



Project Management - WP1

Francesca Viero - PENTA

PediCAP Fifth General Assembly TC - 7th December 2020



This project is part of the EDCTP2 programme supported by the European Union under Grant Agreement RIA2017MC - 2023

WP1 activities

1.1 Set up and steering of governance bodies:



- Project Management Team
- General Assembly
- Core GA
- Ethics Advisor

1.1 Project coordination & 1.4 Quality assurance and risk management:



- Monitor and support activities and timelines
- WP calls
- Quality control of Deliverables

1.2 Technical and financial reporting:



- Internal reporting
- Periodic reporting to EDCTP

1.3 Contractual and Legal Management:



- Setting up First Project Amendment

WP1 activities

1.1 Set up and steering of governance bodies:



- Project Management Team (UCL, PENTA, SGUL): meets every 2 weeks
- General Assembly: meets every 3 months
- Core GA: members to be identified
- Ethics Advisor: invited to all calls and meetings

1.1 Project coordination &

1.4 Quality assurance and risk management:



- Monitor and support activities and timelines
- WP calls / ad hoc calls
- Quality control of Deliverables

Grant Agreement & Annexes as key reference document

Summary of project progress - WP2 Trial

Ms. Number	Milestone Title	Due date	Status
MS2.1	Trial infrastructure (CRFs, database) ready for recruitment	Nov 2020	Achieved
MS2.2	Trial open for recruitment in at least one country	Dec 2020	Achieved

Del. Number	Deliverable Title	Lead beneficiary	Due date	Status
D2.1	Trial Protocol	UCL	Dec 2019	Submitted
D2.2	Ethics advisor report Year 1	UCL	March 2020	Submitted
D2.3	Drug Procurement	PENTA	Oct 2020	Being prepared
D2.4	CRFs and Database	UCL	Nov 2020	Being prepared
D2.5	Incidental Findings Policy	UCL	Nov 2020	Being prepared
D2.6	Statistical Analysis Plan	UCL	Nov 2020	Being prepared
D2.7	TSC and DSMB Charters	UCL	Dec 2020	Being prepared
D2.8	Data management plan	UCL	Dec 2020	Being prepared
D2.9	MTAs and import/export licenses for shipment of samples	UCL	Dec 2020	To postpone
D2.10	First study subject approvals package	UCL	Dec 2020	Being prepared

Summary of Project Progress - Substudies (WP3, WP4, WP5)

<u>Ms. Number</u>	Milestone Title	Due date	Status
MS3.1	Ethical and regulatory approval of sub-study protocol (as part of main trial protocol) in at least one Sub-Saharan African country	Nov 2020	Achieved
MS3.2	Staff trained on PK substudies procedures in at least one contry	Dec 2020	To postpone
MS4.1	Develop survey to collect data on methods to detect respiratory pathogend, associated antibiotic resistance and their local prevalence	Jul 2019	Achieved
MS4.2	Clinical sites trained in microbiological sampling, processing and storage	March 2020	To postpone
MS5.1	IRB approval	Nov 2020	To postpone

<u>Del. Number</u>	Deliverable Title	Lead beneficiary	Due date	Status
D3.1	Weight-banded dosing table for trial	UCT	Dec 2019	Submitted
D3.2	PK sub-study protocol/Standard Operating Procedure	UCT	Dec 2019	To postpone

Summary of project progress - WP6 Capacity building and WP7 communication/networking

<u>Ms. Number</u>	Milestone Title	Due date	Status
MS6.1	Immediate training needs specific to the trial and individual study sites have been identified	Dec 2019	To postpone
MS6.2	First tools to meet knowledge gaps available	March 2020	To postpone
MS7.1	First meeting held by at least one national community advisory group	March 2020	Achieved
MS7.2	Training for communication and optimal antibiotic prescribing	March 2020	To postpone
MS7.3	Completion of stakeholder mapping	March 2020	Achieved
MS7.4	Key stakeholder meeting	Sept 2020	To postpone

<u>Del. Number</u>	Deliverable Title	Lead beneficiary	Due date	Status
D6.1	Online knowledge exchange hub	UOXF	Sept 2019	Submitted
D6.2	Assessment of baseline research capacity	UNZA/SOM	March 2020	To Postpone
D7.1	Project Website	PENTA	June 2019	Submitted
D7.2	Communications and educational material for training	SGUL	March 2020	Submitted
D7.3	Dissemination, Exploitation and Communications strategy	UZCHS	March 2020	To draft
D7.4	Information sheet written about the program for key stakeholders	UZCHS	March 2020	To draft

