

Congenital CMV in Europe

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Venice

Paul D. Griffiths MD, DSc, FRCPath

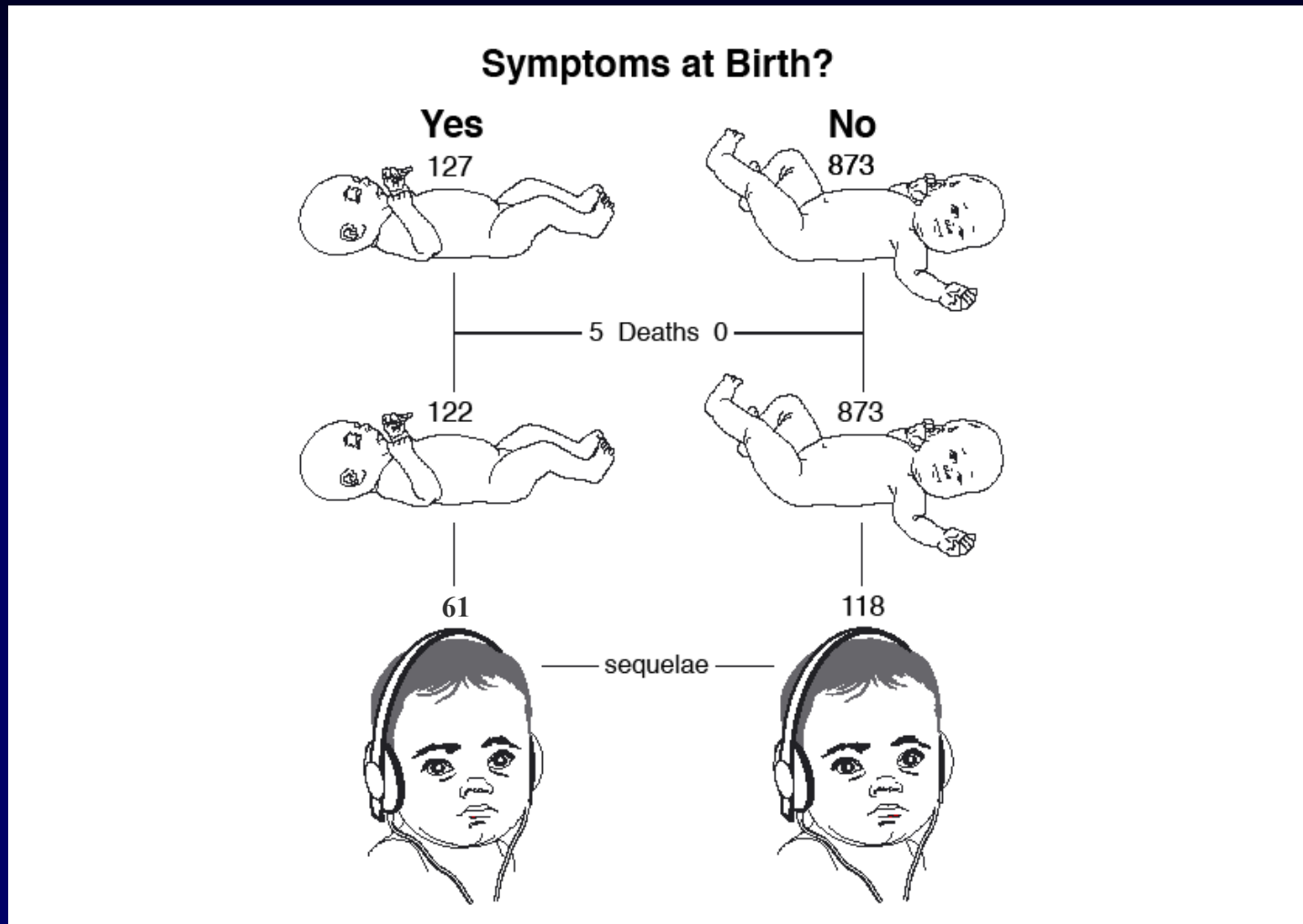
Professor of Virology

