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Nationales
d'Infectiologie

Bordeaux
et l'interrégion Aquitaine § Limousin



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Palais des Congrès de Bordeaux

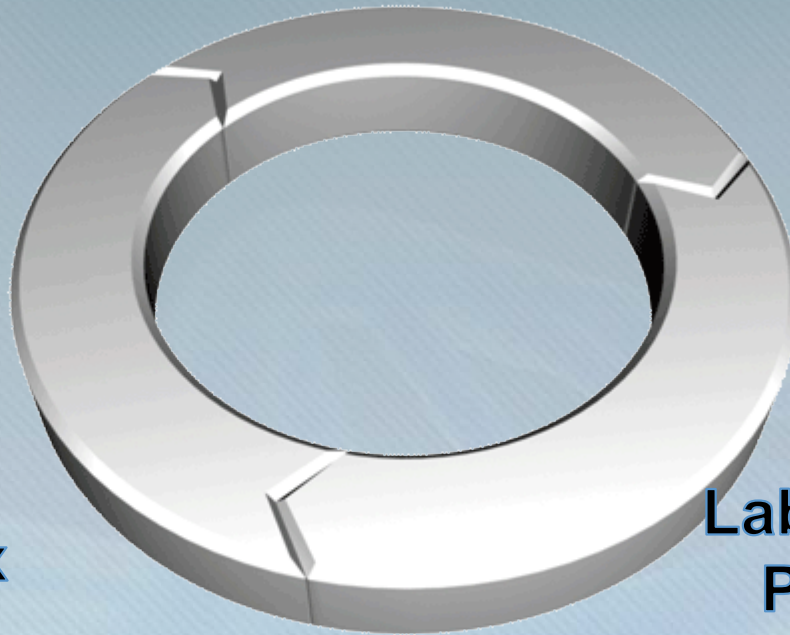
Infections a Campylobacter: une perspective mondiale

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Laboratoire
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GLOBAL FOOTPRINT

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MADAGASCAR*
Rodolphe Mérieux Laboratory in Antananarivo

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Objectifs Gabriel



- Renforcer les capacités de recherche dans les pays en développement
 - Construction de laboratoires
 - Formation de chercheurs
 - transfert de technologies
 - Développement d'une stratégie et agenda de recherche national et regional
 - Mener des études multicentriques S-S et N-S



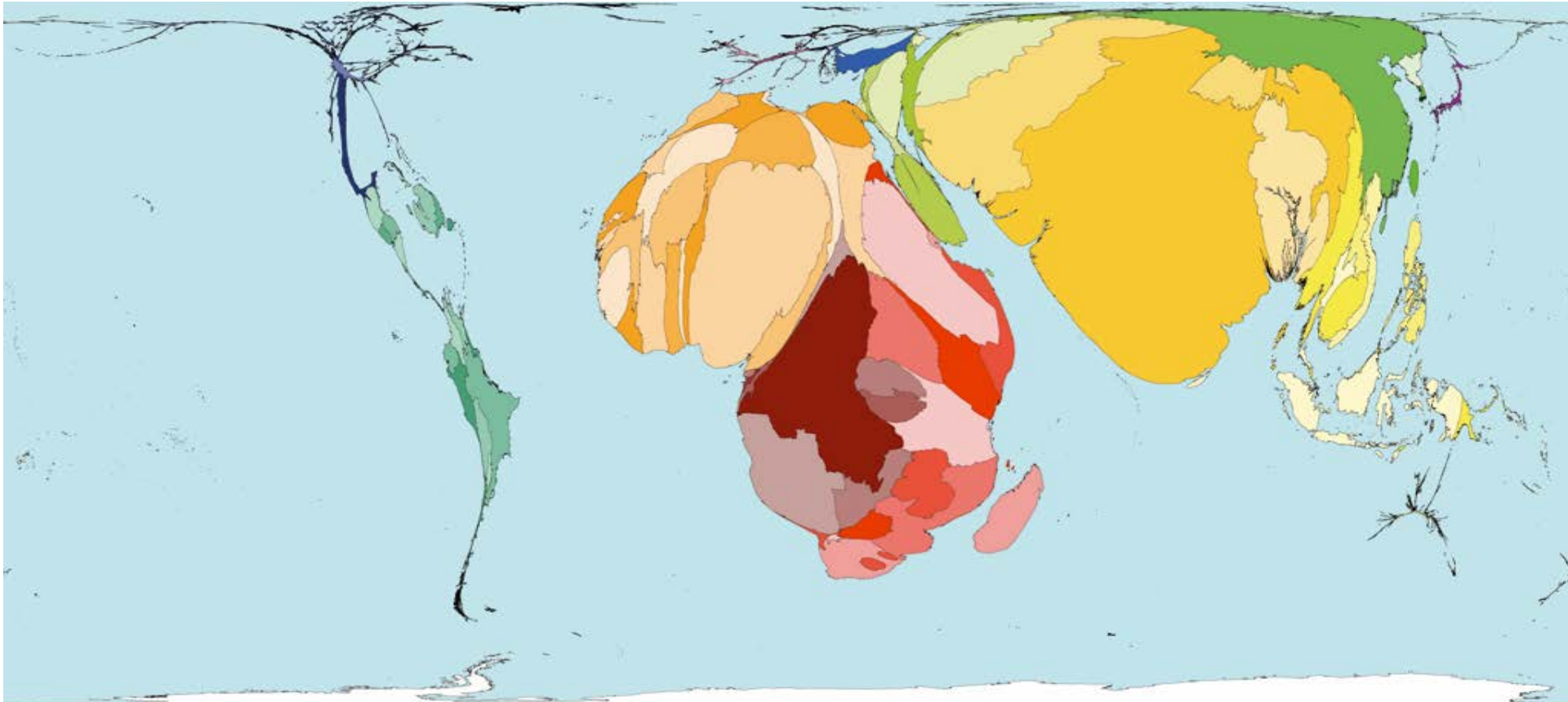
Rodolphe Mérieux Laboratory Antananarivo, Madagascar



Rodolphe Mérieux Laboratory Antananarivo, Madagascar



Mortalité maladies diarrhéiques incidence de la campylobacteriose?