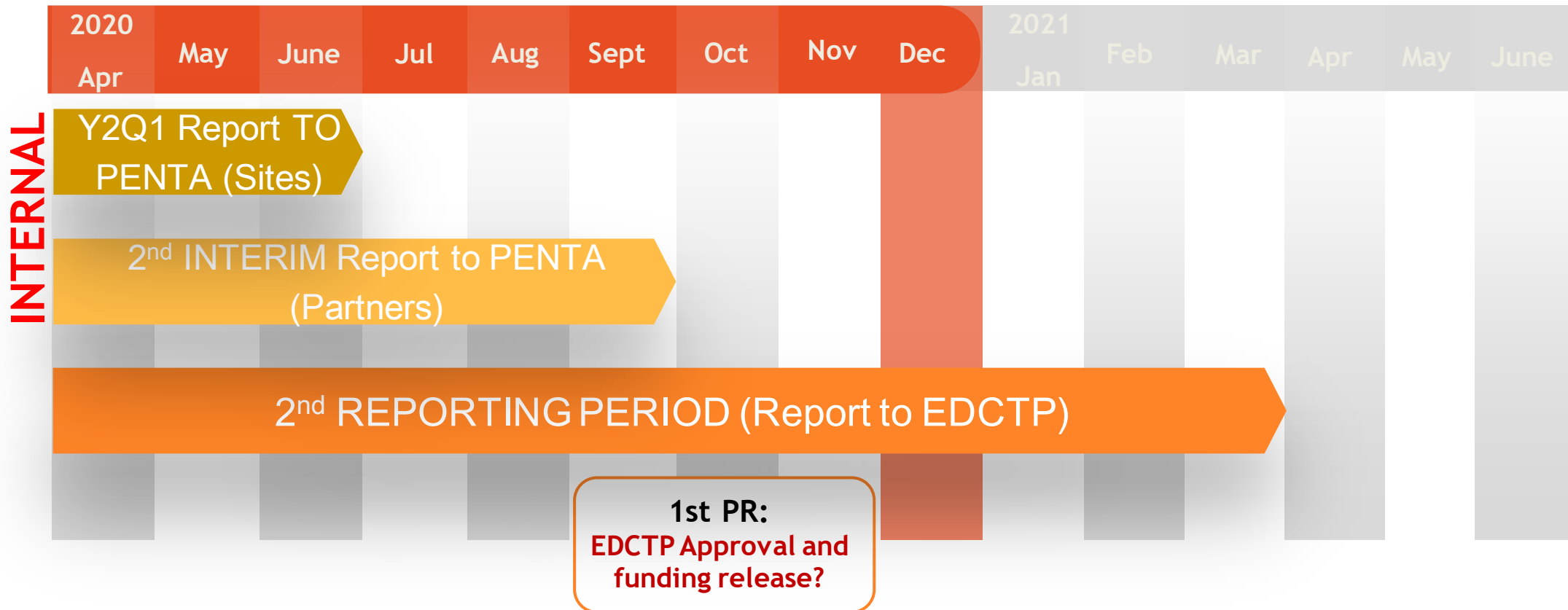
WP1 activities

1.2 Technical and financial reporting:



- Internal reporting
- Periodic reporting to EDCTP (*art.20 GA*)

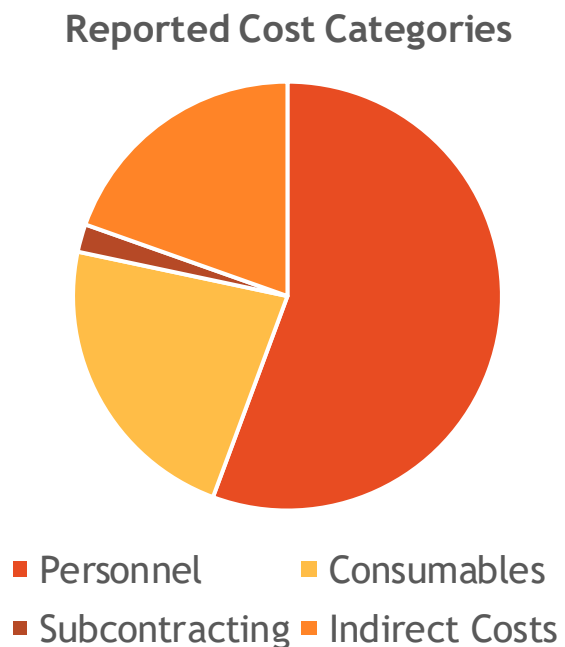
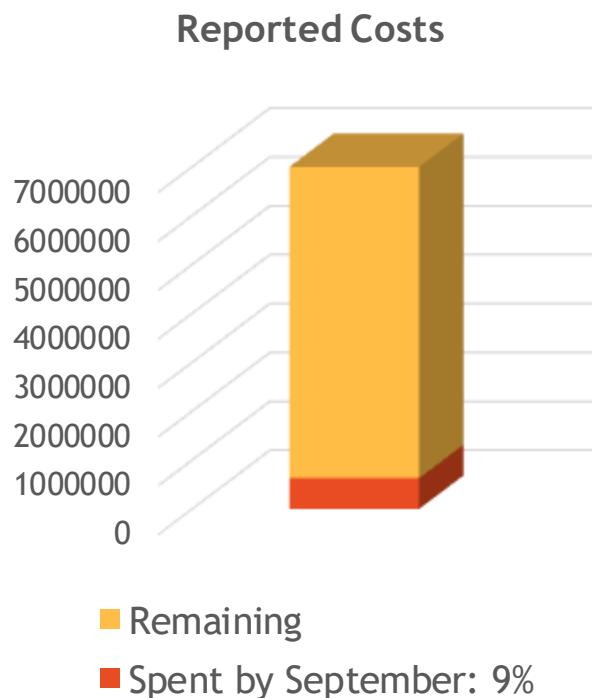
Task 1.2 - Technical and Financial Reporting 1/2



➤ **Financial management:** budget forecast for 2021

Task 1.2 - Technical and Financial Reporting 2/2

Expenditures by September 2020 (provisional)



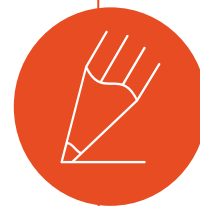
Recurrent inaccuracies:

- ▶ **Discrepancies** from original budget need to be justified (*Budget: Annex 2 to GA*)
- ▶ **WP allocation & cost categories**
- ▶ **Personnel costs:** actual time worked in the project & Person Months calculation (*chapt.3 GA + EDCTP Financial Guidelines*)