University College London Medical School

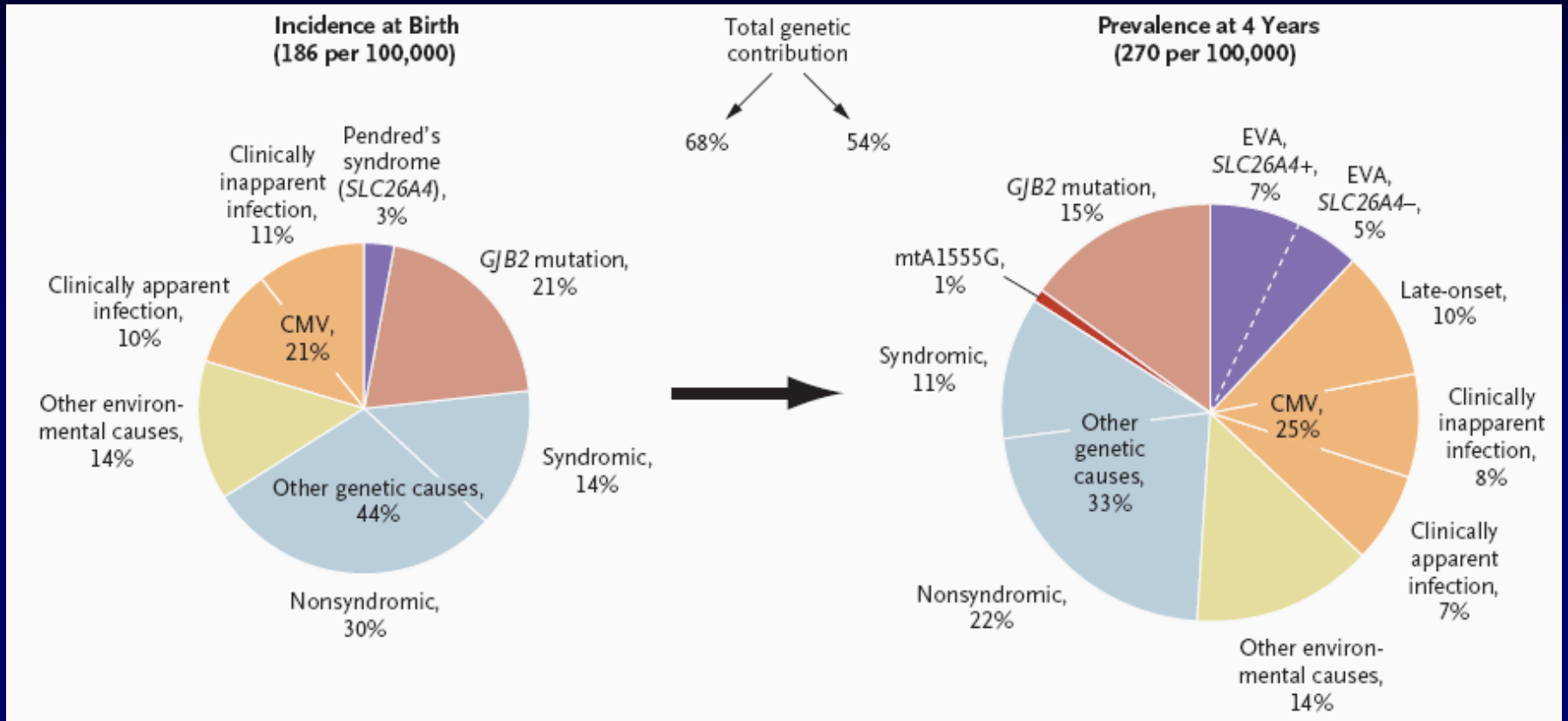
Europe



Disease Outcome per 1000 Babies with Congenital CMV



Causes of SNHL in USA



Overviews of European Countries

