28-Oct-25		DEPARTAMENTO MEDICINA
103	NIVEL DE APOYO SOCIAL PERCIBIDO Y ADHERENCIA AL EJERCICIO TERAPÉUTICO DOMICILIARIO EN PACIENTES CON DOLOR LUMBAR CRÓNICO DEL HOSPITAL REGIONAL DE LORETO, IQUITOS 2026	ARIANA SÁNCHEZ ARRIETA		PREGRADO	ESTUDIO OBSERVACIONAL TRANSVERSAL PROSPECTIVO	SI	SI	C.I.E.I.	C.E.I.-HRL	103– CIEI – HRL – 2025	28-Oct-25		DEPARTAMENTO DE MEDICINA FÍSICA Y REHABILITACIÓN
104	FACTORES OCUPACIONALES Y SÍNDROME VISUAL INFORMÁTICO EN PERSONAL ADMINISTRATIVO CON EXPOSICIÓN A PANTALLAS DEL HOSPITAL REGIONAL DE LORETO, 2025	CINTHYA GIOVANA REATEGUI MORI		POSGRADO	OBSERVACIONAL ANALITICO CUANTITATIVO Y PROSPECTIVO	SI	SI	C.I.E.I.	C.E.I.-HRL	104– CIEI – HRL – 2025	28-Oct-25		DIRECCION ADMINISTRATIVA
105	FACTORES RELACIONADOS A CESÁREAS DE EMERGENCIA EN DOS HOSPITALES PÚBLICOS DE LORETO DE ENERO A JULIO 2025	LADY DHU SOPLOPUCO LÓPEZ	STEPHANIE DEL ROSARIO AMASIFUEN SÁNCHEZ	PREGRADO	observacional, transversal, RETROSPECTIVO CASOS Y CONTROLES	SI	SI	C.I.E.I.	C.E.I.-HRL	105– CIEI – HRL – 2025	28-Oct-25		DPTO ESTADISTICA Y DPTO GINECOLOGIA
106	MICROBIOMA "UNA SOLA SALUD" DEL PUEBLO MATSÉS: INTEGRANDO RESERVORIOS MICROBIANOS ANIMALES Y AMBIENTALES PARA ENTENDER UN ESTADO ANCESTRAL DE LA BIOLOGÍA HUMANA	JHOSEPHI JHAMPIER VÁSQUEZ ASCATE	RAUL YHOSSEF TITO TADEO	POSGRADO	OBSERVACIONAL TRANSVERSAL DESCRIPTIVO ANALITICO COMPARATIVO	SI	SI	C.I.E.I.	C.E.I.-HRL	106– CIEI – HRL – 2025	28-Oct-25		PUEBLO MATSES, LORETO
107	METAHEMOGLOBINEMIA INDUCIDA POR PRIMAQUINA: SERIE DE CASOS	WILFREDO MARTÍN CASAPÍA MORALES		PREGRADO	OBSERVACIONAL TRANSVERSAL SERIE DE CASOS	SI	SI	C.I.E.I.	C.E.I.-HRL	107– CIEI – HRL – 2025	28-Oct-25		DPTO INFECTOLOGIA
108	MORTALIDAD NEONATAL EN LORETO Y SU RELACIÓN CON LOS INDICADORES PERINATALES: APGAR, TIPO DE PARTO, PESO Y MALFORMACIONES CONGÉNITAS 2025	JESUS ABRAHAM AGUILAR GARCIA	JORGE IGNACIO CARRASCO CELI, RICHARD TOM INGA SAQUIRAY, YELITZA SKARLET MARINHO VAQUERO, BARBARA ISABEL RODRIGUEZ RODRIGUEZ, MÓNICA LUCIA TRUJILLO NARVAJA y KARY KCAMILA VELA TELLO	PREGRADO	OBSERVACIONAL ANALITICO RETROSPECTIVO CASO-CONTROL	SI	SI	C.I.E.I.	C.E.I.-HRL	108– CIEI – HRL – 2025	31-Oct-25		DPTO ESTADISTICA Y DPTO NEONATOLOGIA
109	COMPARACIÓN DE PARÁMETROS HEMATOLÓGICOS EN TUBERCULOSIS PULMONAR Y NEUMONÍA ADQUIRIDA EN LA COMUNIDAD, HOSPITAL REGIONAL DE LORETO 2025	ALFREDD JOSSUE MORENO SOTO		PREGRADO	OBSERVACIONAL TRANSVERSAL RETROSPECTIVO ANALITICO	SI	SI	C.I.E.I.	C.E.I.-HRL	109– CIEI – HRL – 2025	3-Nov-25		DPTO ESTADISTICA
110	PLATAFORMA WEB INTELIGENTE PARA LA IDENTIFICACIÓN AUTOMÁTICA DE TIPOS DE LEUCEMIA USANDO DEEP LEARNING	BRUNO ALEJANDRO SANTILLAN CHOTA	ALESSANDRA DEL PILAR MENDOZA RIOS	PREGRADO	OBSERVACIONAL TRANSVERSAL DE EXACTITUD DIAGNOSTICA BASADA EN APRENDIZAJE PROFUNDO	SI	SI	C.I.E.I.	C.E.I.-HRL	110– CIEI – HRL – 2025	5-Nov-25		DEPARTAMENTO DE PATOLOGÍA CLÍNICA Y ANATOMÍA PATOLÓGICA

111	PREVALENCIA DE RESISTENCIA ANTIMICROBIANA EN ESCHERICHIA COLI AISLADOS DEL AGUA DE CONSUMO DOMICILIARIO EN IQUITOS: IMPLICACIONES PARA SALUD PÚBLICA, 2025	NORMAN MARCELO NAJAR LINARES		PREGRADO	OBSERVACIONAL CUANTITATIVO DESCRIPTIVO TRANSVERSAL	SI	SI	C.I.E.I.	C.E.I.-HRL	111– CIEI – HRL – 2025	5-Nov-25		IQUITOS, LORETO
112	FACTORES DE RIESGO FÍSICO ASOCIADOS A PACIENTES CON NEUROPATÍA DIABÉTICA ATENDIDOS EN UN HOSPITAL DE IQUITOS 2025	BRAULIO AYDE FERNANDEZ	LUIS RIOJA RAMIREZ	PREGRADO	OBSERVACIONAL TRANSVERSAL PROSPECTIVA	SI	SI	C.I.E.I.	C.E.I.-HRL	112– CIEI – HRL – 2025	6-Nov-25		DPTO ESTADISTICA, DPTO MEDICINA Y DPTO DE EMERGENCIA Y CUIDADOS CRITICOS
113	CONTROLANDO Y PREVINIENDO LA INFECCIÓN EN LA AMAZONIA PERUANA. LLEVAR LA PREVENCIÓN DONDE MÁS SE NECESITA. PROGRAMA INTEGRAL DE PREVENCIÓN Y CONTROL DE INFECCIÓN Y PROA EN HOSPITAL REGIONAL DE LORETO FELIPE ARRIOLA IGLESIAS. IQUITOS PERÚ	MARTIN CASAPIA MORALES		EXTRAINSTITUCIONAL	ESTUDIO OBSERVACIONAL PROSPECTIVO DE ANALISIS DE PREVALENCIA	SI	SI	C.I.E.I.	C.E.I.-HRL	113– CIEI – HRL – 2025	10-Nov-25		DPTO MEDICINA, DPTO CIRUGIA, DPTO PEDIATRIA, DPTO GINECOLOGIA
114	IMPACTO DE LA MUERTE MATERNA EN LA SOBREVIVENCIA DEL HIJO Y SU INFLUENCIA EN EL ÁMBITO FAMILIAR. HOSPITAL REGIONAL DE LORETO 2022	GISELA FLORES FERNANDEZ		PREGRADO	ESTUDIO OBSERVACIONAL CUANTITATIVO-CUALITATIVO ANALITICO COHORTE PROSPECTIVO	SI	SI	C.I.E.I.	C.E.I.-HRL	ID-114-CIEI-2025	10-Nov-25		DPTO ESTADISTICA
115	IMPACTO DEL TIEMPO DE ESPERA EN LA CALIDAD DE VIDA DE PACIENTES PROGRAMADOS PARA COLECISTECTOMÍA ELECTIVA EN UN HOSPITAL DE LORETO, 2025–2026	GIAMPIERO KEYTARO SAMAMÉ DEL CASTILLO VASQUEZ		PREGRADO	ESTUDIO OBSERVACIONAL TRANSVERSAL DESCRIPTIVO	SI	SI	C.I.E.I.	C.E.I.-HRL	ID-115-CIEI-2025	10-Nov-25		DPTO CIRUGIA
116	GRADO DE DISCAPACIDAD FUNCIONAL EN SUPERVIVIENTES DE ACCIDENTE CEREBROVASCULAR DURANTE EL AÑO 2024 EN EL HOSPITAL REGIONAL DE LORETO	STEFANO VLADIMIR DAVILA PHILIPS	RITA ANGULO QUINTANILLA, ANTONY MARÍN ARBILDO, TEDDY PÉREZ PINEDO, JHOYNER SANTIAGO SALAZAR PÉREZ	PREGRADO	OBSERVACIONAL DESCRIPTIVO COHORTE PROSPECTIVO	SI	SI	C.I.E.I.	C.E.I.-HRL	ID-116-CIEI-2025	10-Nov-25		DPTO MEDICINA, DPTO CIRUGIA
117	INTERVENCIÓN NUTRICIONAL EN ALIMENTACIÓN, ACTIVIDAD FÍSICA, INDICADORES ANTROPOMÉTRICOS Y RIESGO CARDIOMETABÓLICO DE ADULTOS ATENDIDOS EN LA IPRESS I-4 SAN JUAN DE MIRAFLORES, 2025	SISSY SUNAMITA GARCÍA ACHONG	BARBARA FRANCHESCA RUIZ TAPULLIMA	PREGRADO	ESTUDIO CUASI-EXPERIMENTAL LONGITUDINAL PROSPECTIVO PRE Y POST TEST DE UN GRUPO	SI	SI	C.I.E.I.	C.E.I.-HRL	ID-117-CIEI-2025	11-Nov-25		DPTO ESTADISTICA
118	EFICACIA DE UNA INTERVENCIÓN EDUCATIVA VIRTUAL EN AUTOCUIDADO Y CONTROL GLICÉMICO DE PACIENTES DIABÉTICOS DE CONSULTORIO EXTERNO DEL HRL, 2026	MARÍA CLAUDIA HINOJOSA RÍOS		PREGRADO	ESTUDIO CUASI-EXPERIMENTAL ANALITICO DE COHORTE PROSPECTIVO CASO-CONTROL	SI	SI	C.I.E.I.	C.E.I.-HRL	ID-118-CIEI-2025	11-Nov-25		DPTO MEDICINA
119	CALIDAD DE SERVICIO Y SATISFACCIÓN DEL USUARIO DEL DEPARTAMENTO DE MEDICINA FÍSICA Y REHABILITACIÓN DE UN HOSPITAL DE LORETO, 2025	ROSA ENCARNACIÓN MERA ARO		POSGRADO	ESTUDIO CUANTITATIVO NO EXPERIMENTAL TRANSVERSAL CORRELACIONAL SIMPLE	SI	SI	C.I.E.I.	C.E.I.-HRL	ID-119-CIEI-2025	12-Nov-25		DPTO MEDICINA FISICA Y REHABILITACION
120	FACTORES ASOCIADOS A LA CALIDAD DE VIDA DERMATOLÓGICA EN PACIENTES CON ENFERMEDAD RENAL CRÓNICA EN HEMODIÁLISIS EN EL HOSPITAL REGIONAL DE LORETO, 2025	ANA TUESTA ALVARADO	CARLOS UBALDO RENGIFO, ENZO FABIO MIGUEL VALDIVIA RUIZ, JAMES LUIS VÁSQUEZ LECHUGA, PATRICK JOSEPH VÁSQUEZ QUIROZ, DAFNE ZORELLA DE LA	PREGRADO	ESTUDIO OBSERVACIONAL TRANSVERSAL ANALITICA	SI	SI	C.I.E.I.	C.E.I.-HRL	ID-120-CIEI-2025	13-Nov-25		DPTO ESTADISTICA
121	NIVEL DE HEMOGLOBINA DEL SEGUNDO TRIMESTRE Y SEVERIDAD DE PREECLAMPSIA EN GESTANTES DE UN HOSPITAL REGIONAL DE IQUITOS 2025	LILIAN MARINA PAREDES DEL CASTILLO		PREGRADO	ESTUDIO OBSERVACIONAL ANALITICO TRANSVERSAL RETROSPECTIVO	SI	SI	C.I.E.I.	C.E.I.-HRL	ID-121-CIEI-2025	14-Nov-25		DPTO ESTADISTICA
122	CARACTERÍSTICAS CLÍNICAS, EPIDEMIOLÓGICAS Y DESENLACES INTRAHOSPITALARIOS DE MORDEDURAS POR SERPIENTES ATENDIDAS EN DOS HOSPITALES DE LA AMAZONIA PERUANA, 2023-2024	EDGAR ANTONIO RAMÍREZ GARCÍA		POSGRADO	ESTUDIO OBSERVACIONAL ANALITICO TRANSVERSAL RETROSPECTIVO	SI	SI	C.I.E.I.	C.E.I.-HRL	ID-122-CIEI-2025	14-Nov-25		DPTO ESTADISTICA
123	AUDITORIA – CALIDAD DE DATOS EN VIGILANCIA EPIDEMIOLÓGICA IPRESS I-1 CAMPO SERIO, LORETO, PERÚ - 2025	BELÉN MARINA GÓMEZ VALCÁRCEL		EXTRAINSTITUCIONAL	OBSERVACIONAL, DESCRIPTIVO, TRANSVERSAL, TIPO AUDITORIA DE LA CALIDAD	SI	SI	C.I.E.I.	C.E.I.-HRL	ID-123-CIEI-2025	17-Nov-25		IPRESS I-1 CAMPO SERIO, LORETO
124	CARACTERÍSTICAS CLÍNICAS Y EPIDEMIOLÓGICAS DEL BROTE DE DENGUE EN LA LOCALIDAD DE SANTA CLOTILDE, RÍO NAPO, LORETO, 2024	PEDRO JULIO SALIRROSAS FERNÁNDEZ		EXTRAINSTITUCIONAL	ESTUDIO OBSERVACIONAL DESCRIPTIVO TRANSVERSAL Y RETROSPECTIVO	SI	SI	C.I.E.I.	C.E.I.-HRL	ID-124-CIEI-2025	17-Nov-25		SANTA CLOTILDE, RÍO NAPO, LORETO
125	NIVEL DE CONOCIMIENTO Y CONCIENCIA SOBRE SÍNDROME METABÓLICO Y SU ASOCIACIÓN CON EL ESTADO Y HÁBITOS NUTRICIONALES EN INTERNOS DE MEDICINA HUMANA DE LA UNAP, 2025	ANGELES GUERRA FLORES	JULIO FERNANDO GUERRERO PINEDO, SILVANO ENRIQUE HUAYMACARI, JOSE LOPEZ RUIZ, MELITA NATALY MARIN VASQUEZ	PREGRADO	ESTUDIO NO EXPERIMENTAL, OBSERVACIONAL, TRANSVERSAL, CORRELACIONAL	SI	SI	C.I.E.I.	C.E.I.-HRL	ID-125-CIEI-2025	24-Nov-25		DPTO MEDICINA, DPTO CIRUGIA, DPTO PEDIATRIA, DPTO GINECOLOGIA
126	ASOCIACIÓN ENTRE IMC E HIPERTENSIÓN ARTERIAL EN PACIENTES ATENDIDOS EN EL HOSPITAL REGIONAL DE LORETO, PRIMER TRIMESTRE DEL 2025	CARLOS JAVIER RUIZ PEREZ	DAVID MARTIN RUIZ RUIZ, ADRIANO BARRESI SILVA GONZALEZ, MICHEL GABRIEL TRIGOZO PARRA, VALERIA IVONNE SOTO DEL	PREGRADO	ESTUDIO NO EXPERIMENTAL, OBSERVACIONAL, TRANSVERSAL, DESCRIPTIVO-ASOCIATIVO	SI	SI	C.I.E.I.	C.E.I.-HRL	ID-126-CIEI-2025	24-Nov-25		DPTO ESTADISTICA, DPTO MEDICINA
127	INFLUENCIA DE FACTORES SOCIODEMOGRÁFICOS, COMPORTAMIENTOS EN SALUD Y COMORBILIDADES EN LA SEVERIDAD DE LA PSORIASIS, EN PACIENTES DE UN HOSPITAL DE IQUITOS, 2025	HUGO PERCY ZAMORA PEREA		POSGRADO	a) Estudio observacional cuantitativo, transversal analítico. b) Revisión exploratoria de alcance (scoping review). c) Reporte de caso clínico.	SI	SI	C.I.E.I.	C.E.I.-HRL	ID-127-CIEI-2025	25-Nov-25		DPTO MEDICINA
128	CARACTERÍSTICAS CLÍNICO-EPIDEMIOLÓGICAS DE LOS CASOS DE OROPUCHE EN LA REGIÓN LORETO DURANTE EL PERIODO 2023-2025	JEYDY SOLYBEL CONDORI VILCA	CATHERINE ALEXA DIAZ RODRIGUEZ, VALERIA FERNANDA DIAZ VELA, JOSÉ ALEJANDRO	PREGRADO	estudio observacional, descriptivo, transversal y retrospectivo	SI	SI	C.I.E.I.	C.E.I.-HRL	ID-128-CIEI-2025	26-Nov-25		DPTO ESTADISTICA
129	EPIDEMIOLOGÍA Y CLÍNICA DE LA LEISHMANIASIS TEGUMENTARIA EN EL PERÚ	DR. JUAN FRANCISCO SANCHEZ		EXTRAINSTITUCIONAL	estudio transversal de vigilancia pasiva	SI	SI	C.I.E.I.	C.E.I.-HRL	ID-129-CIEI-2025	28-Nov-25		HOSPITAL REGIONAL DE LORETO Y HOSPITAL MILITAR

ANEXO 03

CARTAS DE APROBACIÓN DE CADA PROTOCOLO EN EL 2025

"HOSPITAL REGIONAL DE LORETO "FELIPE ARRIOLA IGLESIAS"

CONSTANCIA No 002– CIEI – HRL – 2025

El Presidente del Comité Institucional de Ética é Investigación del Hospital Regional de Loreto, (CIEI) a través de la Oficina de Apoyo a la Docencia é Investigación, **HACE CONSTAR** que el presente proyecto de Investigación, consignado líneas abajo, fue **APROBADO**, en cumplimiento de los estándares del Instituto Nacional de Salud (INS), acorde con las prioridades Regionales de Investigación, Balance Riesgo/beneficio y confiabilidad de los datos, entre otras. Siendo catalogado como: **ESTUDIO CLINICO CON RIESGO MEDIO**, según detalle:

Título del Proyecto:	**"PRUEBA DE NUEVOS DISPOSITIVOS DE DIAGNÓSTICO PARA ENFERMEDADES FEBRILES"**
Código de Inscripción:	**ID-61-CIEI-2024.**
Modalidad de investigación :	***EXTRAINSTITUCIONAL.***
Investigador (es):	**ISABEL BAZAN ARISTA**

Cualquier eventualidad durante su ejecución, los investigadores reportarán de acuerdo con las Normas y plazos establecidos, así mismo emitirán el informe final socializando los **RESULTADOS** obtenidos. El presente documento tiene vigencia hasta el 06 de enero del 2026. El trámite para su renovación será un mínimo de 30 días antes de su vencimiento.

Punchana, 06 de Enero del 2025.

Hospital Regional del Oriente "Felipe Arriola Iglesias"
DR. CESAR J. RAMAL ASEN...

NADIA MONTES CRCOLLA
05396304
08/01/2025

JRMALL/RCHH/CIRA/JLGP/JERR.

"HOSPITAL REGIONAL DE LORETO "FELIPE ARRIOLA IGLESIAS"

CONSTANCIA No 011– CIEI – HRL – 2025

El presidente del Comité Institucional de Ética é Investigación del Hospital Regional de Loreto, (CIEI) a través de la Oficina de Apoyo a la Docencia é Investigación, HACE **CONSTAR** que el presente proyecto de Investigación, consignado líneas abajo, fue **APROBADO**, en cumplimiento de los estándares del Instituto Nacional de Salud (INS), acorde con las prioridades Regionales de Investigación, Balance Riesgo/beneficio y confiabilidad de los datos, entre otras. Siendo catalogado como: **ESTUDIO CLINICO SIN RIESGO,** según detalle:

Título del Proyecto:	**"FACTORES CONDICIONANTES EN LA ETAPA PRENATAL PARA EL DESARROLLO DEL TRANSTORNO DEL ESPECTRO AUTISTA"**
Código de Inscripción:	**ID-011-CIEI-2025.**
Modalidad de investigación :	*EXTRA-INSTITUCIONAL*
Investigador (es):	Ing. JOSÉ MARÍA HERRERA ROSAS.

Cualquier eventualidad durante su ejecución, los investigadores reportarán de acuerdo con las Normas y plazos establecidos, así mismo emitirán el informe final socializando los **RESULTADOS** obtenidos. El presente documento tiene vigencia hasta el 04 de Marzo del 2026. El trámite para su renovación será un mínimo de 30 días antes de su vencimiento.

Punchana, 04 de Marzo del 2025.

Hospital Regional de Loreto
"Felipe Arriola Iglesias"
Comité Institucional de Ética e Investigación

DR. CÉSAR J. RAMAL ASAYAS
Presidente

JRMALL/RCHH/CJRA/JLGP/JERR.

"HOSPITAL REGIONAL DE LORETO "FELIPE ARRIOLA IGLESIAS"

CONSTANCIA No 012– CIEI – HRL – 2025

El presidente del Comité Institucional de Ética é Investigación del Hospital Regional de Loreto, (CIEI) a través de la Oficina de Apoyo a la Docencia é Investigación, HACE **CONSTAR** que el presente proyecto de Investigación, consignado líneas abajo, fue **APROBADO**, en cumplimiento de los estándares del Instituto Nacional de Salud (INS), acorde con las prioridades Regionales de Investigación, Balance Riesgo/beneficio y confiabilidad de los datos, entre otras. Siendo catalogado como: **ESTUDIO CLINICO CON RIESGO MEDIO,** según detalle:

Título del Proyecto:	**"DESCIFRANDO LA ARQUITECTURA GENÉTICA DE LAS ENFERMEDADES AUTOINMUNES EN POBLACIONES INDÍGENAS DEL PERÚ"**
Código de Inscripción:	**ID-012-CIEI-2025.**
Modalidad de investigación :	***EXTRA - INSTITUCIONAL***
Investigador (es):	**WILFREDO MARTIN CASAPIA MORALES, MD**

Cualquier eventualidad durante su ejecución, los investigadores reportarán de acuerdo con las Normas y plazos establecidos, así mismo emitirán el informe final socializando los **RESULTADOS** obtenidos. El presente documento tiene vigencia hasta el 04 de Marzo del 2026. El trámite para su renovación será un mínimo de 30 días antes de su vencimiento.

Punchana, 04 de marzo del 2025.

Hospital Regional de Loreto
"Felipe Arriola Iglesias"
Comité Institucional de Ética e Investigación
DR. CÉSAR J. RAMAL ASAYA
Presidente del Comité Institucional de Ética e Investigación

JRMALL/RCHH/CJRA/JLGP/JERR.

"HOSPITAL REGIONAL DE LORETO "FELIPE ARRIOLA IGLESIAS"

CONSTANCIA No 016– CIEI – HRL – 2025

El presidente del Comité Institucional de Ética é Investigación del Hospital Regional de Loreto, (CIEI) a través de la Oficina de Apoyo a la Docencia é Investigación, HACE **CONSTAR** que el presente proyecto de Investigación, consignado líneas abajo, fue **APROBADO**, en cumplimiento de los estándares del Instituto Nacional de Salud (INS), acorde con las prioridades Regionales de Investigación, Balance Riesgo/beneficio y confiabilidad de los datos, entre otras. Siendo catalogado como: **ESTUDIO CLINICO CON RIESGO MEDIO,** según detalle:

Título del Proyecto:	"MEJORANDO LA IDENTIFICACIÓN DEL TRANSTORNO NEUROCOGNITIVO ASOCIADO A VIH (TNAV)EN LATINOAMÉRICA; UN ENFOQUE MULTIMODAL EN PERÚ"
Código de Inscripción:	**ID-016-CIEI-2025.**
Modalidad de investigación :	***EXTRA-INSTITUCIONAL***
Investigador (es):	**MÓNICA MARÍA DÍAZ.MD, MS** **CÉSAR RAMAL ASAYAG, MD** **MARTIN CASAPIA.MD**

Cualquier eventualidad durante su ejecución, los investigadores reportarán de acuerdo con las Normas y plazos establecidos, así mismo emitirán el informe final socializando los **RESULTADOS** obtenidos. El presente documento tiene vigencia hasta el 27 de marzo del 2026. El trámite para su renovación será un mínimo de 30 días antes de su vencimiento.

Punchana, 27 de Marzo del 2025.

31/04/25
14:35 p.m.

JRMALL/RCHH/RAAM/JLGP/JERR.

"HOSPITAL REGIONAL DE LORETO "FELIPE ARRIOLA IGLESIAS"

CONSTANCIA No 015– CIEI – HRL – 2025

El presidente del Comité Institucional de Ética é Investigación del Hospital Regional de Loreto, (CIEI) a través de la Oficina de Apoyo a la Docencia é Investigación, HACE **CONSTAR** que el presente proyecto de Investigación, consignado líneas abajo, fue **APROBADO**, en cumplimiento de los estándares del Instituto Nacional de Salud (INS), acorde con las prioridades Regionales de Investigación, Balance Riesgo/beneficio y confiabilidad de los datos, entre otras. Siendo catalogado como: **ESTUDIO CLINICO SIN RIESGO,** según detalle:

Título del Proyecto:	**"DESARROLLANDO Y MEJORANDO ESTRATEGIAS PARA LA PREVENCIÓN DEL CÁNCER DE CUELLO UTERINO EN EL PERÚ"**
Código de Inscripción:	**ID-055-CIEI-2021.**
Modalidad de investigación :	***EXTRA-INSTITUCIONAL***
Investigador (es):	**DRA. VALERIE PAZ SOLDAN.**

Cualquier eventualidad durante su ejecución, los investigadores reportarán de acuerdo con las Normas y plazos establecidos, así mismo emitirán el informe final socializando los **RESULTADOS** obtenidos. El presente documento tiene vigencia hasta el 20 de marzo del 2026. El trámite para su renovación será un mínimo de 30 días antes de su vencimiento.

Punchana, 20 de Marzo del 2025.

Cristina Hidalgo
16/04/2025

Hospital Regional de Loreto
Felipe Arriola Iglesias
Comité Institucional de Ética e Investigación

DR. CESAR J. LAGUNA AGUAYA

JRMALL/RCHH/CJRA/JUGP/JERR.

"HOSPITAL REGIONAL DE LORETO "FELIPE ARRIOLA IGLESIAS"

CONSTANCIA No 018– CIEI – HRL – 2025

El presidente del Comité Institucional de Ética é Investigación del Hospital Regional de Loreto, (CIEI) a través de la Oficina de Apoyo a la Docencia é Investigación, HACE **CONSTAR** que el presente proyecto de Investigación, consignado líneas abajo, fue **APROBADO**, en cumplimiento de los estándares del Instituto Nacional de Salud (INS), acorde con las prioridades Regionales de Investigación, Balance Riesgo/beneficio y confiabilidad de los datos, entre otras. Siendo catalogado como: **ESTUDIO CLINICO RIESGO ALTO,** según detalle:

Título del Proyecto:	**"ANÁLISIS GENÓMICO DE BACTERIAS KAPEc RESISTENTES A ANTIBIÓTICOS DE DIFERENTES REGIONES DE PERÚ PARA ELUCIDAR RUTAS DE TRANSMISIÓN MEDIANTE EL ENFOQUE ONE HEALTH "**
Código de Inscripción:	**ID-018-CIEI-2023.**
Modalidad de investigación :	***EXTRA-INSTITUCIONAL***
Investigador (es):	**LUCIANO AUGUSTO PALOMINO KOBAYASHI**

Cualquier eventualidad durante su ejecución, los investigadores reportarán de acuerdo con las Normas y plazos establecidos, así mismo emitirán el informe final socializando los **RESULTADOS** obtenidos. El presente documento tiene vigencia hasta el 07 de abril del 2026. El trámite para su renovación será un mínimo de 30 días antes de su vencimiento.

Punchana, 07 de Abril del 2025.

Hospital Regional de Loreto
"Felipe Arriola Iglesias"
DR. CESAR J. RAMAL ASAYA

JRMALL/RCHH/RAAM/JLGP/JERR.

"HOSPITAL REGIONAL DE LORETO "FELIPE ARRIOLA IGLESIAS"

CONSTANCIA No 017– CIEI – HRL – 2025

El presidente del Comité Institucional de Ética é Investigación del Hospital Regional de Loreto, (CIEI) a través de la Oficina de Apoyo a la Docencia é Investigación, HACE **CONSTAR** que el presente proyecto de Investigación, consignado líneas abajo, fue **APROBADO**, en cumplimiento de los estándares del Instituto Nacional de Salud (INS), acorde con las prioridades Regionales de Investigación, Balance Riesgo/beneficio y confiabilidad de los datos, entre otras. Siendo catalogado como: **ESTUDIO CLINICO BAJO RIESGO,** según detalle:

Título del Proyecto:	"EVALUACIÓN DE DOS TÉCNICAS DIAGNÓSTICAS PARA LA DETECCIÓN DE HISTOPLASMOSIS EN UNA REGIÓN CON ELEVADO RIESGO DE ADQUISICIÓN "
Código de Inscripción:	**ID-053-CIEI-2023.**
Modalidad de investigación :	***EXTRA-INSTITUCIONAL***
Investigador (es):	**MC. JUAN CARLOS CELIS SALINAS.** **MC. EDGAR ANTONIO RAMIREZ GARCIA.** **MC. WILFREDO MARTIN CASAPIA MORALES.**

Cualquier eventualidad durante su ejecución, los investigadores reportarán de acuerdo con las Normas y plazos establecidos, así mismo emitirán el informe final socializando los **RESULTADOS** obtenidos. El presente documento tiene vigencia hasta el 03 de abril del 2026. El trámite para su renovación será un mínimo de 30 días antes de su vencimiento.

Punchana, 03 de Abril del 2025.

Hospital Regional de Loreto
"Felipe Arriola Iglesias"
DR. CESAR J. RAMAL ASAYAG

JRMALL/RCHH/RAAM/JLGP/JERR.

"HOSPITAL REGIONAL DE LORETO "FELIPE ARRIOLA IGLESIAS"

CONSTANCIA No 020– CIEI – HRL – 2025

El director del Hospital Regional de Loreto; a través de la Oficina de Apoyo a la Docencia e Investigación, y el Comité Institucional de Ética en Investigación (CIEI), **HACE CONSTAR** que el presente proyecto de Investigación, consignado líneas abajo, fue **APROBADO**, en cumplimiento de los estándares del Instituto Nacional de Salud (INS), acorde con las prioridades Regionales de Investigación, Balance Riesgo/beneficio y confiabilidad de los datos, entre otras. Siendo catalogado como: **ESTUDIO CLÍNICO CON RIESGO MEDIO**, según detalle:

Título del Proyecto:	**"RECOLECCIÓN DE MUESTRAS CLÍNICAS DE ENFERMEDADES TROPICALES E INFECCIOSAS, ENFERMEDADES AUTOINMUNE Y DONANTES SANOS" VERSIÓN 3.5 DE FECHA 20 DE FEBRERO 2024-PROTOCOLO #: CRSPTL-00001(BB-ID-061).**
Código de Inscripción:	**ID-14-CIEI-2022.**
Modalidad de investigación :	**EXTRAINSTITUCIONAL.**
Investigador (es):	**DR. JUAN CARLOS HINOJOSA BOYER.**

Cualquier eventualidad durante su ejecución, los investigadores reportarán de acuerdo con las Normas y plazos establecidos, así mismo emitirán el informe final socializando los **RESULTADOS** obtenidos. El presente documento tiene vigencia hasta el 08 de abril del 2026. El trámite para su renovación será un mínimo de 30 días antes de su vencimiento.

Punchana,08 de Abril del 2025.

Hospital Regional de Loreto
"Felipe Arriola Iglesias"
DR. CESAR J. RAMAL ASAYA

JRMALL/RCHH/CJRA/JLGP/JBRR.

"HOSPITAL REGIONAL DE LORETO "FELIPE ARRIOLA IGLESIAS"

CONSTANCIA No 021– CIEI – HRL – 2025

El Director del Hospital Regional de Loreto; a través de la Oficina de Apoyo a la Docencia é Investigación, y el Comité Institucional de Ética en Investigación (CIEI), **HACE CONSTAR** que el **"CONSENTIMIENTO INFORMADO PARA PADRES"** para participar en el estudio de investigación del protocolo de Investigación, **"COLECCIÓN DE MUESTRAS CLÍNICAS VOLUNTARIOS PEDIATRICOS SALUDABLES. VERIÓN 2.0 DE FECHA 20 DE FEBRERO 2024-PROTOCOLO CRSPTL - 00072,** fue **APROBADO,** en cumplimiento de los estándares del Instituto Nacional de Salud (INS), acorde con las prioridades Regionales de Investigación, Balance Riesgo/beneficio y confiabilidad de los datos, entre otras.

Se detalla a continuación los datos del proyecto.

Título del Proyecto:	**"COLECCIÓN DE MUESTRAS CLÍNICAS VOLUNTARIOS PEDIÁTRICOS SALUDABLES" VERSION 2.0 - PROTOCOLO CRSPTL-00072).**
Código de Inscripción:	**ID-15-CIEI-2022**
Modalidad de investigación :	**EXTRAINSTITUCIONAL**
Investigador (es):	**DR. JUAN CARLOS HINOJOSA BOYER.**

Cualquier eventualidad durante su ejecución, los investigadores reportarán de acuerdo con las Normas y plazos establecidos, así mismo emitirán el informe final socializando los **RESULTADOS** obtenidos. El presente documento tiene vigencia hasta el 08 de abril del 2026. El trámite para su renovación será un mínimo de 30 días antes de su vencimiento.

Punchana, 08 de abril del 2025.

Hospital Regional de Loreto
"Felipe Arriola Iglesias"

JRMALL/RCHH/CJRA/JLGP/JERR.

"HOSPITAL REGIONAL DE LORETO "FELIPE ARRIOLA IGLESIAS"

CONSTANCIA No 022– CIEI – HRL – 2025

El director del Hospital Regional de Loreto; a través de la Oficina de Apoyo a la Docencia e Investigación, y el Comité Institucional de Ética en Investigación (CIEI), **HACE CONSTAR** que el presente proyecto de Investigación, consignado líneas abajo, fue **APROBADO**, en cumplimiento de los estándares del Instituto Nacional de Salud (INS), acorde con las prioridades Regionales de Investigación, Balance Riesgo/beneficio y confiabilidad de los datos, entre otras. Siendo catalogado como: **ESTUDIO CLÍNICO CON RIESGO MEDIO**, según detalle:

Título del Proyecto:	**COLECCIÓN DE MUESTRAS CLÍNICAS VOLUNTARIOS PEDIÁTRICOS SALUDABLES. PROTOCOLO # CRSPTL-00072. VERSIÓN 2.0 DEL 20 DE FEBRERO 2024.**
Código de Inscripción:	**ID-09-CIEI-2023.**
Modalidad de investigación :	**EXTRAINSTITUCIONAL.**
Investigador (es):	**DR. JUAN CARLOS HINOJOSA BOYER.**

Cualquier eventualidad durante su ejecución, los investigadores reportarán de acuerdo con las Normas y plazos establecidos, así mismo emitirán el informe final socializando los RESULTADOS obtenidos. El presente documento tiene vigencia hasta el 08 de abril del 2026. El trámite para su renovación será un mínimo de 30 días antes de su vencimiento.

Punchana, 08 de Abril del 2025.

Hospital Regional de Loreto
"Felipe Arriola Iglesias"
Comité Institucional de Ética en Investigación

DR. CESAR J. RAMAL ASAYA
Presidente del Comité Institucional de Ética en Investigación

JRMALL/RCHH/CJRA/JLGP/JERR.

"HOSPITAL REGIONAL DE LORETO "FELIPE ARRIOLA IGLESIAS"

CONSTANCIA No 023– CIEI – HRL – 2025

El Director del Hospital Regional de Loreto; a través de la Oficina de Apoyo a la Docencia é Investigación, y el Comité Institucional de Ética en Investigación (CIEI), **HACE CONSTAR** que el **"ASENTIMIENTO INFORMADO"** para Niños/participantes entre 8 años y 17 años de edad, participar en el estudio de investigación del protocolo de Investigación, **"COLECCIÓN DE MUESTRAS CLÍNICAS VOLUNTARIOS PEDIATRICOS SALUDABLES. VERSIÓN 2.0 DE FECHA 20 DE FEBRERO 2024-PROTOCOLO CRSPTL-00072,** fue **APROBADO**, en cumplimiento de los estándares del Instituto Nacional de Salud (INS), acorde con las prioridades Regionales de Investigación, Balance Riesgo/beneficio y confiabilidad de los datos, entre otras.

Se detalla a continuación los datos del proyecto.

Título del Proyecto:	**"COLECCIÓN DE MUESTRAS CLÍNICAS VOLUNTARIOS . PEDIATRICO SALUDABLES VERSION 2.0 -PROTOCOLO CRSPTL-00072.**
Código de Inscripción:	**ID-18-CIEI-2024.**
Modalidad de investigación :	**EXTRAINSTITUCIONAL**
Investigador (es):	**DR. JUAN CARLOS HINOJOSA BOYER.**

Cualquier eventualidad durante su ejecución, los investigadores reportarán de acuerdo con las Normas y plazos establecidos, así mismo emitirán el informe final socializando los RESULTADOS obtenidos. El presente documento tiene vigencia hasta el 08 de abril del 2026. El trámite para su renovación será un mínimo de 30 días antes de su vencimiento.

Punchana, 08 de abril del 2025.

Hospital Regional de Loreto
"Felipe Arriola Iglesias"
Comité Institucional de Ética en Investigación

DR. CESAR J. RAMAL ASAYA
Presidente del Comité Institucional de Ética en Investigación

JRMALL/RCHH/CJRA/JLGP/JERR.

"HOSPITAL REGIONAL DE LORETO "FELIPE ARRIOLA IGLESIAS"

CONSTANCIA No 024– CIEI – HRL – 2025

El Director del Hospital Regional de Loreto; a través de la Oficina de Apoyo a la Docencia é Investigación, y el Comité Institucional de Ética en Investigación (CIEI), **HACE CONSTAR** que el **"CONSENTIMIENTO INFORMADO DE ADULTOS PARA PARTICIPAR EN UN ESTUDIO DE INVESTIGACION"** para la , **"RECOLECCIÓN DE MUESTRA CLÍNICA DE ENFERMEDADES TROPICALES E INFECCIOSAS, ENFERMEDADES AUTOINMUNE Y DONANTES SANOS.** fue **APROBADO**, en cumplimiento de los estándares del Instituto Nacional de Salud (INS), acorde con las prioridades Regionales de Investigación, Balance Riesgo/beneficio y confiabilidad de los datos, entre otras.

Se detalla a continuación los datos del proyecto.

Título del Proyecto:	**"RECOLECCIÓN DE MUESTRAS CLÍNICAS DE ENFERMEDADES TROPICALES E INFECCIOSAS, ENFERMEDADES AUTOINMUNE Y DONANTES SANOS" VERSION 3.5 DE FECHA 20 DE FEBRERO 2024-PROTOCOLO CRSPTL-00001(BB-ID-061).**
Código de Inscripción:	**ID-19-CIEI-2024.**
Modalidad de investigación :	**EXTRAINSTITUCIONAL**
Investigador (es):	**DR. JUAN CARLOS HINOJOSA BOYER.**

Cualquier eventualidad durante su ejecución, los investigadores reportarán de acuerdo con las Normas y plazos establecidos, así mismo emitirán el informe final socializando los RESULTADOS obtenidos. El presente documento tiene vigencia hasta el 08 de abril del 2025. El trámite para su renovación será un mínimo de 30 días antes de su vencimiento.

Punchana, 08 de abril del 2025.

Hospital Regional de Loreto
"Felipe Arriola Iglesias"
Comité Institucional de Ética e Investigación

DR. CESAR J. RAMAL ASAYA
Presidente Comité Institucional de Ética e Investigación

JRMALL/RCHH/CJRA/JLGP/JERR.