WP1 activities

1.3 Contractual and Legal Management:

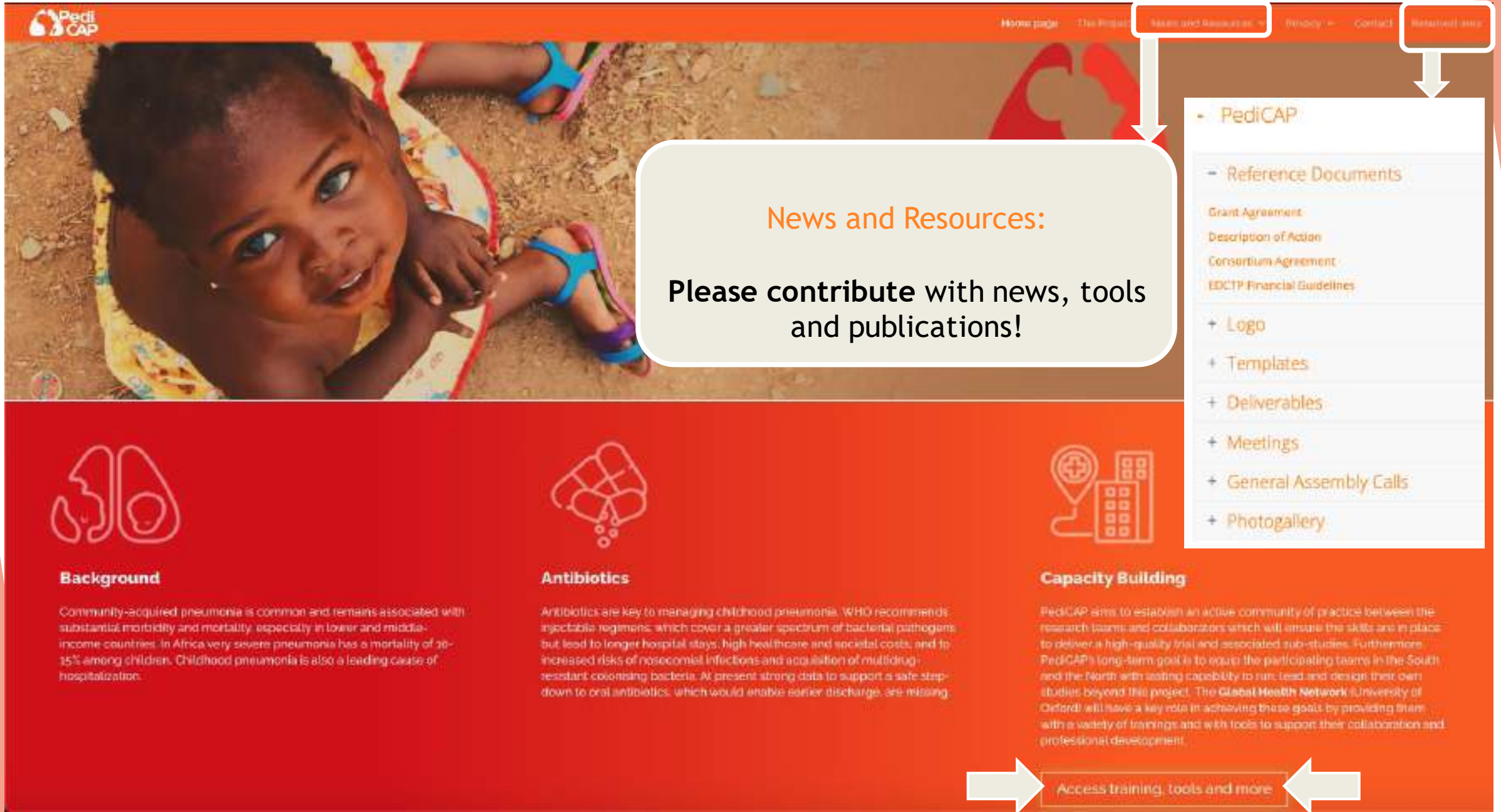
- Setting up First Project Amendment (**by January 2021?**)
 - Correcting timelines
 - Fixing budget categories



PediCAP Annual Consortium Meeting:

Provisional date in Fall 2020?

WP7 - PediCAP Website: www.projectpedicap.org



The image shows a screenshot of the PediCAP website. At the top, there is a navigation bar with links for 'Home page', 'The Project', 'News and Resources', 'Privacy', 'Contact', and 'Retained area'. Below the navigation bar is a large image of a young child sitting on the ground. A callout box with a white background and a grey border is overlaid on the image, containing the text: 'News and Resources: Please contribute with news, tools and publications!'. To the right of the callout box, a dropdown menu is open, showing a list of links: 'PediCAP', 'Reference Documents', 'Grant Agreement', 'Description of Action', 'Consortium Agreement', 'EDCTP Financial Guidelines', 'Logo', 'Templates', 'Deliverables', 'Meetings', 'General Assembly Calls', and 'Photogallery'. Below the image, there are three columns of content, each with an icon and a title: 'Background' (with a brain icon), 'Antibiotics' (with a pill icon), and 'Capacity Building' (with a building icon). At the bottom of the page, there is a button labeled 'Access training, tools and more' with two arrows pointing towards it.

News and Resources:
Please contribute with news, tools
and publications!

- PediCAP
- Reference Documents
 - Grant Agreement
 - Description of Action
 - Consortium Agreement
 - EDCTP Financial Guidelines
- + Logo
- + Templates
- + Deliverables
- + Meetings
- + General Assembly Calls
- + Photogallery

Background

Community-acquired pneumonia is common and remains associated with substantial morbidity and mortality, especially in lower and middle-income countries. In Africa very severe pneumonia has a mortality of 30-15% among children. Childhood pneumonia is also a leading cause of hospitalization.

Antibiotics

Antibiotics are key to managing childhood pneumonia. WHO recommends injectable regimens, which cover a greater spectrum of bacterial pathogens, but lead to longer hospital stays, high healthcare and societal costs, and to increased risks of nosocomial infections and acquisition of multidrug-resistant colonising bacteria. At present strong data to support a safe step-down to oral antibiotics, which would enable earlier discharge, are missing.