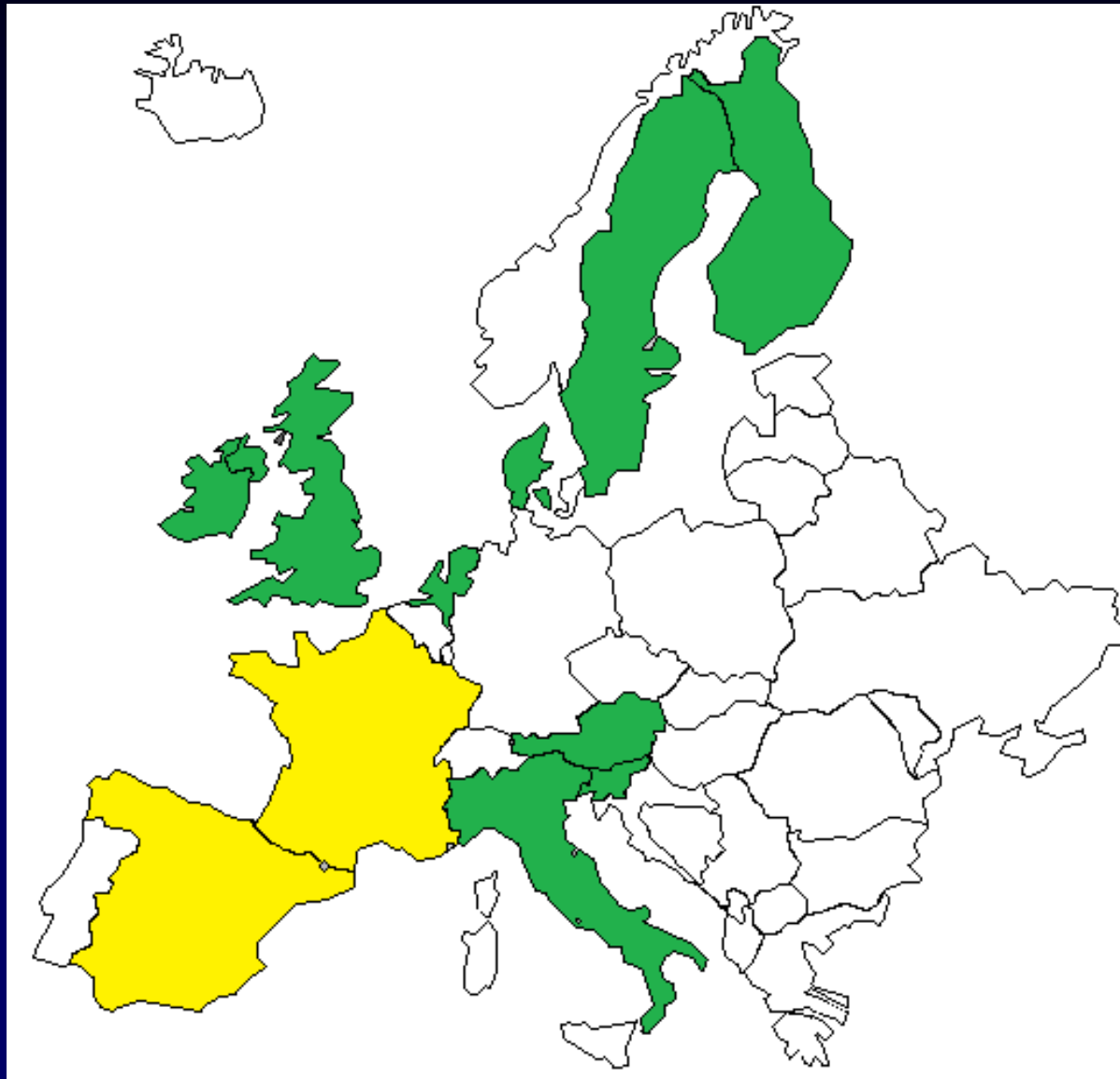
Central estimates from systematic reviews:

- Kenneson Rev Med Virol 17:253;2007
- Dollard Rev Med Virol 17:355;2007
- Cannon Rev Med Virol 20:202;2010
- Hyde Rev Med Virol 20:311;2010

