Breakout Session #5: Retinopathy of Prematurity

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International Neonatal Consortium

EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

CRITICAL PATH INSTITUTE
a decade of excellence

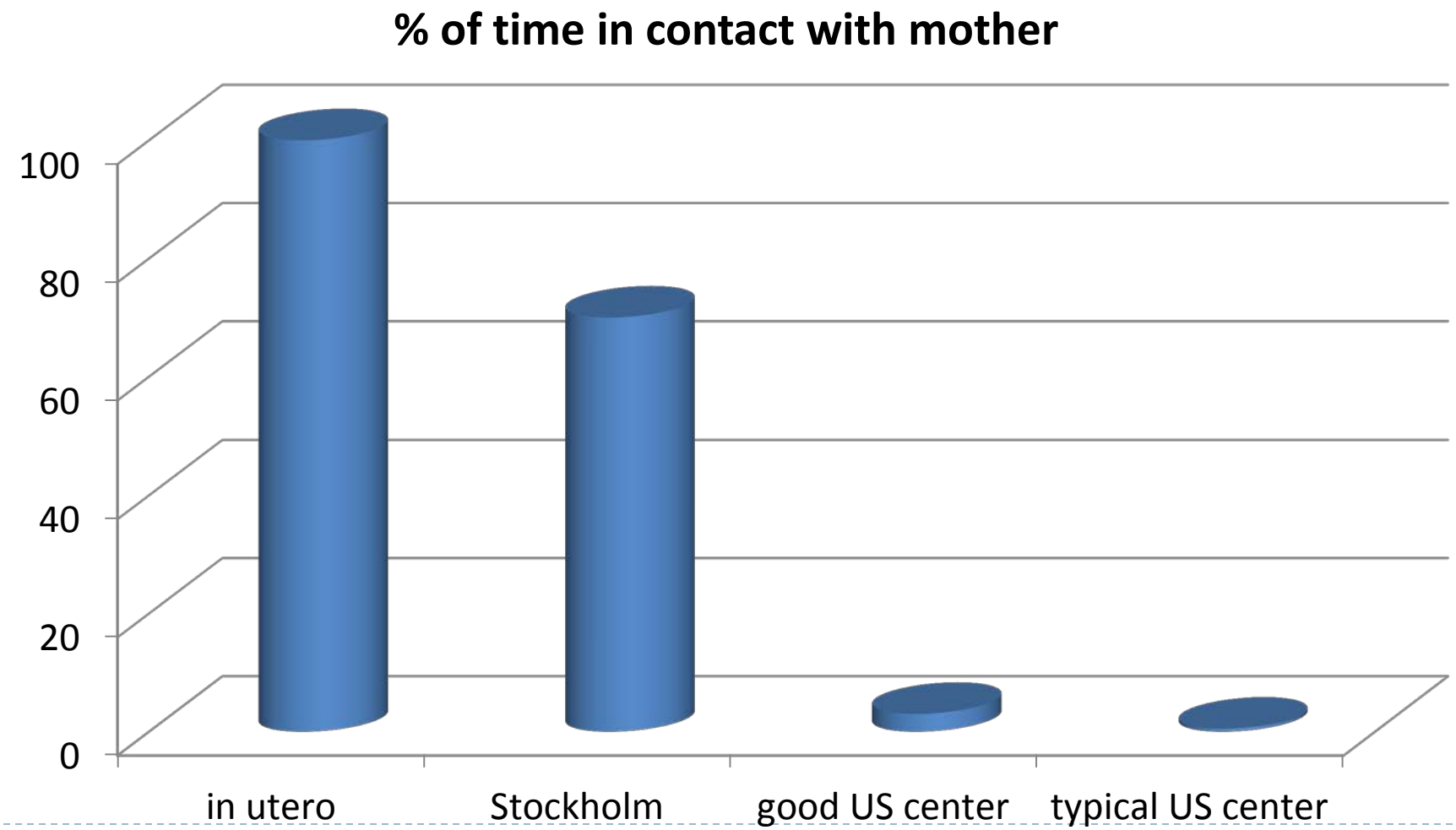
10 YEARS

…Standard of care?