Capacity Building

PediCAP aims to establish an active community of practice between the research teams and collaborators which will ensure the skills are in place to deliver a high-quality trial and associated sub-studies. Furthermore, PediCAP's long-term goal is to equip the participating teams in the South and the North with lasting capability to run, lead and design their own studies beyond this project. The **Global Health Network** (University of Oxford) will have a key role in achieving these goals by providing them with a variety of trainings and with tools to support their collaboration and professional development.

Access training, tools and more



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Trial Set-up and Management

MRC CTU at UCL

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Protocol v3.0

- ▶ This has now been finalised and sent to sites.
- ▶ Sites are in the process of submission to ethics and regulatory bodies.

Trial Set-up

- ▶ We are open!
- ▶ v1.0 of the database is now live. Continuing straight on with phase 2 development.
- ▶ Plan to perform local monitor training early 2021.

Sites

- ▶ Uganda - Opened on 04-Dec-2020.
- ▶ Zambia – SIV conducted 02-Oct-2020. Hoping to open as soon as possible. Slight delay with getting IMP out to the site as courier was unable to find a flight to Zambia. This is now on it's way.
- ▶ South Africa – plan to conduct SIV in January and open early 2021.
- ▶ Zimbabwe – plan to conduct SIV in January and open early 2021.



Using the SureScreen CRP Test

- Dr Julia Bielicki -

- St George's University of London -

with thanks to the Paediatric Study Centre Team at the University of Basel Children's Hospital



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Preparation - materials



Hospital/standard supplies: Skin disinfectant, fingerprick (smallest lancet), plaster, pads



Provided by SureScreen: Test cassette, Dropper, Buffer tube

Setting up



Unpack test cassette and place on clean and level surface



Take out one disposable pipette – make sure not to bend/break pipette tip



Unscrew green AND white top of buffer tube and place on clean and level surface



Clean patient's finger with alcohol swab



Prepare fingerprick lancet



Perform fingerprick

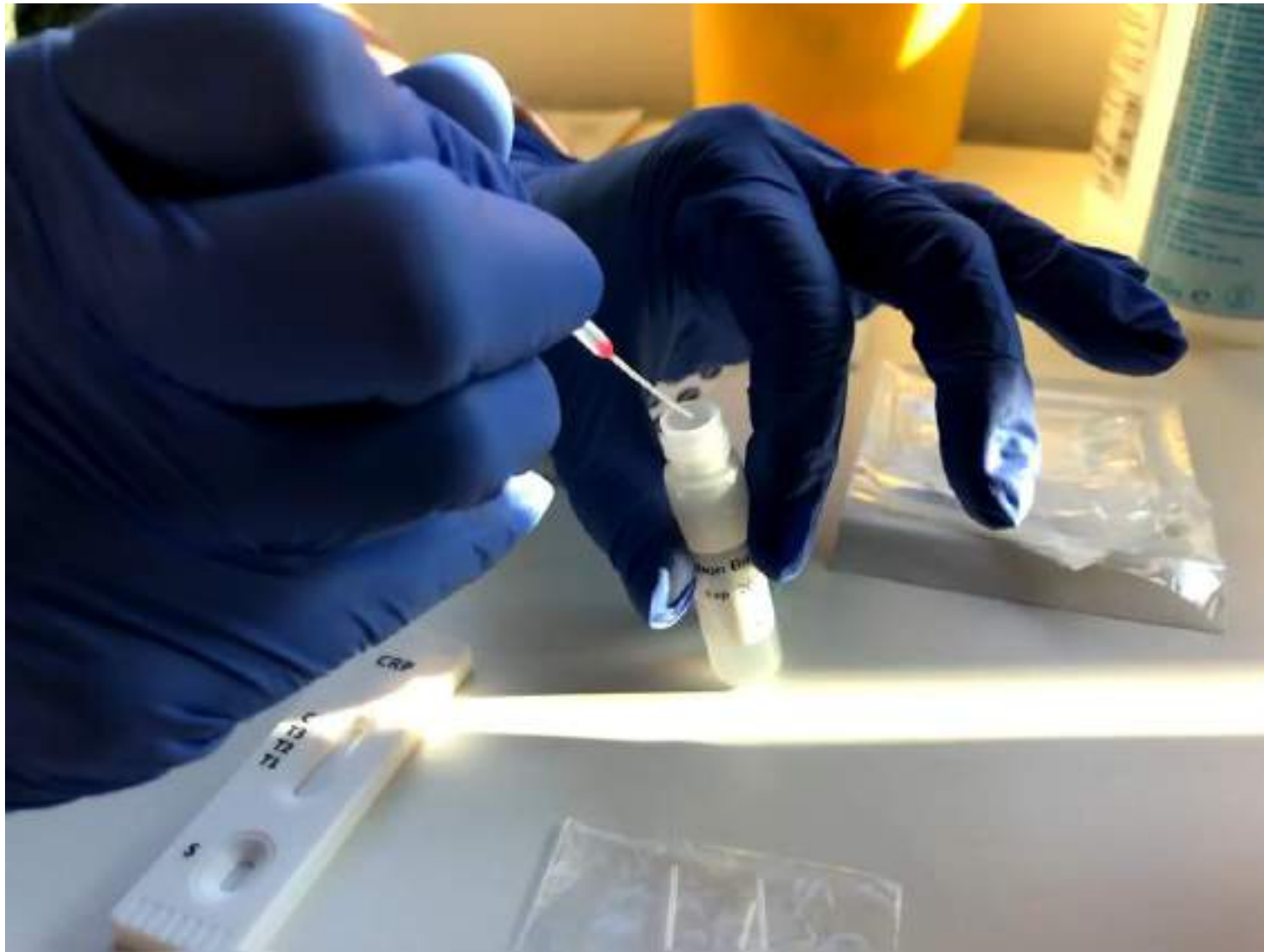


Wipe away first drop of blood
with dry swab



Collect subsequent drop of blood with pipette – SLOWLY!

Pipette tip must be filled.