Ask if different countries seem higher or lower:

- Small numbers
- Historical

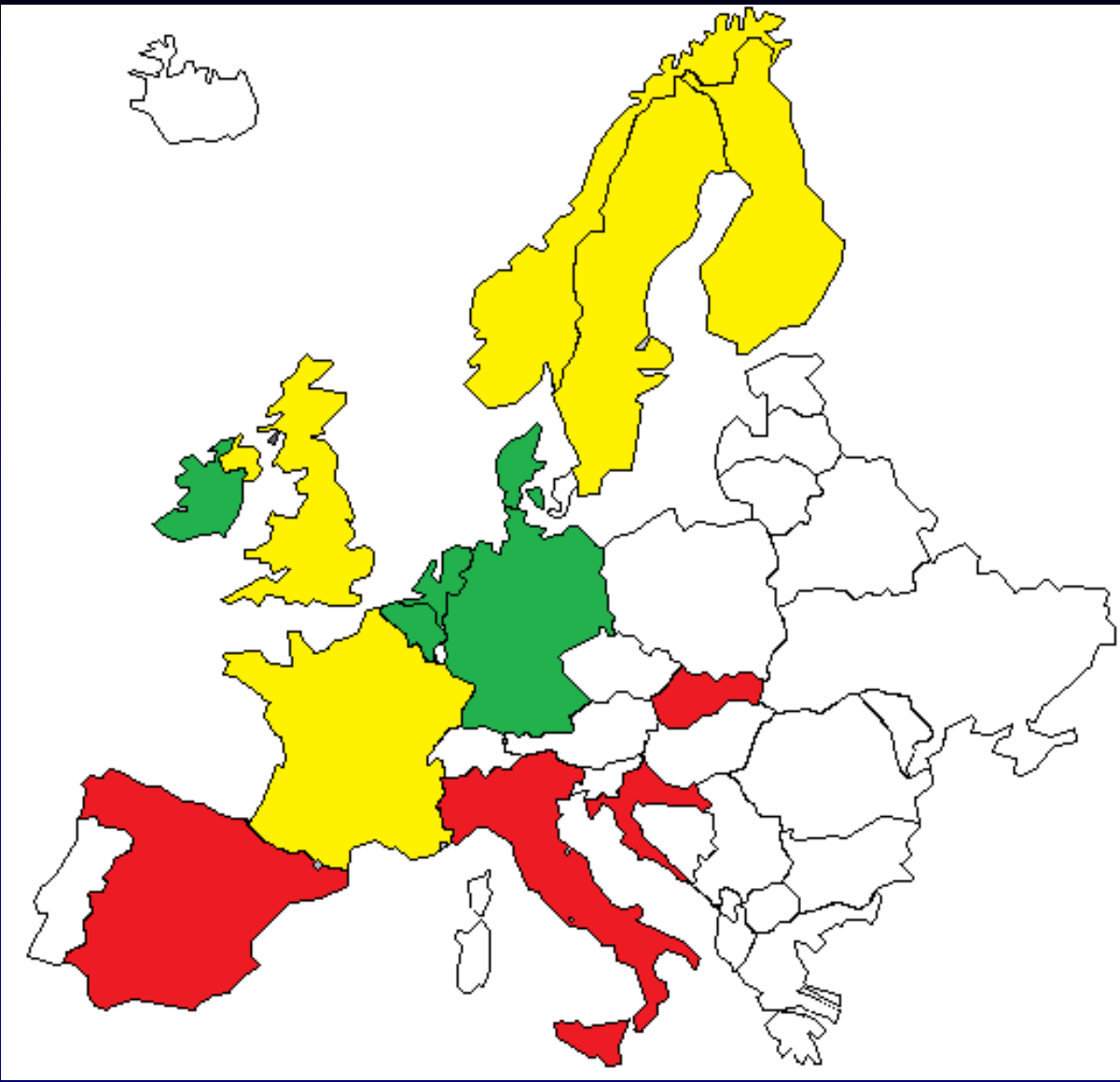
Incidence Congenital CMV (7/1000)