32-weeks GA, just a few hours old…

…wireless system / telemetry allows monitoring

We have a long way to go…



The Sahlgrenska Center for
Pediatric Ophthalmology Research

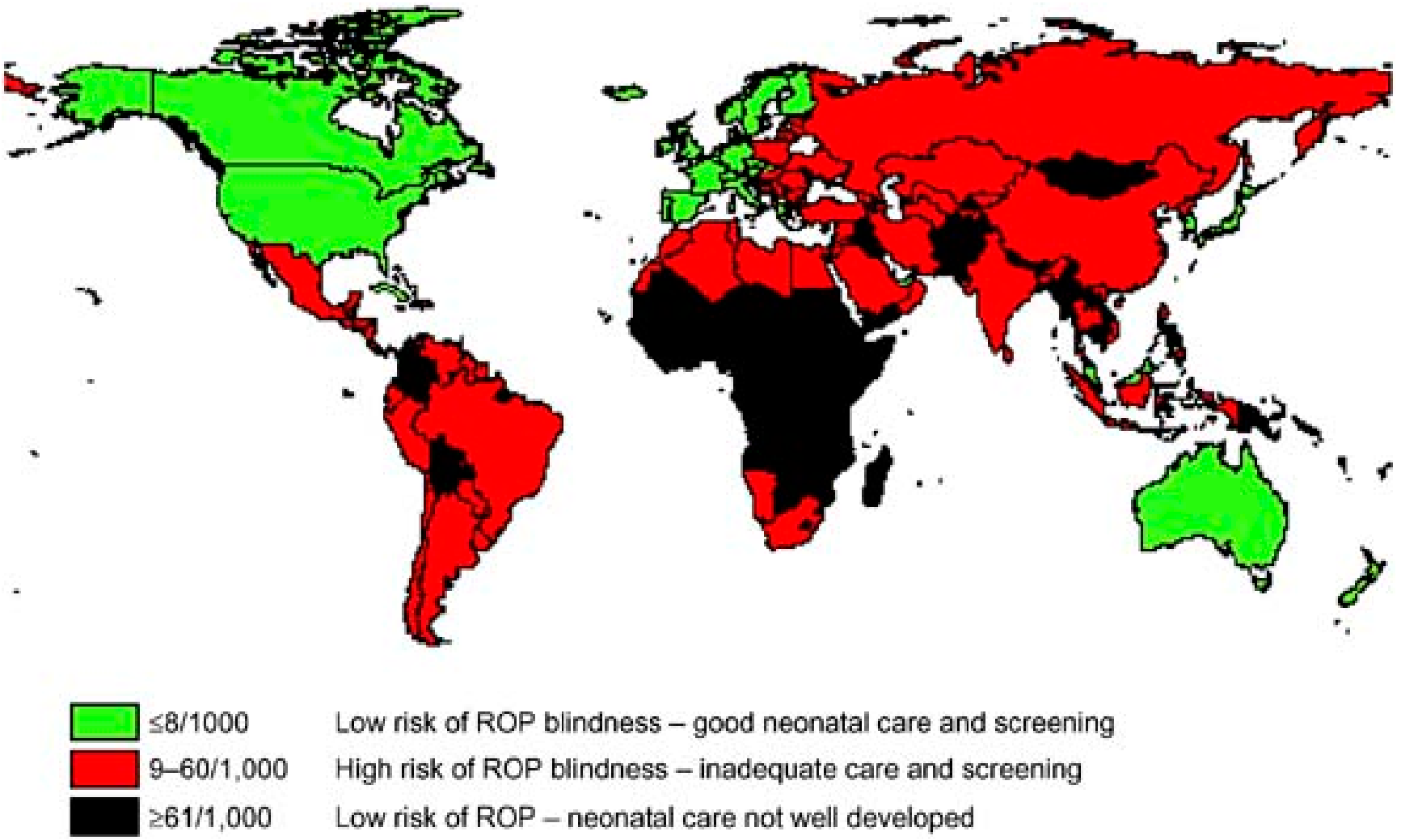
UNIVERSITY OF GOTHENBURG

Background

- ROP is a blinding disease
- ROP is a marker for neonatal health
  - Strong predictor for longterm cognitive, cardiovascular and metabolic outcomes. Farooqii, Kistner, Beardsall

- Incidence 200 000 infants
  - < 31 Wks (high performing NICUs)
  - > 34 Wks (developing world) Blencow

ROP- geographically



Background

- ROP is a preventable disease
  - Oxygen
  - Nutrition
  - Substitution of critical factors (growth factors, fatty acids)
  - Optimal neonatal care (sepsis, PDA, BPD, NEC)

- ROP acute phase is treatable
  - Laser
  - Anti VEGF (Bevacizumab, Ranibizumab)

Implication and Readiness

- Implication
  - Rated high by INC survey
  - Reduce morbidity and blindness
  - Vision 2020 WHO goal- the right to sight

- Readiness
  - Implementation of optimal oxygen delivery
  - 2 ongoing trials in phase II and II/III
    - IGF-1(prevention)
    - Ranibizumab (acute phase treatment)

Unmet needs to be approved by EMA & FDA

- In order to facilitate drugs to market for ROP we ask C-Path and INC to help with
  - Masterprotocol for ROP
    - Short term
    - Long term
  - Biomarkers (weight, B-glucose..)
    - Prediction
    - Prognosis

Action in order to fulfill unmet needs

- Constitute a ROP expert group
  - ROP specialist
  - Neonatologist
  - Regulatory
  - Stakeholders and parental organisation
  - Industry
- Facilitate the work process
- Estabiish FDA and EMA approval

- Optimal oxygen delivery in developing countries
  - Gates foundation?

Response to Breakout Question #1

- For Retinopathy of Prematurity, what indication(s) are in most need of effective therapies? Include an estimate of the incidence and severity.

Response to Breakout Question #2

- For prevention or treatment of ROP, what non-clinical studies need to be carried out prior to designing clinical trails of new and/or existing drugs?
  - What juvenile animal toxicity studies are needed?
  - Are animal models available for the indication (e.g. gestational age equivalent)?
  - Can the non-clinical data be extrapolated to inform clinical development, including initial dosing?

Response to Breakout Question #3

- For prevention or treatment of ROP, what information would be needed before starting a clinical trial?
  - Can existing pediatric or adult studies be extrapolated to neonates?
  - Could a master protocol be developed for use when evaluating treatments for this indication?
  - Would the use of different drug classes alter the inclusion/exclusion criteria?
  - Do the inclusion criteria drive formulation, mode of administration and/or dose?
  - What parameters are needed for constructing a meaningful modelling and simulation tool?

Response to Breakout Question #4

- Are there impediments to establishing a master protocol (do multiple approaches exist – comparative effectiveness studies)? Is there equipoise?

Response to Breakout Question #5

- What potential biomarkers and clinical trial endpoints could be used?
  - Are adequate clinical outcome measures available? If not can they be developed?
  - Are any prognostic, predictive, pharmacodynamic, and safety biomarkers available? Are any regulatory ready?

Response to Breakout Question #6

- What long-term outcome measures are available to assess the safety and efficacy of the therapy?

Response to Breakout Question #7

- In light of your responses to Questions 1-6, where are the gaps in knowledge and how would you prioritize the studies needed to approach the For prevention or treatment of ROP?