Drip complete sample from pipette into prepared buffer tube



Put screw top on buffer tube
and GENTLY invert 4-5 times



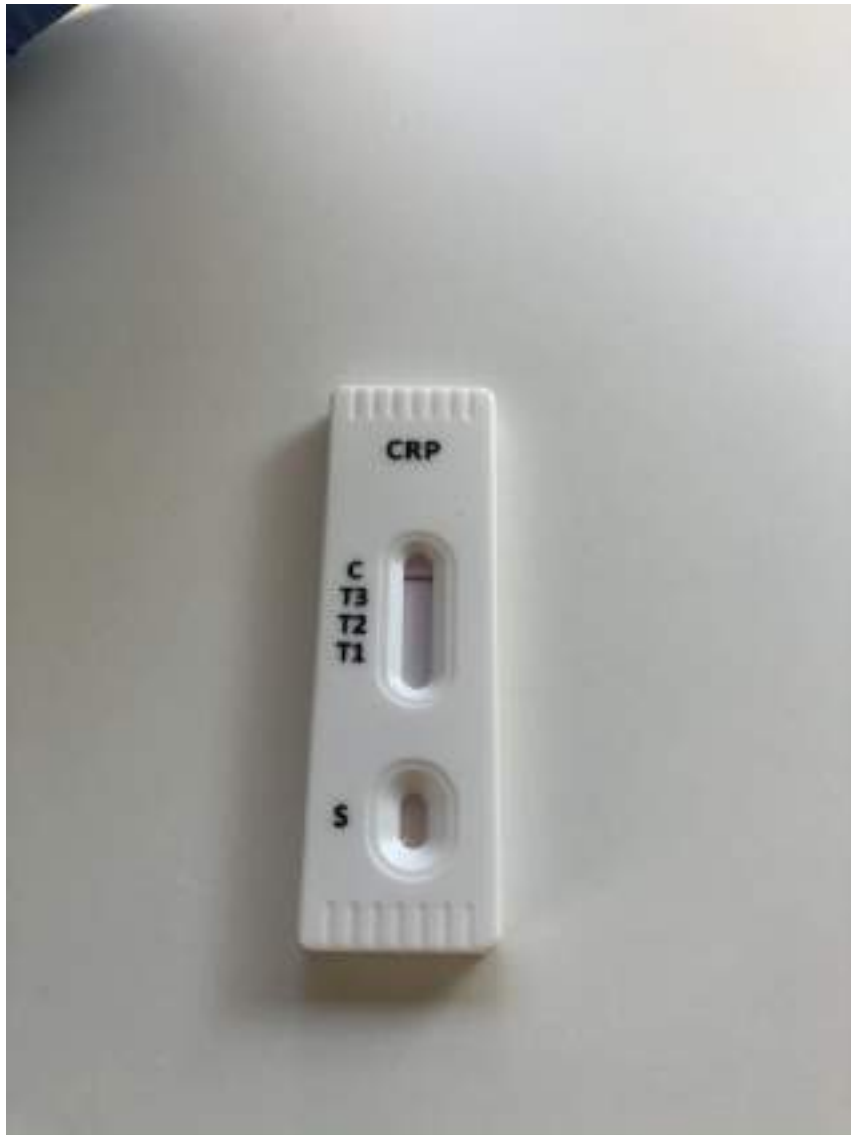
Unscrew white top from buffer tube



Use buffer tube to apply
THREE drops into cassette well



Three drops...



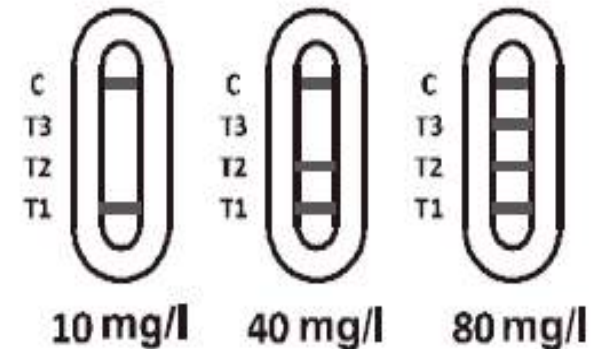
Read test result at 5-8 minutes
– set a timer.

This one is negative 😊

Positive Test Result

- ▶ All positive results mean that the patient meets the eligibility criterion for CRP result.
- ▶ One colour line appears in the control region (C)
- ▶ And at least one colour line appears in the test region (T)

Test line (T)	Semi quantitative result	Eligibility
Only T1 appears	CRP level is 10mg/L at least	Potentially eligible
Only T1 and T2 appear	CRP level is 40mg/L at least	Potentially eligible
T1, T2 and T3 appear	CRP level is above 80mg/L	Potentially eligible



Negative Test Result

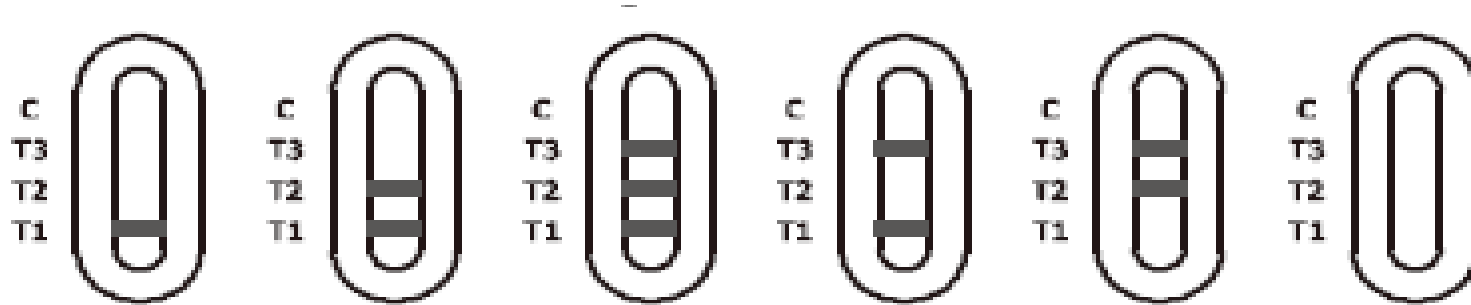
- ▶ A negative result means the patient is not eligible for PediCAP.
- ▶ One colour line appears in the control region (C).
- ▶ No apparent purple line appears in the test region (T).