“Congenital CMV is Less Common in Europe”

- This would still make it the second most common cause of SNHL**
- It remains the only cause that is potentially treatable**

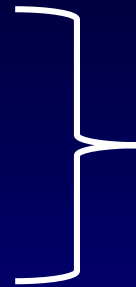
Proportion of IgG Positive (60%)



Types of Maternal Infections

Primary

Reinfection



Exogenous

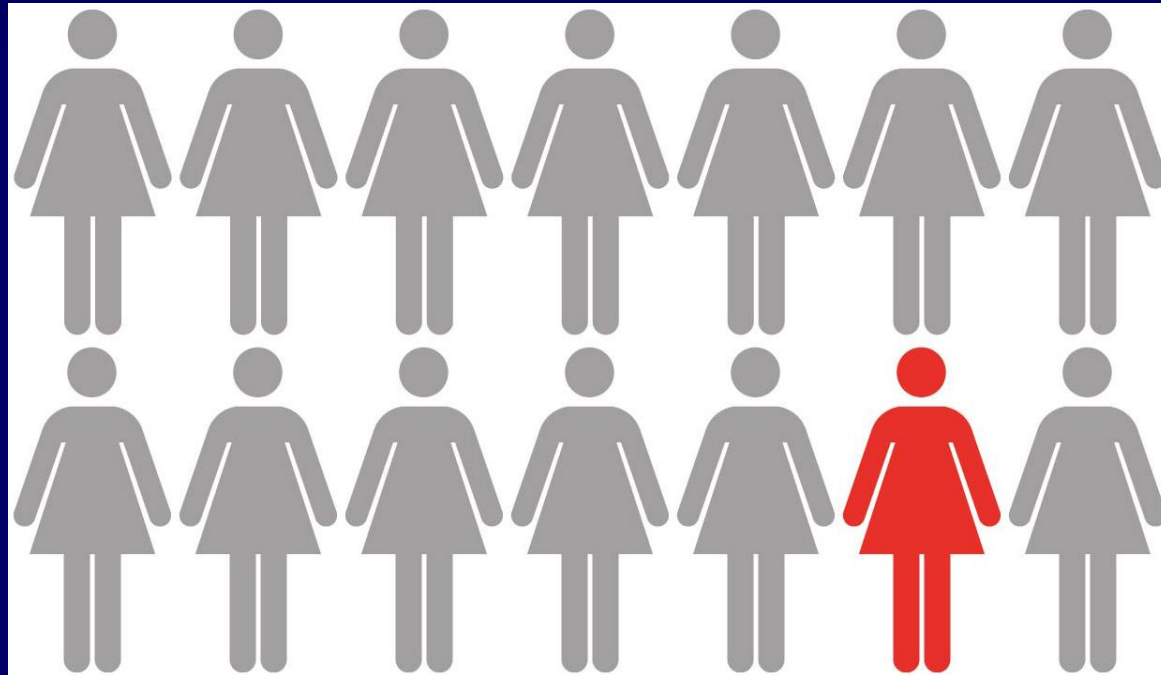
Reactivation

Endogenous

Mother with primary infection



Mothers of babies with cCMV



CMV Vaccines Needed

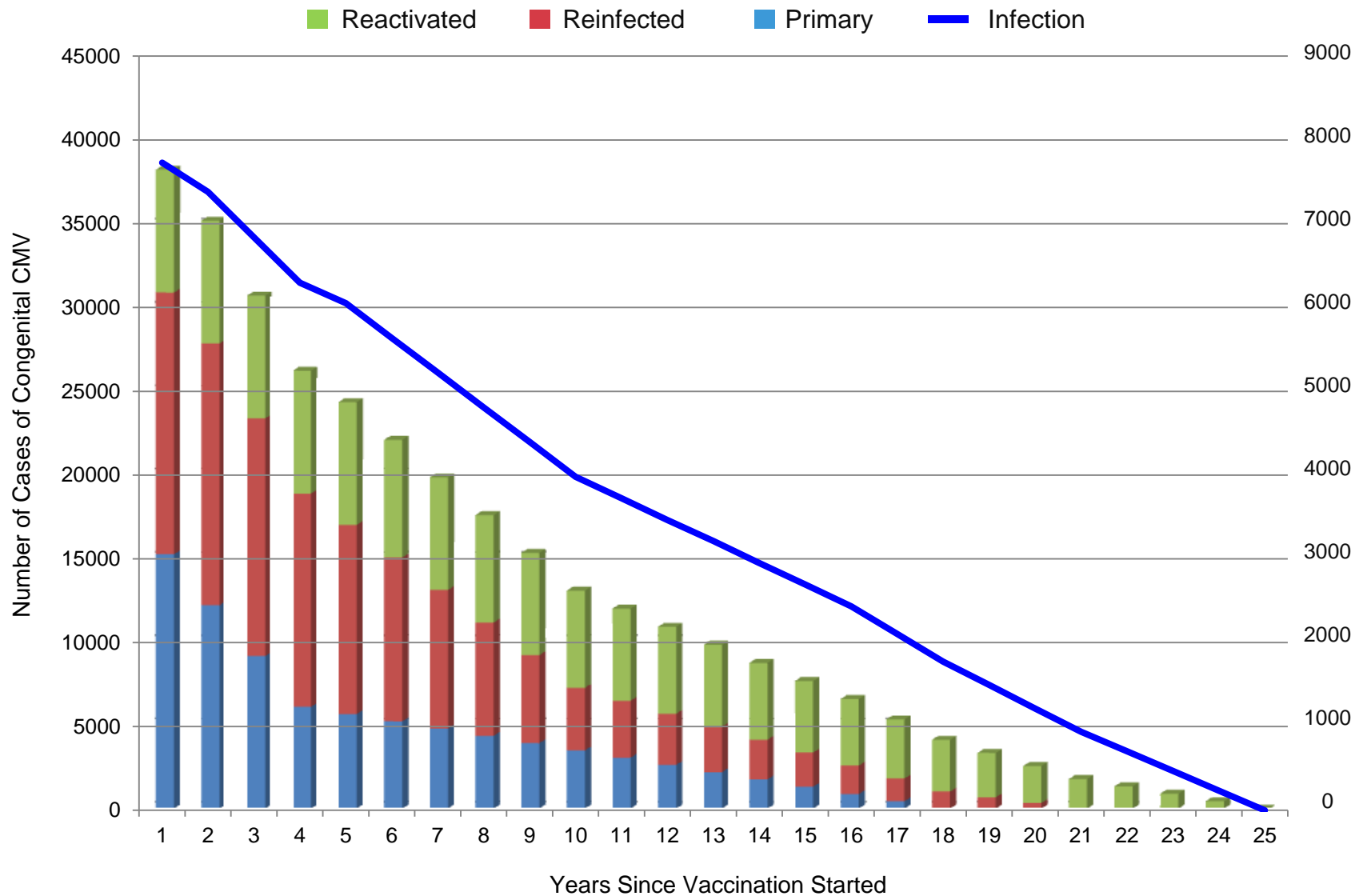
To protect against primary infection

- **Toddlers**
- **Teenagers**
- **Women of child-bearing age**

To boost natural immunity

- **Reinfection**
- **Reactivation**

Possible effect of vaccine



Symptomatic Congenital CMV

- **Microcephaly**
- **Petechiae**
- **Jaundice**
- **Hepatosplenomegaly**
- **Lymphadenopathy**
- **Blueberry muffin rash**
- **Intrauterine growth retardation**
- **(Sensorineural hearing loss)**

Could the Symptomatic Classification be Improved?