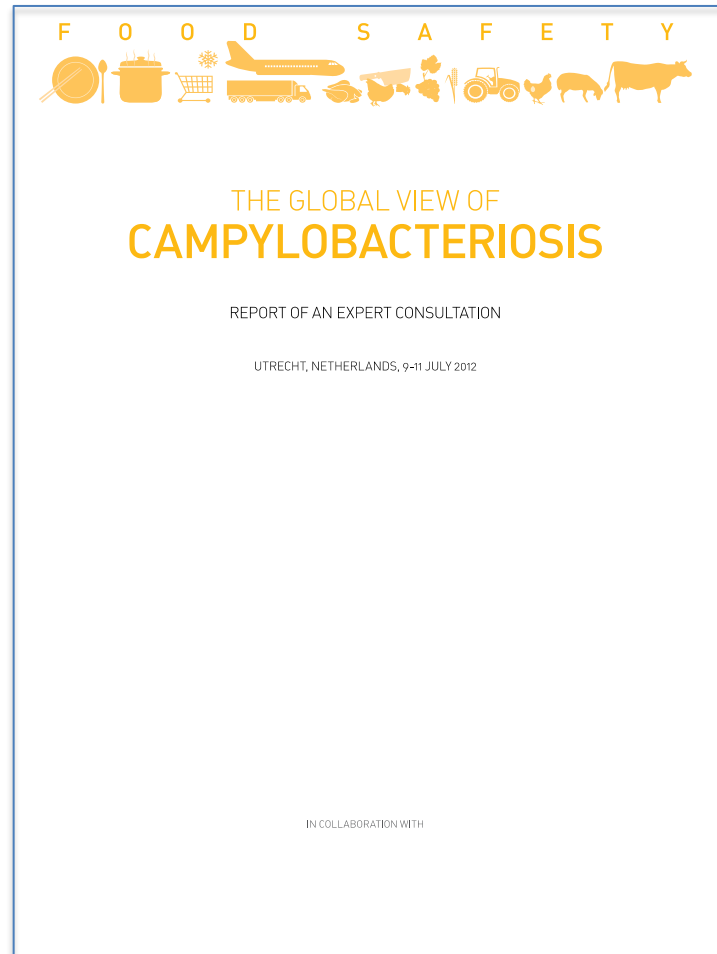
Incidence of Campylobacteriosis

- True incidence poorly known
- UK: 9.3 per 1000 person years
- Netherlands: 5.8 per 1000 person years
- USA: 4.4 per 100 person years
- Global Burden of Disease Study:
 - Campylobacter: 8.4% of total diarrheal burden
 - Campylobacter ranks 3rd after rota and crypto

Murray et al. Lancet 2010; Tam et al. Gut 2012; Havelaar et al Int J Food Microbiol 2009



WHO consultation d'expert 2013



Source attribution

approches microbiologiques

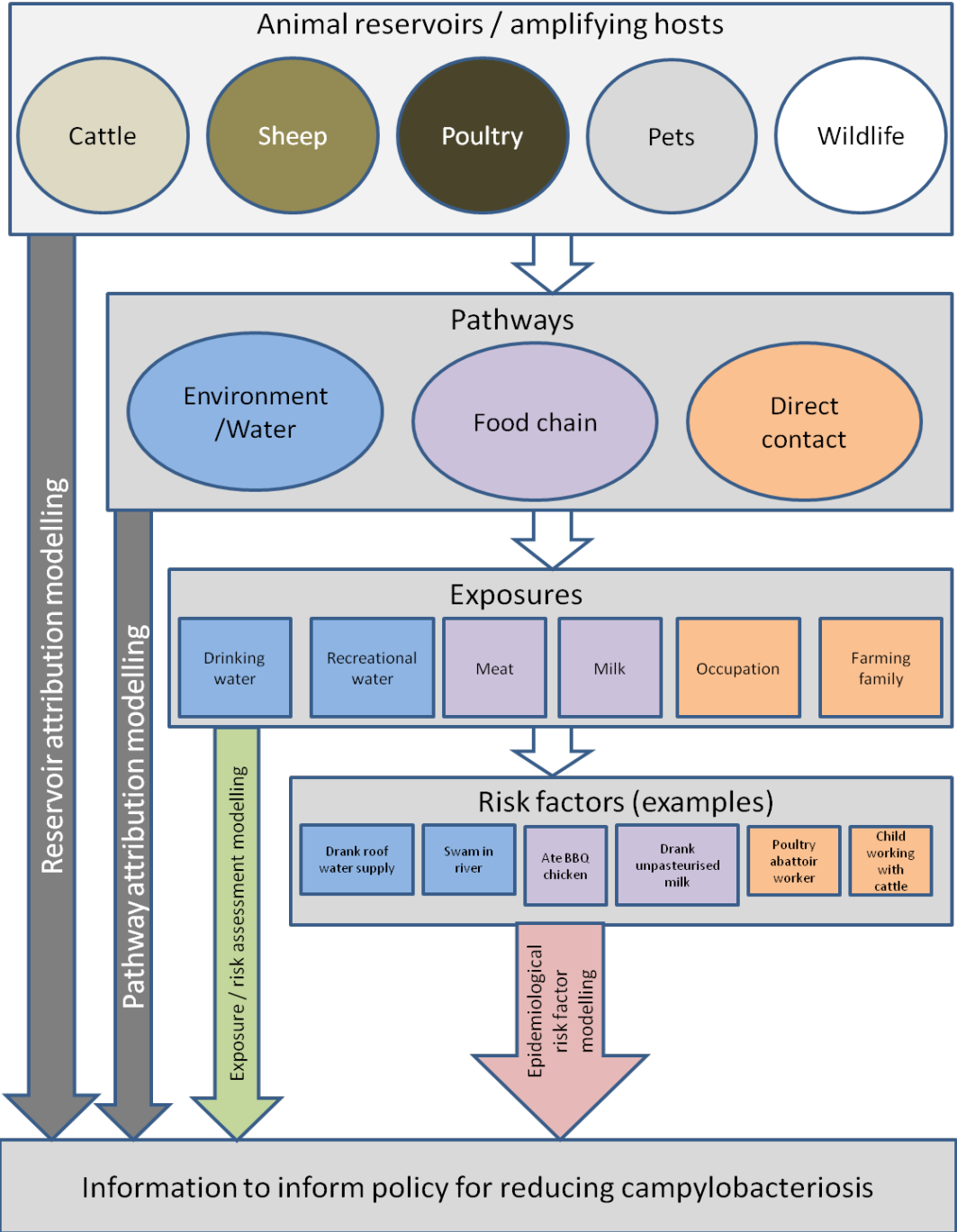
- Comparer de la distribution des soustypes microbiennes (MLST)
- Identifier les sources primaires
- Déterminer leur contribution à la charge de morbidité
- Dynamic reservoir attribution modelling

WHO 2013: Global view on campylobacteriosis



Transmission framework of Campylobacteriosis

- 1. Reservoirs**
(amplifying hosts)
- 2. Pathways**
(primary route; voie de transmission)
- 3. Exposures**
(secondary exposures)
- 4. Risk factors**
(facteur/comportement à risque)



Nigel French in: WHO report :Global view of Campylobacteriosis (2013); Pires 2009

Source attribution

knowledge gaps

- Need for more rapid, less expensive typing tools for source attribution
- Few data of systematic typing from multiple sources in different geographical location over time
- Few data from developing countries

Séquelles et complications

- Syndromes de Guillain-Barré et Miller Fisher
- Arthrite réactive
- Troubles fonctionnels intestinaux
 - *Syndrome du colon irritable*
- Inflammatory bowel disease
- Maladie coeliaque

WHO 2013: Global view on campylobacteriosis



La paralysie ascendante aiguë de Landry

GAZETTE HEBDOMADAIRE

II.