Test line (T)	Semi quantitative result	Eligibility
No line	CRP level is lower than 10mg/L	Not eligible



Invalid Test Result

- ▶ There is no result and therefore eligibility cannot be confirmed.
- ▶ C line fails to appear.



- ▶ An invalid result is most likely due to insufficient specimen volume or incorrect procedural techniques.
- ▶ Review the procedure and repeat the test with a new test cassette.
- ▶ If the problem persists, discontinue using the test kit immediately and contact MRC CTU.



Dissolving the IMP

- with thanks to the Study Team from Uganda!!



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Co-amoxiclav – 5 tablets.

FORMULATION	WEIGHT BAND	# TABLETS AM	# TABLETS PM	# TABLETS DAILY	DAILY DOSE (MG)
Amoxicillin (250mg tablets)	3 - <6kg	1	1	2	500
	6 - <10kg	2	1	3	750
	10 - <14kg	2	2	4	1000
	14 - <20kg	3	3	6	1500
	20 - <25kg	4	4	8	2100
	25 - <35kg	5	5	10	2500
Co-amoxiclav 7:1 (200/28.5mg tablets)	3 - <6kg	1	1	2	400/57
	6 - <10kg	2	2	4	800/114
	10 - <14kg	3	2	5	1000/142.5
	14 - <20kg	4	4	8	1600/228
	20 - <25kg	5	5	10	2000/285
	25 - <35kg	6	6	12	2400/342



Durban site

Anne Derache - AHRI (Durban)

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Durban site

- ▶ Protocol and ICF amendment submitted to Wits HREC (David)
- ▶ Participants documents translated into isiZulu
- ▶ SLA with Enhancing Care Foundation to be finalised before the end of the year
- ▶ Procurement for medical equipment + swabs done
- ▶ Recruitment process for research nurse and medical doctor ongoing > team should be in place by January

Outstanding

- SAHPRA submission – to be done before the end of the year
- SLA with Site monitor – pending draft
- AHRI shut down – December 18th to January 5th



Presentation Title

Veronica Mulenga - UNIVERSITY TEACHING HOSPITAL- CHILDREN'S HOSPITAL,
LUSAKA, ZAMBIA

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UTH-ZAMBIA

- ▶ Ethics and Regulatory approvals
 - ▶ Protocol version 2.0 - Local ethics, Drug regulatory and National ethics approvals obtained.
 - ▶ Submission of amended protocol 3.0 and PIS ver 4.0 to be done week starting 14th December, waiting for translated versions of short patient Information leaflet.
- ▶ Facility readiness: Staff identified, contracts being prepared.
 - ▶ SIV virtual training took place 2nd October 2020 ,12 staff members trained via zoom.
 - ▶ CRFs version 1.0 received 26TH Nov 2020
 - ▶ Pedi CAP A MOP and CRF completion guide- received 26th Nov 2020- staff to go through it
 - ▶ Drug import permit obtained-27th OCT 2020 forwarded to MRC, Drug shipment in process.

Pending: contract with trial monitor

Training of data personnel, Arrival of trial drug, refresher training and commencement of recruitment January 2021.

Title

- ▶ *Please, briefly list any major achievement / Deliverable achieved / Milestone met since April 2020.*
- ▶ *Please, summarize the upcoming steps for the next few months and their realistic timelines.*
- ▶ ***For Microbiology, PK, HEA:** please, provide an updated timeline of your whole substudy including start/end, analysis and any major intermediate step.*
- ▶ *Please mention any PediCAP-related publication or dissemination activity you engaged in so far (e.g. presenting your work in PediCAP at a conference, posters, webinars, ...)*



PK Sub-study

Roeland Wasmann & Paolo Denti - UCT, South Africa

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Deliverables

- ▶ 3.1 Weight-banded dosing table for trial
 - ▶ Completed
- ▶ 3.2 PK sub-study protocol/Standard Operating Procedure
 - ▶ Draft MOP is finished, and will be send to the sites today for feedback