"HOSPITAL REGIONAL DE LORETO "FELIPE ARRIOLA IGLESIAS"

CONSTANCIA No 029– CIEI – HRL – 2025

El presidente del Comité Institucional de Ética é Investigación del Hospital Regional de Loreto, (CIEI) a través de la Oficina de Apoyo a la Docencia é Investigación, HACE **CONSTAR** que el presente proyecto de Investigación, consignado líneas abajo, fue **APROBADO**, en **cumplimiento de los estándares del Instituto Nacional de Salud (INS), acorde con las** prioridades Regionales de Investigación, Balance Riesgo/beneficio y confiabilidad de los datos, entre otras. Siendo catalogado como: **ESTUDIO CLINICO SIN RIESGO,** según detalle:

Título del Proyecto:	**"EVALUACIÓN DE LA RESPUESTA TEMPRANA A UNA SOLA DOSÍS DE ARTESUNATO INTRAVENOSO EN MALARÍA GRAVE: UN ESTUDIO PROSPECTIVOEN UN ENTORNO CON RECURSOS LIMITADOS "**
Código de Inscripción:	**ID-029-CIEI-2025.**
Modalidad de investigación :	**EXTRA - INSTITUCIONAL**
Investigador (es):	**Dra. LIVIA BRESCIANE**

.

Cualquier eventualidad durante su ejecución, los investigadores reportarán de acuerdo con las Normas y plazos establecidos, así mismo emitirán el informe final socializando los **RESULTADOS** obtenidos. El presente documento tiene vigencia hasta el 12 de Mayo del 2026. El trámite para su renovación será un mínimo de 30 días antes de su vencimiento.

Punchana, 12 de Mayo del 2025.

Hospital Regional de Loreto
"Felipe Arriola Iglesias"

JRMALL/RCHH/CJRA/JLGP/JERR.

"HOSPITAL REGIONAL DE LORETO "FELIPE ARRIOLA IGLESIAS"

CONSTANCIA No 030– CIEI – HRL – 2025

El presidente del Comité Institucional de Ética é Investigación del Hospital Regional de Loreto, (CIEI) a través de la Oficina de Apoyo a la Docencia é Investigación, HACE **CONSTAR** que el presente proyecto de Investigación, consignado líneas abajo, fue **APROBADO**, en cumplimiento de los estándares del Instituto Nacional de Salud (INS), acorde con las prioridades Regionales de Investigación, Balance Riesgo/beneficio y confiabilidad de los datos, entre otras. Siendo catalogado como: **ESTUDIO CLINICO SIN RIESGO,** según detalle:

Título del Proyecto: **"EVALUACIÓN RETROSPECTIVA DEL ACLARAMIENTO DE PARASITEMIA TRAS UNA DOSIS ÚNICA DE ARTESUNATO INTRAVENOSO PARA MALARIA GRAVE" : EVALUACIÓN DEL POTENCIAL DE TRANSICIÓ N TEMPRAMA A TRATAMIENTO ORAL EN CONTEXTOS CON RECURSOS LIMITADOS.**

Código de Inscripción: **ID-030-CIEI-2025.**

Modalidad de investigación : **EXTRA - INSTITUCIONAL**

Investigador (es): **Dra. LIVIA BRESCIANE**

.

Cualquier eventualidad durante su ejecución, los investigadores reportarán de acuerdo con las Normas y plazos establecidos, así mismo emitirán el informe final socializando los **RESULTADOS** obtenidos. El presente documento tiene vigencia hasta el 12 de mayo del 2026. El trámite para su renovación será un mínimo de 30 días antes de su vencimiento.

Punchana, 12 de Mayo del 2025.

Hospital Regional de Loreto
"Felipe Arriola Iglesias"
Comité Institucional de Ética e Investigación

DR. CESAR J. RAMAL ASAYA
Presidente del Comité Institucional de Ética e Investigación

JRMALL/RCHH/CJRA/JLGP/JEGR.

12/5/25

"HOSPITAL REGIONAL DE LORETO "FELIPE ARRIOLA IGLESIAS"

CONSTANCIA No 041– CIEI – HRL – 2025

El presidente del Comité Institucional de Ética é Investigación del Hospital Regional de Loreto, (CIEI) a través de la Oficina de Apoyo a la Docencia é Investigación, HACE **CONSTAR** que el presente proyecto de Investigación, consignado líneas abajo, fue **APROBADO**, en cumplimiento de los estándares del Instituto Nacional de Salud (INS), acorde con las prioridades Regionales de Investigación, Balance Riesgo/beneficio y confiabilidad de los datos, entre otras. Siendo catalogado como: **ESTUDIO CLINICO SIN RIESGO** , según detalle:

Título del Proyecto:	**"CARACTERISTICAS CLINICAS Y EPIDEMIOLOGICAS DE LA EPIDEMIA DE VIRUS OROPOUCHE EN LA REGION LORETO, PERU"**
Código de Inscripción:	**ID-041-CIEI-2025.**
Modalidad de investigación :	***EXTRA-INSTITUCIONAL***
Investigador (es):	**MIGUEL ANGEL ROJO PEREZ**

Cualquier eventualidad durante su ejecución, los investigadores reportarán de acuerdo con las Normas y plazos establecidos, así mismo emitirán el informe final socializando los **RESULTADOS** obtenidos. El presente documento tiene vigencia hasta el 21 de Mayo del 2026. El trámite para su renovación será un mínimo de 30 días antes de su vencimiento.

Recibido
el 22/5/25
11:15 a.m.

Punchana, 21 de Mayo del 2025.

Hospital Regional de Loreto
"Felipe Arriola Iglesias"
Comité Institucional de Ética e Investigación

DR. CESAR J. RAMAL ASAYA
Presidente del Comité Institucional de Ética e Investigación

JRMALL/RCHH/CJRA/JLGP/JERR.

"HOSPITAL REGIONAL DE LORETO "FELIPE ARRIOLA IGLESIAS"

CONSTANCIA No 049– CIEI – HRL – 2025

El presidente del Comité Institucional de Ética é Investigación del Hospital Regional de Loreto, (CIEI) a través de la Oficina de Apoyo a la Docencia é Investigación, HACE CONSTAR que el presente proyecto de Investigación, consignado líneas abajo, fue APROBADO, en cumplimiento de los estándares del Instituto Nacional de Salud (INS), acorde con las prioridades Regionales de Investigación, Balance Riesgo/beneficio y confiabilidad de los datos, entre otras. Siendo catalogado como: ESTUDIO CLINICO CON RIESGO MINIMO, según detalle:

Título del Proyecto:		**"ESTUDIO OBSERVACIONAL DE SEPSIS EN IQUITOS, PERÚ"**
Código de Inscripción:		**ID-032-CIEI-2024.**
Modalidad de investigación	:	**EXTRA - INSTITUCIONAL**
Investigador (es):		**BIOLOGA CAROLINA GUEVARA**

Cualquier eventualidad durante su ejecución, los investigadores reportarán de acuerdo con las Normas y plazos establecidos, así mismo emitirán el informe final socializando los RESULTADOS obtenidos. El presente documento tiene vigencia hasta el 29 de Mayo del 2026. El trámite para su renovación será un mínimo de 30 días antes de su vencimiento.

Punchana, 29 de Mayo del 2025.

Hospital Regional de Loreto
"Felipe Arriola Iglesias"
Unidad de Docencia e Investigación
DR. CESAR J. [illegible] ASAYA

JRMALL/RCHH/CJRA/JLGP/JERR.

29/05/25

"HOSPITAL REGIONAL DE LORETO "FELIPE ARRIOLA IGLESIAS"

CONSTANCIA No 057– CIEI – HRL – 2025

El presidente del Comité Institucional de Ética é Investigación del Hospital Regional de Loreto, (CIEI) a través de la Oficina de Apoyo a la Docencia é Investigación, HACE CONSTAR que el presente proyecto de Investigación, consignado líneas abajo, fue APROBADO, en cumplimiento de los estándares del Instituto Nacional de Salud (INS), acorde con las prioridades Regionales de Investigación, Balance Riesgo/beneficio y confiabilidad de los datos, entre otras. Siendo catalogado como: ESTUDIO CLINICO SIN RIESGO MEDIO, según detalle:

.

Título del Proyecto:		**"UNA APLICACIÓN DE TELÉFONOS INTELIGENTES BASADA EN UNA RED NEURONAL ARTIFICIALES PARA DIAGNÓSTICO EN EL PUNTO DE ATENCIÓN DE LA MALARIA EN LA AMAZONIÍA PERUANA"**
Código de Inscripción:		**ID-024-CIEI-2024.**
Modalidad de investigación	:	**EXTRAINSTITUCIONAL.**
Investigador (es):		**DR. MARTIN CASAPIA MORALES.**

Cualquier eventualidad durante su ejecución, los investigadores reportarán de acuerdo con las Normas y plazos establecidos, así mismo emitirán el informe final socializando los RESULTADOS obtenidos. El presente documento tiene vigencia hasta el 19 de Junio del 2026. El trámite para su renovación será un mínimo de 30 días antes de su vencimiento.

Punchana, 19 de Junio del 2025.

Hospital Regional de Loreto
"Felipe Arriola Iglesias"

20/06/25

JRMALL/RCHH/CJRA/JLGP/JERR.

"HOSPITAL REGIONAL DE LORETO "FELIPE ARRIOLA IGLESIAS"

CONSTANCIA No 058– CIEI – HRL – 2025

El presidente del Comité Institucional de Ética é Investigación del Hospital Regional de Loreto, (CIEI) a través de la Oficina de Apoyo a la Docencia é Investigación, HACE CONSTAR que el presente proyecto de Investigación, consignado líneas abajo, fue APROBADO, en cumplimiento de los estándares del Instituto Nacional de Salud (INS), acorde con las prioridades Regionales de Investigación, Balance Riesgo/beneficio y confiabilidad de los datos, entre otras. Siendo catalogado como: ESTUDIO CLINICO SIN RIESGO MEDIO, según detalle:

Título del Proyecto:		**"TUBERCULOSIS RESISTENTE: FACTORES PREDICTIVOS DE RESULTADOS NO EXITOSOS AL TRATAMIENTO EN LA REGIÓN LORETO, PERÚ, 2015-2023"**
Código de Inscripción:		**ID-058-CIEI-2025.**
Modalidad de investigación	:	**EXTRAINSTITUCIONAL.**
Investigador (es):		**BLGA. EVELYN GENTHELL CÓRDOVA PISCO** **BLGO. GEORGE OBREGON BOLTAN.** **DRA. KARINE ZEVALLOS VILLEGAS.** **BLGA. ESTELA ALEJANDRA HUAMÁN ANGELES.** **DRA. TERY VASQUEZ HASSINGER.**

Cualquier eventualidad durante su ejecución, los investigadores reportarán de acuerdo con las Normas y plazos establecidos, así mismo emitirán el informe final socializando los RESULTADOS obtenidos. El presente documento tiene vigencia hasta el 23 de Junio del 2026. El trámite para su renovación será un mínimo de 30 días antes de su vencimiento.

Punchana, 23 de Junio del 2025.

Hospital Regional de Loreto
"Felipe Arriola Iglesias"
Comité Institucional de Ética e Investigación
DR. CESAR J. RAMAL ASAYA

30-06-2025.
8:56 am.

JRMALL/RCHH/CJRA/JLGP/JERR.

"HOSPITAL REGIONAL DE LORETO "FELIPE ARRIOLA IGLESIAS"

CONSTANCIA No 059– CIEI – HRL – 2025

El presidente del Comité Institucional de Ética é Investigación del Hospital Regional de Loreto, (CIEI) a través de la Oficina de Apoyo a la Docencia é Investigación, HACE CONSTAR que el presente proyecto de Investigación, consignado líneas abajo, fue APROBADO, en cumplimiento de los estándares del Instituto Nacional de Salud (INS), acorde con las prioridades Regionales de Investigación, Balance Riesgo/beneficio y confiabilidad de los datos, entre otras. Siendo catalogado como: ESTUDIO CLINICO SIN RIESGO MEDIO, según detalle:

Título del Proyecto:		**"BROTE DE ENFERMEDAD MENINGOCÓCICA INVASIVA EN LA AMAZONÍA PERUANA"**
Código de Inscripción:		**ID-059-CIEI-2025.**
Modalidad de investigación	:	**EXTRAINSTITUCIONAL.**
Investigador (es):		**DR. JUAN CARLOS CELIS SALINAS.**

Cualquier eventualidad durante su ejecución, los investigadores reportarán de acuerdo con las Normas y plazos establecidos, así mismo emitirán el informe final socializando los RESULTADOS obtenidos. El presente documento tiene vigencia hasta el 30 de Junio del 2026. El trámite para su renovación será un mínimo de 30 días antes de su vencimiento.

Punchana, 30 de Junio del 2025.

1/7/25

Hospital Regional de Loreto "Felipe Arriola Iglesias" Comité Institucional de Ética e Investigación

DR. CESAR J. CAMPOS ASAYAS

JRMALL/RCHH/CJRA/JLGP/JERR.

"HOSPITAL REGIONAL DE LORETO "FELIPE ARRIOLA IGLESIAS"

CONSTANCIA No 061– CIEI – HRL – 2025

El presidente del Comité Institucional de Ética é Investigación del Hospital Regional de Loreto, (CIEI) a través de la Oficina de Apoyo a la Docencia é Investigación, HACE CONSTAR que el presente proyecto de Investigación, consignado líneas abajo, fue APROBADO, en cumplimiento de los estándares del Instituto Nacional de Salud (INS), acorde con las prioridades Regionales de Investigación, Balance Riesgo/beneficio y confiabilidad de los datos, entre otras. Siendo catalogado como: ESTUDIO CLINICO CON RIESGO MEDIO, según detalle:

Título del Proyecto:	**"CARACTERIZACIÓN DE LAS CAUSAS INFECCIOSAS DE LA ENFERMEDAD FEBRIL AGUDA Y EXANTEMÁTICA EN LATINOAMERICA"**
Código de Inscripción:	**ID-037-CIEI-2021.**
Modalidad de investigación :	**EXTRA-INSTITUCIONAL.**
Investigador (es):	**DRA. JULIA SONIA AMPUERO VELA.**

Cualquier eventualidad durante su ejecución, los investigadores reportarán de acuerdo con las Normas y plazos establecidos, así mismo emitirán el informe final socializando los RESULTADOS obtenidos. El presente documento tiene vigencia hasta el 07 de Julio del 2026. El trámite para su renovación será un mínimo de 30 días antes de su vencimiento.

Punchana, 07 de Julio del 2025.

Hospital Regional de Loreto "Felipe Arriola Iglesias" Comité Institucional de Ética e Investigación

DR. CESAR J. KAMAL ASAYA

Presidente del Comité Institucional de Ética e Investigación

Melita Pizango. 08/07/25. 11:08 am.

JRMALL/RCHH/CJRA/JLGP/JERR.

"HOSPITAL REGIONAL DE LORETO "FELIPE ARRIOLA IGLESIAS"

CONSTANCIA No 067– CIEI – HRL – 2025

El presidente del Comité Institucional de Ética é Investigación del Hospital Regional de Loreto, (CIEI) a través de la Oficina de Apoyo a la Docencia é Investigación, HACE CONSTAR que el presente proyecto de Investigación, consignado líneas abajo, fue APROBADO, en cumplimiento de los estándares del Instituto Nacional de Salud (INS), acorde con las prioridades Regionales de Investigación, Balance Riesgo/beneficio y confiabilidad de los datos, entre otras. Siendo catalogado como: ESTUDIO CLINICO CON RIESGO MINIMO, según detalle:

Título del Proyecto:	**"ESTUDIO OBSERVACIONAL DE SEPSIS EN IQUITOS, PERU"** **PROTOCOLO DEL ESTUDIO VERSION 12 -05-2025.** **CONSENTIMIENTO INFORMADO VERSION 2.0, 12-05-2025.** **REPORTE DE CASO, VERSION 2.0 – ACTUALIZADO 12-06-2025.**
Código de Inscripción:	**ID-032-CIEI-2024.**
Modalidad de investigación :	**EXTRA-INSTITUCIONAL.**
Investigador (es):	**BIOLOGA. CAROLINA GUEVARA**

Cualquier eventualidad durante su ejecución, los investigadores reportarán de acuerdo con las Normas y plazos establecidos, así mismo emitirán el informe final socializando los RESULTADOS obtenidos. El presente documento tiene vigencia hasta el 21 de Julio del 2026. El trámite para su renovación será un mínimo de 30 días antes de su vencimiento.

Punchana, 21 de Julio del 2025.

Hospital Regional de Loreto "Felipe Arriola Iglesias"
DR. CESAR J. RAMAL ASAYA

21-07-2025 10:37

JRMALL/RCHH/CJRA/JLGP/JERR.

"HOSPITAL REGIONAL DE LORETO "FELIPE ARRIOLA IGLESIAS"

CONSTANCIA No 070– CIEI – HRL – 2025

El presidente del Comité Institucional de Ética é Investigación del Hospital Regional de Loreto, (CIEI) a través de la Oficina de Apoyo a la Docencia é Investigación, HACE CONSTAR que el presente proyecto de Investigación, consignado líneas abajo, fue APROBADO, en cumplimiento de los estándares del Instituto Nacional de Salud (INS), acorde con las prioridades Regionales de Investigación, Balance Riesgo/beneficio y confiabilidad de los datos, entre otras. Siendo catalogado como: ESTUDIO CLINICO SIN RIESGO, según detalle:

Título del Proyecto:		**"PREVALENCIA Y FACTORES ASOCIADOS A TRANSTORNOS NEUROCOGNITIVOS EN PACIENTES CON VIH EN IQUITOS, PERÚ"**
Código de Inscripción:		**ID-070-CIEI-2025.**
Modalidad de investigación	:	**EXTRA - INSTITUCIONAL.**
Investigador (es):		**WILFREDO MARTIN CASAPIA MORALES**

Cualquier eventualidad durante su ejecución, los investigadores reportarán de acuerdo con las Normas y plazos establecidos, así mismo emitirán el informe final socializando los RESULTADOS obtenidos. El presente documento tiene vigencia hasta el 01 de Agosto del 2026. El trámite para su renovación será un mínimo de 30 días antes de su vencimiento.

Punchana, 01 de Agosto del 2025.

GERENCIA REGIONAL DE LORETO
HRL "FELIPE ARRIOLA IGLESIAS"
COMITÉ INSTITUCIONAL DE ÉTICA EN INVESTIGACIÓN
Q.F. ROY A. ALVAREZ MARREROS

01 AGO 2025
47249433
Henrry Alejandro Reyes Vasquez

JRMALL/RCHH/RAAM/JLGP/JERR.

"HOSPITAL REGIONAL DE LORETO "FELIPE ARRIOLA IGLESIAS"

CONSTANCIA No 071– CIEI – HRL – 2025

El presidente del Comité Institucional de Ética é Investigación del Hospital Regional de Loreto, (CIEI) a través de la Oficina de Apoyo a la Docencia é Investigación, HACE CONSTAR que el presente proyecto de Investigación, consignado líneas abajo, fue APROBADO, en cumplimiento de los estándares del Instituto Nacional de Salud (INS), acorde con las prioridades Regionales de Investigación, Balance Riesgo/beneficio y confiabilidad de los datos, entre otras. Siendo catalogado como: ESTUDIO CLINICO SIN RIESGO, según detalle:

Título del Proyecto:	**"EFECTO DE UNA INTERVENCIÓN EDUCATIVA EN PERSONAL DE SALUD SOBRE SATISFACCIÓN LABORAL Y EL COMPROMISO INSTITUCIONAL EN UN HOSPITAL RURAL II-1 SANTA CLOTILDE, MAYNAS, 2024 Y 2025"**
Código de Inscripción:	**ID-096-CIEI-2024.**
Modalidad de investigación :	**EXTRA - INSTITUCIONAL.**
Investigador (es):	**LIC.ENF. LILA YANABEL FERNANDEZ BURGA.**

Cualquier eventualidad durante su ejecución, los investigadores reportarán de acuerdo con las Normas y plazos establecidos, así mismo emitirán el informe final socializando los RESULTADOS obtenidos. El presente documento tiene vigencia hasta el 31 de Julio del 2026. El trámite para su renovación será un mínimo de 30 días antes de su vencimiento.

Punchana, 31 de Julio del 2025.

Hospital Regional de Loreto "Felipe Arriola Iglesias" Comité Institucional de Ética e Investigación

Mirely Madrid Piñedo
71471968
8:39 am
01/08/2025

JRMALL/RCHH/CJRA/JLOP/JERR.

"HOSPITAL REGIONAL DE LORETO "FELIPE ARRIOLA IGLESIAS"

CONSTANCIA No 074– CIEI – HRL – 2025

El presidente del Comité Institucional de Ética é Investigación del Hospital Regional de Loreto, (CIEI) a través de la Oficina de Apoyo a la Docencia é Investigación, HACE CONSTAR que el presente proyecto de Investigación, consignado líneas abajo, fue APROBADO, en cumplimiento de los estándares del Instituto Nacional de Salud (INS), acorde con las prioridades Regionales de Investigación, Balance Riesgo/beneficio y confiabilidad de los datos, entre otras. Siendo catalogado como: ESTUDIO CLINICO SIN RIESGO, según detalle:

Título del Proyecto:		**"DIAGNÓSTICO DE TUBERCULOSIS MAMARIA, ENTIDAD DESATENDIDA EN LA PRÁCTICA CLÍNICA : EVALUACIÓN MULTICÉNTRICA DEL RENDIMIENTO DE GENEXPERT MTB/RIF ULTRA Y STANDARD M10 EN EL PERÚ"**
Código de Inscripción:		**ID-074-CIEI-2025.**
Modalidad de investigación	:	**EXTRA-INSTITUCIONAL.**
Investigador (es):		**DRA. LIVIA TUCKER BRESCIANI**

Cualquier eventualidad durante su ejecución, los investigadores reportarán de acuerdo con las Normas y plazos establecidos, así mismo emitirán el informe final socializando los RESULTADOS obtenidos. El presente documento tiene vigencia hasta el 07 de Agosto del 2026. El trámite para su renovación será un mínimo de 30 días antes de su vencimiento.

Punchana, 07 de Agosto del 2025.

08/8/25
11:50 am

GERENCIA REGIONAL DE LORETO
"FELIPE ARRIOLA IGLESIAS"
COMITÉ INSTITUCIONAL DE ÉTICA E INVESTIGACIÓN
D.P. ROY A. JIMÉNEZ MARREROS

JRMALL/RCHH/RAAM/JLGP/IBRR.

"HOSPITAL REGIONAL DE LORETO "FELIPE ARRIOLA IGLESIAS"

CONSTANCIA No 079– CIEI – HRL – 2025.

El presidente del Comité Institucional de Ética é Investigación del Hospital Regional de Loreto, (CIEI) a través de la Oficina de Apoyo a la Docencia é Investigación, HACE CONSTAR que el presente proyecto de Investigación, consignado líneas abajo, fue APROBADO, en cumplimiento de los estándares del Instituto Nacional de Salud (INS), acorde con las prioridades Regionales de Investigación, Balance Riesgo/beneficio y confiabilidad de los datos, entre otras. Siendo catalogado como: ESTUDIO CLINICO CON RIESGO MEDIO, según detalle:

Título del Proyecto:		**"COLECCIÓN DE MUESTRAS CLINICAS VOLUNTARIOS PEDIATRICOS SALUDABLES.PROTOCOLO # CRSPTL – 00072. VERSION 2.0**
Código de Inscripción:		**ID-009-CIEI-2023.**
Modalidad de investigación	:	EXTRA - INSTITUCIONAL
Investigador (es):		**DR.JUAN CARLOS HINOJOSA BOYER.**

Cualquier enmienda, desviaciones, eventualidad durante su ejecución, los investigadores reportarán de acuerdo con las Normas y plazos establecidos, así mismo emitirán el informe final socializando los RESULTADOS obtenidos. El presente documento tiene vigencia hasta el 08 de Setiembre del 2026. El trámite para su renovación será un mínimo de 30 días antes de su vencimiento.

Punchana, 08 de Setiembre del 2025.

Hospital Regional de Loreto
Felipe Arriola Iglesias"
DR. CESAR J. RAMAL ASAYA

JRMALL/RCHH/CJRA/ELRD/JERR.

Jimmy Pandura Bocanegra
10-09-2025
13:49 HRS.

"HOSPITAL REGIONAL DE LORETO "FELIPE ARRIOLA IGLESIAS"

CONSTANCIA No 080– CIEI – HRL – 2025

El presidente del Comité Institucional de Ética é Investigación del Hospital Regional de Loreto, (CIEI) a través de la Oficina de Apoyo a la Docencia é Investigación, HACE CONSTAR que el " **ASENTIMIENTO INFORMADO** " para niños/ participantes entre 08 y 17 años de edad, participar en el estudio de investigación del protocolo " **COLECCIÓN DE MUESTRAS CLINICAS VOLUNTARIOS PEDIATRICOS SALUDABLES , PROTOCOLO # CRSPTL – 00072, VERSION 2.0,** fue APROBADO, en cumplimiento de los estándares del Instituto Nacional de Salud (INS), acorde con las prioridades Regionales de Investigación, Balance Riesgo/beneficio y confiabilidad de los datos, entre otras. Siendo catalogado como: ESTUDIO CLINICO CON RIESGO MEDIO, según detalle:

Título del Proyecto:		**"COLECCIÓN DE MUESTRAS CLINICAS VOLUNTARIOS PEDIATRICOS SALUDABLES PROTOCOLO # CRSPTL – 00072, VERSION 2.0"**
Código de Inscripción:		**ID-018-CIEI-2024.**
Modalidad de investigación	:	*EXTRA - INSTITUCIONAL*
Investigador (es):		**DR. JUAN CARLOS HINOJOSA BOYER.**

Cualquier enmienda, desviaciones, eventualidad durante su ejecución, los investigadores reportarán de acuerdo con las Normas y plazos establecidos, así mismo emitirán el informe final socializando los RESULTADOS obtenidos. El presente documento tiene vigencia hasta el 02 de SETIEMBRE del 2026. El trámite para su renovación será un mínimo de 30 días antes de su vencimiento.

Punchana, 02 de Setiembre del 2025.

Hospital Regional de Loreto
"Felipe Arriola Iglesias"
Comité Institucional de Ética e Investigación

DR. CESAR J. RAMAL ASAYA

Jimmy Pandura Babilonia
11-09-2025
13:50 HRS.

JRMALL/RCHH/CJRA/ELRC/JEBR.

"HOSPITAL REGIONAL DE LORETO "FELIPE ARRIOLA IGLESIAS"

CONSTANCIA No 081– CIEI – HRL – 2025

El presidente del Comité Institucional de Ética é Investigación del Hospital Regional de Loreto, (CIEI) a través de la Oficina de Apoyo a la Docencia é Investigación, HACE CONSTAR que el " **CONSENTIMIENTO INFORMADO PARA PADRES** " para participar en el estudio de investigación del protocolo " **COLECCIÓN DE MUESTRAS CLINICAS VOLUNTARIOS PEDIATRICOS SALUDABLES , PROTOCOLO # CRSPTL – 00072, VERSION 2.0,** fue APROBADO, en cumplimiento de los estándares del Instituto Nacional de Salud (INS), acorde con las prioridades Regionales de Investigación, Balance Riesgo/beneficio y confiabilidad de los datos, entre otras. Siendo catalogado como: ESTUDIO CLINICO CON RIESGO MEDIO, según detalle:

Título del Proyecto:		**"COLECCIÓN DE MUESTRAS CLINICAS VOLUNTARIOS PEDIATRICOS SALUDABLES PROTOCOLO # CRSPTL – 00072, VERSION 2.0"**
Código de Inscripción:		**ID-015-CIEI-2022.**
Modalidad de investigación	:	*EXTRA - INSTITUCIONAL*
Investigador (es):		**DR. JUAN CARLOS HINOJOSA BOYER.**

Cualquier enmienda, desviaciones, eventualidad durante su ejecución, los investigadores reportarán de acuerdo con las Normas y plazos establecidos, así mismo emitirán el informe final socializando los RESULTADOS obtenidos. El presente documento tiene vigencia hasta el 02 de SETIEMBRE del 2026. El trámite para su renovación será un mínimo de 30 días antes de su vencimiento.

Punchana, 02 de Setiembre del 2025.

Hospital Regional de Loreto
"Felipe Arriola Iglesias"
Comité Institucional de Ética e Investigación
DR. CÉSAR J. RAMOS ASAYA

Jimmy Panduro Babilonia
11-09-2025
13:51 HRS.

JRMALL/RCHH/CJRA/ELRC/JEBR.

GERENCIA REGIONAL DE SALUD - LORETO
HOSPITAL REGIONAL DE LORETO "FELIPE ARRIOLA IGLESIAS

CONSTANCIA No 092– CIEI – HRL – 2025

El presidente del Comité Institucional de Ética é Investigación (CIEI) del Hospital Regional de Loreto a través de la Oficina de Apoyo a la Docencia é Investigación, HACE CONSTAR que el presente proyecto de Investigación, consignado líneas abajo, fue APROBADO, en cumplimiento de los estándares del Instituto Nacional de Salud (INS), acorde con las prioridades Regionales de Investigación, Balance Riesgo/beneficio y confiabilidad de los datos, entre otras. Siendo catalogado como: ESTUDIO CLINICO CON RIESGO MEDIO, según detalle:

Título del Proyecto:	**"MICROBIOME OBSERVATORY OF INDUSTRALIZATION"**
Código de Inscripción:	**ID-044-CIEI-2021**
Modalidad de investigación:	**EXTRAINSTITUCIONAL**
Investigador (es):	**RAUL YHOSSEF TITO TADEO, PHD.** **GRACIELA ROCIO MEZA SANCHEZ, MD, MPH.** **JEROEN RAES, PHD.**

Cualquier eventualidad durante su ejecución, los investigadores reportarán de acuerdo con las Normas y plazos establecidos, así mismo emitirán el informe final socializando los RESULTADOS obtenidos. El presente documento tiene vigencia hasta el 09 de Octubre del 2026. El trámite para su renovación será un mínimo de 30 días antes de su vencimiento.

Punchana, 09 de Octubre del 2025.

Hospital Regional de Loreto
"Felipe Arriola Iglesias"
Comité Institucional de Ética e Investigación
DR. CESAR J. [illegible] ASAYA
Presidente del Comité Institucional de Ética en Investigación

CJRA/ELRDC/GRMS/TYH

GERENCIA REGIONAL DE SALUD - LORETO
HOSPITAL REGIONAL DE LORETO "FELIPE ARRIOLA IGLESIAS"
COMITÉ INSTITUCIONAL DE ÉTICA EN INVESTIGACIÓN

CONSTANCIA No 099 – CIEI – HRL – 2025

El presidente del Comité Institucional de Ética e Investigación (CIEI) del Hospital Regional de Loreto a través de la Oficina de Apoyo a la Docencia é Investigación, **HACE CONSTAR** que el presente proyecto de Investigación, consignado líneas abajo, fue **APROBADO**, en cumplimiento de los estándares del Instituto Nacional de Salud (INS), acorde con las prioridades Regionales de Investigación, Balance Riesgo/beneficio y confiabilidad de los datos, entre otras. Siendo catalogado como: **ESTUDIO CLINICO CON RIESGO MEDIO**, según detalle:

Título del Proyecto:	**"APROVECHAMIENTO DE LA RESPUESTA DEL HUÉSPED FRENTE A LA LEPTOSPIROSIS PARA EL DIAGNÓSTICO Y PRONÓSTICO" VERSION 1.2**
Código de Inscripción:	**ID-084-CIEI-2024**
Modalidad de investigación:	**EXTRAINSTITUCIONAL.**
Investigador (es):	**JUAN CARLOS CELIS SALINAS**

Cualquier eventualidad durante su ejecución, los investigadores reportarán de acuerdo con las Normas y plazos establecidos, así mismo emitirán el informe final socializando los **RESULTADOS** obtenidos. El presente documento tiene vigencia hasta el 15 de Octubre del 2026. El trámite para su renovación será un mínimo de 30 días antes de su vencimiento.

Punchana, 15 de Octubre del 2025.

Hospital Regional de Loreto
"Felipe Arriola Iglesias"

CJRA/ELRDC/TVH

44

1231
2025

CARGO

GERENCIA REGIONAL DE SALUD - LORETO
HOSPITAL REGIONAL DE LORETO "FELIPE ARRIOLA IGLESIAS"
COMITÉ INSTITUCIONAL DE ÉTICA EN INVESTIGACIÓN

BELÉN GÓMEZ VALCÁRCEL
28 nov. 2025
11:30 h.

CONSTANCIA DE ÉTICA

El presidente del Comité Institucional de Ética e Investigación (CIEI) del Hospital Regional de Loreto a través de la Oficina de Apoyo a la Docencia é Investigación, **HACE CONSTAR** que el presente proyecto de Investigación, consignado líneas abajo, fue **APROBADO**, en cumplimiento de los estándares del Instituto Nacional de Salud (INS), acorde con las prioridades regionales de Investigación, balance riesgo-beneficio y confiabilidad de los datos, entre otras. Siendo catalogado como: **ESTUDIO CLÍNICO SIN RIESGO**, según detalle:

Codificación del documento:	**N° 123-CIEI-HRL-2025**
Código de Inscripción:	**ID-123-CIEI-2025**
Título del Proyecto:	**"AUDITORIA – CALIDAD DE DATOS EN VIGILANCIA EPIDEMIOLÓGICA IPRESS I-1 CAMPO SERIO, LORETO, PERÚ - 2025"**
Modalidad de investigación:	**EXTRAINSTITUCIONAL**
Investigador (es):	**BELÉN MARINA GÓMEZ VALCÁRCEL**

Al tratarse de un estudio observacional descriptivo transversal de auditoría de calidad de datos, basado en el análisis de información previamente registrada en las bases de datos institucionales, no se identificaron riesgos adicionales para los pacientes ni se realizaron intervenciones directas sobre ellos. Durante la ejecución del estudio no se reportaron eventualidades que afectaran la confidencialidad o el adecuado manejo de los datos. El equipo investigador ha presentado al CIEI el informe final del estudio, socializando los **RESULTADOS** obtenidos conforme a la normativa vigente. El CIEI ratifica la clasificación del proyecto como **ESTUDIO CLÍNICO SIN RIESGO.** Los miembros participantes declaran no presentar conflictos de interés con el protocolo evaluado.

El presente documento deja constancia de la revisión ética de un estudio ya culminado y de su clasificación como **ESTUDIO CLÍNICO SIN RIESGO**, para los fines administrativos y académicos que correspondan. No aplica trámite de renovación, por tratarse de una auditoría de calidad de datos concluida.

Punchana, 17 de noviembre del 2025.

Hospital Regional de Loreto
"Felipe Arriola Iglesias"
Comité Institucional de Ética e Investigación

DR. CESAR J. RAMAL ASAYA
Presidente del Comité Institucional de Ética e Investigación

CJRA/ELRDC/TVH

124-2025

CARGO

BELEN GÓMEZ VALCÁRCEL

28 nov. 2025 11:30 h

GERENCIA REGIONAL DE SALUD - LORETO
HOSPITAL REGIONAL DE LORETO "FELIPE ARRIOLA IGLESIAS"
COMITÉ INSTITUCIONAL DE ÉTICA EN INVESTIGACIÓN

CONSTANCIA DE ÉTICA

El presidente del Comité Institucional de Ética e Investigación (CIEI) del Hospital Regional de Loreto a través de la Oficina de Apoyo a la Docencia é Investigación, **HACE CONSTAR** que el presente proyecto de Investigación, consignado líneas abajo, fue **APROBADO**, en cumplimiento de los estándares del Instituto Nacional de Salud (INS), acorde con las prioridades regionales de Investigación, balance riesgo-beneficio y confiabilidad de los datos, entre otras. Siendo catalogado como: **ESTUDIO CLÍNICO SIN RIESGO**, según detalle:

Codificación del documento:	**Nº 124-CIEI-HRL-2025**
Código de Inscripción:	**ID-124-CIEI-2025**
Título del Proyecto:	**"CARACTERÍSTICAS CLÍNICAS Y EPIDEMIOLÓGICAS DEL BROTE DE DENGUE EN LA LOCALIDAD DE SANTA CLOTILDE, RÍO NAPO, LORETO, 2024"**
Modalidad de investigación:	**EXTRAINSTITUCIONAL**
Investigador (es):	**PEDRO JULIO SALIRROSAS FERNÁNDEZ**

Al tratarse de un estudio observacional descriptivo transversal basado en el uso de datos secundarios previamente registrados en las bases de datos del Hospital II-1 Santa Clotilde, y ejecutado únicamente mediante revisión documental sin contacto con pacientes ni intervenciones directas, no se identificaron riesgos adicionales para los participantes. Durante la ejecución del estudio no se reportaron eventualidades que afectaran la confidencialidad o el adecuado manejo de los datos. El equipo investigador ha presentado al CIEI el informe final del estudio, socializando los **RESULTADOS** obtenidos conforme a la normativa vigente. El CIEI ratifica la clasificación del proyecto como **ESTUDIO CLÍNICO SIN RIESGO**. Los miembros participantes declaran no presentar conflictos de interés con el protocolo evaluado.

El presente documento deja constancia de la revisión ética de un estudio ya culminado y de su clasificación como **ESTUDIO CLÍNICO SIN RIESGO**, para los fines administrativos y académicos que correspondan. No aplica trámite de renovación, por tratarse de una auditoría de calidad de datos concluida.

Punchana, 17 de noviembre del 2025.

Hospital Regional de Loreto "Felipe Arriola Iglesias"
Comité Institucional de Ética e Investigación

DR. CESAR J. RAMAL ASAYA
Presidente del Comité Institucional de Ética e Investigación

CJRA/ELRDC/TVH

CARE

Erika Pinedo
05/12/2025
8:00am

GERENCIA REGIONAL DE SALUD - LORETO
HOSPITAL REGIONAL DE LORETO "FELIPE ARRIOLA IGLESIAS"
COMITÉ INSTITUCIONAL DE ÉTICA EN INVESTIGACIÓN

CONSTANCIA DE ÉTICA

El presidente del Comité Institucional de Ética en Investigación (CIEI) del Hospital Regional de Loreto a través de la Oficina de Apoyo a la Docencia e Investigación, **HACE CONSTAR** que el presente proyecto de Investigación, consignado líneas abajo, fue **APROBADO**, de acuerdo con la normativa nacional vigente y los procedimientos del CIEI-HRL, la evaluación riesgo-beneficio y confiabilidad de la información. El proyecto fue clasificado como **ESTUDIO CON RIESGO MÍNIMO** y aprobado mediante revisión expedita, según detalle:

Codificación del documento:	**N° 129-CIEI-HRL-2025**
Código de Inscripción:	**ID-76-CIEI-2024**
Título del Proyecto:	**"EPIDEMIOLOGÍA Y CLÍNICA DE LA LEISHMANIASIS TEGUMENTARIA EN EL PERÚ". VERSIÓN 28AUG2025**
Modalidad de investigación:	**EXTRAINSTITUCIONAL**
Investigador (es):	**DR. JUAN FRANCISCO SANCHEZ**

La presente aprobación corresponde a la renovación de la constancia ética previamente otorgada al protocolo NAMRU6.2020.0005, el cual contempla la evaluación clínica y epidemiológica de casos sospechosos o confirmados de leishmaniasis tegumentaria en establecimientos del Ministerio de Salud incluyendo la región Loreto. Durante su ejecución, cualquier eventualidad será reportada al CIEI conforme a las normas y plazos vigentes; al término del estudio, el equipo investigador presentará el informe final socializando los **RESULTADOS** obtenidos. El Comité clasificó el proyecto como estudio observacional con **RIESGO MÍNIMO**, dado que los procedimientos se ajustan a las recomendaciones nacionales para el diagnóstico de leishmaniasis, se cuenta con consentimiento informado y asentimiento para los menores de edad, y se han descrito medidas adecuadas de confidencialidad y manejo de muestras. Los miembros participantes declararon no presentar conflictos de interés con el protocolo evaluado.

El presente documento tiene vigencia hasta el 28 de noviembre del 2026. El trámite para su renovación se realizará con un mínimo de 30 días de anticipación a su vencimiento.

Punchana, 28 de noviembre del 2025.