TRAVAUX ORIGINAUX.

NOTE SUR LA PARALYSIE ASCENDANTE AIGUE,
par le docteur O. LANDRY.

L'objet de ce
et généralement
affections les p

Dans un asse

la qualification générale d'*extenso-progressives*, les troubles fonctionnels, d'abord restreints à une partie limitée du corps, s'irradient graduellement plus ou moins loin de leur point de départ. Cette propagation s'effectue tantôt de proche en proche, et d'après un ordre bien déterminé; tantôt, au contraire, sans régularité et comme au hasard. On peut appeler les paralysies de ce dernier

« Le début des accidents paralytiques peut être précédé d'un sentiment de faiblesse et de crampes abdominales



Jean Baptiste Octave Landry de Thézillat (1826-1865)

Gaz Hebd Med Chir 1859,6:472-4 et 486-8

Guillain-Barré syndrome

- Rapidly evolving symmetrical weakness with areflexia
- Frequent involvement of respiratory muscles leading to artificial respiration
- Selflimiting and most severe at 2-4 weeks
- CSF findings: high protein levels and low white blood cell count
- Mortality 3-5%, disabling residual deficits 20%
- Incidence 1-2/100.000/year, 40.000-80.000 new cases/year worldwide
- **Proof of recent campylobacter infections in approx 30% of the GBS patients**



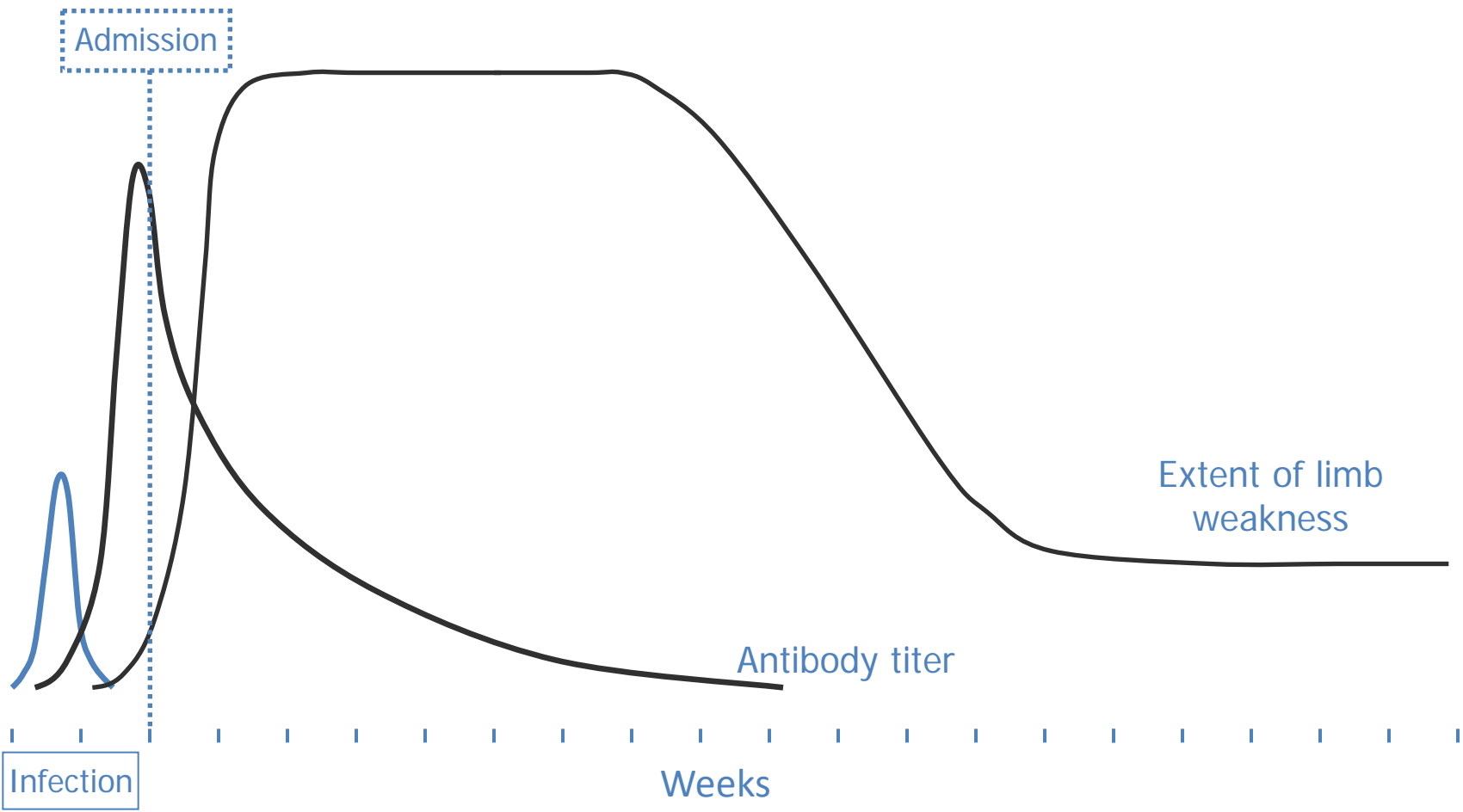
Erasmus Medical Center Rotterdam



Dhaka Medical College & Hospital

Progression Plateau phase Recovery phase Disability

Admission



Infection

Weeks

Antibody titer

Extent of limb weakness

Serum antibodies to gangliosides



GBS incidence in the World (All Ages)