PK sampling schedule

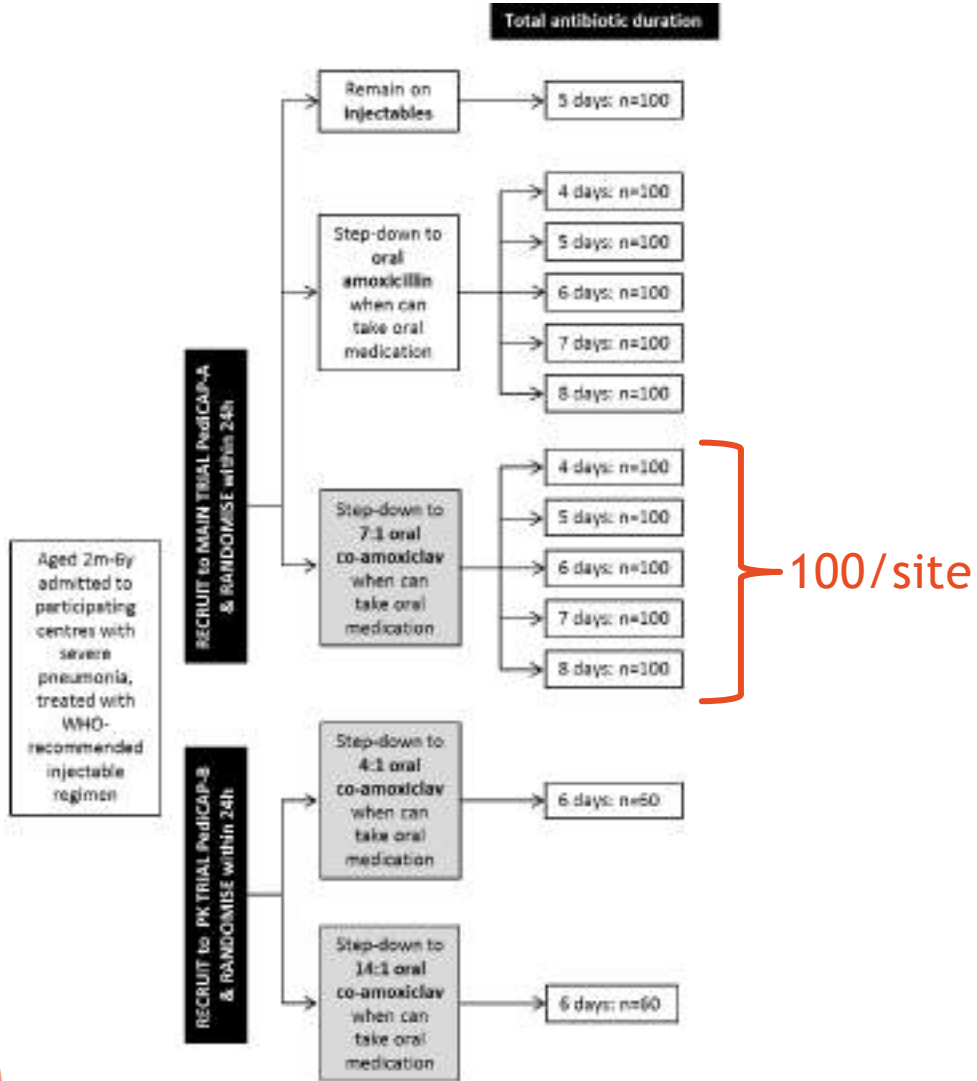
Time relative to morning drug intake ^a	Procedure	Details
-1 hr	Confirm participation PK Sub-Study	
	Apply EMLA cream	
-15 mins	Insert cannula	
0 hr	Take pre-dose PK sample (PK 1)	2 mL, K2 EDTA tube 
	Administer study drug	
	Administer breakfast ^b	
1 hr	Take 2 nd PK sample (PK 2) ^c	2 mL, K2 EDTA tube 
2 hr	Take 3 rd PK sample (PK 3) ^c	2 mL, K2 EDTA tube 
3 hr	Take 4 th PK sample (PK 4) ^c	2 mL, K2 EDTA tube 
6 hr	Take 5 th PK sample (PK 5)	2 mL, K2 EDTA tube 
	Remove cannula	
	Evaluation by study doctor	
	PK Sub-Study completed	

c. Less samples are drawn for children below 5 kg.

- Children between 4 and 5 kg skip 1 of the PK samples
- Children below 4 kg skip 2 of the PK samples

Personal on site can choose which sample to skip. They can choose to skip the 1 h (PK2), 2 h (PK3), or 3h (PK4) sample. The first (PK1, predose) and the last (PK5, 6h after dose) sample must ALWAYS be taken.

PediCAP-A - Enrollment in PK sub-study



► Recruitment of children in PK sub-study possible if:

1. Child participates in PediCAP-A
2. Child is randomized to Co-amoxiclav arm

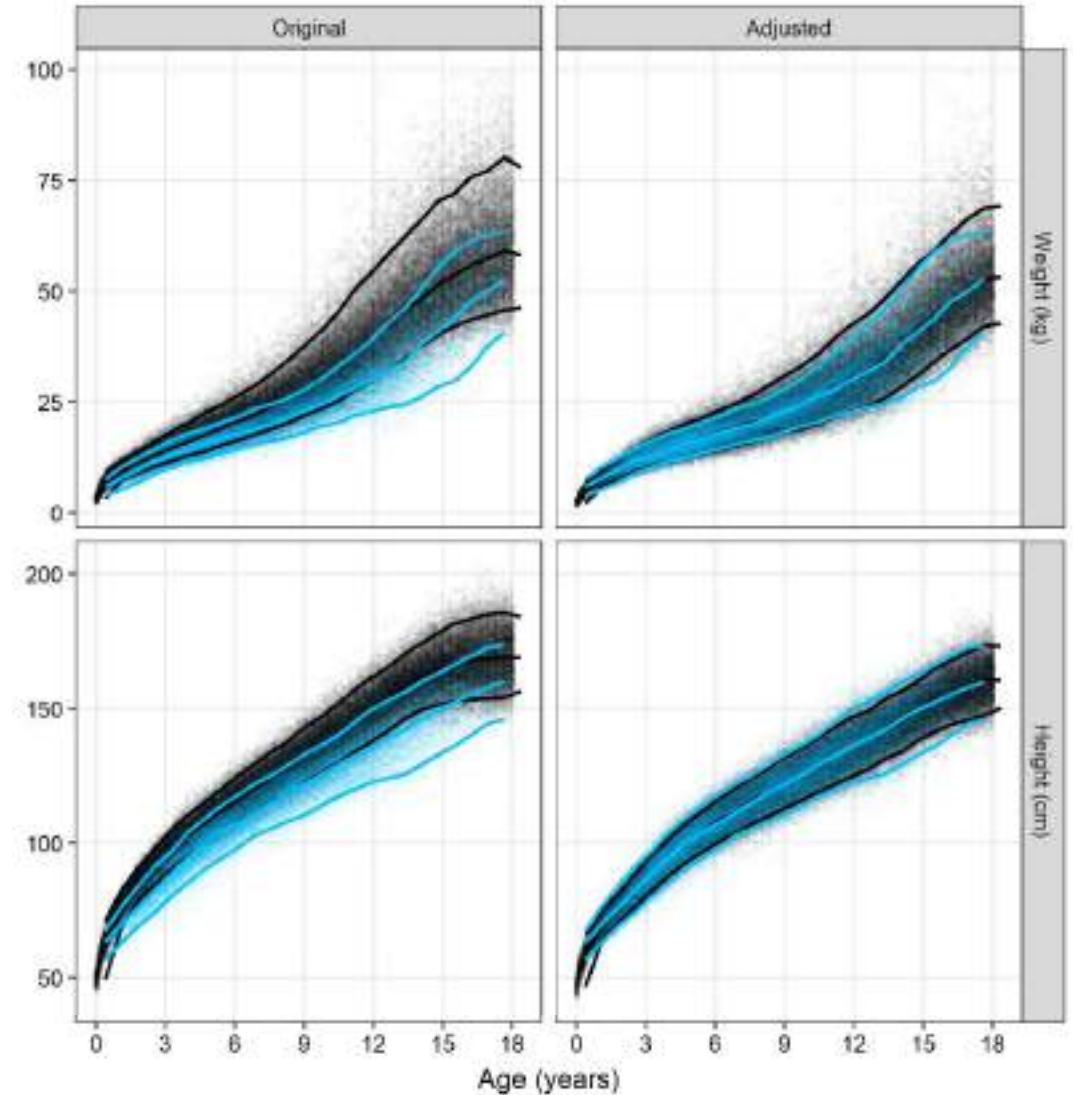
► What is the percentage of children that will participate?