V° B°
Dr. JUAN M. L.
Presidente

Hospital Regional de Loreto
"Felipe Arriola Iglesias"
Comité Institucional de Ética en Investigación

DR. JUAN MARÍN LIZARRAGA
Presidente del CIEI

JML/ELADC/tyd

ANEXO 04

LISTA DE PUBLICACIONES INDEXADAS EN EL 2025

#	Título de Publicación	Primer Autor(a)	Autor o coautor con filiación institucional (en caso sea diferente al 1er autor)	Tipo de Estudio (Posgrado, Institucional, Colaborativo, Otro, Pregrado*)	Diseño de Estudio: Análisis de Datos Secundarios, Estudios Primarios, Ensayo Clinico, Revisiones Sistemáticas, Reportes de Casos, Otro)	Es un publicación sobre innovación? Si/No	Fondos (Autofinanciado, Institucional, Otros-especificar)	Constancia/Certificado de CEI (#informe/memo)	Fecha de Publicación	Nombre de la Revista	Idioma (Español, Inglés, Otros-especificar)	Link a la publicación	Código DOI
1	In vitro activity of cefiderocol against nosocomial Acinetobacter baumannii	Barbara Ymaña	Martin Casapia-Morales	Colaborativo	Estudio observacional, no experimental, de corte transversal, de laboratorio (in vitro), con alcance descriptivo y analítico–correlacional	SI	Institucional + Otros (PROCIENCIA; Universidad Científica del Sur; CYTED; Shionogi)	Universidad Cientifica del Sur (code: 066-2020-PRO99)	2025	Microbiology Spectrum	Ingles	https://journals.asm.org/doi/full/10.1128/spectrum.00644-25?ref=E	10.1128/spectrum.00844-25
2	High Rate of Human T-Cell Lymphotropic Virus-2 in Patients with HIV in the Peruvian Amazon	Silvia Otero-Rodriguez	Martin Casapia-Morales	Colaborativo	Estudio observacional, no experimental, transversal, descriptivo y analitico	SI	Otros (Universidad Miguel Hernández de Elche–UMH-GVA 2022/0005-11-134-4-2023-0133; ISABIAL 2024-0181; Instituto de Salud Carlos III–ISCIII CM23/00050)	CIEI HRL ID-018-CIEI-2013	2025	Tropical Medicine and Infectious Disease	Ingles	https://www.mdpi.com/2414-6366/10/9/267	10.3390/tropicalmed10090267
3	Screening for Trypanosoma cruzi in patients living with the human immunodeficiency virus (PWH) in the Peruvian Amazon	Silvia Otero-Rodriguez	Martin Casapia-Morales	Colaborativo	Estudio observacional, no experimental, prospectivo y de corte transversal,	SI	Otros (Programa de Cooperación al Desarrollo UMH–Generalitat Valenciana [UMH-GVA 2022/0005, 11-134-4-2023-0133]; ISABIAL [2024–0181]; ISCIII + European Social Fund Plus [CM23/00050])	CIEI HRL ID-018-CIEI-2023	2025	Travel Medicine and Infectious Disease	Ingles	https://www.sciencedirect.com/science/article/pii/S1477893925001334?via%3Dihub	10.1016/j.tmaid.2025.102927
4	Genotype distribution and molecular characterization of HPV in the Peruvian amazon: insights into prevalence, lineage diversity, and viral integration	Lesly Solis-Ponce	Greisi Curicó; Heidy Sanchez-Grandez; Cesar Ramal-Asayag; Renzo Lopez	Colaborativo	Observacional, de corte transversal, descriptivo, con componente de laboratorio/molecular	SI	Otros (Karolinska Institutet Research Foundation 2022-1790; Concytec–Prociencia PE501093868-2024; UICC Fellowship Programme; donación de kits Allplex HPV28 por Gen Lab del Perú)	CIEI-HRL ID-042-CIEI-HRL-2023	2025	Nature Oscientific Reports	Ingles	https://www.nature.com/articles/s41598-025-18455-3	10.1038/s41598-025-18455-3
5	Characterization of the clinical features, laboratory findings, and outcomes of human fascioliasis in a global network: a retrospective mutlicenter study	Andrés F Henao-Martínez	Juan C Celis-Salinas, Martin Casapia-Morales, Edgar A Ramirez-García	Colaborativo	Estudio observacional, no experimental, retrospectivo, multicéntrico, tipo serie de casos / cohorte descriptiva basada en una base de datos secundaria	SI	Autofinanciado	No aplica	2025	Therapeutic Advances in Infectious Disease	Ingles	https://journals.sagepub.com/doi/10.1177/20499361251365508	10.1177/20499361251365508
6	GENOMIC DIVERSITY OF UROPATHOGENIC Escherichia coli IN CLINICAL ISOLATES FROM SIX LATIN AMERICAN COUNTRIES, 2018-2023	Francesca Caballero	Alexander Briones-Alejo	Colaborativo	Estudio observacional, no	SI	Otros (Universidad Peruana Unión, Res. N.° 0935-2018-UPEU-FCS-CF + Fogarty/NIH D43 TW007393	CEI Universidad Peruana Unión (N2019-CEUPeU-0001) + CIEI-UPCH (SIDISI N.° 214524 y 214927)	2025	Rev Peru Med Exp Salud Publica	Ingles/Espanol	https://rpmesp.ins.gob.pe/index.php/rpmesp/article/view/14299	10.17843/rpmesp.2025.422.14299
7	Cryptococcus gattii meningitis in an immunocompromised patient in a hospital in the Peruvian Amazon: case report	Angel A Moreno-Soto	Jorge Sibina-Vela, Edgar A Ramírez-García, Juan C Celis-Salinas, Wilfredo M Casapia-Morales	Institucional	Reporte de caso	SI	Autofinanciado	CIEI-HRL 046-CIEI-HRL-2024	2025	Rev Peru Med Exp Salud Publica	Ingles/Espanol	https://rpmesp.ins.gob.pe/index.php/rpmesp/article/view/14195	10.17843/rpmesp.2025.422.14195
8	Twenty-five years of pertussis outbreaks in the Peruvian Amazon: a call to strengthen equity in vaccination and control	Juan C Celis-Salinas	Edgar A Ramírez-García, Wilfredo M Casapia-Morales	Colaborativo	Comment basado en análisis descriptivo de datos secundarios de vigilancia epidemiológica	SI	Autofinanciado	No aplica	2025	The Lancet Regional Health – America	Ingles	https://www.thelancet.com/journals/lanam/article/PIIS2667-193X(25)00265-0/fulltext	10.1016/j.lana.2025.101255
9	Polymerase Chain Reaction-Confirmed Oropouche Virus Disease in Loreto, Perú: A Case Series From December 2023 Through September 2024	Edgar A Ramirez-García	Juan C Celis-Salinas, Cesar Ramal-Asayag, Martín Casapia Morales	Colaborativo	Comment basado en análisis descriptivo de datos secundarios de vigilancia epidemiológica	SI	Autofinanciado	No aplica	2025	Tropical Medicine and Infectious Disease	Ingles	https://www.acpjournals.org/doi/10.7326/ANNALS-25-02192?url_ver=Z39.88-2003&rfr_id=ori:rid:crossref.org&rfr_dat=cr_pub%20%200pubmed	10.7326/ANNALS-25-02192.
10	Impact of antiparasitic therapy on cardiovascular outcomes in chronic Chagas disease. A systematic review and meta-analysis	Anis Rassi Jr	Edgar A. Ramírez-García, Martin Casapia	Colaborativo	Revisión sistemática y meta-análisis	SI	Autofinanciado	No aplica	2025	eClinicalMedicine	Ingles	https://pubmed.ncbi.nlm.nih.gov/39410639/	10.1016/j.eclinm.2024.102972

Anexo 04- Formato Publicaciones Indexadas

Responsable del Informe:

Institución:

04

AMERICAN SOCIETY FOR MICROBIOLOGY | Microbiology Spectrum

3 | Antimicrobial Chemotherapy | Research Article

In vitro activity of cefiderocol against nosocomial *Acinetobacter baumannii*

Barbara Ymaña,[1] Rocío Egoávil-Espejo,[1] Rosario Huerto-Huánuco,[1] Rosario Oporto-Llerena,[1] Carla A. Alonso,[2] Angie K. Castil Luciano A. Palomino-Kobayashi,[1] Carmen Valera-Krumdieck,[3] Gabriela Soza,[4] Tamin Ortiz-Gomez,[5] Patricia Gonzales,[6] Ma López,[7] Gina Salvador-Luján,[8,9] Beatriz Rojo-Bezares,[7] Martin Casapia,[10,11] Paula Toledano,[7] Joseph Pinto,[12] Maria Ramos Chirin Yolanda Sáenz,[7] Maria J. Pons,[1] Joaquim Ruiz[1]

AUTHOR AFFILIATIONS See affiliation list on p. 8.

ABSTRACT The emergence and spread of third-/fourth-generation cephalosporin and/or carbapenem-resistant *Acinetobacter baumannii* have become a significant global public health concern, making new treatment alternatives necessary. Thus, the present study aimed to assess *in vitro* cefiderocol activity against clinical isolates of *A. baumannii* and analyze their relationship with extended-spectrum β-lactamases (ESBLs) and carbapenemases. Ninety-five *A. baumannii* clinical isolates were included in the study. Susceptibility to 12 antimicrobial agents was established by automated methods and/or disk diffusion, while that of colistin was determined following microdilution and that of cefiderocol by microdilution using iron-depleted broth. The presence of bla_{CTX-M}, bla_{PER}, bla_{VEB}, bla_{GES}, bla_{VIM}, bla_{IMP}, bla_{IMI}, bla_{KPC}, bla_{NDM}, $bla_{OXA-23G}$, $bla_{OXA-24G}$, $bla_{OXA-48G}$, and $bla_{OXA-58G}$ was established by PCR. The results showed extremely high levels of resistance (>80%) to all the tested antibacterial agents except colistin (11.6%) and cefiderocol (Clinical and Laboratory Standards Institute [CLSI]: 0%; US Food and Drug Administration [FDA]: 1.1%). Following FDA criteria, 22.1% of isolates were intermediate to cefiderocol, with 68.4% of isolates surpassing the European Committee on Antimicrobial Susceptibility Testing epidemiological cut off. Seven colistin-resistant isolates were only susceptible to cefiderocol following CLSI breakpoints, four of them qualifying as cefiderocol-intermediate following FDA breakpoints. No association between the presence of ESBLs or carbapenemases and cefiderocol minimum inhibitory concentration levels was observed. The present results show the potential utility of cefiderocol in the treatment of *A. baumannii* infections, highlighting the need for judicious use and continuous surveillance to prevent the emergence of cefiderocol-resistant *A. baumannii* clones.

IMPORTANCE Antibiotic resistance is a silent pandemic challenging the treatment of infectious diseases worldwide, but also other medical practices, as, for instance, organ transplantation procedures. In Peru, current levels of antimicrobial resistance are worrisome. In this scenario, we have determined the *in vitro* activity of cefiderocol against a series of *Acinetobacter baumannii* exhibiting high levels of resistance to commonly used antibiotics. This activity is independent of the presence of the most common extended-spectrum beta-lactamases or carbapenemases. Obtained results showed the potential of cefiderocol to become an alternative for the treatment of this type of microorganism, but the high number of isolates bordering the considered breakpoint, despite the lack of use of cefiderocol in the country, also shows the need for a prudent use of this antibiotic to maximize its utility while minimizing the selection of resistant isolates.

Editor Ayesha Khan, UCI Health, Orange, California, USA

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Barbara Ymaña and Rocío Egoávil-Espejo contributed equally to this article. The author order was determined based on time of entry to the center.

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See the funding table on p. 9.

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KEYWORDS cefiderocol, beta-lactamases, antibiotic resistance, middle-income countries, carbapenemases, OXA-24

Antimicrobial resistance is a growing phenomenon affecting microorganisms of all environments (1–4), but it is especially worrisome in clinical settings, where the lives of the most vulnerable patients may be at risk (5). This problem not only jeopardizes the effectiveness of antibiotic treatments when needed, but it also has a serious impact on other human health aspects, such as surgical prophylaxis or the use of antibiotics in at-risk populations, such as post-transplant patients (6, 7).

In fact, antimicrobial resistance is considered one of the leading public health threats of the 21st century and also severely impacts both direct and indirect economic costs (8, 9), qualifying among the World Health Organization (WHO) urgent health challenges for the decade (https://www.who.int/news-room/photo-story/detail/urgent-health-challenges-for-the-next-decade). In this sense, the most recent data have shown that antibiotic resistance was the cause of 1.27 million deaths in 2019 and was involved in an additional 4.95 million deaths (10). Although all microorganisms and environments may be affected, a series of microorganisms are of special concern, being collectively known under the acronym ESKAPE (*Enterococcus faecium, Staphylococcus aureus, Klebsiella pneumoniae, Acinetobacter baumannii, Pseudomonas aeruginosa,* and *Enterobacter cloacae*) or E-ESKAPE, ESKAPE-Ec when also considering *Escherichia coli*.

As indicated above, *A. baumannii* is a member of the ESKAPE group, which is often isolated as a cause of infection in patients attending intensive care units (11, 12). Carbapenems have been considered the treatment of choice for this microorganism, but the increase in the current rates of carbapenem resistance alerts about the need for alternative treatment strategies (13). Indeed, carbapenem-resistant *A. baumannii* (CR*Ab*) is included among the WHO critical priority microorganisms due to the lack of alternative treatments (https://www.who.int/news/item/17-05-2024-who-updates-list-of-drug-resistant-bacteria-most-threatening-to-human-health), which are often limited to colistin or a combination of antibacterial agents (13, 14). Of note, *A. baumannii* exhibiting colistin resistance has been isolated in different areas, opening the door to the isolation of pan-drug-resistant isolates (12, 15, 16).

In this scenario, new alternatives able to fight infections by CR*Ab* are an emerging need worldwide. Cefiderocol is a recently developed siderophore cephalosporin, which enters the bacterial cell through classical cephalosporin routes (17), as well as via iron transporters thanks to a C-3 side chain, which has a chlorocatechol group at the end of the C-3 side chain that confers the above-indicated siderophore ability (17, 18). This increased intake, together with a high degree of stability versus the activity of a great variety of β-lactamases, also related to the above-mentioned chlorocatechol group (17), results in promising activity against a variety of Gram-negative microorganisms, including *A. baumannii* (19, 20).

Most of the studies published on cefiderocol activity have been conducted in high-income countries (19–21), making studies of microorganisms of clinical interest from other areas, such as Peru, necessary. Peru is a middle-income country in which current data about CR*Ab* have shown their presence in a large series of health centers, with resistance rates to other antimicrobial agents commonly being higher than 50%. (15, 16, 22), and with emerging descriptions of colistin-resistant isolates (15, 16).

Thus, this study aimed to determine the *in vitro* activity of cefiderocol against third-/fourth-generation cephalosporins and/or CR*Ab* isolated in different areas of Peru.

RESULTS

Eighty-nine isolates were confirmed as *A. baumannii* by matrix-assisted laser desorption/ionization time-of-flight (MALDI-TOF). The remaining six were classified as *A. baumannii* following the amplification of $bla_{OXA\text{-}51}$ and/or the amplification and sequencing of 16S rRNA.

Overall, high levels of antimicrobial resistance were observed. Thus, the *A. baumannii* isolates presented non-susceptibility levels higher than 90% to almost all classical antibacterial agents, except for ampicillin plus sulbactam (83.2%), ceftazidime plus avibactam (87.4%), gentamicin (89.5%), and colistin (11.6%) (Table 1). Not taking into account cefiderocol, 7 out of 11 (63.6%) colistin-resistant isolates showed non-susceptibility to all antibacterial agents included in the study and were thereby classified as potential pan-drug-resistant isolates. Three of these isolates presented a minimum inhibitory concentration (MIC) of cefiderocol of 1 µg/mL, qualifying as susceptible both by Clinical and Laboratory Standards Institute (CLSI) and U.S. Food and Drug Administration (FDA) breakpoints. The remaining four presented a MIC of 2 µg/mL and were therefore classified as intermediate by FDA breakpoints.

Regarding cefiderocol, the MICs ranged from 0.125 µg/mL to 4 µg/mL, with a MIC_{50} and MIC_{90} of 1 µg/mL and 2 µg/mL, respectively. Only one isolate presented a MIC = 4 µg/mL being classified as susceptible according to CLSI criteria, but resistant by FDA criteria. Furthermore, following the FDA breakpoints, additional 21 (22.1%) isolates were classified as intermediate, resulting in 22 (23.2%) non-susceptible to cefiderocol based on FDA criteria (Table 2; Fig. 1).

On bacterial population terms, following the European Committee on Antimicrobial Susceptibility Testing (EUCAST), 65 (68.4%) isolates were over the epidemiological cut-off (ECOFF) of 0.5 µg/mL.

Regarding extended-spectrum β-lactamases (ESBLs), no bla_{CTX-M} was found, with three isolates presenting bla_{VEB}, one bla_{PER}, and one bla_{GES} (while the latter was classified here as ESBL, in the absence of a full gene amplification and sequencing, it cannot be definitively determined as an ESBL or carbapenemase). Interestingly, all ESBLs were present concomitantly with a carbapenemase.

The most common carbapenemase genes belonged to the bla_{OXA-24} group, which was present alone in 71 (74.7%) isolates, and concomitantly with another carbapenemase or an ESBL in other 7 (7.4%) isolates: bla_{VEB} in 3 cases and with bla_{PER}, $bla_{OXA-23G}$, $bla_{OXA-48G}$, and bla_{NDM} in one isolate each. The bla_{OXA-23} gene was found alone in 8 (8.4%) isolates, and together with a bla_{GES} in one isolate. The bla_{NDM} gene was also present alone in another isolate. Seven (7.4%) isolates did not present any ESBL or carbapenemase sought (Table 3).

No association was observed between the presence of ESBLs or carbapenemases and the final cefiderocol MIC levels, with the isolate with the highest MIC of cefiderocol (4 µg/

TABLE 1 Susceptibility to antibacterial agents[a]

AA	S (No, %)	I (No, %)	R (No, %)	NS (No, %)
SAM	16 (16.8)	16 (16.8)	63 (66.3)	79 (83.2)
TZP	3 (3.2)	4 (4.2)	88 (92.6)	92 (96.8)
ATM	1 (1.1)	7 (7.4)	87 (91.6)	94 (98.9)
CTX	0 (0.0)	3 (3.2)	92 (96.8)	95 (100.0)
CAZ	4 (4.2)	3 (3.2)	88 (92.6)	91 (95.8)
FEP	7 (7.4)	8 (8.4)	80 (84.2)	88 (92.6)
CZA	12 (12.6)	–	83 (87.4)	83 (87.4)
IPM	4 (4.2)	0 (0.0)	91 (95.8)	91 (95.8)
MEM	3 (3.2)	1 (1.1)	91 (95.8)	92 (96.8)
CIP	6 (6.3)	0 (0.0)	89 (93.7)	89 (93.7)
GEN	10 (10.5)	7 (7.4)	78 (81.1)	85 (89.5)
AMK	9 (9.5)	5 (5.3)	81 (83.5)	86 (90.5)
CST	84 (88.4)	–	11 (11.6)	11 (11.6)
FDC (FDA)	73 (76.8)	21 (22.1)	1 (1.1)	22 (23.2)
FDC (CLSI)	95 (100.0)	0 (0.0)	0 (0.0)	0 (0.0)

[a]AA, antimicrobial agent; S, susceptible; I, intermediate; R, resistant; NS, non-susceptible SAM, ampicillin plus sulbactam; TZP, piperacillin plus tazobactam; ATM, aztreonam; CTX, cefotaxime; CAZ, ceftazidime; FEP, cefepime; CZA, ceftazidime plus avibactam; IPM, imipenem; MEM, meropenem; CIP, ciprofloxacin; GEN, gentamicin; AMK, amikacin; CST, colistin; FDC, cefiderocol; FDA, U.S. Food and Drug Administration; CLSI, Clinical and Laboratory Standards Institute breakpoint. The hyphen symbolizes the non-established intermediate category.

TABLE 2 Distribution of the MICs of cefiderocol

	No	MIC_{50}	MIC_{90}	Mode	MIC cefiderocol (µg/ml)					
					0.125	0.25	0.5	1	2	4
A. baumannii	95	1	2	2	4	7	19	43	21	1
CLSI[a]					S	S	S	S	S	S
FDA[b]					S	S	S	S	I	R

[a]CLSI, Clinical and Laboratory Standards Institute.
[b]FDA, U.S. Food and Drug Administration.

mL), only being susceptible to ampicillin plus sulbactam and colistin and presenting bla_{VEB} and $bla_{OXA\text{-}24G}$.

DISCUSSION

Resistance to antibacterial agents is an increasingly worrisome problem that seriously challenges current medical practice. While this phenomenon affects all countries and environments, it is of special concern in low- and medium-income countries. These countries usually present economic restrictions, which often lead to limited treatment alternatives, and/or restrictions or difficulty in achieving access to health facilities, safe water, or sanitation, in addition to social factors including over-the-counter access to antibacterial agents and lack of health education among most of the population (24).

In Peru, most reports describe a dreadful panorama, with prevalence of self-medication of antibiotics around 50%, extremely high levels of resistance to a variety of antibacterial agents by pathogens isolated in health facilities (11, 15, 25), and the isolation of multidrug-resistant or extensively drug-resistant microorganisms outside clinical settings. The present data confirm these high levels of resistance to antimicrobial agents in CR*Ab*, with colistin as the only alternative showing resistance levels less than 80%. Nevertheless, colistin should be used with caution because of its toxicity (26). Furthermore, resistance to this agent is emerging in the area (15, 16), with this issue being also confirmed in the present study. Although data are scarce, in Peru, fatality rates of 42.9% have been described in patients with bloodstream infections (16) and of 27.6% in patients with extensively drug-resistant *A. baumannii* infections treated with colistin (26). These findings indicate the urgent need to introduce new treatment alternatives in the area.

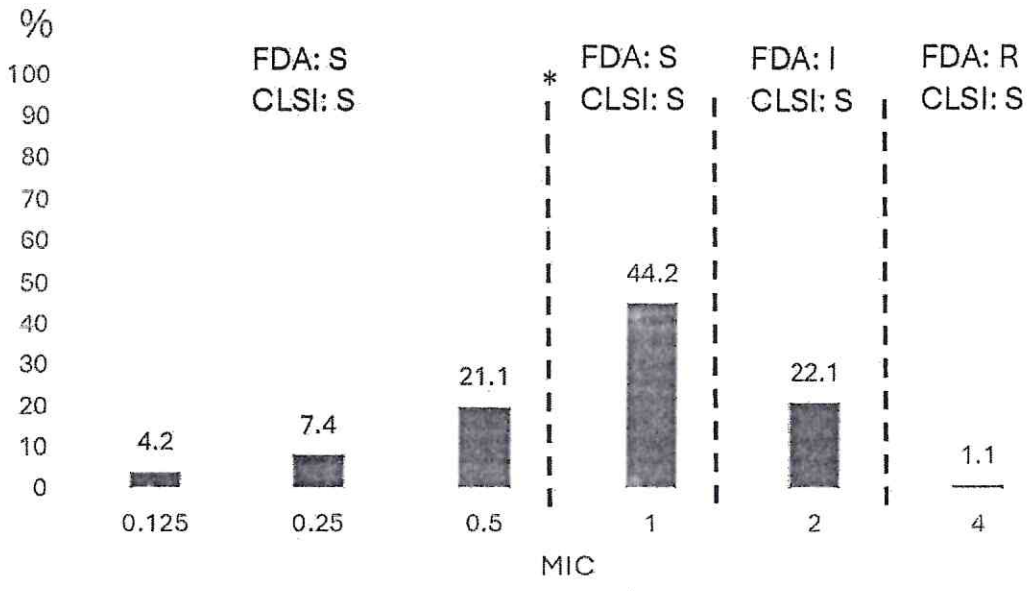

FIG 1 MIC (µg/ml) distribution. The asterisk marks the alert of the European Committee on Antimicrobial Susceptibility Testing regarding risk isolates (23).

TABLE 3 Association of ESBLs and carbapenemases with final MIC levels to cefiderocol

Carbapenemases	ESBLs[a]	No	Cefiderocol MIC					
			0.125	0.25	0.5	1	2	4
---[b]	---	7			2	5		
NDM	---	1					1	
OXA-23G	---	8	1			5	2	
OXA-24G	---	71	3	5	16	31	16	
OXA-23G	GES[c]	1		1				
OXA-24G	VEB	3				1	1	1
OXA-24G	PER	1			1			
OXA-24G + OXA-23G	---	1			1			
OXA-24G + OXA-48G	---	1		1				
OXA-24G + NDM	---	1					1	

[a]ESBLs, extended-spectrum β-lactamases.
[b]The lack of carbapenemases and/or ESBLs is noted by hyphens.
[c]Although classified as ESBL, in the absence of a full-gene amplification and sequencing, it cannot be definitively determined as an ESBL or carbapenemase.

Cefiderocol is a new antibacterial agent, a siderophore-cephalosporin, which has shown good activity levels against relevant pathogens, including *A. baumannii* (19, 20). Although cefiderocol has yet to be introduced in clinical practice in Peru, it may be a potential alternative to treat pathogens, such as CR*Ab*, and therefore evaluation of its *in vitro* activity is important.

The present results show that cefiderocol is, by and large, the most active antibacterial agent tested versus the current collection of *A. baumannii* analyzed (almost all CR*Ab*), regardless of the presence of ESBLs or carbapenemases, as shown by other studies (27, 28). No isolate was found to be resistant according to CLSI breakpoints, but one was resistant, and 21 showed intermediate resistance following FDA criteria. This difference between the two criteria is related to the high number of isolates with a MIC = 2 µg/mL. With respect to colistin-resistant isolates, the MIC of cefiderocol was 1–2 µg/mL, being a relatively high MIC according to EUCAST ECOFF (29). Of note, EUCAST, in the line of FDA breakpoints, suggests that cefiderocol MICs of 1–2 µg/mL may lead to an impaired clinical response, with 64 isolates (67.4%) presenting MIC values ≥1 µg/mL (25). The above-mentioned data highlight a serious question about the lack of standardization of susceptibility breakpoints, which might impact the correct patient management.

Studies developed in other areas show levels of cefiderocol resistance higher than those observed in the present study. Thus, a recent study analyzing 402 carbapenem-resistant *Acinetobacter calcoaceticus-baumannii* complex from the United States showed rates of resistance of 7% and 20.6%, as for CLSI and FDA, respectively, with additional series of intermediate isolates (30). Similarly, a study developed in Vietnam showed c. 15% of resistance (as for CLSI breakpoints) among *A. baumannii* colonizing ICU patients (31). Differences in the origin of samples and/or methodologies to determine susceptibility levels as well as the levels of cefiderocol use in clinical practice may underline the differences in the levels of cefiderocol resistance.

In the present series, the $bla_{\text{OXA-24G}}$ genes were the most common carbapenemases among the isolates analyzed, with $bla_{\text{OXA-23G}}$ being the second most common. The presence of other carbapenemases was testimonial. This agrees with studies in the area in which the presence of members of these OXA groups has been identified as the most common carbapenemases in CR*Ab*. Thus, different authors have described a scenario in which members of the $bla_{\text{OXA-24G}}$ (e.g., $bla_{\text{OXA-72}}$) were the most common carbapenemases amongst CR*Ab*, followed by $bla_{\text{OXA-23G}}$ (22, 32, 33).

While the role of $bla_{\text{OXA-24G}}$ and $bla_{\text{OXA-23G}}$ in the development of cefiderocol resistance seems null (28), it has been proposed that specific β-lactamases, such as those belonging to the bla_{PER} and bla_{NDM} families, might play a role in the development of resistance to cefiderocol (34, 35). In the present study, the low number of isolates possessing these β-lactamases does not allow conclusions to be obtained, with the only

isolate possessing bla_{PER} showing a MIC of 0.5 µg/mL, and the two isolates possessing bla_{NDM} presenting MICs of 2 µg/mL, therefore classified as intermediate following FDA criteria, and being over the EUCAST ECOFF. Nevertheless, these MIC values are within the range of those obtained by Poirel et al. when cloned several PER and NDM encoding genes in *A. baumannii* CIP70.10, showing that, while contributing to the final cefiderocol MIC levels, these alone are not enough to clearly surpass the established breakpoints (34).

The analysis of cefiderocol susceptibility showed a scenario in which 68.4% of isolates were over EUCAST ECOFF (29). This finding strongly suggests that, apart from the scarce presence of NDM or PER, the presence of mechanisms able to slightly increase the MIC to cefiderocol should be considered. The present data highlight not only cefiderocol as a potential alternative to current treatments for *A. baumannii* infections but also the need to use this agent with caution.

While approved in countries such as the United States, country members of the European Union, United Kingdom, or Japan, and with application under study in others, such as Australia (https://www.shionogi.com/global/en/news/2025/04/20250402.html; https://www.shionogi.com/global/en/news/2022/06/20220616.html), cefiderocol is accessible under early access programs (compassionate use) in a long series of countries, mostly qualifying as low- or middle-income countries (https://www.shionogi.com/us/en/innovation/expanded-access-policy.html; https://www.inceptua.com/inceptua-group-expands-early-access-program-to-latin-america/). In low- and middle-income countries, stable access to modern antimicrobial agents has a series of challenging questions, with the antibiotic cost as a severe limiting factor (36). Regarding cefiderocol, in June 2022, Shionogi, the Global Antibiotic Research and Development Partnership, and The Clinton Health Access Initiative signed an agreement to facilitate the access to cefiderocol in 135 countries (https://www.shionogi.com/global/en/news/2022/06/e220615.html).

The correct identification of *A. baumannii* is challenging, because several closely related species may be indistinguishable or easily mistakenly identified. MALDI-TOF is a reliable methodology, but the presence of bacterial misidentification has also been reported (37), and the continuous description of new species may result in different bacterial identification as for version of database (38). The non-identification of the specific β-lactamases is one of the limitations of the study, but the results showed good parameters of cefiderocol activity, irrespective of the presence or absence of the most common *A. baumannii* β-lactamases. While not a limitation, the inclusion criteria should be taken into account, and therefore the present levels of antimicrobial resistance are those of third-/fourth-generation cephalosporin-resistant *A. baumannii* and/or CR*Ab*. In any case, the levels of resistance to these agents in Peru among *A. baumannii* isolates are extremely high (16, 39), surpassing 80% according to some reports (15).

At present, cefiderocol remains to be introduced in clinical practice in the area. *In vitro* activity levels showed that cefiderocol might play a role in the treatment of extensively drug-resistant CR*Ab*, but MIC values highlight the need for judicious use and continuous surveillance to avoid or minimize the risk of the development of resistance.

MATERIALS AND METHODS

Microorganisms

Ninety-five non-duplicate third-/fourth-generation cephalosporins and/or CR*Ab* were isolated from different clinical samples in different health centers in Peru between 2020 and 2022 (Table 4). All isolates were identified by VITEK-2 as belonging to the *Acinetobacter calcoaceticus-baumannii* complex and were sent to the Hospital Universitario San Pedro (Logroño, Spain) to be confirmed at the species level by MALDI-TOF using the MBT Compass Library V11.0.0.0 (July 2021). Isolates with no conclusive MALDI-TOF results were confirmed by the amplification of an internal 353 bp fragment of bla_{OXA-51} and/or amplification and sequencing of 16S rRNA (40, 41).

cefiderocol. Susceptibility differences of one dilution were considered as an inherent methodological error. The *E. coli* ATCC 25922 was used as the quality control in all experiments.

In the text, the term non-susceptible refers to the sum of intermediate and resistant isolates.

In addition, the ecological distribution of MICs was also analyzed following EUCAST guidelines (29).

ESBL and carbapenemase detection

The presence of the ESBL families CTX-M, PER and VEB, GES (ESBLs or carbapenemases), and carbapenemases type VIM, IMP, IMI, KPC, NDM, OXA-23, OXA-24, OXA-48, and OXA-58 was determined by PCR as previously described (Table 5) (45–48). In the text, the OXA-encoding genes sought are indicated with a final "G" or with the word "group" to avoid misinterpretation, because the primers used allow the amplification of a series of related genes.

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TABLE 4 Origin of the samples[a]

Health center	No	City	Location	Region
A	53	Lima	Metropolitan Lima	Coast
B	14	Lima	Metropolitan Lima	Coast
C	12	Lima	Metropolitan Lima	Coast
D	8	Lima	Metropolitan Lima	Coast
E	3	Iquitos	Loreto (Northern Peru)	Jungle
F	2	Lima	Metropolitan Lima	Coast
G	2	Piura	Piura (Northern Peru)	Coast
ND	1	Lima	Metropolitan Lima	Coast

[a]ND, not determined.

Susceptibility to antimicrobial agents

The susceptibility levels to ampicillin plus sulbactam, piperacillin plus tazobactam, aztreonam, cefotaxime, ceftazidime, cefepime, ceftazidime plus avibactam, imipenem, meropenem, ciprofloxacin, gentamicin, and amikacin were established using disk diffusion. Susceptibility to colistin was established according to CLSI guidelines (42). Susceptibility to cefiderocol was determined by microdilution in iron-depleted broth (Remel, Lenexa, USA) as previously described (42, 43). Briefly, a preliminary MIC was established using a range of cefiderocol concentrations containing from 0.06 µg/mL to 2 µg/mL, in the wells of 96-microwell plates. Isolates growing on wells containing 2 µg/mL cefiderocol were tested again in 96-well plates containing up to 64 µg/mL of cefiderocol. A growth control (tested bacteria cultured in media without cefiderocol) and a blank (non-inoculated media without cefiderocol) were used as controls in all determinations. Plates were read at 600 nm in an enzyme-linked immunosorbent assay reader (SYNERGY LX, Biotek, Santa Clara, USA). Bacterial growth was considered when the optical density (OD) was >0.100 (approximately 2.5 times higher than absorbance values of blank wells) (43). Isolates with absorbance values ranging from 0.09 to 0.110 were classified as uncertain and tested again (43).

The susceptibility data were interpreted according to CLSI (42). In the absence of a specific breakpoint, data of ceftazidime-avibactam were interpreted based on *P. aeruginosa* breakpoints. In addition, cefiderocol susceptibility was also interpreted as per the FDA guidelines (44).

As an internal control, susceptibility levels were determined up to three times in a series of randomly selected isolates, as well as in those growing on ≥2 µg/mL of

TABLE 5 Primers used in this study to detect ESBLs and carbapenemases

Gene	Primer sequence		Size[a]	Ann[b]	Ref[c]
	Forward (5′ → 3′)	Reverse (5′ → 3′)			
$bla_{\text{CTX-M-like}}$	CGATGTGCAGTACCAGTAA	TTAGTGACCAGAATCAGCGG	585	60	(48)
bla_{GES}	CTGGCAGGGATCGCTCACTC	TTCCGATCAGCCACCTCTCA	600	57	(45)
bla_{PER}	AGTGTGGGGGCCTGACGAT	GCAACCTGCGCAATRATAGCTT	725	57	(45)
bla_{VEB}	CGACTTCCATTTCCCGATGC	TGTTGGGGTTGCCCAATTTT	376	57	(45)
bla_{KPC}	TCGCCGTCTAGTTCTGCTGTCTTG	ACAGCTCCGCCACCGTCAT	353	57	(45)
bla_{NDM}	ACTTGGCCTTGCTGTCCTT	CATTAGCCGCTGCATTGAT	603	57	(45)
bla_{IMI}	CTACGCTTTAGACACTGGC	AGGTTTCCTTTTCACGCTCA	482	57	(47)
bla_{VIM}	TGTCCGTGATGGTGATGAGT	ATTCAGCCAGATCGGCATC	437	57	(45)
bla_{IMP}	ACAYGGYTTRGTDGTKCTTG	GGTTTAAYAAARCAACCACC	387	57	(45)
$bla_{\text{OXA-23-like}}$	TACAAGGGATTCGGCATCG	TAATGGCCTGTTCCCATGTG	570	52	(46)
$bla_{\text{OXA-24-like}}$	AAAATCTGGGTACGCAAACG	ACATTATCCGCTGGAACAGG	271	52	(46)
$bla_{\text{OXA-48-like}}$	ATGCGTGTATTAGCCTTATCG	CATCCTTAACCACGCCCAAATC	265	57	(45)
$bla_{\text{OXA-58-like}}$	TCGACACACCTTGGTCTGAA	AACTTCCAACTTTGCCATGC	477	52	(46)

[a]Size in base pairs (bp).
[b]Annealing temperature (°C).
[c]References.

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ETHICS APPROVAL

The project was approved by the Institutional Review Board of the Universidad Cientifica del Sur (code: 066-2020-PRO99).

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Tropical Medicine and Infectious Disease

Article

High Rate of Human T-Cell Lymphotropic Virus-2 in Patients with HIV in the Peruvian Amazon

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Abstract

HTLV-1/2 in people with HIV (PWH) has been little studied in the Peruvian Ama an endemic area for both viruses. We aimed to estimate its prevalence and describe main clinical and epidemiological features of individuals with HTLV-HIV co-existence conducted a cross-sectional study (October–December 2023) at the Division of Infect Diseases and Tropical Medicine at the Regional Hospital of Loreto in Iquitos. We perfor a screening test (recombinant HTLV I+II ELISA) and confirmed the results with IN LIA. Among 293 PWH analyzed, 14 (4.8%) were HTLV-positive: 1/293 was HTI positive (0.3%; 95% CI 0.06–0.9), 11/293 were HTLV-2-positive (3.8%; 95% CI 2.1– and 2/293 were non-typeable (0.7%; 95% CI 0.1–2.7). Compared with HIV-monoinfe individuals, superinfected patients were older (55 vs. 39 years; $p = 0.001$). Low educa was more frequent in the univariate analysis (35.7% vs. 15.4%; $p = 0.05$) but was not reta in the multivariable model. In conclusion, HIV–HTLV-2 co-existence is relatively comu (~4%) in the Peruvian Amazon, particularly among older individuals, highlighting the r for targeted screening and prevention strategies. Integrating HTLV testing into routine clinic workflows, along with brief and focused counseling for superinfected patients, help optimize follow-up and care.

Keywords: HTLV; HTLV-2; human T-cell lymphotropic virus; human immunodefici virus; HIV; Peru; Amazon

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1. Introduction

Infection with Human T-Cell Lymphotropic Virus Types I and II (HTLV-1/2) repres an underestimated public health issue, with a heterogeneous geographic distribution a significant burden in endemic areas of Latin America, particularly in Brazil and I HTLV-1 affects more than 10 million people worldwide [1] and is associated with se

conditions such as adult T-cell leukemia/lymphoma and HTLV-1–associated myelopathy. In contrast, HTLV-2, which is considered less pathogenic, predominates among Indigenous populations and people who inject drugs [2–8].

HTLV-1/2 is primarily transmitted through sexual contact, vertical transmission (particularly via breastfeeding), blood transfusions, and, in certain regions, through exposure to contaminated blood through unsterile practices, such as scarification rituals or poorly hygienic procedures. These transmission routes are shared with the human immunodeficiency virus (HIV) [2].

The presence of both HIV and HTLV-1 in an individual's immune system promotes immune dysregulation, characterized by paradoxical expansion of dysfunctional $CD4^+$ and $CD8^+$ T cells and chronic immune activation, ultimately leading to immune exhaustion despite elevated lymphocyte counts [9]. While some reports suggest that HIV–HTLV-2 coinfection may be linked to a 'long-term non-progressor' phenotype, evidence remains inconclusive and clinically controversial [1]. These interactions may influence HIV progression and outcomes, underscoring the importance of HTLV testing in HIV-positive patients—particularly those with compatible ethnic backgrounds and unexpectedly high CD4 counts—and the need for vigilance regarding HTLV-associated conditions such as HAM/TSP, adult T-cell leukemia/lymphoma, and *Strongyloides* hyperinfection [10,11].

In Brazil, the prevalence of HTLV/HIV co-existence is heterogeneous, ranging from 1.3% to 7%. HTLV-1a is the predominant subtype in the Amazon region, while a high endemicity of HTLV-2 has been observed among Indigenous populations and drug users. In Peru, although data are more limited, HTLV-1/2 infection has been documented in both urban and rural populations, with transmission hotspots in the Amazon region and evidence of circulation among Indigenous communities and individuals with similar risk factors to those reported in Brazil [5–7,10,12–14].

The Peruvian Amazon is a key area for HIV transmission, with the second-highest cohort of patients in the country receiving antiretroviral treatment after Lima [15]. Some studies have also revealed very high HIV rates in isolated indigenous populations, mainly due to sexual exposure without protection (including polygamy and homosexual practices), as there is little knowledge about the infection [16,17]. The absence of systematic screening programs for HIV and limited clinical awareness hinder detection and control of the infection, highlighting the urgent need to strengthen epidemiological surveillance and research efforts in the region [2–5].

The aim of this study is to assess the prevalence of HTLV-1/2 infection in a pilot sample of PWH in the Peruvian Amazon, describe the clinical and epidemiological characteristics of superinfected individuals, and analyze differences compared to HIV-monoinfected patients.

2. Materials and Methods

2.1. Study Design and Setting

A cross-sectional study was conducted among PWH who were receiving care at the Division of Infectious Diseases and Tropical Medicine of the Regional Hospital of Loreto "Felipe Santiago Arriola Iglesias" in Iquitos, Peru. The study period was from 20 October 2023 to 31 December 2023.

2.2. Study Population and Enrollment Criteria

Adults aged 18 years and older with confirmed HIV infection who were receiving outpatient care at the Regional Hospital of Loreto were eligible for inclusion. After providing informed consent, participants completed a semi-structured oral interview that collected

data on demographics, clinical history and potential epidemiological risk factors. After that, a blood sample was obtained.

We planned to estimate the prevalence of HTLV coinfection among ~1000 PWH in care. Using an expected prevalence of 10% according to a previous meta-analysis in Peru [18], 95% confidence, and ±3% absolute precision, the required sample for a single proportion was 384. After applying the finite-population correction for N = 1000, this became 278. Allowing 6% for non-evaluable/losses, the final target sample was ≈295 participants.