1-2 / 100.000 / year

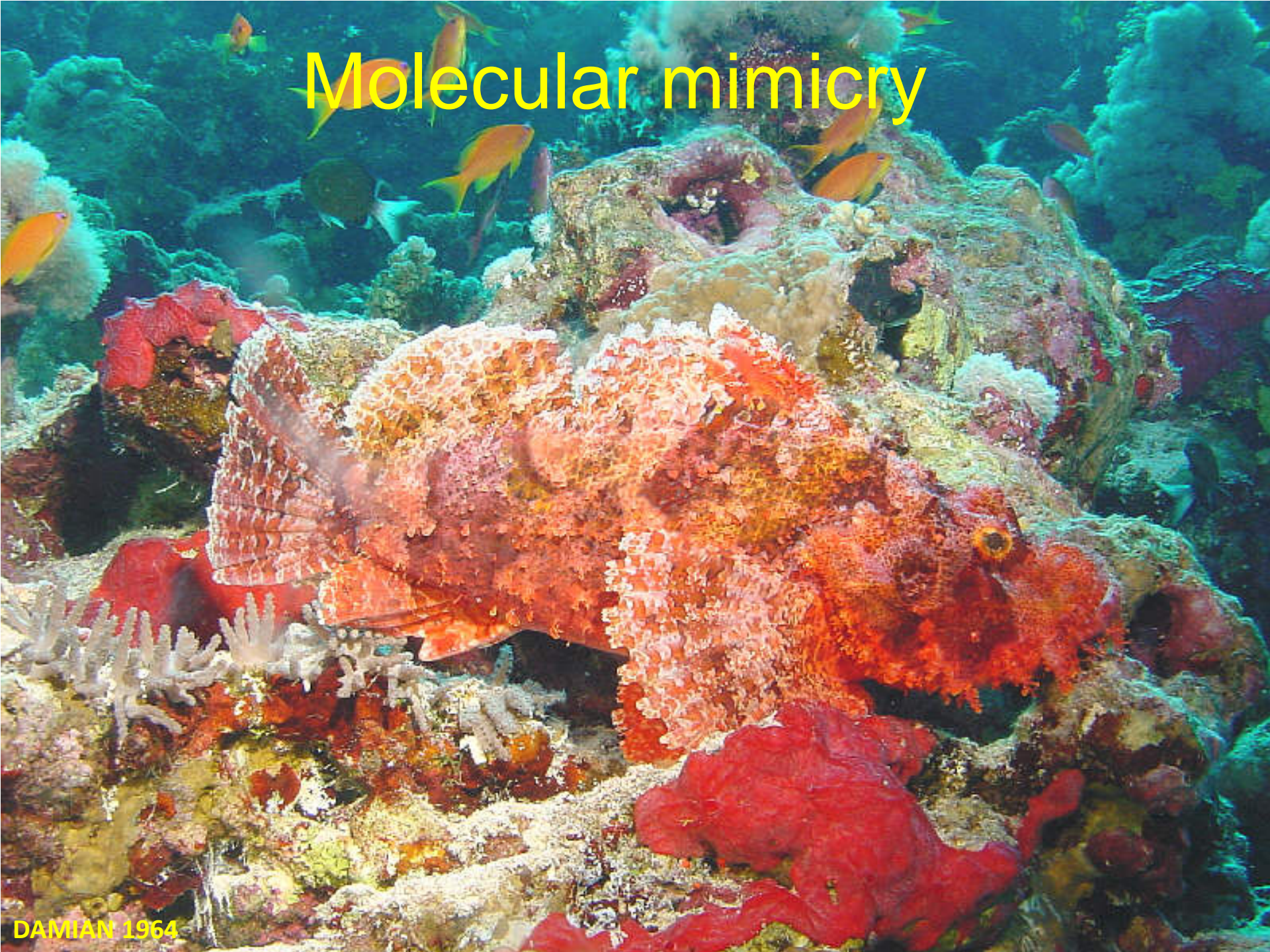
GBS incidence in the World (Children)

0.6 / 100.000/ year

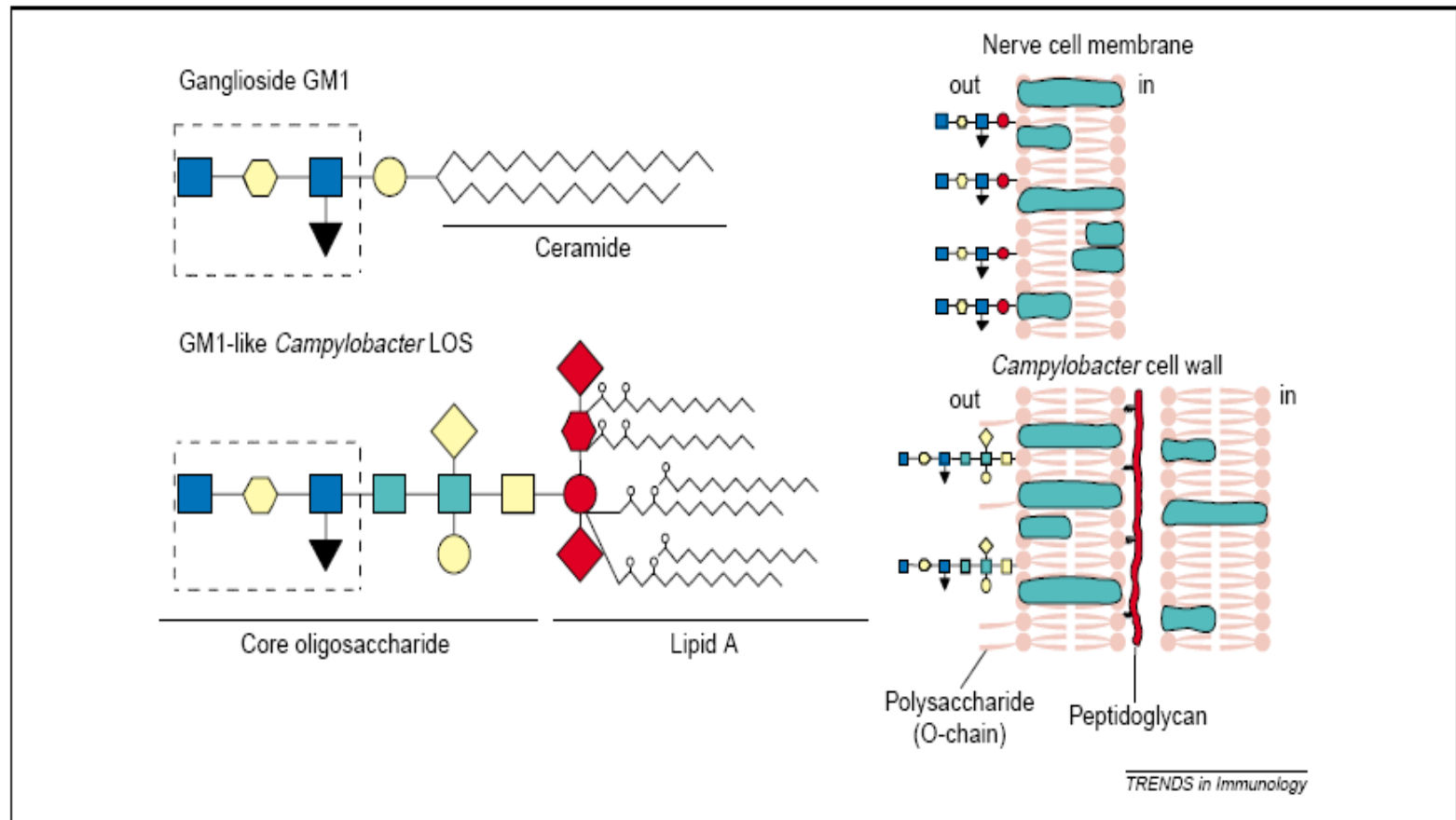
McGroarty et al 2007



Molecular mimicry



Molecular mimicry of gangliosides and *Campylobacter* LOS



Est-ce que dans les pays en développement et a haute incidence de diarrhée, l'incidence du syndrome de GBS est aussi élevé?