- Considering they do participate in the main trial
- That they must stay an extra day in the hospital
 - Considering COVID

Dissemination

▶ Manuscript

- ▶ *Constructing a representative in-silico population for pediatric simulations: application to HIV positive African children*
- ▶ RE Wasmann, EM Svensson, AS Walker, MN Clements, P Denti
- ▶ British Journal of Clinical Pharmacology
 - ▶ Submitted: June 29, 2020
 - ▶ Accepted: November 30, 2020





WP4 MICROBIOLOGY SUB-STUDY

Surbhi Malhotra-Kumar - UNIVERSITY OF ANTWERP

Tomislav Kostyanev - UNIVERSITY OF ANTWERP

Juan Pablo Rodriguez-Ruiz - UNIVERSITY OF ANTWERP

Christine Lammens - UNIVERSITY OF ANTWERP

VICTOR MUSIIME - MAKERERE UNIVERSITY

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Microbiology update

▶ **Achievements:**

- ▶ *Laboratory manual - close-to-final draft*

▶ **Next steps:**

- ▶ *Send out laboratory manual to study team for review and finalize it - December 2020*
- ▶ *Biobank set-up: Some information regarding the main study is required. 2-3 months needed (database, labels, kit preparation and shipping)*
- ▶ *Summer school postponed to 2022*

▶ **Microbiology sub-study:**

- ▶ **Start:** *April 2021, depending on biobank set-up and site familiarity with protocol*
- ▶ **End:** *Depending on enrolment speed*
- ▶ **Analysis:** *As soon as first shipments are received*
 - ▶ *DNA extraction*
 - ▶ *Sequencing*
 - ▶ *Bioinformatic analysis*
 - ▶ *Result dissemination*



Work Package 5 Health Economic Analysis

Günther Fink; Gillian Levine - Swiss TPH
Susan Cleary; Lucy Cunnama - University of Capetown

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Health Economic Analysis Update

- ▶ Deliverables since April 2020: Not applicable
- ▶ Next steps:
 - ▶ Review pilot data to assess validity/comprehension of items
- ▶ Timeline: No required revisions projected
- ▶ *Analysis of cost and consumption of amoxicillin and co-amoxiclav: ongoing*
- ▶ *Systematic review of cost effectiveness analysis methods: ongoing*
- ▶ *UCT Health Research Ethics Committee application: planned for January 2021*



WP6 Update

Trudie Lang - The Global Health Network

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Ongoing WP6 activities

▶ **Development of training (M6.1/M6.2)**

- ▶ *General training available through the PediCAP knowledge hub: pedicap.tghn.org*
- ▶ *Study-specific e-learning to be released January/February 2021 (protocol training and child pneumonia training)*
- ▶ *Development of site training to be assessed as sites recruit*

▶ **Establishing the Professional Development Scheme (M6.3/D6.2)**

- ▶ *A toolkit has been development to support enrolment into the PDS*
- ▶ *WP6 are engaging site coordinators to introduce teams to the PDS and enrol*

▶ **Linking study sites with regional initiatives (M6.5)**

- ▶ *The Global Health Network with the EDCTP NoE, PANDORA and ALERRT have delivered a series of skills-based workshop opportunities which are open to PediCAP teams. This will continue through 2021.*

Next steps through 2021

- ▶ Introduce sites to WP6 and The Global Health Network as teams are recruited
- ▶ Initiate working groups across PediCAP sites
- ▶ Enrol teams in the Professional Development Scheme
- ▶ Assess training and development needs and develop training and tools to meet these
- ▶ Initiate PediCAP skills-sharing workshops with the EDCTP NoE, ALERRT and PANDORA



Presentation Title

Hilda angela Mujuru- UZCRC

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Title

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- ▶ *Please mention any PediCAP-related publication or dissemination activity you engaged in so far (e.g. presenting your work in PediCAP at a conference, posters, webinars, ...)*

▶ D7.3 – Dissemination, Exploitation and Communications Strategy

Community Advisory Groups

- ▶ UZCRC – formed and met twice now
- ▶ Uganda – formed and met
- ▶ Zambia – work in progress

Information To Stakeholders

Submitted to Penta

Ready for sharing

Initial plan- sharing with Paediatricians and MOHCC

▶ Thank you