- **Sensitive investigations**
 - **US, MRI**
 - **Hearing loss in neonates**

- **2 RCTs for ganciclovir treatment**
 - **6 weeks vs no treatment**
 - **6 weeks vs 6 months**

Features of CMV Justifying Treatment 2016

- **Microcephaly**
- **Intracranial calcifications**
- **Ventriculomegaly**
- **Sensorineural hearing loss**

Treat More Benign Symptoms?

- **Concern about committing 6 months of treatment for all with symptoms**
- **What about isolated purpura?**
- **Could a RCT be justified?**
 - **6 weeks**
 - **CNS endpoint**

For Children Older Than 1 Month

- **No evidence**
- **Unmet medical need**
- **RCT needed**
- **Drug vs placebo**
- **6 weeks**
- **CASG 403 started**
 - **VGCV vs placebo**
- **Fair comparison of drug**

PI's for 9 UK Sites for DMID 11-0069 Study

Newcastle 280 **Dr Marieke Emonts**

T: 0191 282 6536

E: marieke.emonts@newcastle.ac.uk

Manchester 296 **Dr Paddy McMaster**

T: 0161 922 3880

E: Paddy.McMaster@pat.nhs.uk

Sheffield 297 **Dr Fiona Shackley**

T: 0114 271 7000

E: Fiona.Shackley@sch.nhs.uk

Birmingham 285 **Dr Scott Hackett**

T: 012 1424 2696

E: scott.hackett@heartofengland.nhs.uk

Oxford 282 **Dr Dominic Kelly**

T: 01865 231693

E: dominic.kelly@paediatrics.ox.ac.uk

Copy In:

Professor Andrew Pollard

T: 018 6522 1060

E: andrew.pollard@paediatrics.ox.ac.uk

Bristol 283 **Dr Jolanta Bernatoniene**

T: 011 7342 0172

E: jolanta.bernatoniene@bristol.nhs.uk

Copy In:

Professor Adam Finn

T: 011 7342 0172

E: adam.finn@bristol.ac.uk

Southampton 286 **Prof Saul Faust**

T: 023 8120 4989 / 023 8120 6883

E: s.faust@soton.ac.uk

London, GOSH 292 **Prof Nigel Klein**

T: 0207 905 2891

E: n.klein@ucl.ac.uk

London, St Georges 281 **Prof Mike Sharland**

T: 020 8725 3922

E: mike.sharland@stgeorges.nhs.uk

**UCL Medical School, Royal Free Campus
(Coordinating Centre) 152**

Professor Paul Griffiths (UK CI)

T: 020 7830 2997

E: p.griffiths@ucl.ac.uk



Why Not Treat All Children?

1 Month ✓

6 weeks, 12 weeks, 6 months?

For evidence-based practice

- Evidence of efficacy
- Evidence of safety

Progressive disease may not be driven by viral replication

Drug activity in vitro \neq clinical efficacy

If adverse event occurs, defensible

Evidence-Based Medicine

- **Logical, stepwise interventions offering progressive control of disease**
- **Parents need to buy into the concept of randomisation and appropriate controls**
- **Essential to persuade regulators to take CMV seriously**
- **They will ignore case series**

“The plural of anecdote is not data”

Then Introduce New Drugs

Establish treatment duration VGCV

Compare VGCV with new drug

- **Maribavir**
- **Brincidofovir**
- **Letermovir**
- **Combination therapy?**

A Vision of the Future

European countries will introduce:

Screening of newborns

- **Epidemiology congenital CMV**
- **Symptoms → treatment + RCTs**
- **No symptoms → RCTs treatment**
- **Monitor efficacy of vaccination**

Screening of pregnant women

- **Epidemiology CMV in community**
- **Diagnosis primary → treatment RCTs**
- **Link with cases of congenital CMV**
- **Monitor efficacy of vaccination**

What can we do meanwhile?

Suggestions

Europe has a substantial CMV problem

Europe has specialist expertise

Countries would benefit from:

- **Better coordination of activity**
- **Applying best practice widely**
- **Training, then return home**
- **Collaboration on RCTs**
 - **Congenital CMV**
 - **CMV in Pregnancy**
- **European Union Funding**