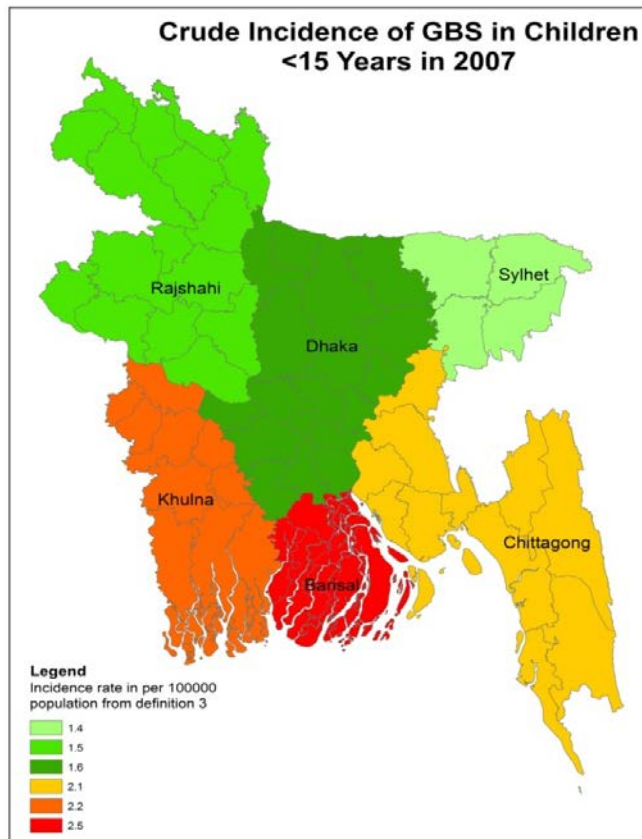


icddr,b Dhaka, Bangladesh



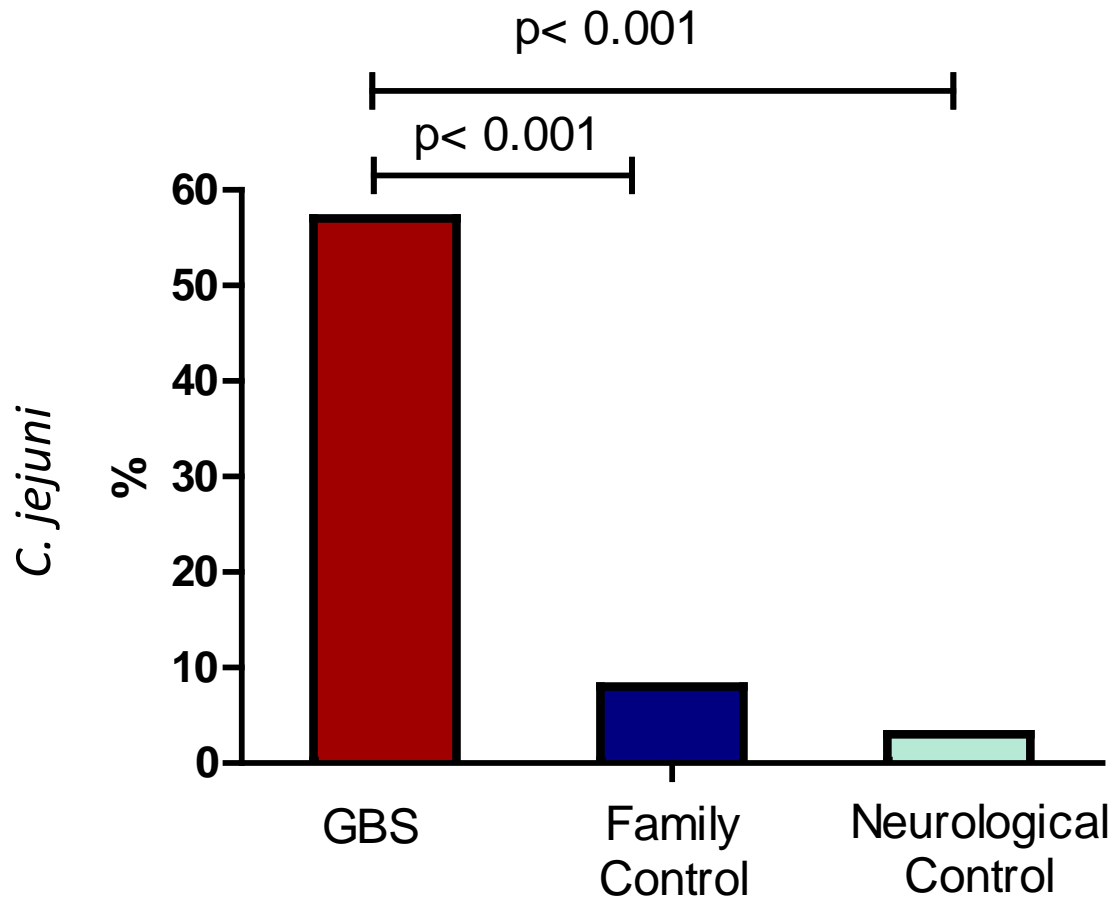
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GBS incidence in Bangladesh (children <15 years)

