Agenda

- Network structure
- Network capacity
- Clinical trials
- Efforts to develop rapid clinical response to EID
- Collaboration with other networks
- Sustainability
- Opportunities for international actions
PREPARE Platform for European Preparedness Against (Re-)emerging Epidemics

2014-2019

Partners:
Academia, clinical networks, industry societies

Coordinator:
Herman Goossens (University of Antwerp)

Deputy Coordinator:
Menno de Jong (Academic Medical Center Amsterdam)

Our mission
To establish PREPARE as the European clinical research framework

- for harmonised large-scale clinical research studies on infectious diseases
- prepared to rapidly respond to any severe infectious disease outbreak
- providing real-time evidence for clinical management of patients and for informing public health responses
Overall architecture

PATHOS
European platform for patient oriented PATHOgenesis Studies

PRACTICE
Platform for Harmonised and Rapid response Clinical Trials in Infectious diseases in Children and adults in Europe

PREDICT
European Platform for REsearch and support on Diagnostics for Infectious disease Clinical Trials

CRISP: Clinical Research Information Sharing Platform

CREATE: Clinical Research Education And Training in Europe
Agenda

- Network structure
- Network capacity
- Clinical trials
- Efforts to develop rapid clinical response to EID
- Collaboration with other networks
- Sustainability
- Opportunities for international actions
Primary Care Network:
Build on GRACE FP6 project

> 600 general practitioners
in 19 European countries
Hospital Care Network:
Build on IMI – COMBACTE - ND4BB project and other networks

> 800 hospitals
> 40 European countries
Agenda

- Network structure
- Network capacity
- Clinical trials
- Efforts to develop rapid clinical response to EID
- Collaboration with other networks
- Sustainability
- Opportunities for international actions
Clinical trials in PREPARE

Three observational studies: Multi-centre EuRopean study of MAjor Infectious Disease Syndromes (MERMAIDS) in primary care and hospitalized adult and pediatric patients, comprising:
- Sepsis-like syndrome (SLS) in infants and Acute respiratory infection (ARI) in children (PED-MERMAIDS)
- Acute Respiratory Infections in Adults (ARI)
- Arboviral compatible febrile illness

Two Adaptive platform design studies:
- European multi-centre double-blinded randomised placebo-controlled Interventional Trial on Influenza-Like-Illness (ILI) in Primary Care (ALIC4E)

- Randomized, Embedded, Multifactorial Adaptive Platform trial for Community-Acquired Pneumonia (REMAP-CAP)
Agenda

- Network structure
- Network capacity
- Clinical trials
- Efforts to develop rapid clinical response to EID
- Collaboration with other networks
- Sustainability
- Opportunities for international actions
Concept

European diagnostic laboratory support

Pre-approved protocols

European multi-center clinical trials, adding new arms to adaptive trial design as and when needed

Fit-for-purpose patient oriented pathogenesis studies

Outbreak Preparedness

Inter-epidemic research

Outbreak Response
Interepidemic Research: adaptive platform design

Bayesian Adaptive Clinical Trial design

Novel and innovative trial design and statistical methods to make maximum use of available sample size, identify sub-group effects, rigorously address multiple questions, evaluate interactions and throughout the platform treat the patients as effectively as possible.

• Provides the flexibility to add and drop arms over time.
• Generates estimates of treatment effect depending on different subsets of patients, different healthcare settings and different adjunct therapies.
• Provides the flexibility to substitute new arms, prepared in advance, in the event of pandemic respiratory tract infections.
Outbreak Preparedness and Response

**Inter-Epidemic Mode**

Standing committee that convenes when the Coordinator is contacted in relation to a new specific ID outbreak to discuss the appropriate Outbreak Mode (1, 2 or 3)

**Composition:** Herman Goossens (Chair), Menno de Jong, Marion Koopmans, Peter Horby

---

**Outbreak Preparation Mode**

**Outbreak Advice Committee (OAC):**
Ad-hoc PREPARE expert committee

---

**Outbreak Research Preparation Mode**

**Outbreak Preparation Committee (OPC):**
- PREPARE Executive Board;
- ad-hoc PREPARE experts;

**Outbreak Mobilisation Plan:**
Planning and implementation of preparatory work necessary to achieve operational readiness to initiate clinical research response to specific ID outbreak if and when needed.

---

**Outbreak Research Mobilisation Mode**

**Outbreak Preparation Committee (OPC):**
- PREPARE Executive Board;
- ad-hoc PREPARE experts;

---

**Outbreak Research Response Mode**

**Outbreak Preparation Committee (OPC):**
- PREPARE Executive Board;
- ad-hoc PREPARE experts;
- Ad-hoc external experts if necessary;

**Outbreak Response Plan:**
Planning and implementation of clinical research response to specific ID outbreak, building on the generic clinical research activities and preparedness activities in PREPARE.

---

**Outbreak Mobilisation Plan:**
OUTBREAK MOBILISATION PLANNING AND IMPLEMENTATION

GA decision, EC (tacit) approval

---

**Outbreak Response Plan:**
OUTBREAK RESPONSE PLANNING AND IMPLEMENTATION

GA decision, EC (tacit) approval

---

**Outbreak Mode Committee (OMC):**
Standing committee that convenes when the Coordinator is contacted in relation to a new specific ID outbreak to discuss the appropriate Outbreak Mode (1, 2 or 3)

**Composition:** Herman Goossens (Chair), Menno de Jong, Marion Koopmans, Peter Horby
PREPARE Response to ZIKV Threat

- **Outbreak Mode Committee meeting (3/12/2015):**
  - Develop maternal and neonate ZIKV eCRFs, in collaboration with ISARIC
  - Adapt PREPARE ARBO virus clinical protocol to capture ZIKV cases
  - Establish link with ECDC
  - Expand OMC

- **Outbreak Mode Committee meeting (10/2/2016):**
  - Participation of EC and ECDC
  - Send out ECDC questionnaire on European ZIKV diagnostic capacity to over 400 COMBACTE LAB-Net and PREPARE laboratory contacts
  - Link to other initiatives and networks
A PREPARE Coordinator convenes Outbreak Mode Committee (OMC) meeting to perform an assessment of the appropriate outbreak mode.