Separated serum samples were aliquoted and frozen at −20 °C. When 96 samples were obtained, an ELISA kit was used, never exceeding four weeks. The presence of antibodies against HTLV-1/2 was initially screened using a single ELISA assay (HTLV I+II ELISA recombinant v.4.0 96-well kit, Wiener Lab, Rosario, Argentina; catalog number 1671096). A result was considered positive when the optical density value exceeded the negative control by 0.200, according to the manufacturer's instructions. Due to the lack of local confirmatory testing, the 15 serum samples that were positive for HTLV at screening were sent to a HTLV reference laboratory in Puerta de Hierro University Hospital, Madrid, Spain. To facilitate safe transport from Iquitos without a cold chain, aliquots of frozen serum were applied to Whatman filter paper to create dried serum spots (DSS), which were air-dried, sealed with desiccant, and shipped using standard triple packaging. Upon arrival, DSS were eluted and tested with INNO-LIA HTLV I/II Score (Fujirebio, Tokyo, Japan; catalog number 80540), following standard laboratory procedures. While serum/plasma are the manufacturer's validated matrices, DSS were used exclusively for transport. Molecular assays, including HTLV typing and proviral load, could not be performed, as DNA extracted from cellular fractions (whole blood/PBMCs) was not collected.

We performed serologic testing for *Strongyloides stercoralis* because of its epidemiologic overlap with HTLV in the Amazon and evidence that HTLV-1 coinfection increases the risk of severe/disseminated strongyloidiasis and treatment failure [19,20]. Accordingly, we assessed *Strongyloides*–HTLV coinfection among PWH to inform clinical follow-up in endemic settings. Serology for *S. stercoralis* was performed using a commercial IgG ELISA (Strongyloides IgG IVD ELISA, DRG Instruments GmbH, Marburg, Germany; catalog number EIA-4208), following the manufacturer's instructions; results were interpreted using kit-specified cutoffs.

Those who were positive for HTLV 1/2 were contacted again to conduct a more comprehensive interview on risk factors for transmission, including the origin of their parents.

2.3. Statistical Data Analysis

Categorical variables were summarized as frequencies and percentages, while continuous variables were expressed as medians and interquartile ranges (IQRs). Ninety-five percent confidence intervals (95% CIs) were calculated using the Newcombe method. Comparisons between categorical variables were performed using the Chi-square test or Fisher's exact test when any expected cell count was <5, while continuous variables were analyzed using the Mann–Whitney U test, given the non-normal distribution. Age was analyzed as a continuous variable and, for specific comparisons, dichotomized at the 75th percentile (P75 = 49 years) into <50 vs. ≥50 years. Risk factors associated with HTLV positivity were explored using bivariate analysis, with odds ratios (ORs) used to quantify associations. Subsequently, we fitted a multivariable logistic regression model using a forward stepwise procedure to identify independent risk factors for HTLV positivity. Age and sex were included a priori, and additional covariates with $p < 0.10$ in the univariable analyses were considered eligible for inclusion in the model. Statistical analyses were performed via IBM SPSS Statistics, version 22.0 (IBM Corp., Armonk, NY, USA).

2.4. Ethical Considerations

The study protocol was approved by the Ethics Committee of the Regional Hospital of Loreto in Iquitos, Peru (EXP: ID-018-CIEI-2023) and by the Ethics and Research Integrity Committee of Miguel Hernández University of Elche, Spain (DMC.JMRR.230908). Written informed consent was obtained from all participants. Confidentiality of data was strictly maintained, and results were only disclosed to each participant's HIV care provider, who ensured appropriate follow-up and treatment.

3. Results

3.1. Overview of the Study Population

A total of 293 PWH were included in the study, of whom 66.9% were male, with a median age of 40 years (IQR 30–49). Of the participants, 16.7% had no formal education or had only attended primary school, 21.8% had received a blood transfusion, 94.5% had been breastfed, and 89.9% acquired HIV through sexual transmission. This overview serves as a reference for subsequent subgroup comparisons between HTLV-positive and HTLV-negative participants, described in Table 1.

Table 1. Epidemiological characteristics of study participants (N = 293) and results of HTLV screening.

Variables	Overall (N = 293)	HTLV Positive (N = 14)	HTLV Negative (N = 279)	*p* Value
Epidemiology				
Sex, male, n (%)	196 (66.9%)	9 (64.3)	187 (66,9)	0.789
Age, median (IQR), years	40 (30–49)	55 (52–61)	39 (29–47)	**<0.001**
Age ≥ 50 years, n (%)	72 (24.6)	12 (85.7)	60 (21.5)	**<0.001**
Residence, n (%)				
Iquitos district	97 (33.1)	7 (50.0)	90 (32.3)	0.932
Punchana district	84 (28.7)	4 (28.6)	80 (28.7)	
San Juan district	64 (21.8)	1 (7.1)	63 (22.6)	
Belen district	33 (11.3)	2 (14.3)	31 (11.1)	
Outside of Iquitos city	15 (5.1)	0 (0.0)	15 (5.3)	
Occupation, n (%)				
Unemployed or student	111 (37.9)	5 (35.7)	106 (38.0)	0.54
Self-employment	100 (34.1)	5 (35.7)	95 (34.1)	
Cattle, agriculture or construction	47 (16.0)	3 (21.4)	44 (15.8)	
Intellectual work	28 (9.8)	0 (0.0)	28 (10.7)	
Craft work	7 (2.4)	1 (7.1)	6 (2.2)	
Education, n (%)				
None or only attended primary school	49 (16.7)	5 (35.7)	44 (15.8)	**0.05**
Attended secondary school or university	244 (83.3)	9 (64.3)	235 (84.2)	
Epidemiological risk factors, n (%)				
Breastfeeding	277 (94.5)	13 (92.9)	264 (94.6)	0.55
Blood transfusion	64 (21.8)	3 (21.4)	61 (21.9)	1.0
Comorbidity, n (%)				
Diabetes or high blood pressure	21 (7.2)	2 (14.3)	19 (6.8)	0.26
Digestive disease	12 (4.1)	2 (14.3)	10 (3.6)	0.10
Other cardiovascular disease	10 (3.49)	1 (7.1)	9 (3.2)	0.39

Table 1. *Cont.*

Variables	Overall (N = 293)	HTLV Positive (N = 14)	HTLV Negative (N = 279)	*p* Value
Previous infections, n (%)				
Strongyloides serology positive	167 (57.0)	6 (42.9)	161 (57.7)	0.29
Tuberculosis test positive	55 (18.8)	4 (28.6)	51 (18.3)	0.30
Prior gonorrhea	33 (11.3)	3 (21.4)	30 (10.8)	0.20
Prior syphilis	41 (14.0)	3 (21.3)	38 (13.6)	0.42
Chronic hepatitis	19 (6.5)	2 (14.3)	17 (6.7)	0.23
Prior cerebral toxoplasmosis	13 (4.4)	0 (0.0)	13 (4.7)	0.41
HIV acquisition, n (%)				
Sexual	263 (89.9)	12 (85.7)	251 (90.0)	0.71
Vertical	2 (1.0)	0 (0.0)	3 (1.1)	
Unknown	27 (9.2)	2 (14.39	25 (9.0)	
Virology, Immunology and Adherence of Treatment				
Nadir $CD4^+$/uL, median (IQR)	228 (109–363)	213 (123–360)	230 (109–363)	0.91
Current $CD4^+$, median (IQR)	446 (303–597)	455 (385–613)	441 (299–593)	0.47
Current $CD4^+ < 200$/mL n (%)	22 (10.7)	0 (0.0)	22 (11.3)	0.61
Current undetectable HIV viral load (<20 copies/mL), n (%)	216 (76.3)	12 (92.39	204 (75.6)	0.31
Poor ART adherence, ≤95%), n (%)	22 (13.4)	2 (15.4)	30 (13.3)	0.89

Values with p value ≤ 0.05, which were subsequently included in the multivariate analysis, appear in b
Percentages may not total 100 due to rounding.

3.2. *HTLV Subtypes*

15/293 patients tested positive for HTLV during screening. Of them, 14/293 (4.8 were definitively confirmed: 1/293 was HTLV-1 (0.3% 95% CI 0.06–0.9), 11/293 w HTLV-2 (3.8%, 95% CI 2.1–6.8) and 2/293 (0.7%, 95% CI 0.1–2.7) were non-typeable INNO-LIA HTLV I/II score (Figure 1).

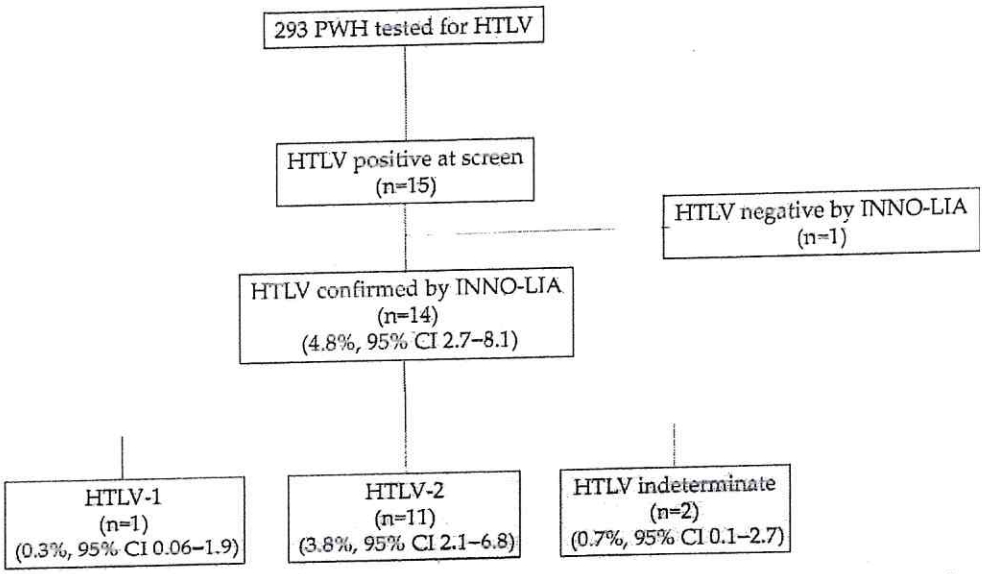

Figure 1. Flow chart of patients with HIV (PWH) who participated in the study and HTLV subty by INNO-LIA HTLV I/II score (number of cases, percentage and 95% confidence interval).

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HIV acquisition, n (%)				
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Vertical	2 (1.0)	0 (0.0)	3 (1.1)	
Unknown	27 (9.2)	2 (14.39	25 (9.0)	
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Values with p value ≤ 0.05, which were subsequently included in the multivariate analysis, appear in bold. Percentages may not total 100 due to rounding.

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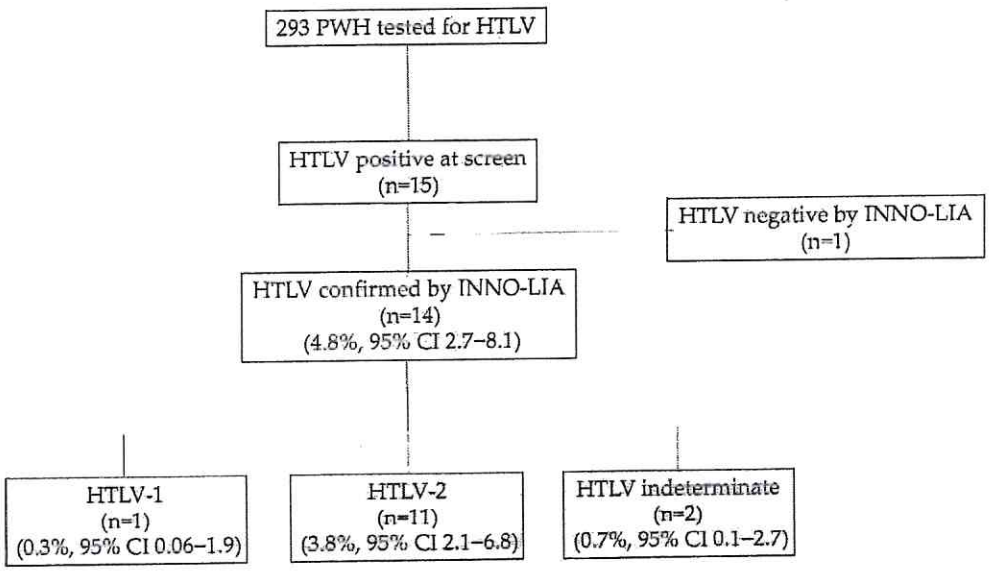

Figure 1. Flow chart of patients with HIV (PWH) who participated in the study and HTLV subtypes by INNO-LIA HTLV I/II score (number of cases, percentage and 95% confidence interval).

Table 2. Characteristics of patients with HIV-HTLV co-existence.

Type of HTLV	Age	Sex	Ethnicity	Origin of Parents	Breast-Feeding	Sexual Behavior/ Number of Sexual Partners	Non-Sterilized Procedures [a]	Transfusion	Living in Rural Area [b]	Chronic Hepatitis	STI [c]	CD4 Count Nadir/Last	HIV Viral Load
HTLV-1	62	M	Mestizo	Tarapoto	Yes	Transgender/<5	No	Yes	No	No	No	479/677	<20
HTLV-2	52	M	Mestizo	Iquitos	Yes	Homosexual/<5	No	No	No	No	No	218/674	<20
HTLV-2	56	M	Kukuma	Marañón River	Yes	Homosexual/<5	No	No	No	No	No	287/684	<20
HTLV-2	60	F	Mestizo	Nauta	Yes	Heterosexual/≥5	No	No	No	No	No	113/113	<20
HTLV-2	61	M	Mestizo	Requena	Yes	Heterosexual/≥5	No	Yes	No	No	No	134/322	<20
HTLV-2	53	M	Mestizo	Cuzco	Yes	Bisexual/≥5	No	Yes	No	Yes	Gonorrhea Syphilis	52/371	<20
HTLV-2	60	M	Mestizo	LOF	Yes	Heterosexual/LOF	LOF	No	No	Yes	No	NA	<20
Non-typable HTLV	43	F	Mestizo	Pebas	Yes	Heterosexual/<5	No	No	No	No	No	261/261	<20
Non-typable HTLV	55	M	Mestizo	Iquitos	Yes	Heterosexual/<5	No	No	No	No	Gonorrhea Syphilis	455/455	<20
HTLV-2	54	F	Mestizo	Marañón River	Yes	Heterosexual/≥5	Scarification	No	No	No	Syphilis	76/525	<20
HTLV-2	64	M	Mestizo	LOF	Yes	Heterosexual/LOF	LOF	No	No	No	No	171/399	<20
HTLV-2	66	F	Mestizo	Ucayali River	Yes	Heterosexual/<5	No	No	No	No	No	519/519	<20
HTLV-2	45	M	Mestizo	Iquitos	Yes	Heterosexual/<5	No	No	No	No	No	434/434	<20
HTLV-2	50	M	Mestizo	Iquitos	No	Heterosexual/<5	No	No	No	No	Gonorrhea	344/344	<20

[a] Non-sterilized procedures: injection, scarification, tattoos, dental procedures, intravenous drugs. [b] Defined as the absence of paved streets. [c] Sexually transmitted infections. LOF: not available due to loss to follow-up. NA: not available in the clinical history.

4. Discussion

This study confirms the relevance of HTLV-HIV coexistence in patients from the Peruvian Amazon, where HTLV-2 predominates over HTLV-1, in contrast to other regions of South America and the world where HTLV-1 is by far more frequent. Two distinct epidemiological patterns of HTLV-2/HIV superinfection have been described: one in Europe, largely associated with people who inject drugs [21], and another in Latin America, particularly in Brazil and Peru. In this region, the prevalence of HTLV-2 among people with HIV is variable and may exceed 3% in certain cohorts [2,8,9,11–14,22,23], with especially high rates reported in indigenous populations of the Amazon, although HIV/HTLV-2 cases have also been documented in urban settings.

In Peru, the Shipibo-Konibo ethnic group in the Amazonian region exhibits a high prevalence of HTLV-1 (5.7%) and HTLV-2 (3.8%) [24]. In other indigenous communities of the Peruvian Amazon, seroprevalence rates of 4.54% for HTLV-1 and 2.38% for HTLV-2 have been documented [25]. Similarly, cross-sectional studies in the Brazilian Amazon have shown a higher prevalence of HTLV-2 than HTLV-1, with seroprevalence rates ranging from 0% to 40% [8]. In general, the overall prevalence of HTLV-2 infection in the indigenous communities of the Amazonian Brazil ranges from 5.7% [26] to 8.1% [6]. Abreu et al. reported a prevalence for HTLV-2 of 18.5% and HTLV-1 of 0.13% in 1452 individuals from the Kayapó ethnic group, and found evidence of intrafamilial transmission in 42.7% of cases [6]. The variability in reported prevalence rates in the literature reflects differences in diagnostic methods, inclusion criteria, and the representativeness of the studied populations. In the Peruvian Amazon, the high proportion of indeterminate INNO-LIA HTLV I/II results underscores the need for confirmatory molecular testing and cautious interpretation of serological results, in line with the recommendations of the Infectious Diseases Society of America and the American Society for Microbiology [25,26]. Additionally, underreporting and the lack of systematic screening hinder the precise estimation of disease burden and the identification of emerging risk factors [8,23,27].

The older age observed in patients with HTLV-HIV co-existence has been observed in previous studies [28]. This may be due to the transmission pattern of HTLV-2, which may be favored by certain practices that were more frequently practiced in indigenous or marginal urban communities some decades ago [29]. In addition, HTLV-2 has lower rates of sexual transmission than HTLV-1 and HIV, with a lower potential for spreading in highly mobile populations with risky sexual behavior, but greater for spreading in those with longer periods of exposure to cumulative risk factors [28]. Although the best-documented risk factors for HTLV-2 infection in Amazonian indigenous populations are age and intravenous drug use, some cultural and socioeconomic factors have been previously associated with HTLV-1 infection. In a cohort of Peruvian women, low educational level (primary education or less) was significantly associated with HTLV-1 infection [30]. In a 10-year analysis from Brazil, an increasing trend in HTLV-1/2 seropositivity was associated with the lowest educational level, which is consistent with our trend [31] and may reflect disparities in access to health information and preventive practices, influencing transmission dynamics [32].

Although at least half of the patients' relatives resided in rural communities along the tributaries and the main course of the Amazon River. The most frequent origin was rural settlements south of Iquitos along the Marañón and Ucayali Rivers, whereas communities along the Amazon River en route to Brazil were less common, which may support the existence of a persistent transmission niche in the Peruvian Amazon [2,5,25].

The clinical course of HTLV-2/HIV co-existence is heterogeneous. Although HTLV-2 is associated with lower pathogenicity than HTLV-1, some studies suggest that it may modulate HIV progression, with reports of "long-term non-progressor" phenotypes and lower

HIV proviral load in individuals with HTLV-2, possibly mediated by increased $CD8^+$ T cytotoxic activity. However, the evidence regarding the clinical impact of superinfec remains controversial and is limited by study heterogeneity and the lack of longitud follow-up [9,25].

One of the main strengths of this study is its focus on epidemiological surveill strategies for HTLV and HIV, particularly in a region where such data are scarce. addressing this neglected area, the study contributes valuable information for public he decision-making and future research planning in the Amazon region. However, the st has several limitations. First, the small sample size limits the generalizability of the find Second, confirmatory testing was performed on eluates from dried serum spots applie Whatman paper, a transport method not formally validated by the INNO-LIA manufact and which may slightly reduce sensitivity in low-titer samples. However, previous stu using dried-spot matrices for HTLV serology report high specificity and variable sensit (≈81–100%), supporting their feasibility in field settings. The results should therefor interpreted cautiously and confirmed with serum or plasma when possible [33]. Anc limitation is the inability to perform molecular characterization (HTLV-1/2 typing by and proviral-load quantification), because cellular specimens (whole blood/PBMCs) not collected. Reliance on serology alone may leave a small proportion of cases unty and precludes analyses relating proviral burden to clinical outcomes. Additionally, g the cross-sectional design, it was not possible to assess the longitudinal clinical im particularly the role of HTLV in HIV disease progression and related complications.

In conclusion, our screening study in the Peruvian Amazon highlights a signifi prevalence of HIV–HTLV co-existence, particularly with HTLV-2. Risk factors inc age over 50 years. However, awareness and identification of HTLV co-existence rer important, as they can guide appropriate patient follow-up and care strategies. Fu multicenter studies with larger cohorts and long-term follow-up are needed to better d the clinical relevance of both HTLV-1 and HTLV-2 in people living with HIV, especial endemic areas such as the Amazon region. From a public-health perspective, the ~4% HTLV coinfection burden supports integrating HTLV testing into HIV clinic workfl linking positive cases to counseling and *Strongyloides* assessment, and strengthening ref networks. Programs should prioritize older PWH in endemic regions, include par testing, and capture cases in surveillance systems to guide resource allocation and effective screening strategies.

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Data Availability Statement: The dataset used and/or analyzed during the current study are available in the Zenodo Repository, under the ORCID: 10.5281/zenodo.14864472.

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Abbreviations

The following abbreviations are used in this manuscript:

HTLV	Human T-cell lymphotropic virus
HIV	Human immunodeficiency virus
PWH	People with HIV
ELISA	Enzyme-linked immunosorbent assay
IQRs	Interquartile ranges
CIs	Confidence intervals
ART	Anti-retroviral therapy

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Screening for *Trypanosoma cruzi* in patients living with the human immunodeficiency virus (PWH) in the Peruvian Amazon

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ABSTRACT

Introduction: Chagas disease (CD) - *Trypanosoma cruzi* infection - in people living with HIV (PWH), partic
those with advanced CD4 T cell depletion, can lead to severe syndromes affecting the central nervous syste
the heart.
Methods: We performed a cross-sectional study to screen for CD among PWH in Iquitos, Peru, between O
2023 and May 2024, with the objective of understanding the frequency of infection in this population.
with confirmed HIV attending outpatient services at two regional hospitals were enrolled. Two ELISA tests (
and recombinant) were used, and discordant results were adjudicated by indirect chemiluminescence i
noassay (CLIA).
Result: Of 534 PWH, the median age was 41 years (IQR 32–49), 66.1 % were male, the median current
count was 443/μL, and 75.8 % had an undetectable viral load. Two discordant serologic results were re
with a negative CLIA, resulting in no confirmed CD cases.
Conclusion: The prevalence of *T. cruzi* infection is likely very low in urban and peri-urban areas of Ic
Continued epidemiological surveillance is essential to monitor potential changes over time.

1. Introduction

Trypanosoma cruzi, the protozoan etiological agent of Chagas disease (CD), is responsible for the highest burden of parasitic disease in the Americas, affecting an estimated 6–8 million people [1]. It is primarily transmitted by infected hematophagous triatomine insects, although congenital exposure, blood transfusion, and ingestion of contaminated food or beverages are also possible routes of transmission [2].

An acute phase of circulating parasitemia develops 1–2 weeks after exposure to *T. cruzi* and can last up to 3 months. Most cases are asymptomatic or present as a non-specific, self-limiting febrile illness. The acute phase ends when the host immune system suppresses pa
replication, causing parasitemia to disappear, however residual
sites often persist in deep muscle and nerve tissues. So begins the ch
phase, which is lifelong in most untreated individuals. Unfortun
20–30 % of those with chronic CD eventually develop irreversibl
potentially fatal end-organ disease, famously manifested as C
cardiomyopathy and/or gastrointestinal megasyndromes [1,3].
complications usually occur after decades of infection and are
associated with significant disability, loss of productivity, and ele
healthcare costs, making CD not only a medical but also a socia
economic problem [2].

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Immunocompromised individuals have a significantly higher risk of morbidity and mortality from CD. In people with chronic CD, advanced CD4 T cell depletion caused by HIV may permit *T. cruzi* reactivation, leading to high levels of circulating parasitemia and a wide range of clinical manifestations, with the most severe syndromes involving the central nervous system and heart [4,5]. The mortality rate of *T. cruzi* reactivation disease in people with HIV (PWH) is greater than 75 %. Beyond HIV, reactivation has also been described in patients undergoing chemotherapy, hematopoietic stem cell transplantation, and immunosuppressive therapies, highlighting the importance of monitoring diverse vulnerable populations [2].

PAHO as well as U.S. and Spanish guidelines recommend that all people with CD risk factors be screened particularly immunocompromised populations like PWH [6,7]. Several studies have evaluated *T. cruzi* epidemiology among PWH in non-endemic and endemic settings [8]. In the UK, Ahmed et al. [9] screened 86 PWH and found no positive cases. In Italy, Rodari et al. [10] evaluated 389 patients, reporting a prevalence of 0.5 %–1.29 % depending on the confirmatory technique. In Spain, Salvador et al. [11] identified a prevalence of 3.9 % among 141 Latin American patients, while Llenas-García et al. [12] reported 1.9 % in a cohort of 155 patients. In a U.S. study, Hayon et al. measured a CD frequency of 2/294 (0.68 %) in PWH screened for CD with serology and PCR [13]. In endemic areas, Stauffert et al. [14] screened 200 PWH in southern Brazil (Rio Grande do Sul) and found a coinfection prevalence of 5 %. In Bolivia, Reimer-McAtee et al. [15] evaluated 116 PWH, reporting a coinfection prevalence of 27.6 %. However, no studies to date have assessed the prevalence of *T. cruzi* infection among PWH in Perú.

In Perú, *T. cruzi* is endemic in several southwestern regions, with a prevalence of around 0.4 % in Arequipa, Moquegua, Tacna, Ayacucho, and Apurímac [16]. Although Loreto has traditionally been considered non-endemic, sporadic acute cases have been reported [17]. In Iquitos, isolated cases (1 of 300) were identified among pregnant women [18], but none in a general population study (n = 394) [19]. To date, no studies have assessed the risk of *T. cruzi* infection or reactivation in PWH, underscoring the need for region-specific research. The objective of study was to perform a serological screening of CD among PWH in the Peruvian Amazon.

2. Material and methods

This was a prospective, cross-sectional study of PWH receiving care between October 20, 2023, and May 20, 2024, at one of two hospitals in Iquitos, Peru: (1) the Regional Hospital of Loreto "Felipe Santiago Arriola Iglesias" and (2) Hospital de Iquitos. Adults aged ≥18 years with confirmed HIV attending outpatient care appointments at either hospital were eligible for enrollment. After providing informed consent, participants underwent an interview detailing their sociodemographic characteristics and awareness of CD. The questionnaire applied is in **annex 1**. They submitted blood samples for *T. cruzi* serological testing.

We used *T. cruzi* IgG antibody assays: Chagatest ELISA lysate (Wiener, Rosario, Argentina) and Chagatest ELISA recombinant v4.0 (Wiener, Rosario, Argentina). We performed the assays according to the manufacturer's instructions, with the positivity threshold set at 0.200 OD units above the mean of two negative controls included per plate). For discordant results, we performed a third serological assay, an indirect chemiluminescence immunoassay (CLIA) for the qualitative detection of IgG antibodies against *T. cruzi* (MAGLUMI Chagas™, Snibe Diagnostics, Peru), following the manufacturer's instructions. We defined a confirmed diagnosis of CD as positive results by two tests. We extracted $CD4^+$ T cell counts and viral loads from medical records within approximately two months of the screening. This study was approved by the Ethics Committee of the Regional Hospital of Loreto (EXP: ID-018-CIEI-2023).

3. Results

We enrolled 534 PWH. The median age was 41 years (IQR: 32–49) and 66.1 % were male, 33.1 % lived in rural areas, 47.9 % lived in houses made of wood or leaves, and 20.4 % reported a history of blood transfusion. The median nadir $CD4^+$ was 238/μL (IQR 117–375), the median $CD4^+$ was 443/μL (IQR, 281–615), and the proportion with an undetectable HIV viral load (<20 copies/ml) was 75.8 % (Table 1). All but five participants were receiving antiretroviral therapy (ART), with more than 95 % adherence in 85.6 % of them. These sociodemographic data reflect the socioeconomic vulnerability of this population, where poor housing and limited access to healthcare may further increase their risk of neglected tropical infections.

Two patients tested positive by either Chagatest ELISA lysate or Chagatest ELISA recombinant; both had discordant results. CLIA was negative for both patients (Table 2), thus we identified no cases of *T. cruzi* infection. Although prevalence was zero in this sample, the possibility of false negatives cannot be excluded, and the findings should be interpreted with caution.

Table 1
Epidemiological characteristics of patients with human immunodeficiency virus (HIV) included in the study.

	Overall (N = 534)
Sex, Male, n (%)	353 (66.1 %)
Age	
Age, median (IQR), years	41 (32–49)
Age ≥50, n (%)	67 (12.5 %)
Hospital attended, n (%)	
Regional Hospital of Loreto	416 (77.9 %)
Hospital of Iquitos	118 (22.1 %)
Residence, n (%)	
Iquitos district	171 (32.0 %)
Punchana district	134 (25.1 %)
San Juan district	109 (20.4 %)
Belen district	87 (16.3 %)
Outside of Iquitos metropolitan area	33 (6.2 %)
Occupation, n (%)	
Unemployed or student	215 (40.3 %)
Self-employment	152 (28.5 %)
Cattle, agriculture or construction	97 (18.2 %)
Intellectual work	45 (8.4 %)
Craft work	25 (4.7 %)
Education, n (%)	
None and attended primary school	113 (21.2 %)
Attended secondary school or university	421 (78.8 %)
Epidemiological risk factors, n (%) φ	
Resides in rural location	177 (33.1 %)
Lives in a house made of wood or leaves	256 (47.9 %)
Blood transfusion	109 (20.4 %)
Risk group, n (%)φ	
Heterosexual	374 (75.4 %)
Non-heterosexual	97 (19.4 %)
HIV acquisition, n (%) φ	
Sexual	463 (86.7 %)
Vertical	3 (0.6 %)
Parenteral	1 (0.2 %)
Unknown	62 (11.6 %)
Antiretroviral treatment	
Yes	529 (99 %)
Adherence[a] < 90 %	33 (7.6 %)
Adherence[a] 90–95 %	6.9 (6.9 %)
Adherence[a] >95 %	374 (85.6 %
Immunology and virology, n (%)	
Nadir $CD4^+$, median (IQR),/uL[b], median (IQR)	238 (117–375)
Current $CD4^+$, median (IQR),/uL[b], median (IQR)	443 (281–615)
Current $CD4^+$ < 200/ml[b], n (%)	52 (13.9 %)
Current undetectable HIV viral load[c], (<20 copies/mL), n (%)	330 (65.8 %)

IQR: interquartile range.
φ Epidemiological risk factors, Risk group, and HIV acquisition may include more than one response per participant.
Data availability varies across variables: [a] information available for 437 participants, [b] for 303 participants; [c] for 374 participants; [d] for 501 participants.

Table 2
Clinical and serological findings in two patients with discordant serological tests.

Patient	Age/ Sex	CD4 cell/ μL	Chagatest ELISA lysate[a] (optical density)	Chagatest ELISA recombinant v4.0[a] (optical density	Indirect chemiluminescence immunoassay[b]
1	46 year/ female	928	0.320, positive	0.08, negative	0.024, negative
2	28 year/ male	444	0.087, negative	0.447, positive	0.179, negative

[a] Results were considered positive when the optical density (OD) value exceeded that of the negative control by 0.200, in accordance with the manufacturer's instructions.

[b] Results were considered positive when the value was ≥1.0 index/ml, in accordance with the manufacturer's instructions.

4. Discussion

Our study identified no cases of *T. cruzi* infection among 534 PWH enrolled in Iquitos, Peru. The prevalence of CD among PWH in Latin American countries varies widely by region, population, and diagnostic method, but is generally reported between 1 % and 28 % in endemic areas. In Bolivia, a cross-sectional study in Cochabamba found a prevalence of 27.6 % among PWH, reflecting the hyperendemic status of Chagas disease in that country [15]. In Brazil, studies using highly specific diagnostic methods report prevalence rates of 0.8 %–2 % among urban HIV cohorts, though older literature and less specific assays have reported rates up to 5 % [20,21]. In Argentina, a retrospective review of PWH in Buenos Aires found that 80 out of 1200 HIV patients (6.7 %) were coinfected with T. cruzi, though this cohort was enriched for individuals with epidemiologic risk factors [22]. Studies of Latin American immigrants with HIV in non-endemic countries (e.g., Spain) report prevalence rates of 1.9 % overall, but much higher rates (up to 21.5 %) among Bolivian migrants [9].

The sensitivity of serological tests is lower in PWH. With very low $CD4^+$ counts, B cells may not function properly, making the humoral response unreliable. Several publications have reported cases of PWH who tested seronegative but positive by PCR [15,23]. Therefore, if PCR had been used, a positive case might have been identified. However, as the average CD4 count of our study population was high (above 200) and with good adherence of treatment, their serologic response was likely intact. Another consideration is the use of rapid diagnostic tests, which, although less sensitive, could play a role in screening at primary care level in endemic areas [24].

This study has several limitations. First, the sample size was not powered to accurately estimate the prevalence of CD in this population; when the expected prevalence is low (e.g., around 1 %), at least 1000 participants would be needed for precise estimates. Second, we did not include a comparison group of HIV-seronegative individuals from the same area, which would have provided additional epidemiological context. Third, PWH with central nervous system manifestations such as meningoencephalitis or cerebral mass lesions were not included, although this population may be at higher risk of *T. cruzi* reactivation. Fourth, parasitological methods to assess parasitemia were not performed, as the protocol focused on serological screening.

Larger studies are therefore required to determine the true prevalence of CD among PWH living in Iquitos and surrounding areas. Future research should also explore the cost-effectiveness of routine screening in HIV programs, integration with existing laboratory infrastructure, and the development of targeted clinical algorithms for immunocompromised patients.

In conclusion, the prevalence of CD is likely very low in urban and peri-urban areas of Iquitos. However, given the high mortality of *T. cruzi* reactivation disease, continued epidemiological surveillance a PWH is essential to detect potential changes over time and to pr future severe reactivation cases in this region, rather than re mending systematic screening at entry-to-care.

CRediT authorship contribution statement

Silvia Otero-Rodriguez: Writing – review & editing, Methodo Investigation, Data curation, Conceptualization. **Martin Casapia rales:** Writing – review & editing, Methodology, Investigation. **Lorena Pinedo-Ramirez:** Writing – review & editing, Investiga Data curation. **Esperanza Merino:** Writing – review & editing, odology. **Eva H. Clark:** Writing – review & editing, Supervision. **Manuel Ramos-Rincón:** Writing – review & editing, Writing – ori draft, Methodology, Data curation, Conceptualization.

Availability of data and materials

The data that support the findings of this study are availabl request from the corresponding author. The data are not pub available due to privacy or ethical restrictions.

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Declaration of competing interest

The authors declare the following financial interests/personal lationships which may be considered as potential competing inter Jose Manuel Ramos Rincon reports article publishing charges equipment, drugs, or supplies were provided by Miguel Hernar University of Elche Faculty of Medicine. If there are other authors, declare that they have no known competing financial interests or sonal relationships that could have appeared to influence the work ported in this paper.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https:// org/10.1016/j.tmaid.2025.102927.

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Genotype distribution and molecular characterization of HPV in the Peruvian amazon: insights into prevalence, lineage diversity, and viral integration

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Cervical cancer remains a leading cause of cancer-related mortality among women in Peru, with the highest death rates reported in the Amazon region. Despite this burden, molecular data on human papillomavirus (HPV) in this area are limited. This study aimed to assess HPV genotype distribution a molecular characteristics in women undergoing cervical screening in the Peruvian Amazon. Between May and November 2024, cervical samples were collected from 503 women aged 25–55, along with an additional subset of 35 women with histologically confirmed CIN2 + lesions. HPV genotyping was performed using the Allplex™ HPV28 assay, and single infections with HPV16 or HPV52 were further analyzed by TaME-seq to determine lineage, intrahost variability, and integration. HPV prevalence w 51.7% (278/538), with high rates of multiple infections (44.2%) and low vaccination coverage (7.8%). Oncogenic HPV types were detected in 35.7% (192/538) of participants, with HPV 16 and HPV 52 bein the most prevalent. Sublineage analysis revealed predominance of A1 variants, while viral integration was detected in nine cases, three associated with CIN2 + lesions. Integration sites occurred mainly in *E1/E2* for HPV16 and *L1/L2* for HPV52. These findings highlight the urgent need to expand vaccinatior and implement molecular screening strategies in the Peruvian Amazon.

Keywords Cervical cancer, Human papillomavirus, Sublineages, Integration, Peruvian amazon, TaME-seq

Cervical cancer remains a major public health challenge globally, particularly in low- and middle-incon countries and rural areas, where access to early detection and treatment remains limited[1]. In Peru, it is one of tl leading causes of cancer-related mortality among women, primarily driven by persistent infection with high-ri human papillomavirus (HPV) genotypes. Although national efforts to expand HPV vaccination and cervic

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screening coverage have yielded progress, significant gaps persist, especially in remote and low-resource areas of the country.[2].

Several studies have assessed HPV prevalence and genotype distribution in Peru. However, most have focused on urban or more accessible populations[3–5]. In contrast, limited molecular epidemiological data are available from the Peruvian Amazon, where health infrastructure is weaker, healthcare access is restricted, and cervical cancer outcomes are among the poorest in the country. The Peruvian Amazon, comprising regions such as Loreto, Ucayali, and Madre de Dios, reports some of the highest cervical cancer mortality rates in the country, exceeding 35 deaths per 100,000 women annually[1,6].

To address these inequities, there is an urgent need to better understand the distribution of HPV genotypes and the molecular characteristics of circulating viral variants in these populations. While HPV16 and HPV18 are the most carcinogenic types globally, other genotypes, such as HPV52, have emerged as important contributors to cervical cancer risk in Latin America[3,7]. Understanding this genotype distribution is critical for tailoring screening strategies and informing vaccine policy.

This study represents the first comprehensive effort to characterize HPV genotype distribution and molecular features in a remote, low-resource population from the Peruvian Amazon. The investigation assessed the prevalence of HPV types and conducted molecular characterization of most predominant genotypes, including lineage assignment, viral integration, and intrahost variability. The objective was to generate insights into the diversity and molecular behavior of high-risk HPV types in this region, contributing to future risk stratification strategies and supporting the development of more effective, locally adapted screening and prevention programs.

Results

Study population characteristics

From May to November 2024, a total of 503 women aged 25–55 years consented to participate in the study. The median age was 39 years (range 25–55). HPV was detected in 251/503 participants (49.90%), of whom 113/251 (45.02%) exhibited multiple HPV infections. (NOTE: Multiple infections included combinations of different risk levels, with high-/low-risk, high-/medium-risk, and medium-/low-risk genotypes detected). Only 42/503 women (8.35%) reported prior HPV vaccination. A summary of the number of participants, age range, HPV status (positive/negative), infection pattern (single or multiple HPV types), and self-reported HPV vaccination status is presented in Table 1. Cytological results were not available for these women, as the protocol focused exclusively on HPV testing.

An additional subset of 35 women with histologically confirmed CIN2 + lesions was recruited from pathology units during the same period (May–November 2024). The median age of this group was 41 years (range 29–55) and none of the participants in this subset had been vaccinated against HPV. Among them, 8/35 (22.86%) were HPV negative, 17/35 (48.57%) had a single HPV infection and 10/35 (28.57%) showed multiple HPV infections. Follow-up biopsies were confirmed (histologically) as CIN2 + lesions.

HPV distribution

We assessed the distribution of HPV genotypes in general and by infection multiplicity (single vs. multiple infections). The overall distribution considering all samples (503 regular screening and 35 confirmed CIN2 + samples) can be seen in Fig. 1.

Considering all 538 women included in the study, a total of 278/538 (51.67%) tested positive for HPV. Among them, 155/278 (51.76%) cases involved single infections and 123/278 (44.24%) involved multiple infections.

Analysis of single infections ($n = 155$) revealed that up to 94/155 (60.65%) were caused by oncogenic HPV types. The most prevalent oncogenic genotypes were HPV16 (22/94, 23.40% of single infections caused by oncogenic types) and HPV52 ($n = 16/94$, 17.02%). High-risk types (HPV16 and HPV18) were identified in 25/94 (26.60%) single infections caused by oncogenic types, while medium-risk types (HPV31, 33, 35, 45, 52, and 58) accounted for 48/94 samples (51.06%), and low-risk types (HPV39, 51, 56, 59, and 68) for 21/94 cases (22.34%). Only 8 of the 155 women (5.16%) with single HPV infections reported prior HPV vaccination. None of them belonged to the group presenting histologically confirmed CIN2 + diagnosis, and only one carried a high- or medium-risk HPV type (HPV58).

Age	n	HPV negative	HPV positive	Single infection	Multiple infection	Non vaccinated	Vaccinated
25–30	97	35	62	29	33	77	20
31–35	94	54	40	23	17	86	8
36–40	108	58	50	26	24	102	6
41–45	77	39	38	21	17	74	3
46–50	86	45	41	30	11	84	2
51–55	41	21	20	9	11	38	3
Total	503	252	251	138	113	461	42

Table 1. Characteristics of women attending cervical screening clinics in loreto, Peru (May–November 2024). The table shows the distribution of participants by age group, HPV status (positive or negative), infection pattern (single or multiple HPV types), and self-reported HPV vaccination status. HPV, human papillomavirus.