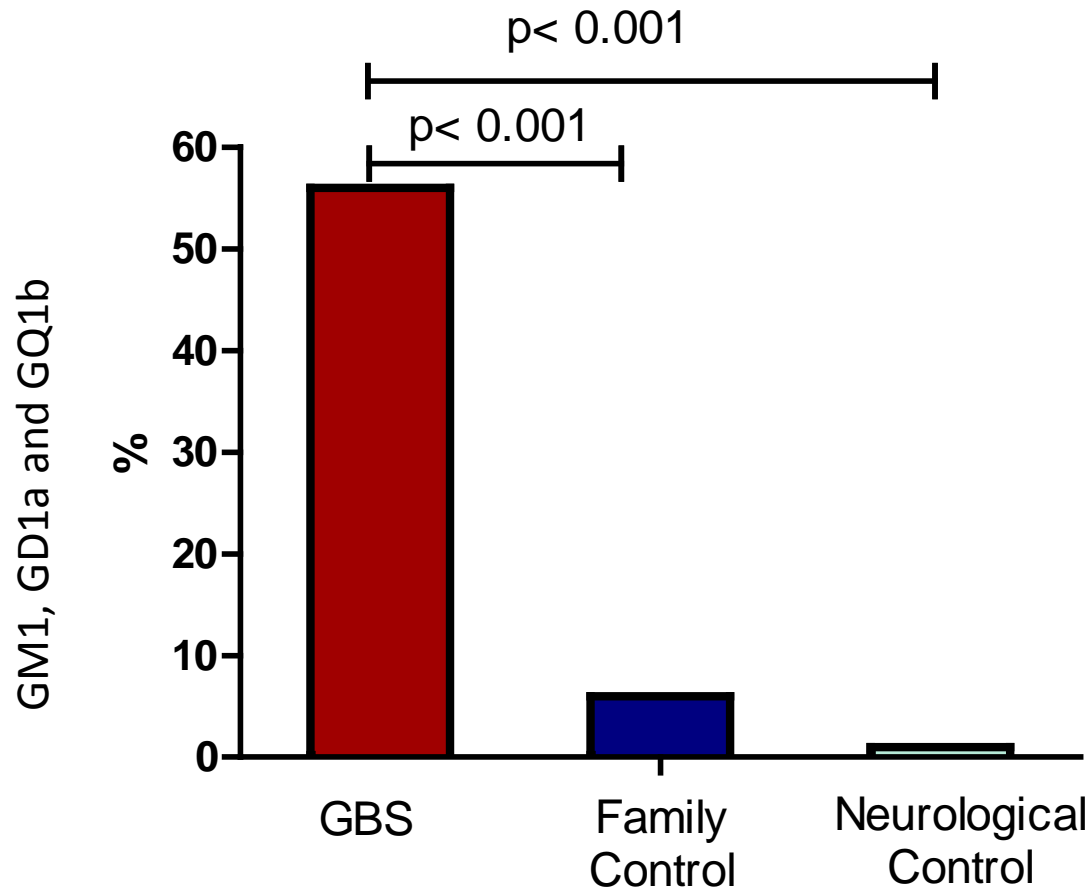


1.5– 2.3/100.000/ year
VS
0.6/100.000/year worldwide

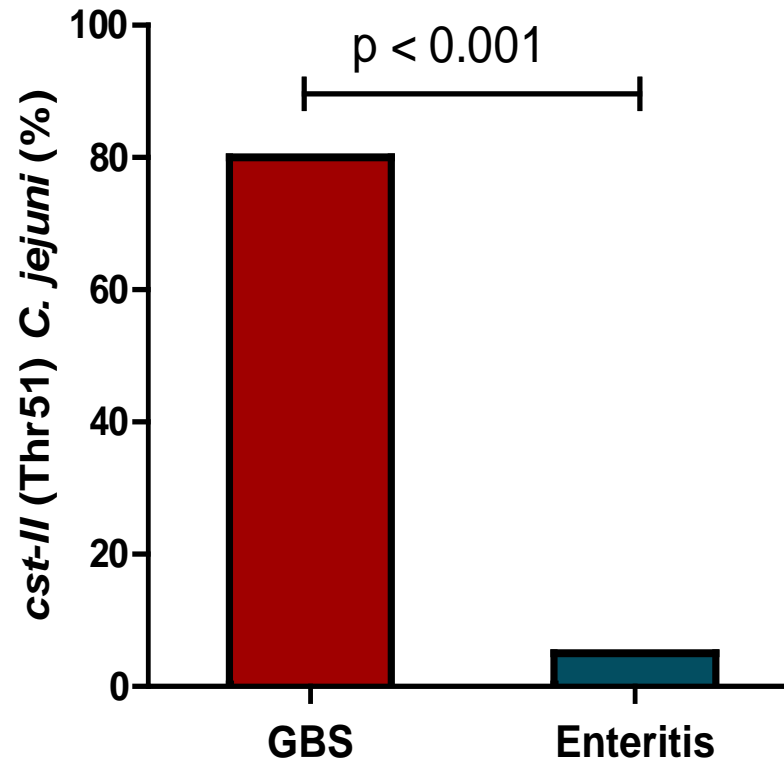
Campylobacter jejuni infection and GBS



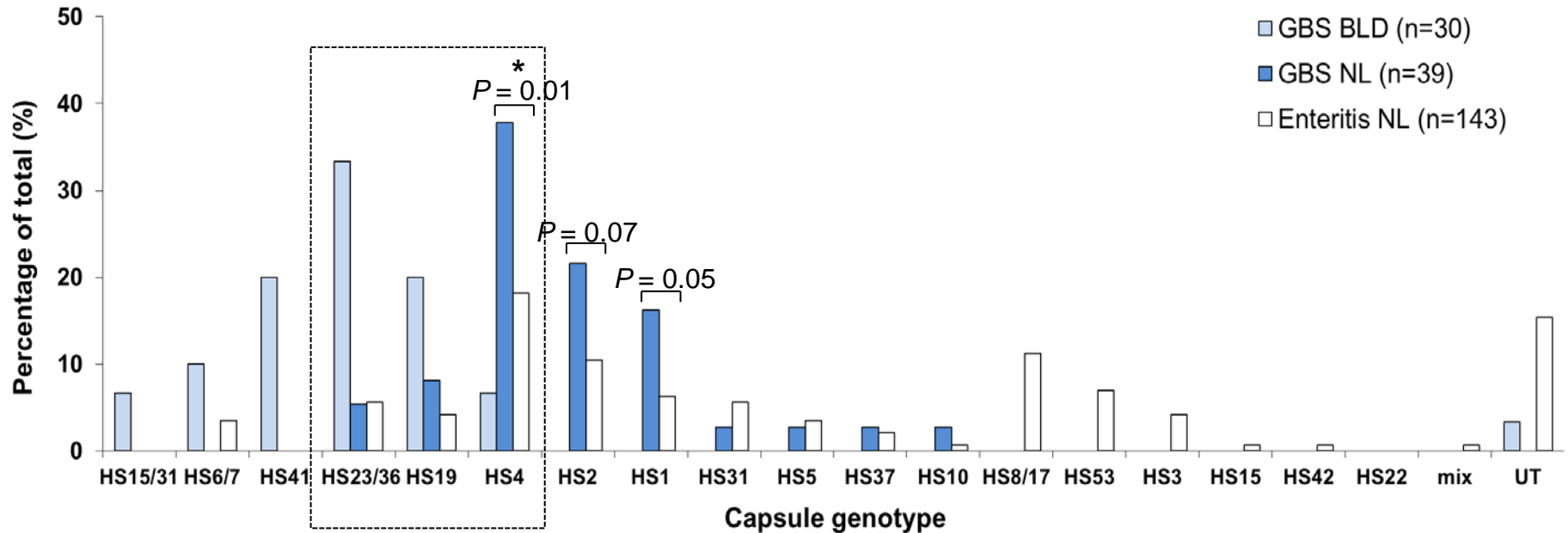
Anti-ganglioside antibodies in GBS



Presence of *C. jejuni* *cst-II* (Thr51) in patients with GBS



Six dominant capsule types within GBS-related *C. jejuni* strains



Heikema et al 2014



Evidence for causal role for *C. jejuni* in pathogenesis of GBS

- Association between *C. jejuni* infections and GBS
- Molecular mimicry between *C. jejuni* LOS and peripheral nerve gangliosides
- Cross-reactive antibodies to *C. jejuni* LOS and gangliosides in serum from GBS patients
- Induction of similar cross-reactive antibodies in rabbit model after immunization with *C. jejuni* LOS
- Pathogenicity of these cross-reactive antibodies in ex vivo animal models
- GBS disease model in Japanese white rabbit



Recommendations on sequelae

WHO should:

- Promote studies on causal associations between Campylobacter and long-term sequelae e.g troubles fonctionels intestinaux
- Promote population studies on antecedent infections and GBS in particular in LIDC
- Promote long term disability studies in GBS
- Promote low-cost case management

International GBS Outcome Study (IGOS)

Cohort study on clinical and biological determinants and outcome

i

- **International**

- >140 centers from 16 countries participating
- Supported by the International Neuropathy Consortium (INC)