OMC advice

0 1 2 3

B PREPARE Coordinator convenes Extraordinary GA conform article 6.2.2.9 of the CA to vote on the decision as advised by the OMC.

GA Decision

0 1 2 3

C PREPARE Coordinator informs European Commission, DG RTD of the GA decision.

No response from EC within 48 hours/
EC agrees with GA decision

PREPARE Mode

0 1 2 3

PREPARE Coordinator is contacted (by European Commission, DG RTD or PREPARE partner) in relation to possible response to a specific ID Outbreak.
Collaboration with Public Health England for validating the transition from “Interepidemic Mode” to “Outbreak Clinical Research Response mode”

- **Period:** 1/2/2017 – 31/1/2018
- **Objectives:**
  - To define a general model and principle for the management of the response phase
  - To consider all activities associated with implementation of the response mode
  - To produce a response plan
  - To bear in mind the interoperability with other networks when developing this plan
PREPARE - PHE Clinical Preparedness Plan

- **Work programme:**
  - Work package 1: Workshop to introduce the outbreak research response mode and consider the implications.
  - Work package 2: Desktop Exercise(s) to practice the switch from normal business to outbreak response mode
  - Work package 3: Command post exercise (optional)
  - Work package 4: Emergency planning support to the PREPARE consortium

- **Final deliverable:**
  - An operational clinical response mode plan, including a plan for updating to provide sustainability
Agenda

- Network structure
- Network capacity
- Clinical trials
- Efforts to develop rapid clinical response to EID
- Collaboration with other networks
- Sustainability
- Opportunities for international actions
WP1: EARL tools used globally

- **Public / Patient / Clinician / Research Acceptability**
  - PUBLIC- 4 focus groups and survey of >8,000 members of public in European, ANZ and Canada- assessing attitudes to pandemic research, consent models, risk : benefit with comparative effectiveness designs and novel interventions
  - Consensus conferences defining researcher priority of pandemic research

- **Barriers and Solutions**
  - Ethical approvals – tracking timelines and accessing country level barriers
  - Contract approvals – Assessing barriers to delayed contracting

- **Improving** PREPARE conduct
  - Embedded barriers studies in ALICE and REMAP CAP, constantly sharpening the saw
  - Patient follow up methodology studies
WP5: Global Adaptive Trial

- **International Protocol:**
  - Protocol has been revised in order to create a modular protocol.
  - Enables us to use globally with appendices describing the interventions and regional requirements.
  - Integrated eCRFs, data dictionary and tables

- **Global and Regional Governance Structure:**
  - **International Trial Steering Committee (ITSC):** responsible changes in trial designs, invite/accept networks for participation, reporting trial results, activating outbreak mode if applicable.
  - **Regional Management Committees (RMCs):** responsible for the conduct of the trial within their region.
  - **Domain specific working group (DSWG) for antibiotics, steroids, ventilation**
  - **International Statistics interest group (ISIG)**
  - New international name and logo.
REMAP-CAP goes global in 2017

- PREPARE (EU FP7 funded project)
  - Marc Bonten (WP5 Lead)
  - EU REMAP-CAP
- ANZICS CTG (Funded by NHMRC of Australia and NRC of New Zealand)
  - Steve Webb (Australia) and Colin McArthur (New Zealand)
  - ANZ REMAP-CAP
- **Canadian Institutes of Health Research**
  - John Marshall
  - Application for partnered funding CAPTIC (Canadian Adaptive Platform Trial in Intensive Care)
Agenda

- Network structure
- Network capacity
- Clinical trials
- Efforts to develop rapid clinical response to EID
- Collaboration with other networks
- Sustainability
- Opportunities for international actions
Merge AMR and EID

**Antimicrobial resistance**
- Fast completion of clinical studies;
- Largest need in bacterial infections (antibiotic resistance)

Similar non-scientific barriers
- Overlapping stakeholders

Need for operational high quality large-scale clinical research infrastructure with European coverage

**Emerging Infectious Diseases**
- Rapid initiation and completion of clinical studies;
- Mostly virus infections

Overlapping stakeholders

Platform forE European Preparedness Against (Re-)Emerging Infectious Diseases (PREPARE)
High-level Roadmap

I. HIGH LEVEL DESIGN
   - High Level design completed 1/11

II. DETAILED DESIGN
   - Detailed Design completed 31/12

III. CONSTRUCTION

IV. IMPLEMENTATION
   - 1/1 ECRAID full launch

Strategic priorities:
- Stakeholder engagement and commitment
- Secure sufficient stable sources of funding
- Embedment of ECRAID in international relevant initiatives
Agenda

- Network structure
- Network capacity
- Clinical trials
- Efforts to develop rapid clinical response to EID
- Collaboration with other networks
- Sustainability
- Opportunities for international actions
Opportunities for international actions: Examples of what PREPARE could offer

- PREPARE Outbreak Mode Response concept
- PREPARE – PHE initiative developing an operational clinical response mode plan in 2017-2018 for Europe
- Tools developed in WP1 (barriers and solutions for contractual and EARL challenges) – Final workshop planned end 2017
- Global adaptive trial in severe CAP – Low cost to add more ICUs (per patient payment)
Many thanks