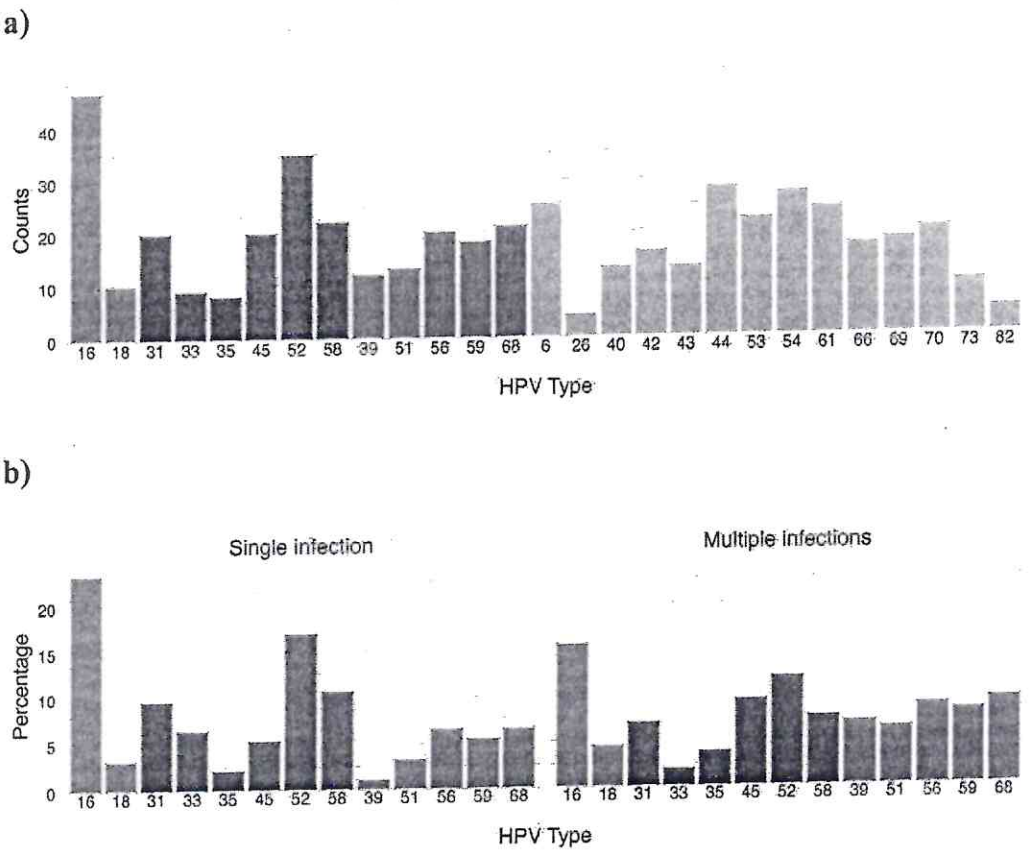

Fig. 1. Distribution of HPV genotypes and oncogenic risk in cervical samples from the Peruvian Amazon. (A) Number of HPV detections by genotype in cervical samples from the Peruvian Amazon. **(B)** Proportion of oncogenic HPV types stratified by infection pattern (single vs. multiple infections). Genotypes are colored as follows: red for high-risk (HPV16, 18), purple for medium-risk (HPV45, 31, 33, 35, 52, 58), green for low-risk (HPV39, 51, 56, 59, 68), and grey for non-oncogenic types.

Among 123 women with multiple infections, oncogenic HPV types were detected in 98/123 (79.67% of multiple HPV infections), with the most frequently detected oncogenic genotypes being HPV 16 ($n=25/98$) and HPV 52 ($n=19/98$). (Fig. 1B) High-risk genotypes were found in 28/98 (28.57%) multiple HPV infections presenting oncogenic types, medium-risk genotypes (excluding samples with high-risk and/or low genotypes) in 45/98 (45.92) samples, and low-risk genotypes (excluding samples with high and/or medium risk types) were detected in 25/98 women (25.51%). Only 10/98 women with multiple infections had reported being vaccinated, of whom 7/10 presented HPV types involving at least one oncogenic HPV type.

Among the 35 women with confirmed CIN2+lesions, 27 of them showed HPV positivity. HPV16 was the most prevalent genotype ($n=11/27$, 40.74%), followed by HPV52 ($n=8/27$, 29.63%) and HPV31 ($n=3/27$, 11.11%). High-risk genotypes (HPV16 and HPV18) were identified in 12/27 cases (44.44%), while medium-risk genotypes (HPV31, 33, 45, 52, and 58), in the absence of high-risk types, were detected in 8/27 cases (29.63%) and low risk types (excluding samples with high and/or medium risk types) in 7/27 samples (25.96%).

Self-reported vaccination status was available for both cohorts. Among the screening women, 42/503 (8.35%) reported prior HPV vaccination. Of these, 18/42 (42.86%) tested HPV-positive. Five out of 18 (27.79%) carried high-risk and/or medium oncogenic HPV types: 2/5 (40.00%) with multiple infections including HPV16/18/52 (with additional low-risk types), 1/5 (20.00%) with HPV33 (with additional non-oncogenic types), and 2/5 (40.00%) with HPV58 (one woman with a single infection and another with additional non-oncogenic types). The remaining infections involved low- or non-oncogenic types. Importantly, none of the 35 women with CIN2+lesions reported previous vaccination.

Summary of sequencing results

All single infections positive for HPV16 or HPV 52 ($n=36$) were sequenced alongside a positive control (HPV16 plasmid) and a negative control (PCR-grade water), generating between approximately 2.3 million and 140 million trimmed reads per sample (Supplementary Table S1). The proportion of reads mapping to the HPV genome varied substantially and showed a strong negative correlation with Allplex28 Ct values for the sequenced type (Supplementary Table S1).

Of the sequenced samples ($n=36$), 29 achieved > 90% genome coverage at a depth of ≥ 10×, and, among those, 24 also reached ≥ 100× coverage across the full viral genome. Sequencing performance was significantly associated with Ct values: both the number of reads mapped to the HPV genome and the mean coverage were strongly negatively correlated with Ct (Spearman's $\rho = -0.98$, $p < 2.2 \times 10^{-16}$).

Sublineage typing results

Sublineage typing was performed for all samples with ≥ 20× coverage across the full viral genome and a minimum genome coverage threshold of 50%, resulting in 13 HPV16 positive and 17 HPV52 positive samples included in the analysis.

Among HPV16 positive samples, most clustered within sublineage A1 (11/13, 84.62%), while one sample each was assigned to D2 and D3. For HPV52, the majority of samples were classified as sublineage A1 (14/17, 82.35%), with three samples assigned to sublineage C2 (17.65%). All HPV52 sublineage assignments were supported by high bootstrap values (≥ 92). In contrast, HPV16 bootstrap support values varied more widely (51–100), with lower values typically observed in samples with a greater proportion of missing genomic positions, which likely reduced the reliability of phylogenetic placement.

Comparison between Peruvian and Norwegian HPV16A1 and HPV52A1 strains

To explore viral diversity across time and geography, Peruvian HPV16 A1 and HPV52 A1 sequences with at least 80% genome coverage were compared to Norwegian sequences from the National Screening Program, previously published by Hesselberg Løvestad et al.[10].

The HPV16 phylogenetic tree revealed a large, well-supported clade (bootstrap = 96) comprising both Peruvian ($n=3$) and Norwegian ($n=10$) sequences (Fig. 2A). In contrast, the HPV52 tree exhibited minimal phylogenetic structure. All sequences were classified as sublineage A1, and most internal branches showed low bootstrap support. Aside from one clade containing three Peruvian samples (bootstrap = 71), the remaining sequences were interspersed throughout the tree without clear clustering by geographic origin or collection period (Fig. 2B).

Mutational signatures of the intrahost variability

All detected iSNVs were classified into the 96 single base substitution (SBS) mutation classes (categories) according to trinucleotide context and substitution type (Fig. 3). In both HPV16 and HPV52, T > C substitutions predominated, followed by C > T and T > G substitutions. The relative distribution of these mutations differed between genotypes: HPV16 exhibited a broader range of T > C and C > T contexts, whereas HPV52 showed a distinct enrichment of specific T > G mutations, particularly within the GTT > GGT trinucleotide motif.

Integrations

Integration events between the HPV genome and the human genome were detected in both HPV16 and HPV52 positive samples using a combination of discordant read pair detection and junction read analysis. In total,

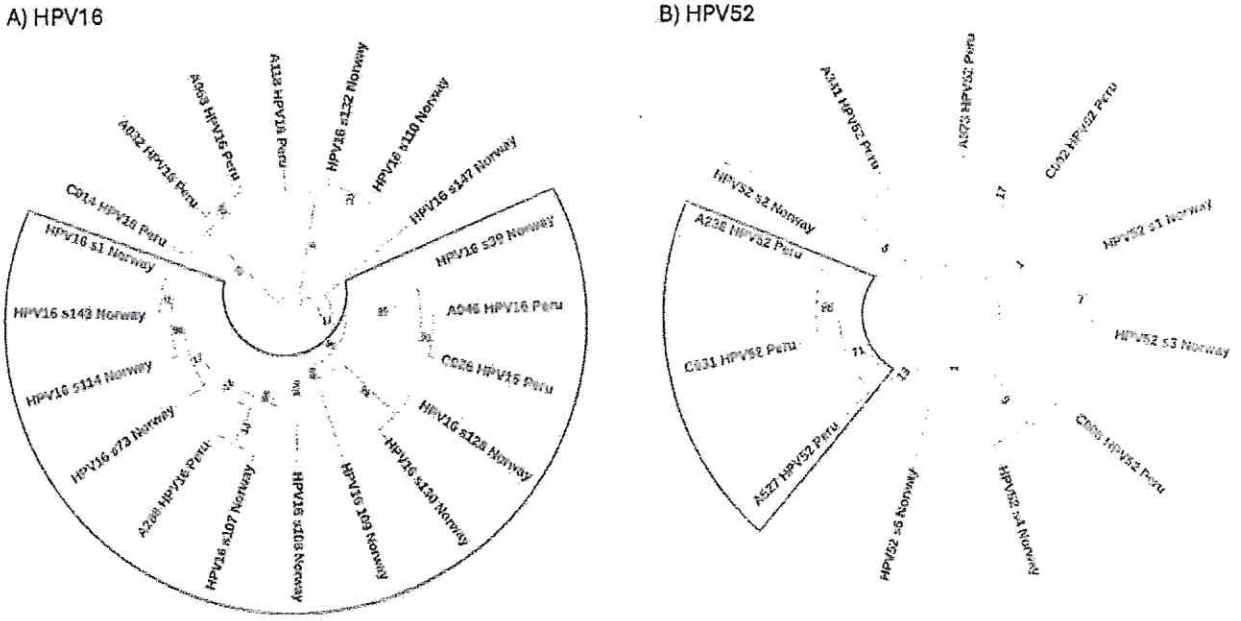

Fig. 2. Phylogenetic comparison of HPV16 and HPV52 A1 sublineages from Peruvian and Norwegian samples. Maximum likelihood phylogenetic trees were constructed using RAxML-NG v1.2.2 under the GTR model, and 1000 bootstrap replicates[18]. Colored labels indicate country of origin (green: Peru; purple: Norway). The boxed clade marks the most strongly supported node.

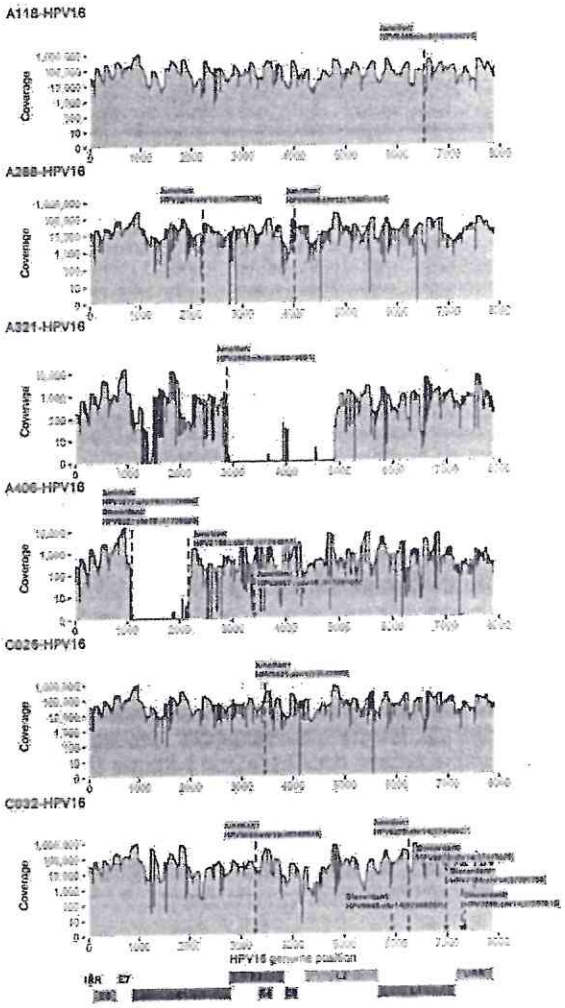

Fig. 4. Integrations sites detected in HPV16 positive samples. The X-axis represents the full-length HPV16 genome (~7906 bp), while the Y-axis shows read coverage depth. Integration sites were detected by the presence of discordant and junction reads. Drops in coverage indicate potential integration breakpoints. The lower panel illustrates the genomic organization of HPV16, including early (*E6*, *E7*, *E1*, *E2*, *E4*, *E5*), late (*L1*, *L2*), and non-coding (URR) regions.

specific host-virus interactions or distinct selective pressures acting on HPV52. The observed differences in mutational context may also be indicative of differential APOBEC activity across HPV genotypes and warran further investigation.

HPV DNA integration into the human genome is a hallmark of cervical carcinogenesis[25]. Integration event were detected in nine samples, including three confirmed CIN2+ cases. Consistent with prior studies, HPV1 integration breakpoints clustered in the E1 and E2 regions of the viral genome, supporting the hypothesis tha disruption of these regulatory genes promotes oncogene overexpression[25]. HPV52 integration breakpoints wer more often located in *L1* and *L2*, possibly reflecting genotype-specific patterns. Integration sites were distributed across multiple human chromosomes, with no apparent enrichment for specific loci, reinforcing the notion tha integration is a largely stochastic process with oncogenic potential. In two samples (A321 and A406), integratio sites coincided with localized drops in sequencing depth, an observation commonly reported for HPV16 an interpreted as indicative of large deletions around integration breakpoints.

This study has several strengths. It provides valuable molecular data from a remote and low-resourc region previously excluded from HPV genomic research and includes cases with confirmed high-grad lesions, strengthening clinical relevance. The application of TaME-seq enabled high-resolution analysis of vira integration and intrahost diversity, features that go beyond conventional genotyping and offer insights into vira behavior. However, limitations must be acknowledged. First, the sample size for CIN2+ lesions was modest, an sequencing performance varied with sample adequacy and viral load, as shown by the strong inverse correlatio between Ct values and sequencing coverage. Second, although international phylogenetic comparisons wer included, the cross-sectional design precludes inferences about transmission dynamics or viral evolution Additionally, progression risk could not be assessed, as longitudinal follow-up data were not available.

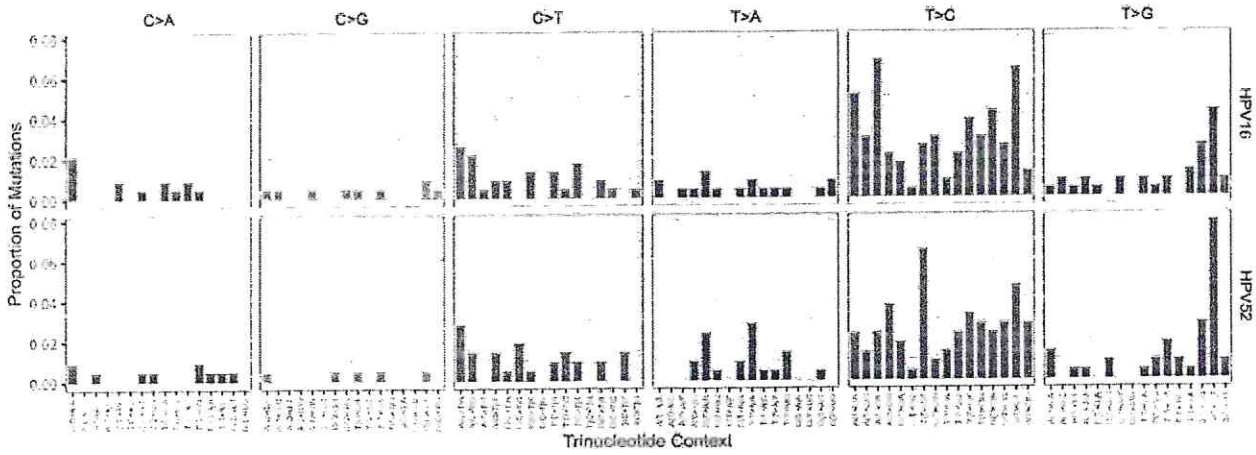

Fig. 3. Mutation signatures of iSNVs. The bar plots show the distribution of 96 trinucleotide-based single base substitution (SBS) classes detected in HPV16 and HPV52 genomes, categorized by substitution type and context. T > C transitions were the most frequent, followed by C > T and T > G substitutions. A notable enrichment of T > G mutations within the GTT > GGT context was observed in HPV52 samples.

six HPV16 positive and three HPV52 positive samples showed evidence of high-confidence integration sites (Figs. 4 and 5). Integrations were also detected in three confirmed CIN2 + cases (C026-HPV16, C032-HPV16, and C031-HPV52). For HPV 16, integration breakpoints were observed across various regions of the viral genome, most frequently within or near the *E1*, *E2*, and *L2* genes (Fig. 4). Several samples exhibited multiple integration sites. In A321 and A406 samples, integration sites were associated with local drops in sequencing depth. Integration breakpoints varied in genomic location on the host side, involving multiple chromosomes. For HPV52, integration was also detected in diverse regions of the viral genome, mostly in *L1* and *L2* (Fig. 5). Integration breakpoints were distributed across several human chromosomes, again without apparent preference for specific genomic features.

Discussion

This study provides the first comprehensive molecular characterization of HPV infections among women undergoing cervical screening in the Peruvian Amazon, a region burdened with some of the highest cervical cancer mortality rates in the country[1,2].

A remarkably high prevalence of oncogenic HPV types (192/538, 35.69%) was detected among women attending screening, with over half exhibiting multiple HPV infections. These findings are consistent with previous reports from Peru's most resource-limited regions and far exceed prevalence rates documented in urban populations[1,19]. Vaccination coverage in this study was low (42/538, 7.81%), mostly among younger women, reflecting the relatively recent introduction of HPV vaccination in Peru (2011). Among vaccinated participants, 42.9% tested HPV-positive, but the majority of infections involved low- or non-oncogenic types. Only five vaccinated women carried oncogenic HPV types, including HPV16/18/52 in multiple infections, HPV33, and HPV58. Importantly, none of the 35 women with histologically confirmed CIN2 + lesions had been vaccinated. These findings are consistent with the expected protective effect of HPV vaccination against high-grade cervical disease, while also highlighting the urgent need to improve vaccine coverage in remote regions such as Loreto.

In line with global and regional trends, HPV16 was the most common genotype identified in both single and multiple infections[9]. Supporting recent data that indicate a shift in type distribution in Latin America[1], HPV18 was relatively rare, while HPV52 was highly prevalent, particularly among CIN2 + cases. Importantly, HPV52 is included in the nonavalent vaccine but not in the bivalent or quadrivalent formulations, underlining its oncogenic potential in this population and reinforcing the importance of implementing broader-valency vaccines in Peru.

Phylogenetic analysis revealed a predominance of A1 sublineages for both HPV16 and HPV52, in agreement with data from other Latin American populations. However, less common sublineages were also identified, including D2 and D3 for HPV16 and C2 for HPV52. These have been associated with increased oncogenicity in other regions[20,21]. Comparative phylogenetic analysis with Norwegian strains revealed tight clustering of some Peruvian HPV16 A1 variants with sequences collected more than a decade earlier in Scandinavia, suggesting that certain A1 variants have circulated globally over extended periods while still accumulating detectable sequence divergence. In contrast, HPV52 sequences showed minimal phylogenetic structure, with weak bootstrap support and no clear geographic or temporal clustering. This may reflect a slower evolutionary rate or higher sequence conservation in HPV52, though additional data are needed to confirm this.

Analysis of iSNVs revealed consistent mutational patterns across HPV16 and HPV52, dominated by T > C and C > T substitutions. These mutations are likely shaped by host deaminase activity, particularly that of the APOBEC3 enzyme family, which is known to introduce such changes in viral genomes[22–24]. The enrichment of specific T > G transversions in the GTT trinucleotide context observed in HPV52 samples is particularly notable, as such mutations are rarely reported in papillomavirus genomes. This atypical pattern may reflect genotype-

Sample collection and DNA extraction

Cervical samples were collected by healthcare professionals using FLOQSwabs® (Copan®) and stored in Copa eNAT® transport and preservation medium to maintain the integrity of the genetic material during transpor and storage. Genomic DNA was extracted using the STARMag 96 ProPrep system (Seegene®), following th manufacturer's instructions for efficient DNA extraction. The extraction was performed using the SEEPREP 3 automated equipment (Seegene®), ensuring reproducibility and consistency across all processed samples.

HPV genotyping and sample selection for variant analysis

HPV genotyping was performed using the Allplex™ HPV28 Detection Kit (Seegene®), which allows for th simultaneous detection of 28 HPV types, using the CFX96 Thermocycler (Biorad®). The manufacturer instructions were followed accordingly.

HPV types were classified as high-risk (HPV16, 18), medium-risk (45, 31, 33, 35, 52, 58) and low-risk (3 51, 56, 59 and 68), based on international evidence from the global attribution analysis of HPV genotypes t invasive cervical cancer[9]. All other types were considered non-oncogenic.

Tagmentation-assisted multiplex PCR enrichment sequencing

The most prevalent HPV genotypes detected in the study cohort were HPV16 and HPV52, both in single an multiple infections. Based on these findings, samples with single infections of HPV16 or HPV52 were selecte for downstream analysis, including variant lineage determination, intrahost variability, and viral integration.

A total of 36 DNA samples, 21 HPV16 positive and 15 HPV52 positive, previously genotyped using th Allplex™ HPV28 Detection Kit (Seegene®), were analyzed using Tagmentation-Assisted Multiplex PCI Enrichment Sequencing (TaME-seq)[10]. Library preparation began with tagmentation using the Illumina DN Preparation Kit (Illumina®), following the manufacturer's protocol. Up to 50 ng of input DNA per sample wa used in a 15 µL reaction volume. A positive control (HPV16 reference plasmid, provided by the Internationa HPV Reference Center, www.hpvcenter.se) and a negative control (PCR-grade water) were included throughou the workflow.

Following tagmentation, multiplex PCR amplification was performed using HPV genotype-specific primer (forward and reverse reactions separated) and unique i5/i7 index adapters, as previously described[10,11]. Amplifie libraries were pooled according to genotype (HPV16 or HPV52), purified using AMPure XP beads (Beckma Coulter®), and normalized prior to sequencing. Libraries were diluted to a final concentration of 1.8 pM an sequenced on the Illumina® NextSeq 500 platform using a paired-end 151 + 151 bp run with the Mid Outpu reagent kit. Sequencing followed the protocols detailed in the Denature and Dilute Libraries Guide v02, NextSe 500 System Guide v02, and NextSeq 500 Kit Reference Guide (revision F).

Bioinformatics and downstream analysis

Bioinformatics analysis of the sequencing data was performed using the TaME-seq Snakemake workflow, whic is publicly available (https://github.com/jean-marc-costanzi/TaME-seq, accessed on 2025-03-25) and has bee validated and published in previous studies[10,11]. The workflow begins with quality control, including trimmin of adapter sequences and filtering of low-quality reads. For alignment, two aligners were used: HISAT2[12] fo mapping the reads to the HPV genome and LAST[13] particularly useful for detecting integration events betwee the HPV genome and the host genome. The final output consists of detailed statistical tables, nucleotide coverag data, and specific information regarding integration sites and intrahost viral variability.

Sublineage typing

Consensus sequences were generated for all samples by selecting the nucleotide with the highest read dept at each genomic position, requiring a minimum coverage of 20×. Sublineage typing was conducted separatel for HPV16 and HPV52 positive samples by aligning each consensus sequence to a panel of genotype-specifi sublineage reference sequences (retrieved from the PaVE database, https://pave.niaid.nih.gov/explore/variants variant_genomes, accessed on 2025-03-25) using MAFFT v7.526[14].

Maximum likelihood phylogenetic trees were constructed using RAxML-NG v1.2.2 under the GTR model with 50 randomized parsimony starting trees and 1000 bootstrap replicates[15]. A sample was assigned to specific sublineage if it clustered within a clade containing the corresponding reference sequence, with bootstra support > 70%.

To explore viral diversity across time and geography, Peruvian HPV16 A1 and HPV52 A1 sublineag sequences were compared with Norwegian sequences obtained between 2009 and 2012 through the Nationa Screening Program, as previously published by Hesselberg Løvestad et al.[10].

Intrahost mutation detection

Intrahost single nucleotide variants (iSNV) detection was performed as previously described[10,11]. In short, raw reads were aligned to the HPV reference genome (HPV16REF, HPV52REF (retrieved from the PaVE database https://pave.niaid.nih.gov/, accessed on 2025-03-25) using HISAT2 (v2.2.1), and nucleotide frequencies wer extracted using BCFtools mpileup (v1.12)[12,16]. iSNVs were identified in a reference-independent manner as th second most abundant base at each position, with minimum ≥ 100× coverage and Phred score ≥ 30. At sites with 100–500× depth, a minimum frequency of 5% was required; for > 500× depth, a 1% threshold was applied. Only samples with ≥ 100× mean sequencing depth were included.

All detected iSNVs were classified into the 96 single base substitution (SBS) mutational signatures based or trinucleotide context. Counts were converted to proportions and visualized per HPV type to explore mutationa patterns.

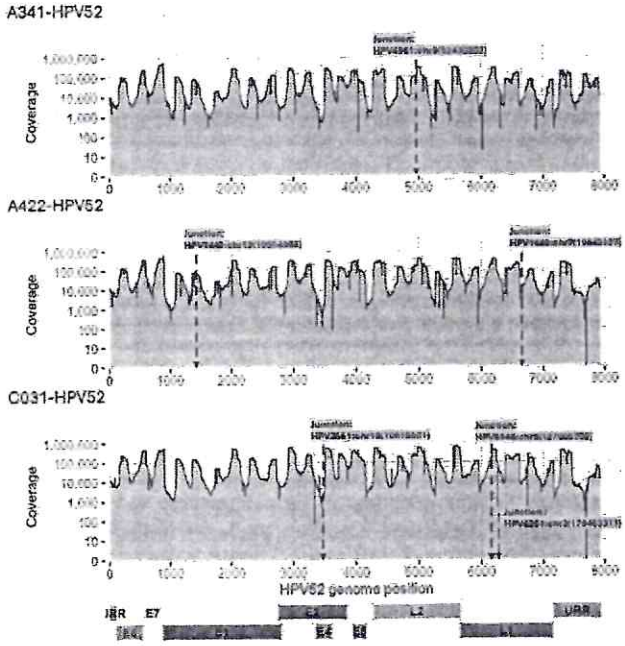

Fig. 5. Integrations sites detected in HPV52-positive samples. The X-axis shows the HPV52 genome (~7961 bp) and the Y-axis displays read coverage. Integration breakpoints were detected predominantly in L1 and L2 regions. The schematic below outlines the structure of the HPV52 genome with annotated coding regions.

The findings of this study have direct public health implications for the Peruvian Amazon. The high prevalence of oncogenic HPV types particularly HPV52, which is not covered by the bivalent or quadrivalent vaccines reinforces the urgent need to implement vaccination schemes using the nonavalent vaccine in regions with a high viral burden. Furthermore, the detection of viral integration in confirmed CIN2+cases supports the use of molecular testing as a primary screening strategy over conventional cytological methods, especially in areas with limited access to clinical follow up. Implementing high-risk HPV based screening, combined with genotyping and integration surveillance, could optimize the identification of women at risk and improve cervical cancer outcomes in vulnerable settings such as Loreto.

In conclusion, this study reveals a high burden of HPV infection, including oncogenic HPV types, in women attending cervical screening in the Peruvian Amazon. The predominance of vaccine-preventable types, combined with low vaccine coverage and confirmed integration in CIN2+cases, underscores the need to scale up HPV vaccination and strengthen molecular screening in nationwide settings. These efforts are critical for developing equitable and effective cervical cancer prevention strategies in Peru and similar high-burden regions.

Methods

Study population

Women aged 25 to 55 years attending cervical screening clinics at Hospital Regional de Loreto "Felipe Santiago Arriola Iglesias" and Hospital de Apoyo de Iquitos "César Garayar García", located in the Loreto region of the Peruvian Amazon, were invited to participate in a study on the distribution of HPV genotypes for cervical HPV infection. The study was conducted between May and November 2024.

Although Peruvian cervical cancer screening guidelines recommend testing for women aged 30–49 years in accordance with World Health Organization (WHO) recommendations[8], this study was carried out in areas with limited access to healthcare services. To address this gap and capture a broader picture of HPV circulation, all women within the approved age range (25–55 years) who attended the participating clinics, regardless of screening eligibility, were offered HPV testing. This also included accompanying women who were not initially seeking screening but agreed to participate. Exclusion criteria included women with no history of sexual activity, pregnancy, women with a history of prior hysterectomy, and those currently undergoing pharmacological or surgical treatment for cervical cancer.

To ensure the inclusion of high-grade lesions, an additional set of samples from women with histologically confirmed CIN2+lesions was included. During the same study period (May to November 2024), all women with a clinical suspicion of CIN2+based on cytological findings who had been referred for biopsy to the Pathology Units at the same hospitals were invited to participate. A cervical sample for HPV testing was collected immediately prior to the biopsy procedure, following written informed consent. Histological examination of the biopsies subsequently confirmed the CIN2+diagnosis.

HPV-human chromosome integration detection

Viral integration analysis followed a previously described approach[10,11]. Potential integration sites were identified by detecting discordant read pairs in the HISAT2 alignment, where one read mapped to the human genome and its mate to HPV. Sites were recorded if at least two such human-mapped reads had unique start or end positions. HISAT2-unmapped reads were re-aligned with LAST to detect junction reads, and integration breakpoints were recorded if they were supported by ≥ 3 junction reads with unique coordinates. All candidate sites were visually inspected in IGV Web App (v2.2.7)[17]. Integrations supported only by split reads, repetitive regions, or likely trimming artefacts were excluded.

Data availability

The data that support the findings of this study are available on request from the corresponding author. The data are not publicly available due to privacy or ethical restrictions. All code used for processing and analysis of sequencing data is publicly available at the TaME-seq GitHub repository: [https://github.com/sinanugur/TaME-seq].

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Author contributions

Data curation: L.S.P., M.S., L.S.A.M. Methodology: G.C., S.E., H.S.G., S.S.H., J.B., K.S., M.A.B., L.H.B., M.Y.R., G.V.Z., R.L., A.M., C.R.A., G.O. Formal analysis, methodology, investigation, validation: L.S.P., M.S., J.B., S.E., S.S.H., L.S.A.M. Resources, conceptualization and project administration: M.A.B., G.O., M.S., K.S., L.S.A.M. Writing-original draft preparation: L.S.P., M.S., L.S.A.M. Writing-review and editing: G.C., S.E., H.S.G., S.S.H., J.B., K.S., M.A.B., L.H.B., M.Y.R., G.V.Z., R.L., A.M., C.R.A., G.O. All the authors have read and approved the final manuscript.

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Declarations

Competing interests

The Allplex™ HPV28 Detection kits used in this study were donated by Gen Lab del Perú. The authors declare that the companies/institutions had no involvement in the design, data collection, analysis, interpretation of the data, or writing of the manuscript. The authors have no conflicts of interest to declare.

Ethics approval

All experiments were performed in compliance with relevant laws and institutional guidelines and in accordance with the ethical standards of the Declaration of Helsinki. This study was approved by the ethics committee of the Hospital Regional de Loreto (ID-042-CIEI-HRL-2023), and all participants provided informed consent prior to inclusion in the study.

Additional information

Supplementary Information The online version contains supplementary material available at https://doi.org/10.1038/s41598-025-18455-3.

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THERAPEUTIC ADVANCES in
Infectious Disease

Original Research

Characterization of the clinical features, laboratory findings, and outcomes of human fascioliasis in a global network: a retrospective mutlicenter study

Ther Adv Infect Dis

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Abstract

Background: Fascioliasis, caused by *Fasciola hepatica* and *F. gigantica*, is a neglected tropical disease that has significant medical and veterinary importance. This foodborne zoonotic trematodiases primarily affects poor rural populations in tropical and subtropical areas, where prevalence can be as high as 21%.

Objective: This study aims to characterize the clinical features, laboratory findings, and outcomes of fascioliasis in a real-world cohort.

Design: Retrospective study.

Methods: Patients ⩾ 18 years old diagnosed with fascioliasis were identified from TriNetX, a global federated research network, on October 26, 2024. We used the International Classification of Diseases results to define fascioliasis (ICD-10 code B66.3) for the period 2021–2024. These data include demographics, diagnoses, comorbidities, procedures, clinical laboratory results, and medications. All variables except outcomes were not time-bound to the diagnosis date.

Results: In a cohort of 174 predominantly middle-aged, female, and Caucasian patients, we found high rates of essential hypertension, neoplasms, heart disease, liver disease, and sleep disorders. Key symptoms included upper abdominal pain, skin complaints, dyspnea, and malaise/fatigue. Some outcomes were hepatomegaly, cholelithiasis, and cholangitis in 10% of patients, with hepatic cirrhosis being rare. Among hospitalized patients within 3 months of diagnosis, 63% experienced abdominal pain. Of the 13 patients who developed cholangitis or cholelithiasis, most were men, had abdominal pain, nausea/vomiting, dysphagia, and ascites with a history of liver or intrahepatic bile neoplasia. A total of 90-day mortality was low (less than 6%). Triclabendazole was reported in only 6% of these patients.

Conclusion: In a large real-world case series of fascioliasis, we found a high frequency of comorbidities and typical gastrointestinal symptoms. The low use of triclabendazole may be due to limited access to the product in certain countries or its omission from the database if prescribed in the outpatient setting. Mortality was very low, but biliary and liver complications warrant characterization through additional prospective clinical studies.

Plain language summary

Clinical outcomes of fascioliasis

Fascioliasis is a parasitic disease, now seen worldwide. Here a summary of cases seen in a multinational database with the goal to report comorbidities and clinical outcomes

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Keywords: complications, *Fasciola hepatica*, Fascioliasis, real-world data

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Introduction

Fascioliasis, caused by *Fasciola hepatica* and *F. gigantica*, is a neglected tropical disease with significant global public health implications, particularly in endemic regions.[1] The foodborne zoonotic trematodiases primarily affect rural populations in tropical and subtropical areas, where prevalence in humans can reach 21%.[2] Over 180 million people are estimated to be at risk of infection worldwide, particularly in areas with high infection rates among ruminant definitive hosts.[3] Human fascioliasis and the other foodborne trematodiases are responsible for 200,000 illnesses and more than 7000 deaths annually, translating to 1066 thousand disability-adjusted life years (DALYs) lost globally.[4] The burden is nevertheless underestimated, as the impact of chronic complications such as anemia, malnutrition, liver fibrosis, and biliary obstruction, which can impair quality of life and necessitate long-term medical care, is difficult to measure.[5,6]

Fascioliasis is also a major veterinary problem, not only in terms of animal morbidity but also in economic losses in the agricultural sector, estimated to be over $3 billion worldwide annually.[7,8] Despite advancements in diagnosis and treatment, a considerable knowledge gap remains regarding long-term outcomes, especially in diverse populations and healthcare settings.

This gap highlights the need for more robust studies to understand the factors affecting disease progression and to inform more effective management strategies for fascioliasis. This study aims to characterize the clinical features, laboratory findings, and outcomes of fascioliasis in a real-world cohort.

Methods

Study design and inclusion criteria

Adult patients (≥18 years) diagnosed with fascioliasis were identified from TriNetX, a global federated research network, on October 26, 2024. We used the International Classification of Diseases to define the fascioliasis (ICD-10 code B66.3) between 2021 and 2024.

Database

TriNetX aggregates anonymized data from approximately 100 million patients across more than 80 medical centers in the United States, Canada, Europe, Australia, Indonesia, and other countries. These data include demographics, diagnoses, procedures, clinical laboratory results, and medications. All variables, except outcomes, were not time-bound to the diagnosis event. Our group has published several large cohort studies using this database.[9–11]

Statistical analysis

Frequency analyses (mean and standard deviations) were completed within the TriNetX platform. Any data displayed on the TriNetX platform in aggregate form, or any patient-level data provided in a data set generated by the TriNetX platform, only contains de-identified data as per the de-identification standard defined in Section 164.514(a) of the Health Insurance Portability and Accountability Act (HIPAA) Privacy Rule.

Ethical considerations

Not applicable. Research utilizing TriNetX does not require ethical approval because patient-identifiable information is inaccessible to users.

Results

Demographics

A total of 174 patients (mean age of 57 ± 20 years) met the inclusion criteria. Among these patients, 95 were women (55%) and 79 were men (45%). Ethnic distribution revealed that the majority were non-Hispanic (62%), and a minority were Hispanic or Latino (8%). Most patients were Caucasian (54%), followed by African or African American (13%), with Asian, Native Hawaiian, or other Pacific Islander groups each representing under 10% (details are in Table 1).

Comorbidities

Common comorbidities included essential hypertension (41%), neoplasms (36%), heart disease

Table 1. Demographic data, clinical features, laboratory findings, and outcomes among patients diagnosed with fascioliasis.

Clinical features	*N*=174
Age (mean ± SD)	57 ± 20
Sex (women)	95 (55%)
Ethnicity	
Not Hispanic	107 (62%)
Unknown	53 (31%)
Hispanic or Latino	14 (8%)
Race	
Caucasian	94 (54%)
Unknown Race	30 (17%)
African or African American	22 (13%)
Other Race	14 (8%)
Asian	13 (7%)
Native Hawaiian or Other Pacific Islander	10 (6%)
Comorbidities	
Essential hypertension	72 (41%)
Neoplasm	62 (36%)
Heart disease	61 (35%)
Liver disease	52 (30%)
Sleep disorders	40 (23%)
Anemia	39 (22%)
Vitamin D deficiency	37 (21%)
DM2	35 (20%)
IBD	31 (18%)
Hypothyroidism	26 (15%)
Chronic kidney disease	21 (12%)
Eosinophilia	15 (9%)
HIV	<10 (<6%)
Symptoms	
Upper abdominal pain	58 (33%)
Skin complaints	57 (33%)
Dyspnea	55 (32%)
Throat or Chest pain	53 (30%)
Malaise and Fatigue	50 (29%)
Headache	49 (28%)
Shortness of breath	47 (27%)
Diarrhea	44 (25%)
Nausea and vomiting	42 (24%)
Cough	41 (24%)
Dyspnea	40 (23%)
Labs (mean ± SD)	
WBC (10^3/μL)	7.1 ± 3.4
Hemoglobin (mg/dL)	13.1 ± 2.0
Hematocrit (%)	39.7 ± 5.5
Eosinophils (%)	3.6 ± 5.9
Platelets (10^3/μL)	240.8 ± 76.5
ALT (U/L)	29.3 ± 23.7
AST (U/L)	30.1 ± 27.5
Creatinine (mg/dL)	0.9 ± 0.6
C-Reactive Protein (mg/L)	14.1 ± 27.6
ESR (mm/hour)	26.7 ± 28.2
Ferritin (ng/mL)	190.3 ± 278.7
LDH (U/L)	1.7 ± 0.9
Antiparasitics	
Praziquantel	20 (11%)
Albendazole	19 (11%)
Ivermectin	11 (6%)
Triclabendazole	10 (6%)
Procedures	
ERCP	12 (7%)
Outcomes	
Hepatomegaly (±1 year)	16 (9%)
Cholangitis/cholelithiasis at 5 years	14 (8%)
Hepatic cirrhosis at 5 years	<10 (<6%)
Portal vein thrombosis at 5 years	<10 (<6%)
Hospitalization (90 days)	50 (29%)
90-day mortality	<10 (<6%)

ALT, alanine aminotransferase; AST, aspartate aminotransferase; CK, chronic kidney disease; DM2, diabetes mellitus type 2; ERCP, endoscopic retrograde cholangiopancreatography; ESR, erythrocyte sedimentation rate; HIV, human immunodeficiency virus; IBD, inflammatory bowel disease; LDH, lactate dehydrogenase.

(35%), liver disease (30%), and sleep disorders (23%). Key symptoms included upper abdominal pain and skin complaints (33% each), dyspnea (32%), and malaise/fatigue (29%).

Laboratory, treatment, and imaging results
Laboratory values showed white blood cells (WBC) of $7.1 \pm 3.4 \times 10^3/\mu L$ with a mean of 3.6% eosinophils and platelets averaging $240.8 \pm 76.5 \times 10^3/\mu L$. There was a wide value range for the C-reactive protein (CRP), averaging 14.1 ± 27.6 mg/L, and the erythrocyte sedimentation rate (ESR) was 26.7 ± 28.2 mm/H. Antiparasitic treatments like praziquantel and albendazole were recorded in 11% of cases, with triclabendazole administered to 10 patients. Endoscopic retrograde cholangiopancreatography (ERCP) was only reported in 7% of the patients.

Twenty-nine percent of the patients were hospitalized. The 90-day mortality was low (<6%). Hepatomegaly, cholelithiasis, and cholangitis occurred in 10% of cases, while hepatic cirrhosis was uncommon. Among hospitalized patients within 3 months of diagnosis, 63% had abdominal pain. Of the 13 patients who developed cholangitis or cholelithiasis, 53% were men (47% women) with abdominal pain, nausea/vomiting, dysphagia, ascites, and liver or intrahepatic bile neoplasia.

Discussion

This cohort of 174 patients with fascioliasis was represented by predominantly middle-aged, female, and Caucasian patients, with a notable Hispanic representation (8%). Fascioliasis is geographically distributed in all continents except Antarctica.[12] Most of these cases may have been diagnosed with fascioliasis in Asia, Africa, or represent imported cases from immigrants in North America, given that most patients were not Hispanic. Diagnosis of fascioliasis remains a challenge since tests for acute fascioliasis are limited in most countries where this disease is endemic.[13] Although coprological studies are widely available, eggs are not usually visualized during the acute phase of the disease because the larvae are still migrating through the peritoneal cavity or liver parenchyma and have not yet matured in the biliary ducts to release eggs. Thus, a point-of-care serological test to detect IgM/IgG for fascioliasis is urgently needed since clinicians in countries where the disease is endemic must still rely on research/outside laboratories to diagnose the disease.[14,15]

The burden of comorbid conditions is not commonly reported for patients with fascioliasis, and is limited to only case reports of hypothyroidism and heart failure in two imported US cases.[16] We found high rates of essential hypertension, neoplasms, heart disease, liver disease, and sleep disorders in this cohort of patients with fasciolasis. Hypertension has been reported as a common comorbidity among cohorts of other neglected tropical diseases like chronic Chagas disease, with a prevalence of over 60%.[17,18] The increasing burden of chronic noninfectious disease is well recognized worldwide; thus, comorbid conditions in this and other cohorts are likely to represent conditions affecting the overall age-matched population and may not be related to their risk of infection. However, whether true associations exist and whether potential interactions of these conditions with neglected tropical diseases are plausible, warrants further investigation.

Symptoms during acute infection include right upper quadrant pain, fever, and hepatosplenomegaly, although many infections can be asymptomatic.[19] Key symptoms in this cohort included upper abdominal pain, skin complaints, dyspnea, and malaise/fatigue. Because we did not necessarily capture symptoms at the time of diagnosis, these may represent acute, residual, and perhaps even unrelated symptoms. For the same reason, although the eosinophilia is a routine finding during acute infection, its duration and magnitude could not be captured. Likewise, antiparasitic treatments and ERCP procedures were infrequent and likely related to limitations of the electronic medical records.

Although up to one-third of patients required hospitalization, the 90-day mortality and complication rates were low. Chronic infection complications usually develop after 6 months and up to 10 years or more after infection[20] and include biliary colic, cholangitis, cholelithiasis, and obstructive jaundice.[21,22] Hepatomegaly, cholelithiasis, and cholangitis were infrequent complications in this, as in other cohorts. Cholangitis and/or cholelithiasis mainly presented with abdominal pain,

nausea, and ascites in men with liver or bile duct neoplasia. Although case series and case reports have reported secondary pancreatitis[23] as a complication in up to 38% of patients, we did not find any cases in our cohort. Liver cirrhosis and cancer are plausible, yet undocumented, complications of chronic liver infections, including fasciolasis, especially since there may be a link with fibrosis.[24] However, rates of cirrhosis and portal vein thrombosis were also infrequent in this cohort. Exploring such long-term associations warrants further studies.

Our study has several limitations. The retrospective design and use of ICD codes for diagnosis may introduce selection bias and the potential for misclassification. We did not have access to microbiology or histology data to confirm cases clinically, identify the parasite species, or determine treatment courses. Other relevant data could not be obtained due to the ICD-10 limitations (e.g., acute vs chronic infection or subcapsular hematoma). However, this is one of the most extensive case series of fascioliasis patients ever described, with close to 200 subjects. In addition, treatment with triclabendazole, the only drug highly effective against this liver fluke, was reported only for a few patients and was surpassed by the frequency with which praziquantel, an ineffective drug against fascioliasis, was prescribed. The limited use of triclabendazole may be attributed to its lack of registration in certain countries. Alternatively, it could be due to insufficient data capture through our federal network, especially if treatment was administered outside the scope of the electronic medical record system. Documentation of treatment response to triclabendazole is of importance because of the increasing reports of drug resistance.[25,26]

In conclusion, in a large real-world case series of fascioliasis, we found a high frequency of comorbidities and typical gastrointestinal symptoms characteristic of this infection. Mortality was low, as were complication rates. However, the role of chronic biliary and liver complications in the development of liver fibrosis and cancer warrants additional clinical prospective studies. Use of triclabendazole in this report was low (6%). Identifying cases of fascioliasis in large clinical networks may uncover new trends in the incidence of this re-emerging zoonotic disease that affects the poorest people on the planet.[27–33]

Declarations

Ethics approval and consent to participate
Not applicable. Research utilizing TriNetX does not require ethical approval because patient-identifiable information is inaccessible to users. Any data displayed on the TriNetX platform in aggregate form, or any patient-level data provided in a data set generated by the TriNetX platform, only contains de-identified data as per the de-identification standard defined in Section 164.514(a) of the Health Insurance Portability and Accountability Act (HIPAA) Privacy Rule.

Consent for publication
Not applicable.

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Competing interests

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Availability of data and materials

The corresponding author had full access to data in the study and was ultimately responsible for submitting the manuscript for publication. The datasets generated and analyzed in the current study are available from those subscribed to TrinetX or from the corresponding author upon reasonable request.

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ORIGINAL ARTICLE

GENOMIC DIVERSITY OF UROPATHOGENIC *Escherichia coli* IN CLINICAL ISOLATES FROM SIX LATIN AMERICAN COUNTRIES, 2018-2023

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ABSTRACT

Objective. To genetically characterize clinical isolates of uropathogenic *Escherichia coli* (UPEC) from hospitals in Peru and contextualize them against 127 additional UPEC genomes reported in six Latin American countries between 2018 and 2023. **Materials and methods.** The genomes of 16 Peruvian UPEC isolates were sequenced, assembled and supplemented with 127 genomes available in the NCBI public database. Serotypes, sequence types (STs), antimicrobial resistance (AMR) genes, and resistance-associated mutations were identified. A phylogenetic analysis was also conducted in order to determine evolutionary relations and distribution in phylogroups. Results. The ST131 clone was the most prevalent (42.7%), followed by ST1193 (13.3%). Phylogroup B2 was widely predominant (83.2%), with serotype O25:H4 standing out. The resistance genes *blaTEM-1*, *blaCTX-M-15*, and *blaCTX-M-27* were identified with high frequency, as well as mutations in *gyrA* and *parC* associated with fluoroquinolone resistance, especially in the ST131 clone. **Conclusion.** Our findings show high circulation of high-risk UPEC clones, such as ST131 and ST1193, in Latin America, along with a notable burden of genes and mutations linked to multidrug resistance, highlighting the need to strengthen regional genomic surveillance.

Keywords: *Escherichia coli*; Uropathogen; UPEC; Bacterial Resistance; Molecular Epidemiology (source: MeSH NLM).

INTRODUCTION

Escherichia coli is a Gram-negative bacillus of the *Enterobacteriaceae* family that is part of the normal intestinal microbiota in most humans. However, there are opportunistic variants, known as uropathogenic *E. coli* (UPEC), capable of colonizing the urinary tract and causing infections [1,2]. These UPEC strains are characterized by the presence of at least three specific virulence factors: *chuA* and *fyuA*, involved in iron acquisition; *vat*, which encodes a vacuolization-inducing autotransporting toxin; and *yfcV*, associated with fimbriae that facilitate adhesion to urothelial cells [3].

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UPEC are the leading cause of urinary tract infections (UTIs) worldwide, affecting approximately 400 million people per year and causing nearly 230,000 deaths annually, according to the 2019 Global Burden of Disease study [4]. These infections are the second most common type in adults [5] and are classified as complicated (cUTI) when there are comorbidities (pregnancy, immunocompromised status) or urinary tract abnormalities (obstruction, hydronephrosis, kidney stones), and uncomplicated (uUTI) in the absence of these conditions [6]. Antibiotics such as ampicillin, sulfamethoxazole, and ciprofloxacin are used to treat uUTIs, while nitrofurans, cephalosporins, and carbapenems are recommended for cUTIs [5].

The inappropriate use and poor regulation of broad-spectrum antibiotics have contributed significantly to the increase in antimicrobial resistance (AMR), particularly in low- and middle-income countries [7]. Regarding UPEC, the most important AMR mechanisms include the production of extended-spectrum beta-lactamases (ESBLs), enzymes capable of hydrolyzing penicillin, beta-lactams, and cephalosporins [8]. Among these enzymes, *blaCTX-M-1* stands out, which is capable of hydrolyzing third-generation cephalosporins and one of the most common beta-lactamases in ESBL-producing *E. coli* [9]. In addition, there are non-enzymatic resistance mechanisms, such as point mutations in target genes: *parC/E* and *gyrA/B* are associated with resistance to fluoroquinolones [10], *glpT* and *uhpT* with fosfomycin [11], and *pmrA/B/D* with colistin [12]. Other non-enzymatic mechanisms include efflux pumps, such as those encoded by the *emrD*, *acrF*, and *mdtM* genes, which are related to multidrug resistance (MDR) [13]. Between 2000 and 2019, in Europe, Asia, and America, high phenotypic resistance to quinolones (49.4%), beta-lactams (36.9%), aminoglycosides (28.7%), and fosfomycin (8.4%) was reported [14].

Advances in genomics in recent decades now allow for the precise identification of sequence types (STs) and high-risk clones. Among these, ST131 stands out as the MDR clone with the highest risk worldwide [15]. In Australia, in 2013, ST131 (27%) and serotype O25b (85%) were found to be the most frequent in urinary isolates from a sample of women of reproductive age [16]. In 2022, in the United States, 23% of *E. coli* isolates belonged to the emerging pandemic clone ST1193, characterized by its resistance to fluoroquinolones, and its prevalence was 51% in China [17].

The lack of information on the genomic diversity and resistance patterns of UPEC in Latin America hinders its monitoring and treatment. Most studies are limited to identifying lineage markers and resistance genes using conventional PCR. Although whole genome sequencing is a key tool for high-resolution, large-scale characterization of isolates, to date few studies in the region have reported using this technique for UPEC. Therefore, in order to better understand the genomic diversity of this pathogen in Latin America, this study aimed to characterize 16 UPEC isolates from hospitals in Peru and analyze them in the context of 127 UPEC genomes reported in six countries in the region between 2018 and 2023.

KEY MESSAGES

Motivation for the study. To contribute to the genomic surveillance of UPEC in clinical samples from Latin America, in response to the growing public health problem represented by UTIs and their resistance to antimicrobials.

Main findings. Our study revealed a high frequency of high-risk clones, such as ST131 and ST1193. Critical mutations were identified in genes associated with resistance to multiple antibiotics, including fluoroquinolones, beta-lactams, and fosfomycin.

Implications. Our results highlight the urgent need to strengthen UPEC surveillance in Latin America. Tracking resistant strains and implementing measures to limit their spread is crucial and has a significant impact on the effectiveness of available treatments.

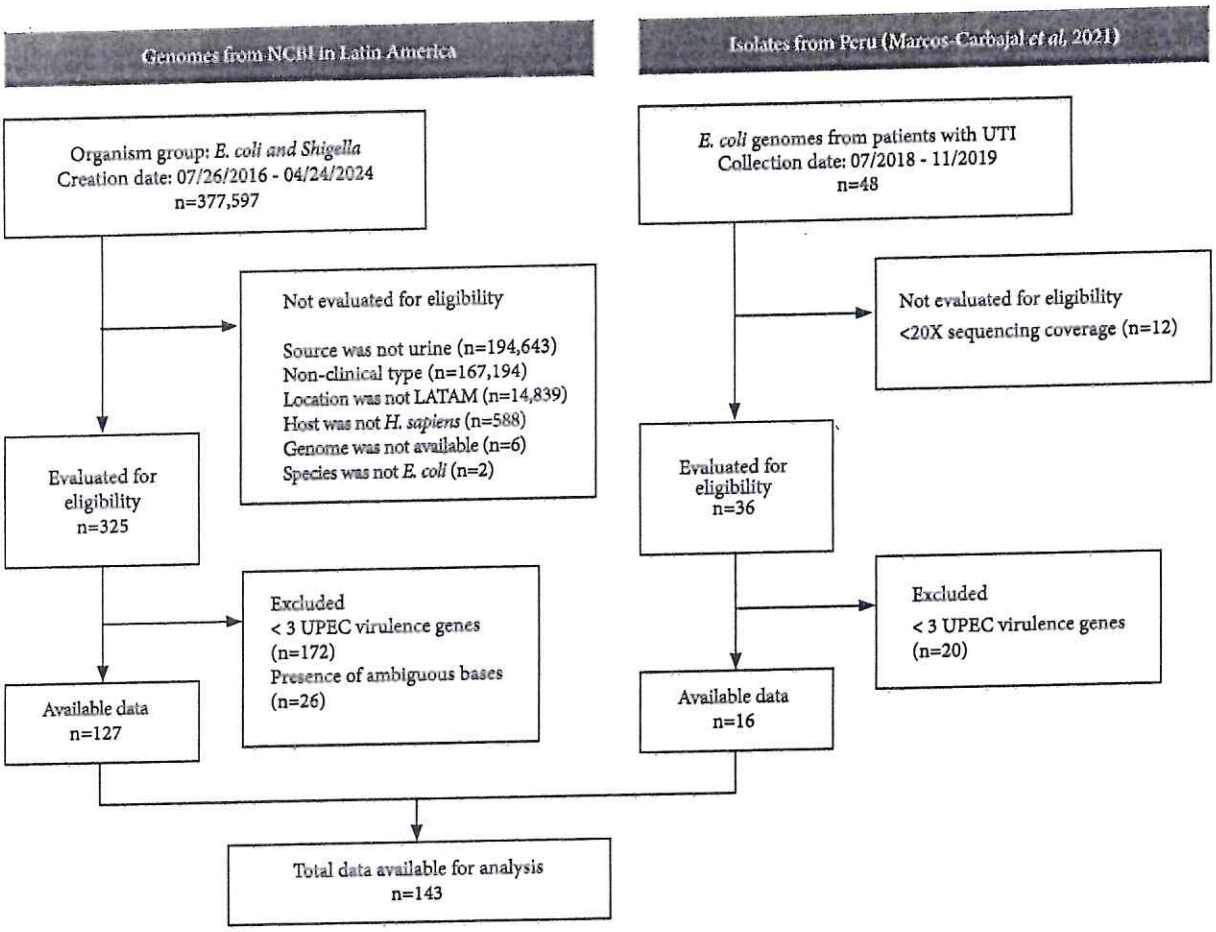
MATERIALS AND METHODS

Study design

We conducted a descriptive study. The study population consisted of 143 UPEC isolates from Latin America. Of these, 127 correspond to genomes from the NCBI public database and 16 from outpatients with a clinical diagnosis compatible with urinary tract infection (UTI) in hospitals in Peru (Figure 1).

Genomic sequencing of UPEC isolates in Peru

E. coli strains previously characterized phenotypically were collected from patients with UTI in eight Peruvian hospitals during 2018–2019 [18]. Total DNA was extracted from 5 ml of liquid culture in TSB medium using the Thermo GeneJet Genomic DNA Purification Kit (Thermo Scientific) in a final volume of 100 µl. DNA quantification was performed with the Qubit 4 fluorometer and the dsDNA HS kit (Thermo Scientific). From the 200 original isolates, 48 were



NCBI: National Center for Biotechnology Information, LATAM: Latin America, UPEC: uropathogenic *E. coli*, UTI: urinary tract infection.

Figure 1. Flowchart showing the search for uropathogenic *E. coli* (UPEC) genomic sequences in the NCBI Isolates Browser database in Latin America and genomes from isolates from patients with UTI in Peru. A total of 127 genomes from Latin America were included from NCBI and supplemented with 16 collected from hospitals in Peru, with a total of 143 UPEC genomes available for analysis.

selected for sequencing using stratified sampling, prioritizing diversity in antimicrobial resistance profiles and geographical representativeness of the collection sites (Figure 1). Genomic libraries were prepared with the NexteraXT kit (Illumina) and sequenced on an Illumina MiSeq instrument at UPCH, using MiSeq v2 500-cycle kits. The raw sequences obtained from sequencing (Fastq format) were subjected to quality control using FastQC v0.12.1 (https://github.com/s-andrews/FastQC). Subsequently, the fastp v0.23.4 program (https://github.com/OpenGene/fastp) was used to remove adapters and low-quality sequences (Q<30 and length <50 bp), generating paired R1 and R2 files. Finally, the processed reads were assembled *de novo* using default parameters with SPAdes v3.15.2 (https://github.com/ablab/spades). The quality of the assembled genomes was evaluated using the QUAST v5.2.0 tool (https://github.com/ablab/quast) (Figure 2). The fastq and fasta files were deposited in the following BioProject: PRJNA1153025.

Public UPEC genomes in Latin America

Genomes assembled in Fasta format were downloaded from the NCBI Isolates Browser (https://www.ncbi.nlm.nih.gov/pathogens/isolates/), along with associated metadata, which included relevant information such as the isolate identifier code, assembly code, year of collection, and country of origin. The selection criteria for the search included the taxonomic group (taxgroup_name) "*E. coli* and *Shigella*"; the isolate type (epi_type) "clinical"; the isolate source (isolation_source) 'urine'; the host (host) "*Homo sapiens*"; and the geographical location (geo_loc_name) limited to "Paraguay," Argentina, Colombia, Brazil, Chile, Peru, Mexico, Bolivia, Costa Rica, Cuba, Ecuador, El Salvador, Guatemala, Haiti,

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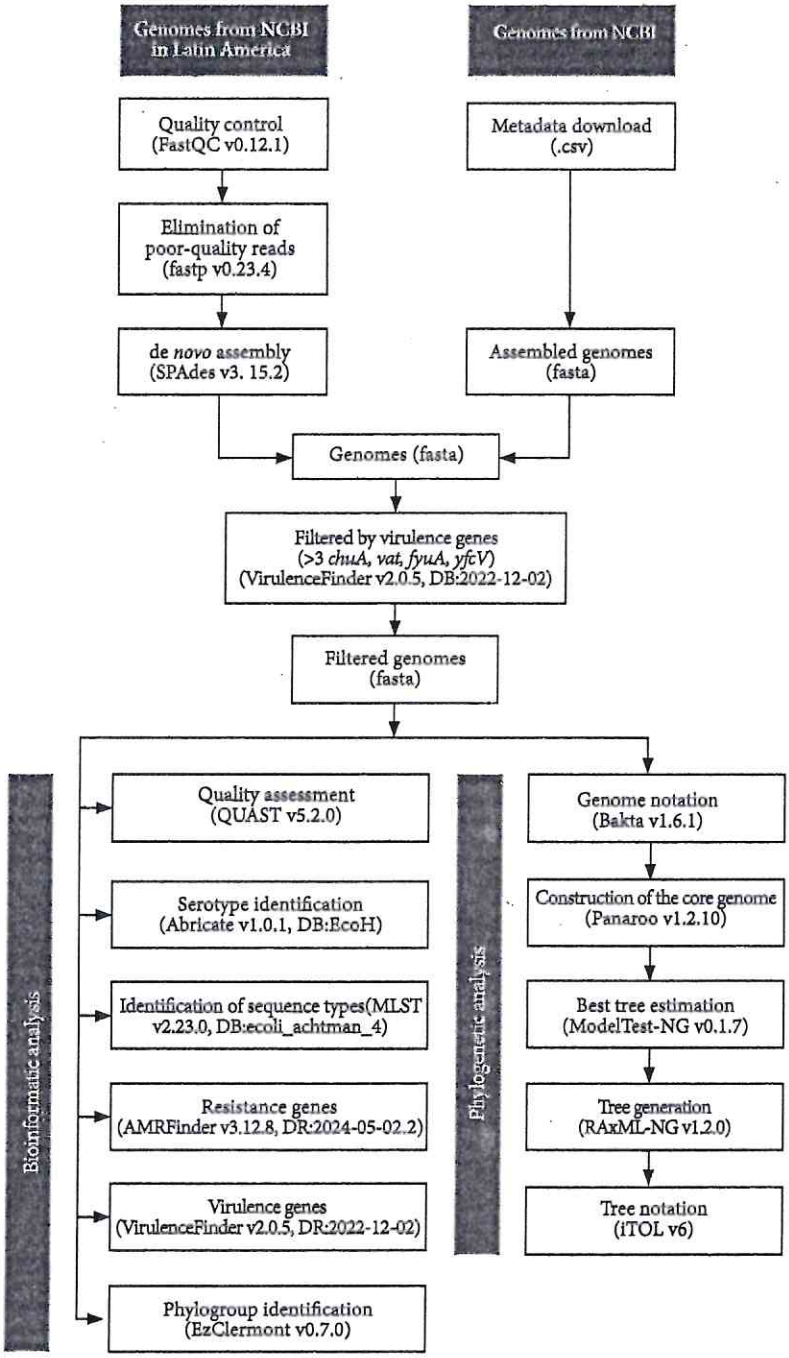

Figure 2. Flowchart of the bioinformatic and phylogenetic analysis. Reads from patients isolated from hospitals in Peru were assembled and processed together with genomes from NCBI using typing and phylogeny tools.

Honduras, Nicaragua, Panama, Dominican Republic, Uruguay, and Venezuela, in the period between 2016 and 2024. A total of 325 public genomes met these criteria (Figure 1).

Refinement of UPEC genome selection

To confirm that the *E. coli* isolates corresponded to the UPEC type, genomes possessing three or more of the virulence factors proposed by Spurbeck *et al.* [3] *chuA*, *vat*, *fyuA*, and *yfcV* were included, indicating a genetic profile consistent with UPEC. In addition, quality filters were applied, requiring sequences to be between 4.5 and 5.5 million base

pairs (Mb) in length, and genomes with ambiguous bases were excluded. After applying these filters, the final number of considered public genomes was 127, to which we added 16 UPEC genomes generated in this study, resulting in a total of 143 genomes analyzed (Figure 1).

Classification, gene identification, and phylogenetic analysis

To identify the serotype of the isolates, we used the ABRicate v1.0.1 tool (https://github.com/tseemann/abricate) with the EcOH database. Sequence types (STs) were determined according to the ecoli_achtman_4 scheme, derived from seven marker genes, using the MLST v2.23.0 program (https://github.com/tseemann/mlst). Antimicrobial resistance genes and mutations were identified using AMRFinderPlus v3.12.8 (https://github.com/ncbi/amr, database 2024-05-02.2). Virulence genes were identified using VirulenceFinder v2.0.5 (database 2022-12-02) available on the Center for Genomic Epidemiology (CGE) server (https://cge.food.dtu.dk/services/VirulenceFinder/). In addition, the phylogroup was identified according to the Clermont scheme using EzClermont v0.7.0 (https://github.com/nickp60/EzClermont). All analyses used a cutoff threshold of 90% for coverage and identity. The assembled genomes were annotated using Bakta v1.6.1 (https://github.com/oschwengers/bakta) and core genome alignment was performed with Panaroo v1.2.10 (https://github.com/gtonkinhill/panaroo). Subsequently, the best model for constructing the phylogenetic tree was determined using ModelTest-NG v0.1.7 (https://github.com/ddarriba/modeltest). Finally, the tree was constructed using the GTR+I+G4 model and performing 100 bootstrap replicates with RAxML-NG v1.2.0 (https://github.com/amkozlov/raxml-ng). An *Escherichia fergusonii* genome (CP083638.1) was used to root the tree. The tree was annotated and visualized using iTOL v6 (https://itol.embl.de/) (Figure 2).

Ethical considerations

This study was evaluated and approved by the Ethics Committee of the Universidad Peruana Unión (N2019-CEU-PeU-0001) and by the Institutional Committee on Research Ethics (CIEI) of the Universidad Peruana Cayetano Heredia (SIDISI No. 214524 and No. 214927). Only bacterial isolates were used, without including or analyzing any personal or clinical information about the patients.

RESULTS

We analyzed 143 UPEC isolates from six Latin American countries: Paraguay (39.2%), Brazil (32.9%), Peru (11.2%), Colombia (8.4%), Argentina (6.3%), and Mexico (2.1%) (Figure 3). The temporal distribution of the isolates was as follows: 2018 (9.8%), 2019 (6.3%), 2020 (8.4%), 2021 (30.1%), 2022 (44.1%), and 2023 (1.4%). The most frequent UPEC sequence types in Latin America were ST131 (42.7%), ST1193 (13.3%), ST648 (8.4%) and ST998 (3.5%). In Peru, the predominant sequence types were ST131 (43.8%) and ST1193 (37.5%); in Brazil, ST131 (40.4%), ST648 (14.9%) and ST127 (10.6%); in Paraguay, ST131 (39.2%), ST1193 (12.5%) and ST73 (7.5%); in Argentina, ST131 (33.3%) and ST1193 (33.3%); in Colombia, ST131 (66.7%) and ST648 (16.7%); and in Mexico no prominent clones were identified (Figure 3). The most frequent serotype was O25:H4 (43.4%), followed by O75:H5 (11.2%), O1:H6 (6.3%) and O2:H6 (3.5%). The Clermont B2 phylogroup was predominant in this dataset (83.2%), followed by phylogroups F (15.4%) and G (1.4%).

The most common beta-lactamases among the antimicrobial resistance (AMR) genes, were *blaTEM-1* (40.0%), *blaCTX-M-15* (32.2%), *blaCTX-M-27* (9.1%), *blaKPC-2* (4.9%), *blaNDM-1* (2.1%), and *blaKPC* (0.7%). The most common genes associated with aminoglycoside resistance were *aph(6)-Id* (35.0%), *aph(3")-Ib* (33.6%), *aadA5* (31.5%), *aac(6')-Ib-cr5* (22.4%), *and aac(3)-IIe* (16.8%). Among the genes related to efflux pumps, *emrD* was found in all isolates (100%), followed by *acrF* (93.0%) and *mdtM* (60.8%). Other genes also stood out, such as *mphA* (43.4%), associated with macrolide resistance; *sul1* (45.5%) and *sul2* (37.1%), associated with sulfonamide resistance; *tetA* (39.9%) and *tetB* (16.8%), related to tetracycline resistance; and *dfrA17* (36.4%), associated with trimethoprim resistance.

Non-synonymous mutations associated with RAM were found in 69.9% of UPEC isolates, with at least one mutation in the *gyrA* gene, which is related to fluoroquinolone resistance. We found that 67.8% of isolates had double mutations in amino acids Ser-83 and Asp-87 of *gyrA*. Regarding the *parC* gene, also associated with fluoroquinolone resistance, 69.2% had at least one mutation, while 46.9% had double mutations in combinations of the amino acids Ala-108, Ala-56, Glu-84, Ser-57, or Ser-80. Regarding the *pmrB* gene, 79.0% of the isolates had at least one mutation related to colistin resistance, and 1.4% had double mutations between the amino acids Glu-123, Pro-94, Val-161, or Tyr-358. Other genes associated with resistance presented single mutations: 86.0% of isolates had a mutation in the *glpT* gene (Glu-448), 69.2% in *uhpT* (Glu-350), 46.2% in *ptsI* (Val-35), and 16.8% in *cyaA* (Ser-352), all associated with fosfomycin resistance. Besides, 72.0% had mutations in *parE*, which confers resistance to fluoroquinolones, frequently in the amino acids

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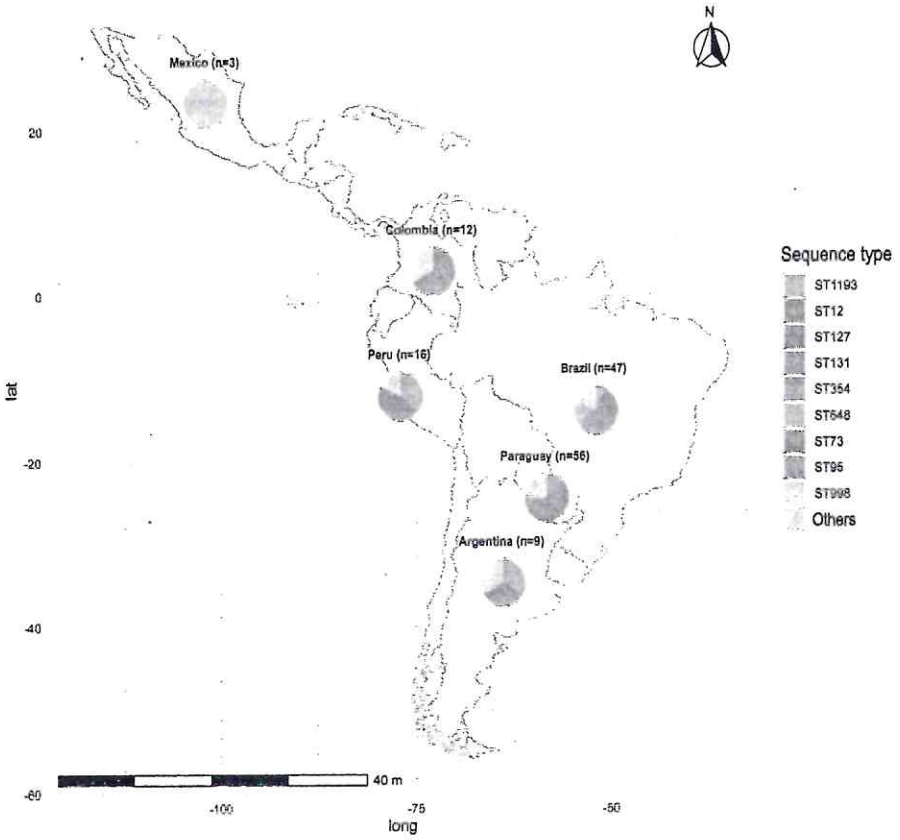

Figure 3. Geographic distribution of uropathogenic *E. coli* (UPEC) clones in Latin America.

Ile-529 (46.2%) and Leu-416 (13.3%). The mutation in *marR* (Ser-3), associated with multidrug resistance to penicillin, phenols, quinolones, rifamycins, and tetracyclines, was identified in 24.5% of the isolates.

Patterns of coincidence between sequencing type, serotype, and point mutations associated with AMR were identified in the 143 analyzed genomes (Table 1). The most frequent pattern includes ST131 with serotype O25:H4 (35.7%), followed by ST1193 with serotype O75:H5 (11.1%). The three most frequent patterns include the point muta-

Table 1. *In silico* prediction of serotype, sequence type, and point mutations associated with resistance in uropathogenic *E. coli* (UPEC) genomes, 2018–2023 (n=143).

Pattern number	Sequence type	Serotype	Mutations associated with antimicrobial resistance	Types of antibiotics	Number of UPEC isolates (%)	Countries (n)
1	131	O25:H4	*glpT*(E448K), *gyrA*(D87N), *gyrA*(S83L), *parC*(E84V), *parC*(S80I), *parE*(I529L), *pmrB*(E123D), *ptsI*(V25I), *uhpT*(E350Q)	3	51 (35.7)	Paraguay (19) Brazil (16) Colombia (8) Peru (6) Argentina (1) Mexico (1)
2	1193	O75:H5	*gyrA*(D87N), *gyrA*(S83L), *marR*(S3N), *parC*(S80I), *parE*(L416F), *pmrB*(E123D), *uhpT*(E350Q)	7	16 (11.1)	Paraguay (7) Peru (6) Argentina (2) Brazil (1)
3	648	O1:H6	*cyaA*(S352T), *glpT*(E448K), *gyrA*(D87N), *gyrA*(S83L), *parC*(S80I), *parE*(S458A)	2	7 (4.9)	Brazil (4) Argentina (1) Colombia (1) Paraguay (1)
4	998	O2:H6	*glpT*(E448K), *marR*(S3N), *pmrB*(E123D)	7	5 (3.5)	Paraguay (3) Argentina (1) Brazil (1)

tions *gyrA* (D87N), *gyrA* (S83L), and *parC* (S80I), all related to fluoroquinolone resistance. However, *glpT* (E448K), *parC* (E84V), *parE* (I529L), *pmrB* (E123D), *ptsI* (V25I), and *uhpT* (E350Q) were also found in pattern 1; *marR* (S3N), *parE* (L416F), *pmrB* (E123D), *uhpT* (E350Q) in pattern 2; and, *cyaA* (S352T), *glpT* (E448K), *parE* (S458A) in pattern 3. Likewise, patterns 2 and 4 had mutations associated with the highest number of antibiotic classes (seven classes) due to the presence of the MDR *marR* gene. In addition, patterns 1, 2, and 4 were more frequent in isolates from Paraguay, and pattern 3 in isolates from Brazil (Table 1).

Phylogenetic analysis identified two main clades according to the Clermont classification: F and G/B2 (Figure 4). The second clade is larger and is divided into a subclade for group G and two large subclades for B2. Clones ST131, ST1193, ST998, and ST127 are restricted to phylogroup B2, while ST648 and ST354 are restricted to phylogroup F, and ST117 is restricted to phylogroup G. Serotypes O25:H4, O75:H5, and O2:H6 are restricted to phylogroup B2, while O1:H6 and O45:H6 are restricted to phylogroup F. It should be noted that all isolates belonging to ST1193 have a double mutation in the *gyrA* gene and most isolates belonging to ST113 have a double mutation in the *gyrA* and *parC* genes simultaneously.

DISCUSSION

This study analyzed 143 UPEC genomes from six Latin American countries, with a predominance of isolates from Paraguay and Brazil. A high frequency of the ST131 clone (42.7%) was identified, mainly related to serotype O25:H4 and phylogroup B2, followed by ST1193 and ST648. Consistent patterns were found between clone, serotype, and mutation, with frequent combinations of resistance to fluoroquinolones and fosfomycin. Phylogenetic analysis revealed the grouping of the dominant clones within phylogroup B2, while others such as ST648 were restricted to phylogroup F, evidencing the genetic diversity and possible regional adaptation mechanisms of UPEC in Latin America.

During the 2018-2023 period, the ST131 clone was identified in 42.7% of the analyzed UPEC genomes. In comparison, a study conducted in Saudi Arabia in 2020 reported a prevalence of 61.7% [19]. ST131 is known to be a high-risk, multidrug-resistant (MDR) pandemic strain and one of the leading causes of difficult-to-treat UTIs and bacteremia. This clone has plasmids that encode additional resistance and virulence genes, facilitating its spread in community and hospital settings [20]. The emerging ST1193 clone, also pandemic and MDR, has also been identified as a cause of UTI and bacteremia [17]. In our study, 13.3% of isolates from the region correspond to ST1193, and in Peru we identified it in 37.5% of cases. This is higher than the 6% reported in Spain in a collection of UPEC from women in primary care centers [21].

Phylogenetic group B2, recognized as the most virulent and highly prevalent in mammals, is associated with persistent extraintestinal infections [22]. In our study, 83.2% of isolates belonged to group B2, with ST131 clones with serotype O25 standing out. A study in Iraq identified that 33.9% of UPEC belonged to phylogroup B2, of which 92.1% corresponded to ST131 and 97.1% were serotype O25 [15]. The O25-B2-ST131 lineage is considered hypervirulent, MDR, and ESBL-producing, underscoring the need to implement control measures to limit its spread [23]. Similarly, a report from Saudi Arabia identified a prevalence of 61.7% for phylogroup B2, with 100% of ST131 clones belonging to this group, a result consistent with our study [19]. In contrast, a previous study in Peru did not identify phylogroups F and G among UPEC isolates [24].

With regard to beta-lactamases, our study highlights the presence of the *blaCTX-M-15* (32.2%) and *blaCTX-M-27* (9.1%) genes. These results differ from a previous study conducted in Peru, which used conventional PCR and reported a frequency of 18% for the *blaCTX* gene, with a different distribution in which *blaCTX-M-1* (72.4%) and *blaCTX-M-9* (25.9%) predominated [8]. These findings underscore the importance of reporting specific beta-lactamase alleles to better understand their distribution and impact on antimicrobial resistance.

When it comes to genes associated with efflux pumps, we found that 100% of the analyzed genomes contained the *emrD* gene and 93.0% contained the *acrF* gene, both of which play a key role in resistance to multiple families of antibiotics through transcriptional regulation [13]. These findings are similar to those reported by a study on UPEC in Iraq, which found a prevalence of 100% for *emrD* and 66% for *acrF* [25]. In addition, the *tetA* gene (39.9%) stood out in resistance to tetracyclines, while *sul1* showed a prevalence of 45.5% in resistance to sulfonamides. In contrast, a study in Iran reported that the *tetB* (66.7%) and *sul1* (45.5%) genes were the most prevalent [26], which could be attributed to geographical differences and the use of molecular techniques for gene identification.

Single nucleotide polymorphisms (SNPs) also play a crucial role in AMR. In Iran, 91.2% of strains with double mutations in *gyrA* (codons 83 and 106) were found to be resistant

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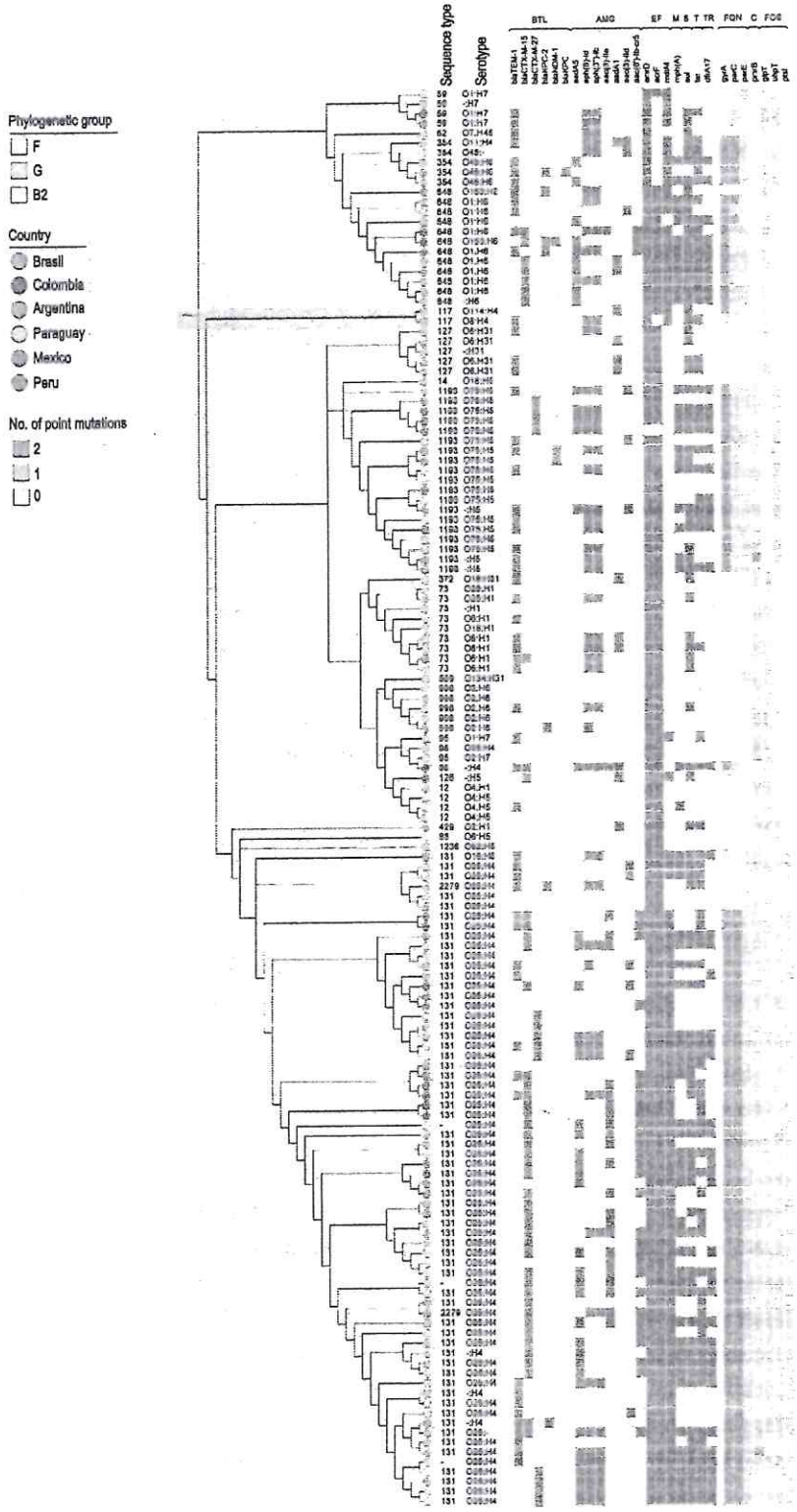

BTL: beta-lactamases, AMG: aminoglycosides, EF: efflux, M: macrolides, S: sulfonamides, T: tetracycline, TR: trimethoprim, FQN: fluoroquinolones, C: colistin, FOS: fosfomycin

Figure 4. Phylogenetic tree of 143 uropathogenic *E. coli* (UPEC) isolates from Latin America during 2018 and 2023.

to fluoroquinolones, with minimum inhibitory concentration (MIC) values of up to 256 µg/mL [10]. In our study, 69.9% of isolates had mutations in the *gyrA* gene, and 67.8% had double mutations (codon 83 and 87). In addition, all ST1193 isolates had double mutations in *gyrA*, which is consistent with a study conducted in the United States indicating that this clone is resistant to fluoroquinolones [27]. In addition, we found that the frequency of double mutations is higher than in other regions, which could be a consequence of the unregulated use of antibiotics in Latin America.

Mutations in *pmrB*, which affect the PmrAB stress response system in enterobacteria, are associated with changes in lipopolysaccharide (LPS), thereby reducing the efficacy of colistin in *mcr*-negative *E. coli* isolates. This effect manifests as a significant increase in MIC to 8 or 16 µg/mL [12]. Although colistin is not recommended as a treatment for UTIs in the region, an increase in the detection of resistant strains in patients with UTIs has been reported over the last decade [28].

One of the main limitations of this study was the small number of analyzed *E. coli* genomes, originating from six Latin American countries, as this may not reflect the actual diversity of UPEC in the region. The years of isolation are not homogeneous across countries, which could influence the reported genomic representativeness. In addition, not all genomes available in the NCBI database are UPEC, despite being classified as UTI by the authors. Finally, although the bioinformatic tools we used are robust and frequently used in genomic studies of AMR, they are constantly updated and may not detect mutations in resistance genes that are clinically relevant in the future.

One of the main strengths of our study lies in the use of a functional definition based on virulence genes to classify UPEC, which provides a solid foundation for future research. This approach not only lays the groundwork for the application of more robust epidemiological designs but, when combined with molecular tools, will enable long-term monitoring with broader and more systematic sampling across different regions and time periods. This will lead to a deeper understanding of the evolution of antimicrobial resistance and the dynamics of UPEC infections, enabling more effective strategies for their control and prevention.

In conclusion, our study identified a high frequency of high-risk uropathogenic *E. coli* clones such as ST131 and ST1193, along with a high frequency of mutations in genes associated with multidrug resistance. These findings underscore the importance of these clones in the epidemiology of UTIs as a public health risk. Therefore, empirical treatment regimens for UTIs should be improved and antimicrobial resistance control policies strengthened. Furthermore, the patterns we report suggest possible clonal spread between countries, highlighting the need for coordinated genomic surveillance efforts at the regional level.

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Author contributions. All authors declare that they comply with the authorship criteria recommended by the ICMJE.

Roles according to CrediT. FC: conceptualization, methodology, software, formal analysis, research, writing (original draft), visualization. AMV: methodology, formal analysis, research, writing (original draft). DC: methodology, software, validation, formal analysis, research, writing (review and editing), supervision. AFL: research, resources. RGA: research, resources. JSP: research, resources. PAM: research, resources. EBY: research, resources. HMF: research, resources. MCQ: research, resources. JPD: research, resources. NLR: research, resources. ABA: research, resources. PDR: research, resources. CPS: research, resources. GS: conceptualization, formal analysis, research. PT: conceptualization, methodology, validation, research, writing (review and editing), supervision. PMC: conceptualization, methodology, research, writing (review and editing), fund acquisition.

Conflict of interest. The authors have no conflicts of interest to declare.

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Supplementary material. Available in the digital version of the RPMESP.

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CASE REPORT

Cryptococcus gattii MENINGITIS IN AN IMMUNOCOMPROMISED PATIENT IN A HOSPITAL IN THE PERUVIAN AMAZON: CASE REPORT

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ABSTRACT

We report a case of *Cryptococcus gattii* meningitis in a patient with HIV in the Peruvian Amazon. A 36-year-old male patient with severe neurological symptoms that was diagnosed by cerebrospinal fluid culture. Although liposomal amphotericin B and flucytosine are considered the standard antifungal therapy, due to a lack of resources, an alternative treatment of amphotericin B deoxycholate and fluconazole was used. Even with this alternative, treatment faced challenges due to the persistence of the microorganism. This case highlights the importance of considering *C. gattii* in the differential diagnosis of cryptococcal meningitis in immunocompromised patients, even in areas where the prevalence of this pathogen is low. The effectiveness of treatment and the patient's survival underscore the need for diagnostic and therapeutic strategies adapted to resource-limited settings.

Keywords. Cryptococcosis, immunocompromised host, amphotericin B. (source: MeSH NLM).

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INTRODUCTION

Cryptococcus species are encapsulated yeasts found in soil and bird feces. These microorganisms mainly affect individuals with compromised immune systems [1]. There are 37 known species of *Cryptococcus*, but only *C. neoformans* and *C. gattii* are pathogenic. Infections caused by *C. gattii* are quite rare [2]. The mortality rate in patients affected by this pathogen is approximately 14% [3].

Cryptococcal meningitis is a severe disease worldwide that mainly affects HIV-positive patients with low CD4 counts and those on immunosuppressive therapy. It is often caused by *C. neoformans* and, to a lesser extent, *C. gattii* [4,5]. Reports show that one million cases are diagnosed each year, resulting in more than 600,000 deaths [6].

Infection with *C. gattii* can affect immunocompetent and immunocompromised hosts. These may be asymptomatic until immunosuppressive factors, such as corticosteroid treatment or HIV infection, facilitate the manifestation of symptoms [7]. The ability of *C. gattii* to cause disease in individuals with intact immune systems is due to its rapid replication in phagocytes before the adaptive immune response is activated [8]. We report the first case of meningitis caused by *C. gattii* in an immunocompromised patient in the Peruvian Amazon.

CASE REPORT

A 36-year-old male patient, born and raised in Iquitos, Peru, with high-risk sexual behavior and no other relevant medical history, was admitted to the emergency department of the Lo-

reto Regional Hospital with three weeks of general malaise and moderate, throbbing frontal headache. Two weeks prior to admission, he experienced nausea, vomiting, and weight loss. One week prior, he reported decreased visual acuity and subjective photophobia (Figure 1).

During the physical examination, the patient was hemodynamically stable, weighing 71 kg, and had paresis in the left lower limb and severe headache. Neurological assessment showed altered mental status and neck stiffness, although cranial nerves were within normal limits. No abnormalities were detected on additional systemic examinations.

HIV infection was confirmed on admission by using a rapid test, subsequently validated by a PCR test, which showed a viral load of 207,000 cells/mL and a CD4 level of 34 cells/mL. The complete blood count showed lymphocytopenia with 800 cells/µL and mild anemia with hemoglobin of 11.4 g/dL. A cerebrospinal fluid (CSF) sample was obtained by lumbar puncture revealing an opening pressure of 30 cm/H2O, leukocytes of 6 cells/mL, glucose of 16.2 mg/dL, proteins of 40.9 mg/dL, and *Cryptococcus* spp. was found by India ink staining (Table 1). A brain CT scan showed an incidental finding of an arachnoid cyst in the posterior fossa (Figure 2).

Given the positive HIV results and the neurological abnormalities found during physical examination, additional tests were conducted. These showed a complete blood count with lymphocytopenia and mild anemia. In addition, a Sabouraud agar culture of a CSF sample isolated *Cryptococcus gattii* within 36 hours, with automated identification using VITEK® 2 Compact.

The patient was hospitalized and treated for cryptococcal meningitis. Antifungal therapy started with amphotericin B deoxycholate at a dose of 50 mg every 24 hours intravenously, plus fluconazole 800 mg daily orally. Adequate fluid and electrolyte replacement was provided before and after each dose. During the first two weeks of induction therapy, therapeutic lumbar punctures were conducted intermittently. The opening pressure was persistently high, with altered cellularity and biochemistry, as well as a sluggish clinical course. CSF culture results showed *C. gattii*. Treatment was extended for an additional two weeks, and the patient experienced significant clinical improvement. Consequently, upon discharge, consolidation therapy started with fluconazole 400 mg orally every 24 hours for 10 weeks.

One week after discharge, the patient attended a follow-up appointment at the infectious disease's outpatient clinic, showing clinical improvement. He was instructed to continue treatment with fluconazole 400 mg and cotrimoxazole 800/160 mg orally every 24 hours for 10 weeks. Five months later, at a follow-up visit, a viral load of <40 copies of RNA was confirmed.

DISCUSSION

Upon admission to the hospital, the patient was diagnosed with cryptococcal meningitis and HIV infection, leading to the immediate start of antifungal treatment. During the disease course, the sluggish clinical response suggested that the causative agent was probably not *Cryptococcus neoformans*. After two weeks of induction therapy, and during hospitalization, a culture result showed *Cryptococcus gattii*.

The low prevalence of *C. gattii* compared to *C. neoformans*, particularly in immunocompromised patients such as those with HIV infection, makes diagnosis difficult [9]. However, recent outbreaks in North America and Australia have expanded the known risk groups to include patients with cancer, solid organ transplants, and other immunodeficiencies [10,11]. In Peru, there is evidence of cases of cryptococcosis caused by *C. neoformans* var. *gatti* (which remains a variant of *C. neoformans* itself) [12], but only one case has

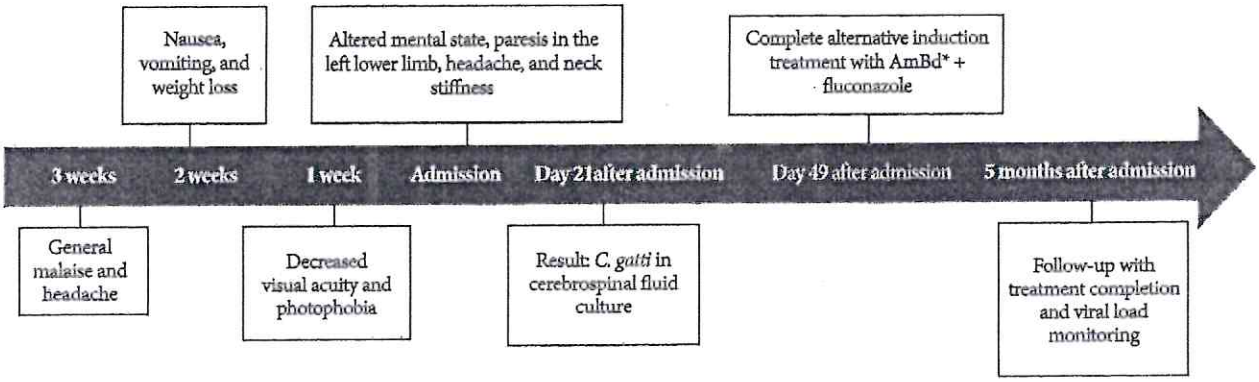

Figure 1. Timeline. *AmBd: Amphotericin B deoxycholate.

Table 1. Laboratory tests on cerebrospinal fluid sample.

CSF	2 days	14 days	19 days	25 days
Leucocytes	6 cel/mm³	2 cel/mm³	2 cel/mm³	3 cel/mm³
Protein	40.9 mg/dL	43 mg/dL	56.3 mg/dL	59.7 mg/dL
Glucose	16.2 mg/dL	35.5 mg/dL	34 mg/dL	37.1 mg/dL
India ink	Positive	Positive	Positive	Positive
Bk staining	Negative	Negative	Negative	Negative
Gram staining	Negative	Negative	Negative	Negative
Opening Pressure	30 cm/H_2O	75 cm/H_2O	58 cm/H_2O	38 cm/H_2O
Culture result	-	Positive (1°LP)	Negative	Negative

*LP: lumbar puncture

been reported for *C. gatti* as a variety, and that was in the Peruvian highlands in an immunocompetent patient [13], unlike this report, in which the patient was immunocompromised.

It is recommended to perform a CSF culture after 2 weeks of induction therapy to assess sterility if clinical symptoms persist, which serves as an indicator of therapy success before proceeding to the consolidation phase [14]. This is consistent with our report, in which the difference between the initial positive culture and the subsequent culture, which was negative, was 12 days, similar to the case of Gutierrez *et al.*, where culture sterility was achieved on day 19 [13].

Current treatment guidelines recommend the use of liposomal amphotericin B and flucytosine to treat cryptococcal meningitis caused by *C. gattii*, with a treatment regimen of 4 to 6 weeks [15,16]. However, in resource-limited settings where these drugs are not available, induction therapy with amphotericin B deoxycholate (AmBd) at a dose of 1 mg/kg per day IV or a combination of AmBd at 0.7 mg/kg per day IV plus fluconazole at 800 mg per day orally is suggested [9]. This approach was used by Lizarazo *et al.* in Colombia, who, in the absence of flucytosine, used amphotericin B deoxycholate together with fluconazole in 90 patients [17], similarly to the study by Gutierrez *et al* [13].

The use of liposomal amphotericin B over deoxycholate is preferred due to the lower probability of developing nephrotoxicity, although studies have shown that its efficacy at 2 and 10 weeks is comparable to the liposomal presentation [18]. Nevertheless, in our report, at 28 days, the patient received a cumulative dose of 1400 mg of AmBd, unlike the 535 mg reached in the report by Gutierrez *et al*, in which the patient only received 11 days of the drug [13]. Despite the cumulative dose used in our patient, he did not develop nephrotoxicity. In contrast, a patient in Cuba with the same diagnosis and etiological agent, also treated with AmBd and

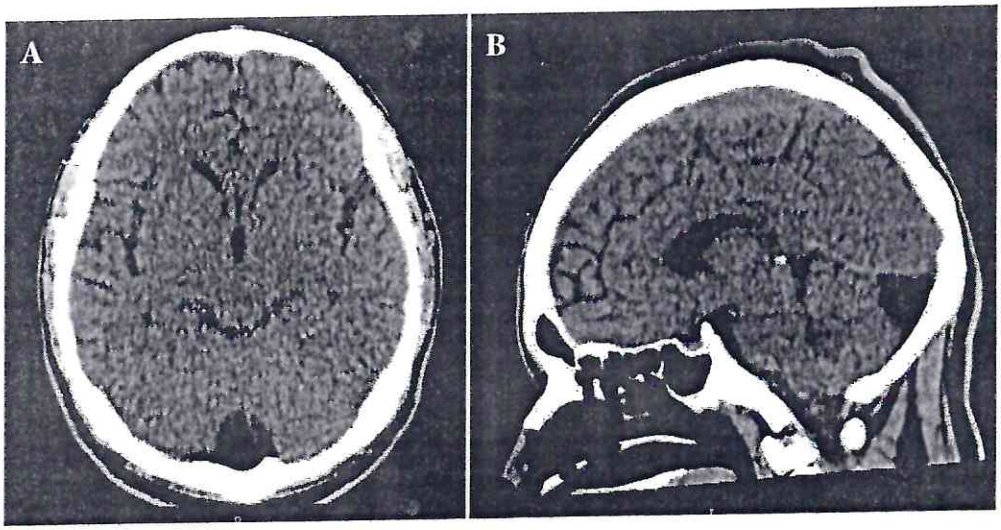

Figure 2. Non-contrast brain CT scan. Axial (A) and sagittal (B) views show a rounded, hypodense image with liquid density located in the midline of the posterior fossa, suggesting an arachnoid cyst. The rest of the brain parenchyma appears normal.

fluconazole, presented nephrotoxicity after a cumulative dose of 1500 mg of AmBd, which forced a change in treatment to the liposomal formulation of amphotericin B [16].

The diagnosis of cryptococcosis caused by *C. gattii* is made through a combination of clinical evaluation, physical examination, and additional tests. The cryptococcal antigen test is the most sensitive, but it does not distinguish between *C. gattii* and *C. neoformans*, so culture remains essential for a definitive diagnosis that differentiates between these species [19]. Initial neurological symptoms often include headache and neck stiffness. As the disease progresses, other neurological signs may appear, such as seizures, cranial nerve abnormalities, cerebellar irregularities, focal weakness in the limbs, and changes in mental status. The average time from the onset of the first symptoms to diagnosis is approximately 45 days [3]. In this case, the initial diagnosis was made at 21 days, indicating probable *C. neoformans* meningitis, but was later adjusted to *C. gattii* after isolation of the pathogen. The patient presented general symptoms, like malaise, progressive headache, nausea, and vomiting. One week before admission, he also experienced decreased visual acuity and photophobia.

The case illustrates unique diagnostic and therapeutic challenges associated with *C. gattii*, highlighting the need for a more intensive and prolonged treatment approach in the presence of severe neurological complications. It also emphasizes the importance of accurate diagnosis through culture to guide treatment and improve clinical outcomes. Furthermore, it highlights the importance of medical awareness and continuing education on the diversity of cryptococcosis in different populations, reaffirming the need for epidemiological surveillance and adaptability in clinical management strategies to optimize care and health outcomes in patients with invasive fungal infections.

In conclusion, *Cryptococcus gattii* should be considered in the differential diagnosis of meningitis in HIV-positive patients with neurological symptoms who do not respond to initial induction therapy, even in regions where its prevalence is low. Increasing awareness of this rare infection and its therapeutic challenges is crucial to improving clinical outcomes in these vulnerable populations.

Ethical criteria. Informed consent was obtained from the patient, and the article has been reviewed by the ethics committee (046-CIEI-HRL-2024) and received institutional permission (3329 - 2024-CRL DRS-L/30.50) from the Felipe Santiago Arriola Iglesias Regional Hospital in Loreto for publication.

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CRediT roles. AMS: Writing – Original draft, Writing – Review and Editing, and Project Administration. RCG: Writing – Original draft, Review and Editing MPO and JVA: Data Curation and Visualization. ERG: Project and Resource Administration. JCS and WCM: Supervision.

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Twenty-five years of pertussis outbreaks in the Peruvian Amazon: a call to strengthen equity in vaccination and control

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The highest global incidence of pertussis (whooping cough) in the past 25 years was registered in 2024, with 137 cases per million population in the context of a global resurgence of cases in 2022 and 2023.[1] This tendency is associated with a global drop in vaccination rates over the past decade, where Latin America and the Caribbean have experienced the most important declines in childhood vaccination coverage.[2] This combination of increasing case numbers and declining vaccine coverage, together with an upsurge in vaccine misinformation and hesitancy has facilitated the arising outbreaks, particularly among vulnerable populations in countries such as Peru, Mexico, and Brazil.[2,3]

In Peru, the national incidence of pertussis increased from 3.9 cases per million inhabitants in 2023 to 7.4 in 2024 and 57.5 up to epidemiological week 33 (EW33) of 2025, with a total of 1956 cases (confirmed and probable) and a case-fatality rate of 1.28%. Children under 12 years of age accounted for 70.5% (1379/1956) of cases, while 73.4% (1436/1956) were concentrated in the Amazonian region of Loreto, where 23 of the 25 reported deaths occurred (92.0% of the national mortality). None of the deceased had received the pertussis vaccine, and most were under one year of age.[4] This region, characterized by persistent geographic barriers and deficient access to basic services, has historically shown the lowest DTP3 vaccination coverage in the country, (2018–2024: 72.8, 82.8, 60.3, 57.6, 71.8, 66.5 and 86.2%), with a recent coverage of only 41.2% (the lowest nationwide) as of June 2025.[5]

At the subnational level, within the Amazon region of Loreto (the largest in the country), cases were disproportionately concentrated in Datem del Marañón Province, with 70.0% (1370/1956) of cases and 76.0% (19/25) of national deaths up to EW33 of 2025.

A historical analysis of the past 25 years (2000–2025-EW33) shows a concentration of pertussis cases in the Loreto region, accounting for 47.5% (7448/15,696) of cases, and within it, in Datem del Marañón Province, which has been the most affected nationally, with a cumulative 25.6% (4022/15,696) of cases over 25 years. This is the same province where, in 2023, a case of vaccine-derived poliovirus type 1 (VDPV1) was reported.[6] Furthermore, during this period, Loreto reported the highest number of cases (ranking first or second nationally) in 21 of the 25 years (Fig. 1).

A recent national study using data from the Demographic and Health Survey (ENDES) between 2015 and 2023 revealed that, despite the recovery of vaccination coverage following the COVID-19 pandemic, marked inequities in childhood immunization persist in Peru. Inequality in vaccine coverage, assessed using the Slope Index of Inequality (SII), consistently showed a pro-rich pattern from 2015 to 2023. The unexpected increase observed in 2023 compared to 2021 and 2022 reflected a significant absolute difference in coverage between the extremes of socioeconomic wealth.[7]

In Peru, a national equity-oriented strategy that prioritized the introduction of new vaccines in the poorest regions with the highest infant mortality rates initially increased coverage in these areas and reduced regional disparities. Nevertheless, socioeconomic inequalities persist at the individual level, underscoring the need to combine geographic targeting with mechanisms for household-level identification and follow-up.[8]

According to Peru's current technical immunization guidelines, children receive five doses of pertussis-containing vaccines: a primary series with DTP-HBV-Hib (pentavalent combined vaccine) at 2, 4, and 6 months of age, followed by DTP boosters at 18 months and 4 years.[9] Since 2019, vaccination during pregnancy has been introduced, with Tdap administered between 27 and 36 weeks of gestation. The estimated coverage among pregnant women in 2022 was 56%. In a case–control study conducted in Peru between 2019 and 2022, infants of mothers vaccinated with Tdap during the third trimester had an 81% lower risk of pertussis than those born to unvaccinated mothers.[10,11]

These data reveal an alarming concentration of cases in Loreto, particularly in the Datem del Marañón Province, in 2025 (as well as over the past 25 years), highlighting a persistent and severe inequity in pertussis immunization at the subnational level. This low coverage in a region that accounts for a large share of pertussis cases demonstrates that lack of access to services and under-vaccination[5] in geographically isolated areas

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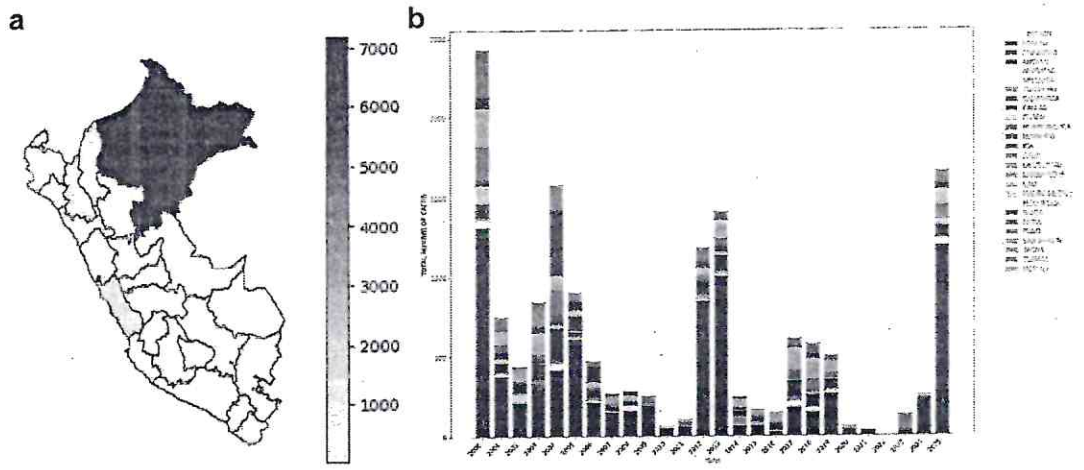

Fig. 1: **Pertussis cases in Peru, 2000–2025 (up to EW33). a.** Cumulative pertussis cases by province, 2000–2025 (up to EW33). The darkest shade corresponds to the province of *Datem del Marañón* (within the Amazon region of Loreto), which reported the highest cumulative number of cases over the 25-year period. **b.** Pertussis cases by year and by region, 2000–2025 (up to EW33). **Note:** Supporting data in https://doi.org/10.17632/htkvfd6grx.1, link: https://data.mendeley.com/datasets/htkvfd6grx/1. Source: Centro Nacional de Epidemiología, Prevención y Control de Enfermedades, Peru.[4] EW: epidemiological week.

remain significant barriers to the control of this disease. They also indicate that the measures implemented over the past 25 years, as well as those taken this year, have been insufficient to solve the problem. Consequently, immediate long-term measures and plans are required, including a comprehensive, equity-focused strategy with targeted interventions that incorporate territorial, community and intercultural components.

Contributors

Juan C. Celis-Salinas: conceptualisation, data curation, formal analysis, validation, visualisation, writing—original draft, and writing—review & editing and decision to submit the manuscript.

Edgar A. Ramírez-García: data curation, formal analysis, validation, visualisation, writing—original draft, and writing—review & editing.

Victor Fiestas Solorzano: data curation, formal analysis, validation, visualisation, writing—original draft, and writing—review & editing.

Martín Casapia-Morales: data curation, formal analysis, validation, visualisation, writing—original draft, and writing—review & editing.

Data sharing statement

Supporting data in Mendeley https://doi.org/10.17632/htkvfd6grx.1, link: https://data.mendeley.com/datasets/htkvfd6grx/1.

Source: Centro Nacional de Epidemiología, Prevención y Control de Enfermedades, Ministerio de Salud; Perú.

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The Lancet Group takes a neutral position with respect to territorial claims in published maps.

Declaration of interests

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Impact of antiparasitic therapy on cardiovascular outcomes in chronic Chagas disease. A systematic review and meta-analysis

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Summary

Background Endemic in more than 20 countries, Chagas disease affects 6.3 million people worldwide, leading to 28,000 new infections and 7700 deaths each year. Previous meta-analyses on antiparasitic treatment need updates to encompass recent studies and to assess key clinically meaningful endpoints. This study aims to evaluate the impact of antitrypanosomal therapy in preventing or reducing disease progression and mortality in chronic Chagas disease.

Methods We performed a systematic review and meta-analysis of studies reporting the cardiovascular outcomes of antitrypanosomal therapy in patients with chronic Chagas disease. We searched Ovid Embase, Ovid MEDLINE, Ovid Global Health, Scopus, Web of Science Core Collection, Cochrane Library, PubMed, Google Scholar, and Virtual Health Library databases from inception to May 18, 2024. We included aggregated data from randomized controlled studies and observational reports (full articles and abstracts) featuring antiparasitic interventions with benznidazole or nifurtimox compared to a control group. Primary outcomes were electrocardiogram (ECG) changes, disease progression, cardiovascular death, and overall mortality. A customized risk of bias scale assessed the methodological quality of studies, and a random-effects model estimated the pooled risk ratios. This investigation was registered in PROSPERO (CRD42023495755).

Findings Out of 4666 reports screened, 23 met the pre-specified inclusion criteria (8972 participants). Compared to no treatment or placebo, antiparasitic treatment led to a reduction in i) ECG changes (17 studies, 4994 participants: risk ratio (RR): 0.48, 95% CI 0.36–0.66, $p < 0.001$; $I^2 = 76.4\%$) with a number needed to treat (NNT) of 5; ii) disease progression (12 studies, 5722 participants: RR: 0.35, 95% CI 0.23–0.51, $p < 0.001$; $I^2 = 72.4\%$) NNT of 6; iii) cardiovascular death (7 studies, 5662 participants: RR: 0.44, 95% CI 0.21–0.95, $p = 0.04$; $I^2 = 50.5\%$) NNT of 22; and iv) overall mortality (10 studies, 7694 participants: RR: 0.54, 95% CI 0.34–0.87, $p < 0.001$; $I^2 = 60\%$) NNT of 23.

Interpretation We found compelling evidence that antiparasitic treatment significantly reduces the risk of ECG changes, disease progression, cardiovascular death, and overall mortality in chronic Chagas disease. Although the quality of evidence ranges from low to intermediate, with considerable heterogeneity across studies, the potential

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benefits are substantial. These findings support the broader use of trypanocidal therapy in the management of Chagas disease, though further research remains necessary.

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Keywords: Chagas disease; Chagas cardiomyopathy; *Trypanosoma cruzi*; Antitrypanosomal therapy; Benznidazole; Nifurtimox; Meta-analysis; Disease progression

Research in context

Evidence before this study

Chagas disease, an infectious disease caused by the parasite *Trypanosoma cruzi*, poses a significant health burden, not only in Latin America, where transmission occurs but also in non-endemic countries due to the migration of infected individuals. It leads to severe complications such as chronic cardiomyopathy characterized by arrhythmias, heart failure, thromboembolic events, and sudden death. We examined the efficacy of antiparasitic treatment for chronic Chagas disease in a PubMed base search using search terms such as chronic Chagas disease, and antitrypanosomal therapy. We saw mixed results, often limited to surrogate endpoints like parasitemia negativization or seroreversion. We assessed several systematic reviews and meta-analyses, including two Cochrane reviews, that explored the efficacy and effectiveness of antitrypanosomal therapy. However, some studies focused only on serological or parasitological outcomes, while those that examined clinical endpoints found the evidence insufficient to reach definitive conclusions. For patients with chronic Chagas cardiomyopathy (CCC) or asymptomatic chronic Chagas disease, the available data does not indicate a clear benefit from etiological treatment. In one Cochrane meta-analysis, only two randomized controlled trials met strict inclusion criteria, resulting in insufficient data for firm conclusions. A second meta-analysis, which applied broader criteria, also failed to demonstrate treatment effectiveness due to inconsistent and low-quality data for key outcomes.

Added value of this study

More recently, new studies have been published, highlighting the need for an updated assessment of the evidence. This study bridges the gap by providing an extensive and updated evaluation of the clinical impact of antitrypanosomal therapy in chronic Chagas disease. We included full-text articles and abstracts published in English, Spanish, or Portuguese that reported primary data from prospective or retrospective cohorts, randomized or quasi-randomized trials, and cross-sectional studies from inception to May 18, 2024. Most studies (50%) exhibited a moderate risk of bias, with a substantial proportion (42%) showing a high risk of bias and a minority having a low risk of bias (8%). Compared to no treatment or placebo, antiparasitic treatment led to a reduction in ECG changes (Risk ratio (RR): 0.48), disease progression (RR: 0.35), cardiovascular death (RR: 0.44), and overall mortality (0.54). Unlike previous analyses, our study incorporated a broader range of study designs and a more extended review period, providing a better understanding of the clinical efficacy of etiologic treatments. Overall, the evidence adds a positive effect of antitrypanosomal therapy in Chagas disease outcomes. The study findings suggest a more liberal approach to antitrypanosomal therapy should be implemented and validated in patients with Chagas disease.

Implications of all the available evidence

Despite several limitations of this meta-analysis, our findings suggest that antiparasitic therapy can significantly reduce the progression and mortality of chronic Chagas disease, challenging the previous belief that these treatments are ineffective in the chronic stage. The evidence suggests treatment benefits in patients with the indeterminate form and potentially even in the early stages of Chagas cardiomyopathy. However, the cutoffs when antiparasitic therapies fail to halt the progression of cardiac disease remain unknown. Nonetheless, our findings underscore the need for policy changes to enhance the availability and distribution of current antiparasitic drugs, ensuring they reach a broader patient population. Another point to consider is the urgency of identifying or developing definitive biological markers of cure. Due to the inherently complex nature of Chagas disease, finding a marker with 100% sensitivity is unlikely. Furthermore, even with such a marker, the limited availability of only two drugs with similar mechanisms of action diminishes the practical importance of declaring a patient cured. Efforts should focus on optimizing existing therapies and expanding their access. While researching new treatments with better efficacies and safety profiles is needed, we must recognize that developing and testing new drugs is lengthy and complex. This concept also applies to new immunotherapies. Balancing the enhancement of current treatments with the pursuit of improved therapies will potentially ensure both immediate and long-term advancements in managing Chagas disease.

Introduction

Chagas disease (American trypanosomiasis) is an infectious disease caused by the blood and tissue parasite *Trypanosoma cruzi*, primarily transmitted through the faeces of Triatomines (kissing bugs), which contaminate mucous membranes or broken skin.[1] Transmission can also occur orally through food and beverage contamination, vertically (from infected mothers to their offspring), transfusion of blood products, solid organ transplantation, and laboratory accidents. Chagas disease is endemic in 21 countries across Latin America, as well as in parts of Texas and potentially other areas in the Southern U.S. According to recent estimates from the Global Burden of Disease Study 2021, Chagas disease affects approximately 6.3 million people worldwide, contributing to 239,000 disability-adjusted life years (DALYs), and causing 7700 deaths annually.[2] These data represent an update from previous estimates, which indicated an annual incidence of 28,000 cases, affecting about 6 million people globally and resulting in approximately 12,000 deaths per year.[3] The disease has become an important health problem in non-endemic countries due to the migration of infected individuals originating from endemic regions of Latin America.

Chagas disease has two sequential clinical phases: acute and chronic, with the former noted previously to be highly susceptible to parasitological cure. A more complicated picture emerges during the chronic phase, which has indeterminate (absence of clinical findings despite infection) and determinate (evidence of clinical expression) forms. The determinate form of chronic Chagas disease poses a significant burden to affected patients. As the illness progresses, it causes substantial morbidity through the development of angina, heart failure, arrhythmia, systemic or pulmonary embolism, megaesophagus, and megacolon.[4] Patients develop cardiomyopathy at an annual rate of 1.9% after being infected.[5] Once present, cardiomyopathy carries an annual mortality rate of 7.9%,[6] which is higher than that for acquired immunodeficiency syndrome (AIDS).[7] Despite advances in vector control and a reduction in disease transmission in some regions, clinical care for patients who are newly infected, as well as those who are diagnosed late, remains limited. Unfortunately, the majority of newly infected patients are asymptomatic and, therefore, go mostly undiagnosed. The window for treating acute Chagas disease successfully is missed, and these patients progress to the chronic phase.

Complicating this picture even further, when patients are diagnosed late, they often have advanced chronic Chagas cardiomyopathy (CCC), which necessitates specialized care that is both costly and time-consuming. Access to newer heart failure drugs, cardiac implantable electronic devices, catheter ablation, and cardiac transplantation is limited to only a few advanced centers. Given these challenges, early diagnosis and the timely use of effective antiparasitic drugs are both fundamental strategies that could significantly improve patient outcomes.

A central question in the antiparasitic treatment of chronic Chagas disease is whether patients in either the indeterminate or determinate forms of the illness would benefit from such therapy. The only specific antiparasitic treatment for this infection consists of two extensively investigated nitroheterocyclic trypanocidal drugs, benznidazole (BZN) and nifurtimox (NFT).[8] Previous studies have clearly shown that both compounds—certainly in the acute phase, but even in many cases in the chronic phase of the illness–frequently elicit a favorable parasitological and serological response.[9,10] However, seroreversion may take decades to be demonstrated, and the reversion of parasitological and molecular tests cannot be considered a surrogate for cure. An important question arises: are these favorable effects in terms of parasitological cure demonstrated by the disappearance of detectable parasites in the blood also translating into clinical improvement for patients? Or is it the case that during the chronic phase, host genetic factors and parasite characteristics become more important, rendering antiparasitic treatment unable to affect the outcome of CCC or other chronic sequelae? In this regard, the effect of antitrypanosomal therapy on disease outcomes has indeed been deemed inconclusive. Several systematic reviews and meta-analyses,[9–11] including two Cochrane reviews,[12,13] have attempted to assess the efficacy and effectiveness of antitrypanosomal therapy. Unfortunately, some reports evaluated only serological or parasitological outcomes,[9,10] while those that evaluated clinical endpoints[11–13] concluded that there was insufficient evidence to draw definitive conclusions. Specifically, for patients with CCC or asymptomatic chronic Chagas disease, the current available evidence suggests there is no clear benefit from etiological treatment. One Cochrane meta-analysis, which included only two randomized controlled trials (RCTs) due to rigid inclusion criteria, was unable to find enough data to provide useful conclusions[12]; the second meta-analysis, which applied broader inclusion criteria, also failed to demonstrate the utility of etiological treatment due to the low quality and inconsistency of the data for key outcomes.[13] Several studies have emerged since these reviews,[14–16] necessitating an updated evaluation of the evidence. We aim to conduct a comprehensive systematic review and meta-analysis to reassess the impact of trypanocidal therapy on Chagas disease progression and mortality, considering the latest available data and addressing the limitations of previous analyses.

Methods

Ethic statement

For this systematic review and meta-analysis, all data were anonymized and could not be traced back to the

original participants in the referenced clinical trials or cohort studies. As a result, obtaining informed consent or requesting an ethical permit specifically for this analysis was deemed unnecessary.

Search strategy and selection criteria

This systematic review and meta-analysis was conducted in accordance with the recommendations of the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) 2020 guidelines.[17] We systematically searched Ovid Embase, Ovid MEDLINE, Ovid Global Health, Scopus, Web of Science Core Collection, Cochrane Library, PubMed, Google Scholar, and Virtual Health Library databases to find relevant articles from inception to May 18, 2024, with no language or publication restrictions. We also screened the reference lists of included full texts and previous relevant systematic reviews and sought input from experts to identify additional articles. Databases were searched using a combination of controlled vocabulary and free text terms for Chagas disease and antitrypanosomal therapy. Details of the search strategy are presented in the Appendix (pp 3–6). We included full-text articles and abstracts published in English, Spanish, or Portuguese that reported primary data from prospective or retrospective cohorts, randomized or quasi-randomized trials, and cross-sectional studies. Case-control studies, case reports, and *in vitro* or animal studies were excluded to focus on human data and minimize publication bias.

The search of the literature was performed by a medical librarian and peer-reviewed by a second librarian using the Peer Review of Electronic Search Strategies (PRESS) guideline. All identified studies were uploaded into Endnote 20 (Clarivate Analytics, Pennsylvania, USA), and Covidence, and duplicate studies were removed. Three reviewers (AHM, ARJ, and FMR) independently screened the titles and abstracts of the studies for eligibility. If a study was judged as potentially relevant based on the title or abstract, the full text was obtained and assessed for inclusion. Disagreements were resolved by discussion among the reviewers or, if needed, by a fourth reviewer. Using Covidence, we generated a PRISMA document[17] detailing the initial number of reports, the number of duplicates removed, the number excluded during title/abstract screening, and the number excluded during full-text assessments, along with reasons for exclusion (Appendix pp 7–13). Reports that met the selection criteria were included in the final analysis.

Inclusion criteria for the studies were: (1) patients with chronic Chagas disease confirmed by serological tests (both children and adults) in either the indeterminate or cardiac forms; (2) studies comparing patients treated with either BZN or NFT to a control group (either untreated or treated with placebo), with no limit on the duration of follow-up; (3) studies reporting at least one of the following outcomes: ECG change, disease progression, cardiovascular death, or overall mortality. The definitions of outcomes varied between studies, but these variations were accepted without the need for standardization, and (4) studies providing sufficient data to estimate a risk ratio.

We excluded reports that met any of the following criteria: use of historical controls, absence of a control group, administration of BZN or NFT in combination with other compounds, focus on acute or congenital infections, emphasis on preventing congenital Chagas disease through treatment of reproductive-age women, or those in the context of organ transplantation or immunocompromised patients. It is important to note that some studies did not distinguish between different groups and analyzed mixed populations together, such as children and adults, patients treated with BZN or NFT, and those with the indeterminate form alongside patients with the cardiac form. Finally, when multiple publications were based on the same cohort, we included data only from the most recent and comprehensive report.

Data analysis

Two reviewers (AHM and ARJ) independently accrued data using a standardized Excel spreadsheet for initial data extraction, and disagreements were resolved through discussion. Once extracted, the data were transferred to Research Electronic Data Capture (REDCap) for further management and analysis. We extracted aggregated data as published, which included author, year and type of publication, country, type of study, population description (children and/or adults, disease stage or form, mean age, and percentage of men), number of participants (total and in each group), intervention (type of medication and dose), control group description, outcomes assessment (ECG change, disease progression, cardiovascular death, and overall mortality), and mean duration of follow-up. The disease stage was categorized into three groups: patients with cardiomyopathy, those exclusively in the indeterminate form, and those in the chronic phase (chronic Chagas disease). It's important to note that the studies classified as chronic Chagas disease included both patients with the indeterminate form and those with mild cardiomyopathy. However, the outcomes were analyzed collectively without distinguishing between patients with indeterminate or determinate forms. This classification approach allows for a comprehensive analysis of disease progression across different stages of Chagas disease while acknowledging the potential overlap between categories, particularly within the chronic phase group. For the pooled mean age and pooled mean follow-up, we used weighted values, which were calculated by multiplying each study's mean by its sample size (the "weight") and then dividing the sum of these values by the total sample size across all studies. This approach ensures that larger, more statistically robust studies have a greater impact on the overall mean, reducing the

potential bias introduced by smaller studies and providing more accurate results. Data related to side effects were not collected as they were either inconsistently reported or not reported at all across the various studies.

ECG alterations were measured as any new significant ECG change recorded during the study. However, in their analysis, some studies included all patients with ECG changes at the end of the follow-up rather than just the new cases. Disease progression was defined as any worsening disease parameter (e.g., worsening cardiomyopathy based on clinical symptoms, chest x-rays, ECG, or echocardiography). As mentioned earlier, there were some discrepancies in these definitions among the studies, but these differences do not significantly impact the analysis of the results.

All extraction forms, tools, and meta-analyses were pilot-tested on two studies and subsequently modified to ensure the extraction of relevant data and confirm the feasibility of our research question. We contacted the study authors to address any relevant ambiguities.

Risk of bias across studies

Two reviewers (AHM, ARJ) independently evaluated the included studies for risk of bias analysis, using a customized scale, with a third reviewer (FMR) resolving any disagreements. The risk of bias was classified as high, moderate, or low for each study (Appendix pp 14–15).

Statistical analysis

Risk ratios (RR) with 95% confidence intervals (CI) were used as the summary measure for all outcomes. These RRs were calculated based on the extracted frequencies and denominators, representing the ratio of outcomes in the antitrypanosomal drug group compared to the control group. Given the differences in study design among the included studies, we assumed a high potential for heterogeneity and used a random-effects model to calculate pooled effects size. Between-study heterogeneity was estimated using the I^2 statistic, representing the proportion of variability not attributable to chance. I^2 values equal to or greater than 50% indicate substantial heterogeneity.[18]

In a sensitivity analysis, the influence of individual studies on the summary statistics was examined by omitting one study at a time from the meta-analysis. We also conducted subgroup analyses for all outcomes based on the following potential sources of heterogeneity: publication type, disease stage, antiparasitic drug used, treatment duration of BZN, study design, population age, risk of bias of included studies, and country. For all subgroup analyses, we assessed whether subgroup effects (interaction) were present.

Meta-regression analyses of numerical variables were performed to examine factors associated with treatment efficacy and contributing to study heterogeneity. Contour-enhanced funnel plots were constructed to assess publication bias, and the Egger test was used to evaluate for a small-study effect.[19] All tests were two-sided, and a p-value <0.05 was considered statistically significant. Statistical analyses were performed using Stata software, version 18.0 (StataCorp), and the protocol was prospectively registered in PROSPERO (CRD42023495755).

Role of the funding source

There was no funding source for this study. The corresponding authors had full access to all the data in the study and took final responsibility for the decision to submit the manuscript for publication.

Results

Literature search for Chagas disease studies with antitrypanosomal therapies

Database searches yielded 4666 citations. After automated duplicate removal, 3273 citations underwent title and abstract screening. Of these, 133 reports met the criteria for full-text review. Following the full-text review, 115 papers were excluded (Appendix pp 7–13), and 5 were manually added (4 abstracts[20–23] and 1 full-text article)[24] (Fig. 1). Ultimately, 23 studies[14–16,20–39] met the inclusion criteria (19 full-text articles[14–16,24–39] and 4 abstracts).[20–23] Notably, one study[15] employed two different designs: a cross-sectional design to evaluate ECG changes and a prospective design to evaluate mortality. Therefore, the percentages provided next refer to the 24 different study designs. Ten (42%) studies were retrospective, 8 (33%) were prospective, 5 (21%) were RCTs, and 1 (4%) was a cross-sectional study. One study[32] used an alternating sequence for randomization (quasi-randomization), and acknowledging the differences between RCT and quasi-randomized study, we included this study among the RCTs. The 23 included studies contained a total of 8972 participants (3859 treated and 5113 control). The number of participants in each study varied from a minimum of 33[21] and a maximum of 2854.[36] The weighted mean age of participants was 43.4 years, with individual study means ranging from 9 years[28] to 55 years[36] (Table 1). Our analysis included 43.6% male subjects. The weighted mean follow-up duration was 6.7 years, ranging from 1[27] to 25 years.[39] For the selected outcomes, we had 17 studies reporting on ECG change, 12 on disease progression, 7 on cardiovascular death, and 10 on overall mortality (Table 1). Disease progression was defined differently across studies. Five studies[14,24,27,30,35] defined it through clinical, electrocardiographic, or echocardiographic radiological changes. Four studies[25,29,32,34] used the Kuschnir classification, defining progression as a change to a more advanced group. Kuschnir groups are based on the presence of abnormal ECG, cardiomegaly, and symptoms of heart failure: Group 0–normal ECG and chest X-ray; Group I–abnormal ECG, normal chest

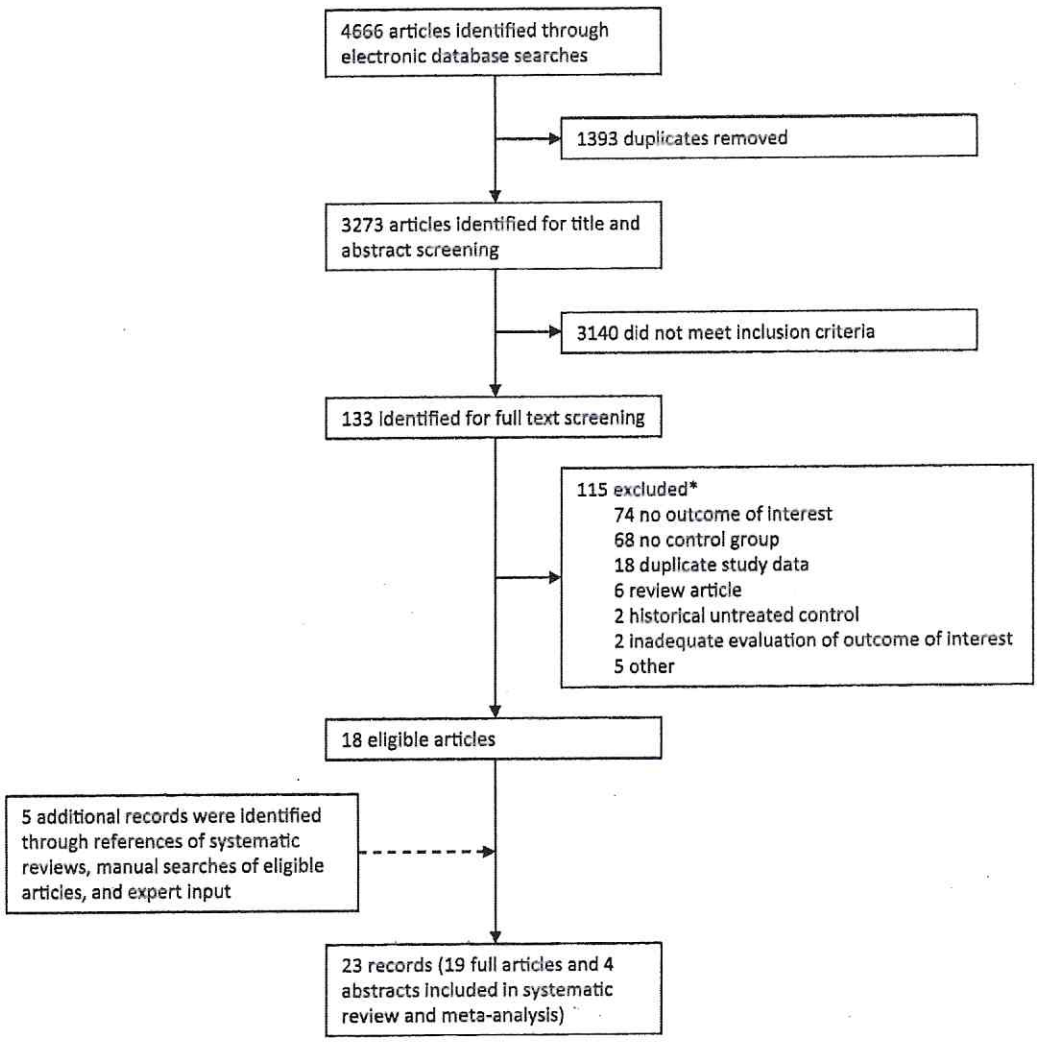


Fig. 1: PRISMA figure. Selection of reports for inclusion in meta-analysis. *The total exceeds 115 because some studies met more than one exclusion criterion.

X-ray; Group II–abnormal ECG and cardiomegaly without heart failure; Group III–cardiomegaly with signs of heart failure. Two studies[16,36] used composite outcomes of cardiovascular events, and one study defined progression as the development of cardiomyopathy with left ventricular ejection fraction (LVEF) < 50%.[23] Most studies (50%) exhibited a moderate risk of bias, with a substantial proportion (42%) showing a high risk of bias and a minority having a low risk of bias (8%) (Appendix p 15).

Key endpoint analysis

In the random-effects model analysis, antitrypanosomal therapy significantly reduced the risk of several key outcomes in patients with chronic Chagas disease compared to placebo or no therapy (Table 2, Fig. 2). The overall risk ratios (RR) were 0.48 (95% CI: 0.36–0.66, $p < 0.001$) for ECG changes with a heterogeneity I^2 of 76.4% and a number needed to treat (NNT) of 5, after a mean follow-up of 9.9 years (4994 participants from 17 studies, 4 RCTs and 13 observational studies); 0.35 (95% CI: 0.23–0.51, $p < 0.001$) for disease progression with a heterogeneity I^2 of 72.4% and an NNT of 6, after a mean follow up of 7.9 years (5722 participants from 12 studies, 3 RCTs and 9 observational studies); 0.44 (95% CI: 0.21–0.95, $p = 0.04$) for cardiovascular mortality with a heterogeneity I^2 of 50.5% and an NNT of 22, after a mean follow up of 7.2 years (5662 participants from 7 studies, 2 RCTs and 5 observational studies); and 0.54 (95% CI: 0.34–0.87, $p < 0.001$) for overall mortality with a heterogeneity I^2 of 60% and an NNT of 23, after a mean follow up of 6.2 years (7694 participants from 10

Author, publication type	Country	Study type	Population age and disease stage	Total of participants (treated/control)	Intervention vs control	Outcomes assessment	Mean follow up, years	BZN/NFT dose (mg/kg/day) and duration of therapy (days)	Age at treatment (mean)	Men (%)	Risk of Bias
Macedo et al. (1987),[20] abstract	Brazil	Retrospective	Adults with chronic indeterminate form	171 (103/68)	BZN/NFT vs placebo	ECG change	7	BZN (7) (30–60) NFT (7–8) (60–90)	NI	NI	High
Ianni et al. (1993),[21] abstract	Brazil	Retrospective	Adults with chronic indeterminate form	33 (15/18)	BZN vs placebo	ECG change	8.1	BZN (5) (60)	NI	NI	High
Miranda et al. (1994),[24] full article	Brazil	Prospective	Children and adults with chronic Chagas disease	120 (76/44)	BZN vs untreated	Disease progression	13[a]	BZN (5)[b] (60)	34	41.7	High
Viotti et al. (1994),[25] full article	Argentina	Retrospective	Children and adults with chronic Chagas disease	201 (131/70)	BZN vs untreated	ECG change, disease progression, CV death and overall mortality	8	BZN (5) (30)	46.6[c]	41.3	Moderate
De Andrade et al. (1996),[26] full article	Brazil	RCT	Children with chronic Chagas disease	129 (64/65)	BZN vs placebo	ECG change	3	BZN (7.5) (60)	9.5[d]	58.9	Moderate
Coura et al. (1997),[27] full article	Brazil	RCT	Adults with chronic indeterminate form[e]	77 (53/24)	BZN/NFT vs placebo	ECG change and disease progression	1	BZN (5) (30) NFT (5) (30)	NI	NI	Moderate
Catalioti et al. (1998),[22] abstract	Venezuela	Prospective	Adults with chronic Chagas disease	539 (74/465)	BZN vs untreated	CV death and overall mortality	5	BZN (5) (60)	41.0[n]	38.6	High
Sosa-Estani et al. (1998),[28] full article	Argentina	RCT	Children with chronic Chagas disease	106 (55/51)	BZN vs placebo	ECG change	4	BZN (5) (60)	9[d]	NI	Moderate
Fabbro de Suasnábar et al. (2000),[29] full article	Argentina	Prospective[e]	Children and adults with chronic Chagas disease	198 (68/130)	BZN/NFT vs untreated	Disease progression, CV death and overall mortality	14	BZN (5)[f] (30) NFT (5–8) (60)	36.5[d]	42.9	High
Gallerano et al. (2000),[30] full article	Argentina	Prospective[g]	Children and adults with chronic Chagas disease	894 (226/668)	BZN/NFT[h] vs untreated	ECG change, disease progression, CV death and overall mortality	6.6[i]	BZN (4–8) (45–60) NFT (10) (45–60)	33.4	49.1	Moderate
Lauria-Pires et al. (2000),[31] full article	Brazil	Retrospective	Adults with chronic Chagas disease	91 (45/46)	BZN/NFT vs untreated	ECG change and overall mortality	10	BZN (10) (20–60) NFT (10) (20–60)	45.5[d]	NI	High
Viotti et al. (2006),[32] full article	Argentina	RCT[j]	Adults with chronic Chagas disease	566 (283/283)	BZN vs untreated	ECG change, disease progression, CV death and overall mortality	9.8	BZN (5) (30)	39.4	46.1	Low
Fabbro et al. (2007),[33] full article	Argentina	Prospective[g]	Adults with chronic indeterminate form	111 (54/57)	BZN/NFT vs untreated	ECG change	21	BZN (5)[f] (30) NFT (8–10) (60)	31.5[d]	31.5	Moderate
Bertocchi et al. (2013),[34] full article	Argentina	Prospective	Adults with chronic Chagas disease	107 (82/25)	BZN vs untreated	ECG change and disease progression	8.8[i]	BZN (5) (30)	35[d]	36.4	Moderate
Machado-de-Assis et al. (2013),[35] full article	Brazil	Retrospective[c]	Children and adults with chronic Chagas disease	58 (29/29)	BZN vs untreated	Disease progression	13	BZN (5) (60)	NI	34.5	Moderate
Morillo et al. (2015),[36] full article	Multiple	RCT	Adults with chronic Chagas cardiomyopathy	2854 (1431/1423)	BZN vs placebo	Disease progression, CV death and overall mortality	5.4	BZN (5) (40–80)	55	49.3	Low
Colantonio et al. (2016),[37] full article	Argentina	Retrospective	Children with chronic indeterminate form	86 (48/38)	BZN vs placebo	ECG change	10.3	BZN (5) (60)	10	48.8	Moderate

(Table 1 continues on next page)

Author, publication type	Country	Study type	Population age and disease stage	Total of participants (treated/control)	Intervention vs control	Outcomes assessment	Mean follow up, years	BZN/NFT dose (mg/kg/day) and duration of therapy (days)	Age at treatment (mean)	Men (%)	Risk of Bias
(Continued from previous page)											
Fragata-Filho et al. (2016),[34] full article	Brazil	Retrospective	Adults with chronic indeterminate form	310 (263/47)	BZN vs untreated	ECG change, disease progression, CV death and overall mortality	19.6	BZN (5) (60)	38.4	34.5	Moderate
Cardoso et al. (2018),[35] full article	Brazil	Cross-sectional/ prospective[o]	Adults with chronic Chagas cardiomyopathy	1813 (493/1320)	BZN vs untreated	ECG change and overall mortality	2[k]	BZN (NI) (NI)	NI	32.2	High/ Moderate[l]
Soverow et al. (2019),[38] full article	USA	Prospective	Adults with chronic Chagas disease	89 (59/30)	BZN/NFT vs untreated	ECG change	3.3[i]	BZN (5) (60) NFT (8–10) (90)	46.7[n]	NI	High
Haslocher-Moreno et al. (2021),[16] full article	Brazil	Retrospective	Adults with chronic indeterminate form	228 (114/114)	BZN vs untreated	ECG change, disease progression and overall mortality	15.1	BZN (5)[m] (30–60)	31.3	70.2	Moderate
Suasnábar et al. (2021),[39] full article	Argentina	Retrospective	Children with chronic Chagas disease	82 (41/41)	BZN/NFT vs untreated	ECG change	25	BZN (5)[f] (30) NFT (12–15) (45–60)	12.1[n]	35.4	High
Jiang et al. (2024),[23] abstract	USA	Retrospective	Adults with Chagas disease[c]	109 (52/57)	BZN/NFT vs untreated	Disease progression	NI	BZN (NI) (NI) NFT (NI) (NI)	57.8	37.6	High

BZN, Benznidazole. CV, cardiovascular. ECG, 12-lead electrocardiogram. NI, not informed. NFT, Nifurtimox. RCT, randomized controlled trial. [a]For studies reporting a range of follow-up periods as this one (10–16 years), the mean follow-up duration was calculated as the average of the minimum and maximum values within the range (13 years). [b]The Benznidazole dose was corrected from 15 mg/kg/day, as stated in the paper, to 5 mg/kg/day, based on communication with the author. [c]For studies not reporting the mean age for the overall population as this one, the weighted mean age was calculated using the mean ages and sample sizes of the treatment and control groups. For example, the authors reported mean ages of 46.0 years (BZN, 131 patients) and 47.7 years (control, 70 patients), resulting in a weighted mean age of 46.6 years [(46 x 131) + (47.7 x 70)], divided by 201. [d]Average of the minimum and maximum values. [e]Deduced from us based on the details provided in the paper, although not specified by the authors. [f]Half dose during the first week. [g]Actually, the authors affirmed that the study was partially retrospective and partially prospective. [h]Patients treated with Allopurinol (n = 309) were excluded. [i]Weighted mean follow-up. [j]Although the authors used an alternating sequence for randomization (quasi-randomization), we included this study among the RCT, acknowledging the differences between RCT and quasi-randomized trials. [k]For the prospective cohort. [l]High for the cross-sectional design and moderate for the prospective cohort. [m]Or 200 mg/day as a fixed dose. [n]Weighted mean age. [o]This study had two epidemiological designs, one cross-sectional and the other prospective.

Table 1: **Characteristics of 23 studies included in the meta-analysis.**

studies, 2 RCTs and 8 observational studies). The intervention may benefit 19.3% of additional patients for ECG changes, 15.6% for disease progression, 4.6% for cardiovascular mortality, and 4.4% for overall mortality (absolute risk reductions). Omitting each study individually did not result in significant changes to the risk ratios in any outcomes, indicating robustness in the findings (Appendix p 16).

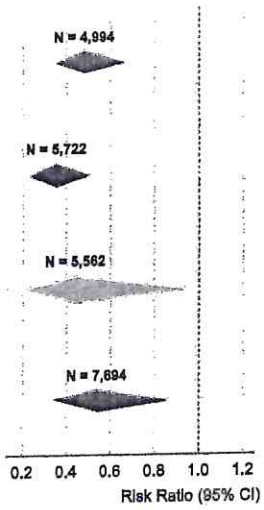
Subgroup analysis

The subgroup analyses for ECG changes, disease progression, cardiovascular death, and overall mortality consistently show that antiparasitic treatment is beneficial compared to control (no treatment or placebo) (Appendix pp 17–19). For ECG changes, significant differences in the magnitude of the treatment effect were observed for disease stage ($p < 0.001$), study type ($p < 0.001$), and country ($p = 0.02$). This indicates that while the treatment effect remains beneficial across all subgroups, its strength varies among them. Other factors such as publication type, selection of antiparasitic drug, treatment duration of BZN, population age, and risk of bias of the studies (low, moderate, or high) showed no significant interaction effects. For disease progression and cardiovascular death, significant quantitative differences were found based on disease stage and country, again indicating variability in effect size but a consistent benefit derived from treatment. The analysis of overall mortality revealed significant differences by country, but the treatment consistently reduced mortality across all subgroups. No qualitative interactions were found for any outcome, meaning the treatment effect was consistently favorable.

Additional analysis

The meta-regression analyses for the four outcomes provide insights into the factors influencing treatment efficacy (Appendix pp 20–24). For ECG changes, age showed a significant negative association ($p = 0.04$), suggesting that older patients benefited more from the treatment. However, it is crucial to note that most observations are based on a mean age of up to 50 years, aligning with current guidelines focused on this age group. Only two studies included patients with a mean age over 50 years.[23,36] These results should not be interpreted as indicating greater benefit for patients older than 50 nor suggesting universal adult benefit over children. Within the studied age range (childhood to

Outcomes	Mean follow-up* (years)	N° of participants (studies)	Control group event rate	Relative effect (95% CI)	Treatment group event rate† (95% CI)	I^2	NNT (95% CI)	Forest plot summary of the 4 major outcomes
ECG changes	9.9	4,994 (17 studies,4 RCT and 13 observational studies)	37.2 per 100	RR 0.48 (0.36 to 0.66)	17.9 per 100 (13.4 to 24.6)	76%	5 (4 to 8)	N = 4,994
Disease progression	7.9	5,722 (12 studies, 3 RCT and 9 observational studies)	24.0 per 100	RR 0.35 (0.23 to 0.51)	8.4 per 100 (5.5 to 12.2)	72%	6 (5 to 8)	N = 5,722
CV death	7.2	5,662 (7 studies, 2 RCT and 5 observational studies)	8.3 per 100	RR 0.44 (0.21 to 0.95)	3.7 per 100 (1.7 to 7.9)	50%	22 (15 to 250)	N = 5,562
Overall mortality	6.2	7,694 (10 studies, 2 RCT and 8 observational studies)	9.6 per 100	RR 0.54 (0.34 to 0.87)	5.2 per 100 (3.2 to 8.3)	60%	23 (16 to 77)	N = 7,694



Forest plots: Each color represents an individual outcome. The center of the diamond plot represents the risk ratio and both ends, the 95% confidence intervals. The control group event rate was calculated by summing the number of events from all included studies (number of events out of number of total control patients). ECG, electrocardiogram. CV, cardiovascular. I^2, the heterogeneity statistic. NNT, number needed to treat (NNT is calculated as 100 divided by the absolute risk difference—i.e., (Control group event rate minus Treatment group event rate) when expressed as a percentage, or as 1 divided by the absolute risk difference when given as a proportion). RCT, randomized control trials. RR, risk ratio. *Weighted means were used for the pooled estimates of the mean follow-up, taking into account each study's sample size. †Was calculated based on the relative effect and its 95% CI applied to the control group event rate.

Table 2: **Summary of the results of meta-analysis comparing antiparasitic treatment versus control on major cardiovascular outcomes in patients with chronic Chagas disease.**

middle adulthood), a trend towards increased benefit with age was observed, possibly driven by differences between pediatric and young adult populations rather than among adults of various ages. Considering changes in life expectancy, particularly for migrants in Western countries with better healthcare access, older patients may exhibit distinct treatment responses. This highlights the need for further research to clarify treatment effects across more specific age groups, especially focusing on potential differences between children, young adults, and older adults. The dose of BZN showed a significant positive association, with 5 mg/kg proving more effective ($p < 0.001$) than higher dose regimens. Notably, only one study in our analysis utilized a 10 mg/kg dose, which limits the generalizability of this finding. Moreover, several confounding factors may have influenced these results. No significant effects were observed for the percentage of men ($p = 0.38$), mean follow-up duration ($p = 0.95$), or NFT dose ($p = 0.98$) regarding ECG changes. In terms of disease progression, cardiovascular death, and overall mortality, none of the factors analyzed showed significant associations.

For analysis of publication bias, the funnel plots for the four outcomes are depicted in the Appendix (pp 25–26). For ECG changes, the symmetrical plot and Egger test ($p = 0.83$) indicate no significant bias. Disease progression shows slight asymmetry with a borderline Egger test result ($p = 0.06$). Cardiovascular death appears symmetrical, and the Egger test ($p = 0.15$) confirms no significant bias. Overall mortality is mostly symmetrical, with the Egger test ($p = 0.67$) indicating no significant bias. Overall, publication bias is not a major concern for these outcomes, although the findings for disease progression suggest that negative studies may have been slightly less likely to be published.

Discussion

We found that antitrypanosomal therapy positively affected relevant cardiovascular outcomes in chronic Chagas disease. The intervention resulted in an NNT of 5, 6, 22, and 23 to prevent one case of ECG change, disease progression, cardiovascular death, and overall mortality, respectively. Despite the considerable risk of bias in most included studies, this comprehensive review synthesized all relevant research on antiparasitic treatment in chronic Chagas disease. The analysis yielded interpretable data within acceptable scientific parameters for the field, providing valuable insights despite limitations. Consistent trends across studies,

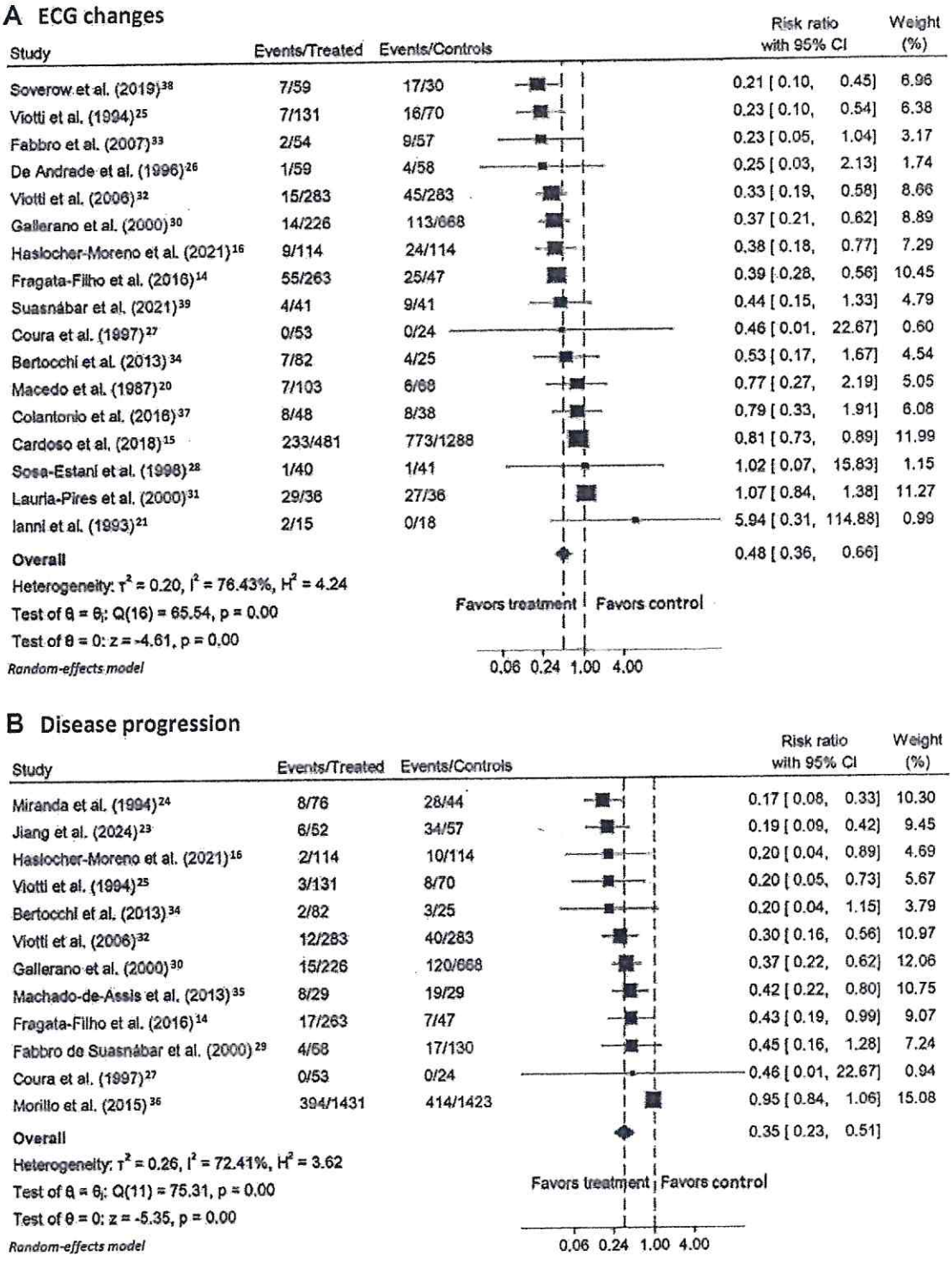


Fig. 2: Forest plots for pooled risk ratios for outcomes: (A) electrocardiogram changes, (B) disease progression, (C) Cardiovascular mortality, and (D) Overall mortality.

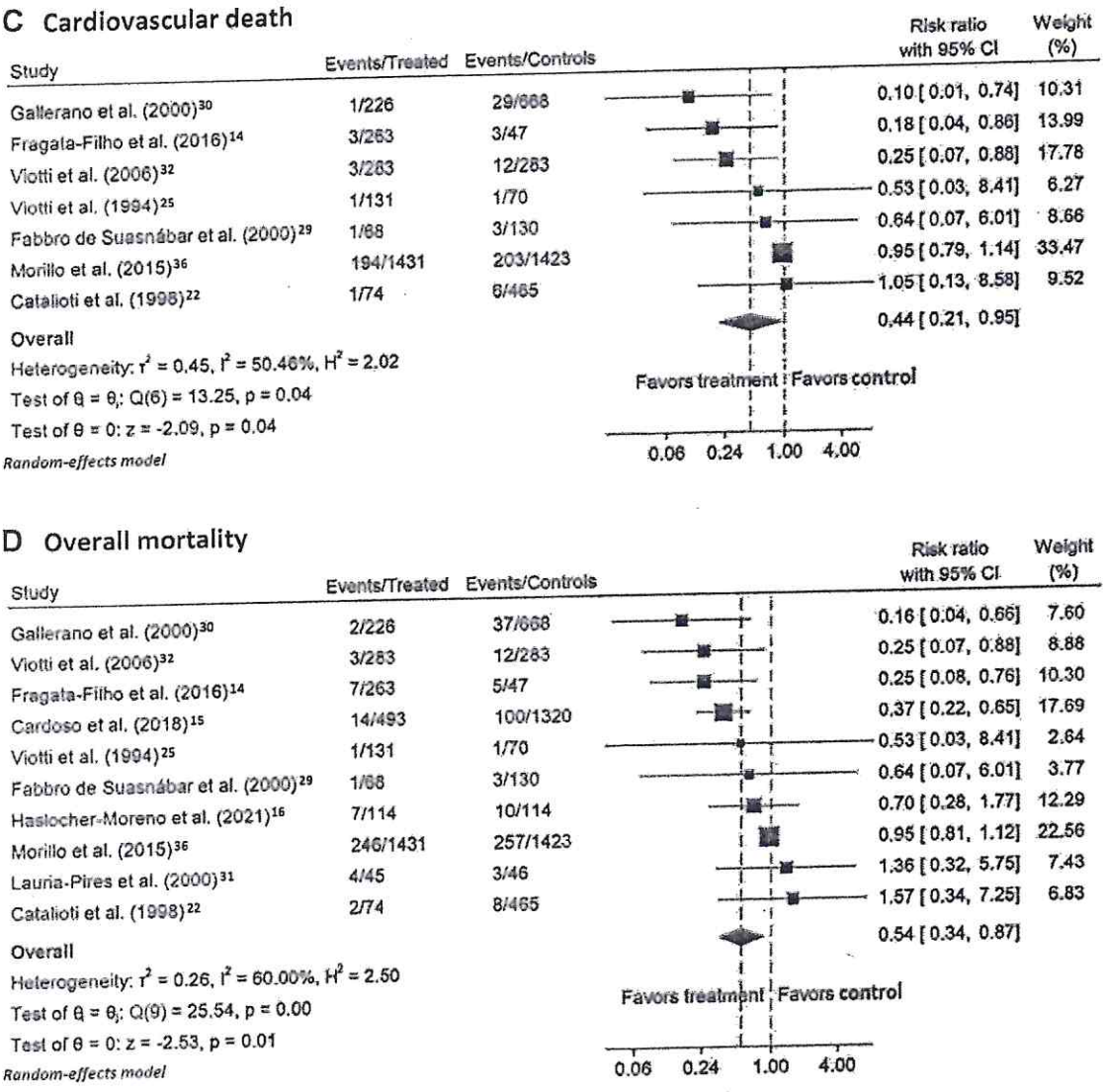


Fig. 2: Continued.

showing reduced risks of various adverse outcomes, strengthen the findings' validity. While acknowledging the need for more robust research, this review offers important guidance for clinical decision-making and future investigations in Chagas disease management.

Our results differ from a recent meta-analysis investigating the use of BZN to treat chronic Chagas disease, which concluded that more data is needed due to a lack of significant impact on cardiovascular outcomes.[11] However, that meta-analysis included only five studies (one randomized and four prospective observational) and considered studies up to 2021, excluding research on NFT, another treatment option. In contrast, our more comprehensive analysis included 23 reports, encompassing a broader range of study designs and extending the review period to 2024. By incorporating studies on BZN and NFT, we aimed to provide a more extensive evaluation of their efficacy in treating chronic Chagas disease. This broader approach highlights potential benefits associated with these treatments that were not evident in the previous, more limited meta-analysis and aligns with the most recent recommendations from the Brazilian Society of Cardiology guidelines.[4]

Direct parasite-mediated cardiac injury, long-standing myocardial fibrosis due to tissue parasite persistence, adverse immune reactions, and reinfections are pivotal in the pathogenesis of CCC.[40–42] Morbidity

and mortality arise primarily from CCC complications, including arrhythmias, biventricular myocardial dysfunction, and thromboembolic events. A recent review highlighted the conspicuous arrhythmogenic feature of CCC, starting with basic electric remodeling at the cellular level and culminating with widespread fibrosis, alongside additional remodeling processes driven by immunological disturbances, coronary microvascular derangements, dysautonomia, and contractile impairment.[43]

Our study endpoints, including ECG alterations and clinical disease progression, are instrumental in detecting ongoing cardiac injury and informing the risk of cardiomyopathy development.[44] In addition, subgroup analysis indicated that earlier stages of the disease (patients with the indeterminate form) might benefit more from trypanocidal therapy, aligning with the potential benefit of reducing parasite tissue burden before further damage occurs.

Recommendations for antiparasitic treatment in chronic Chagas disease are usually based on surrogate outcomes such as short-term parasitemia negativization or long-term seroreversion, which do not clearly relate to cardiac pathogenesis and disease progression. Our findings suggest that antiparasitic treatment may impact disease progression and, to a lesser degree, mortality, even in those with mild cardiomyopathy. Therefore, it is critical to assess each patient individually for therapy, regardless of the stage of the disease, as some patients with early and minor cardiac alterations may still benefit from treatment.

This review has several limitations. There was significant heterogeneity between studies, as demonstrated by a high I^2 statistic. Differences in study designs, heterogeneous populations, varying follow-up durations, and the inclusion of studies with moderate to high risk of bias could distort our findings and misrepresent the effect of antiparasitic therapy. Additionally, the variation in outcome definitions and measurement methods among the studies presents a limitation. Another key issue is that while some studies used only BZN, others included both BZN and NFT (analyzed together), and the control groups varied between placebo and no treatment, which are not equivalent comparisons. Furthermore, several studies combined children and adults, raising concerns about whether the conclusions can be generalized across these different populations.

Another limitation is the use of RR as the effect size metric in retrospective cohort studies. While RR is typically used in prospective designs, we applied it in retrospective cohort studies as well, given the available data on the number of events and total patients in each group. However, this approach may introduce some bias, as odds ratios or rate ratios are often recommended for certain observational designs. That said, since we included only one cross-sectional study and excluded case–control studies, the use of RR becomes less problematic and, in fact, more suitable for integrating these different study designs. Critics may also highlight the methodological weaknesses in mixing randomized and observational studies due to inherent biases and confounders. Nonetheless, non-randomized studies provide the most comprehensive and relevant data currently available. The advantages of incorporating both types of studies in a meta-analysis may outweigh the disadvantages, suggesting that observational studies should not be excluded a priori.[45]

It is important to note that we performed subgroup analyses based not only on study type (RCTs, prospective, retrospective, and cross-sectional) but also on other factors, such as treatment type (BZN vs BZN or NFT), age groups, and publication type, among others. The benefit of antiparasitic therapy remained consistent across these various subgroups. Conducting large-scale, high-quality RCTs in Chagas disease is exceptionally challenging due to the intrinsic characteristics of the disease and logistical and economic constraints. Including abstracts alongside full papers could be seen as another limitation, but as long as the information in the abstracts is sufficient for analysis, their inclusion minimizes potential publication bias and ensures all available studies are considered.

In Chagas disease research, several widely claimed yet inadequately supported narratives dominate the literature. These include the urgent call for novel therapeutic agents, based on the assumption that existing drugs, BZN and NFT, are primarily effective only in the acute phase and pediatric populations, are associated with significant toxicity, and require prolonged treatment durations.[46] Another persistent belief emphasizes the need for a definitive gold-standard test or biomarker for early cure determination, driven by the prolonged persistence of seropositivity post-treatment and the limited reliability of parasitological and molecular assays in chronic cases.[47,48]

However, emerging data challenge these longstanding assertions, suggesting the need to recalibrate research and clinical priorities. Recent evidence supports the tolerability of BZN in chronic Chagas disease. Data from the largest RCT[36] showed that BZN when administered with close monitoring, required permanent discontinuation in only about 10% of cases due to adverse events, a rate comparable to that observed with the newer drug sacubitril/valsartan for treating heart failure from other etiologies.[49] Furthermore, a 30 to 60-day treatment regimen, albeit longer than many other infectious disease treatments, is feasible and justifiable given the chronic nature of Chagas disease and its severe consequences. Some incipient findings suggest that shorter protocol treatments with BZN were well tolerated and effective in adult patients with chronic Chagas disease.[50,51] Nevertheless, it is crucial to recognize that these studies focused solely on parasitological responses and did not evaluate long-term clinical outcomes.

The relentless pursuit of a definitive biomarker of cure warrants reconsideration. In chronic Chagas disease, the serological response to treatment can take decades to resolve, complicating efforts to establish a rapid, reliable marker of successful therapy. Parasitological assays, while valuable when positive, are limited by the low parasitemia in chronic infection, reducing their utility in confirming cure. Therefore, focusing on a single biomarker may divert resources from more impactful, immediate, but potentially beneficial interventions. Given that BZN and NFT have demonstrated efficacy and a manageable safety profile, the immediate focus should be expanding access to these treatments. It's crucial to develop standardized follow-up protocols to address the current gaps in treatment monitoring. This would ensure better patient outcomes and strengthen the conclusions drawn from ongoing and future research. Expanding drug availability through policy reforms, improving distribution systems, and moving these medications beyond governmental facilities to wider commercial availability will help reach a broader patient population.

The emphasis on developing new pharmacotherapies, though important, should not overshadow the immediate need to optimize current treatments. Developing new drugs is a lengthy and uncertain process. In contrast, maximizing the use of existing effective treatments offers a tangible opportunity to mitigate the burden of Chagas disease. This requires efforts to enhance drug availability, optimize treatment protocols, and implement robust public health strategies.

In conclusion, while searching for novel treatments and effective biomarkers of cure and disease progression with trypanocidal therapy remains important, there is an urgent need to adopt a pragmatic approach focused on effectively utilizing existing treatments. Their proven BZN and NFT efficacy—as demonstrated by this systematic review and meta-analysis—and their manageable safety profiles should call for more widely accessible patient treatments. Prioritizing this approach will address immediate therapeutic needs and lay a stronger foundation for future advancements in Chagas disease management. Realigning research and clinical strategies towards solutions that provide an immediate and significant impact on the patient population is imperative.

Contributors

ARJ: conceptualization, methodology, validation, formal analysis, investigaton, data curation, writing-original draft, writing-review & editing, visualization, supervision, project administration, AG: conceptualization, methodology, software, validation, resources, visualization, writing-review & editing, supervision, AS: investigation, data curation, writing-review & editing, RS: investigation, data curation, writing-review & editing, SS: investigation, data curation, writing-review & editing, NIAH: supervision, writing-review & editing, FMR: investigation, data curation, writing-review & editing, MFC: investigation, data curation, writing-review & editing, HMK: investigation, data curation, writing-review & editing, JS: investigation, data curation, writing-review & editing, SK: writing-review & editing, LAM: writing-review & editing, EAR: writing-review & editing, MC: writing-review & editing, PH: writing-review & editing, MEB: writing-review & editing, SP: writing–review & editing, CFP: supervision, writing-review & editing, JAMN: supervision, writing-review & editing, AFHM: conceptualization, methodology, software, validation, formal analysis, investigaton, data curation, writing-original draft, writing-review & editing, visualization, supervision, project administration.

Data sharing statement

The corresponding authors have full access to data in the study and had final responsibility for the decision to submit the manuscript for publication. The datasets generated and analyzed in the current study are available from the corresponding authors at reasonable request.

Declaration of interests

Maria Elena Bottazzi and Peter Hotez are part of a team of scientists advancing research toward the development of a therapeutic Chagas disease vaccine and are listed among the inventors on a Chagas disease vaccine patent submitted by Baylor College of Medicine. Dr. Andres F. Henao-Martinez received educational funds from F2G: Novel Therapeutics for Rare Fungal Infections; and support to attend 3ra Jornada Internacional de Enfermedades Infecciosas y Tropicales as a lecturer in Lima, Peru.

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Appendix. Supplementary data

Supplementary data related to this article can be found at https://doi.org/10.1016/j.eclinm.2024.102972.

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