- **GBS**

- All patients with diagnosis GBS (and variants)
- Aim to include >1000 patients

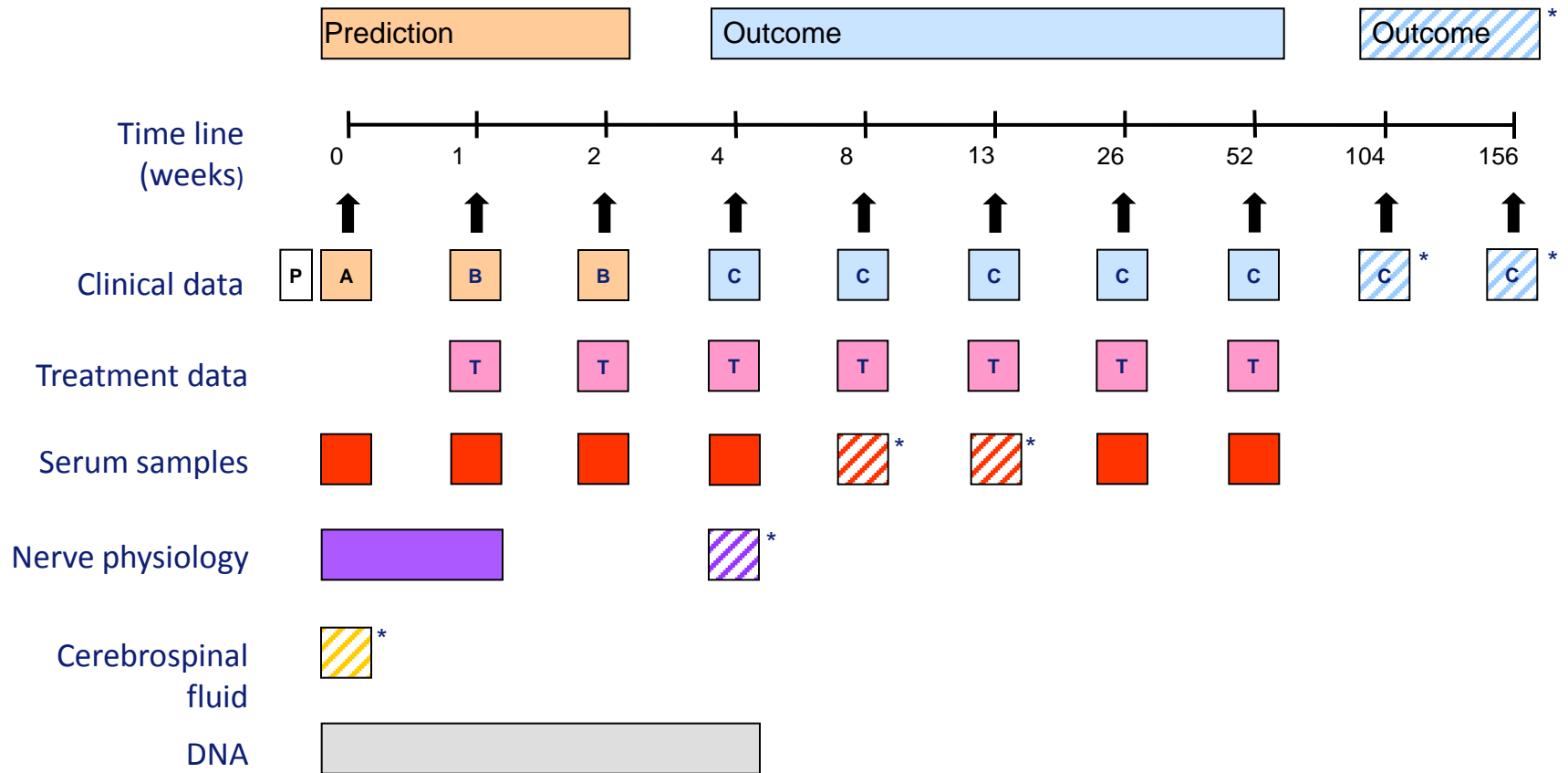
- **Outcome**

- Various outcome measures during follow-up of at least 1 year

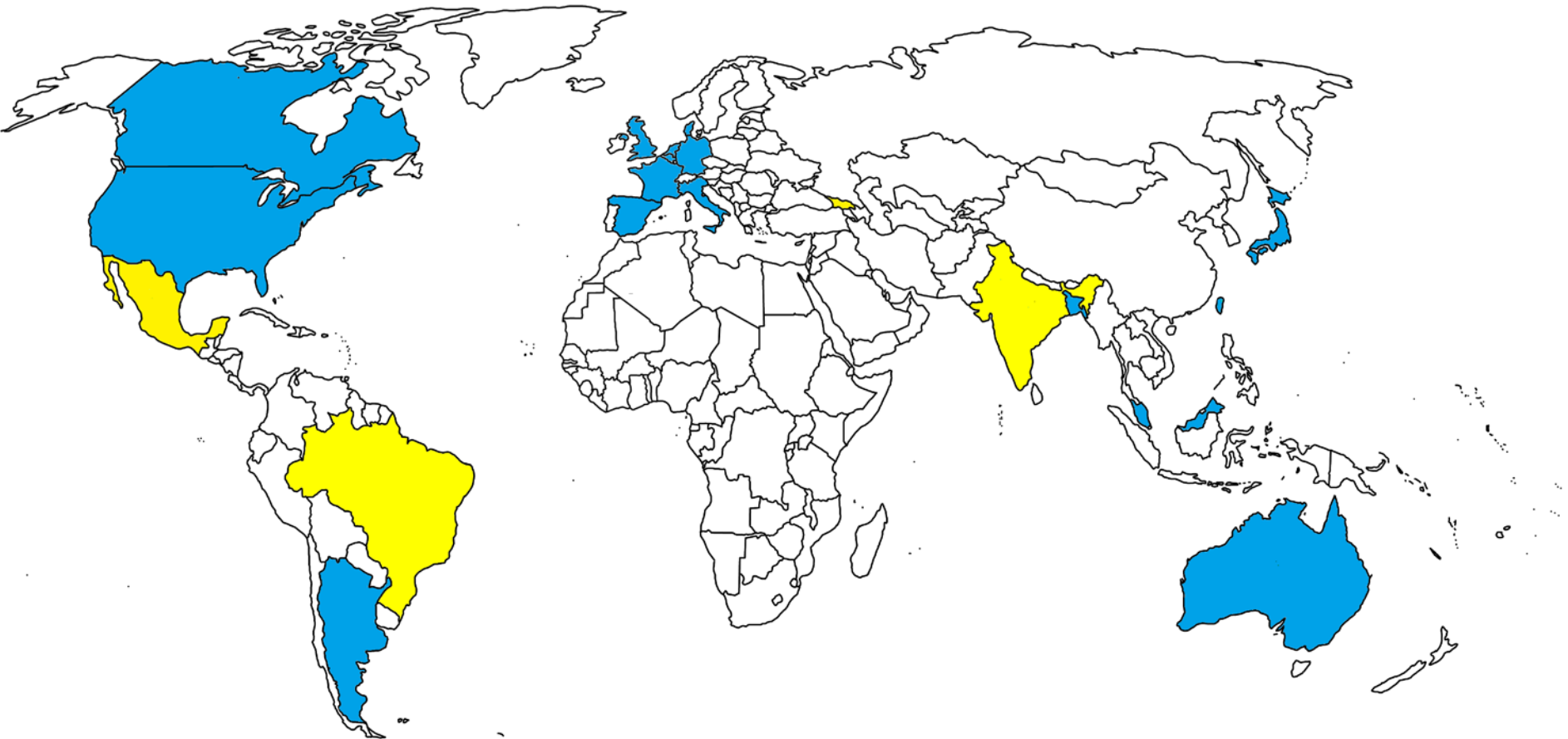
- **Study**

- Web-based supported

International GBS Outcome Study (IGOS)

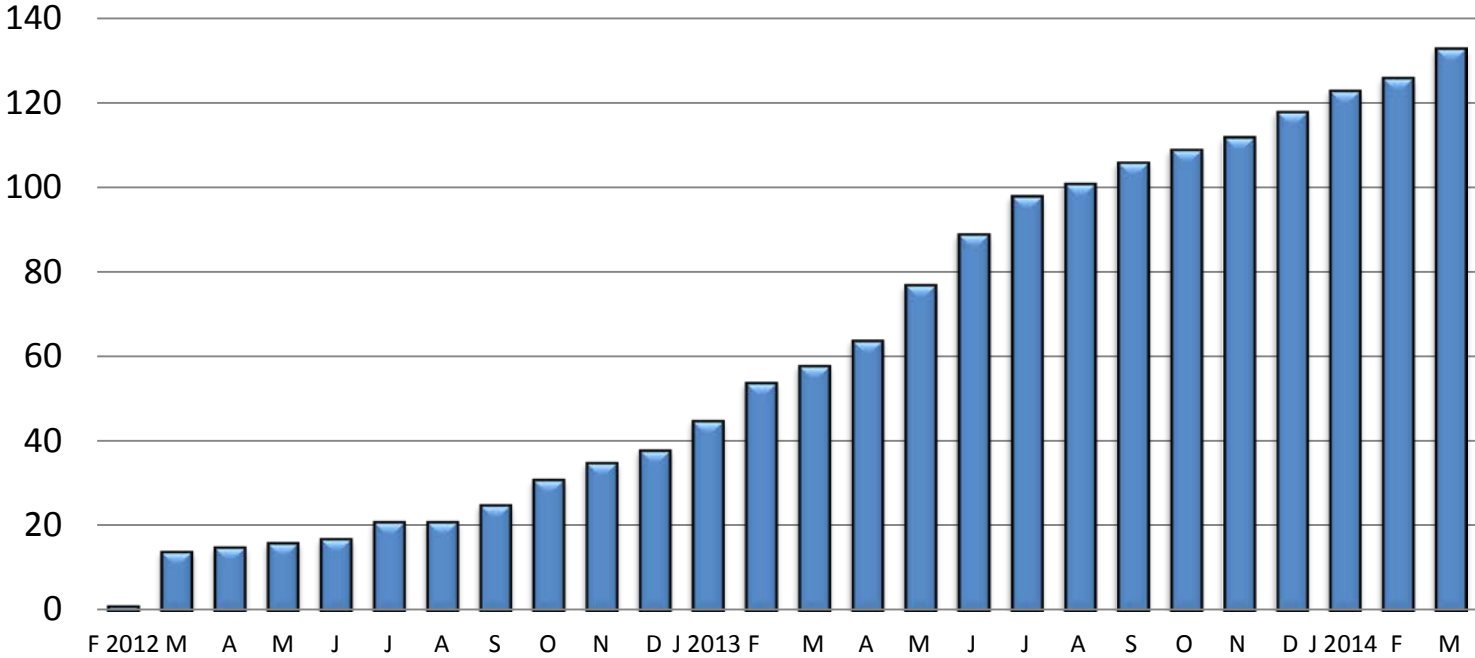


IGOS: a worldwide study



- Inclusion of patients
- In process of IRB approval

Number of hospitals with IRB approval





Déclaration de liens d'intérêt avec les industries de santé en rapport avec le thème de la présentation (loi du 04/03/2002) :

Intervenant : Hubert Philippe Endtz

Titre : Professeur d'Université

L'orateur ne souhaite pas répondre

- Consultant ou membre d'un conseil scientifique
- Conférencier ou auteur/rédacteur rémunéré d'articles ou documents
- Prise en charge de frais de voyage, d'hébergement ou d'inscription à des congrès ou autres manifestations
- Investigateur principal d'une recherche ou d'une étude clinique

OUI NON

OUI NON

OUI NON

OUI NON

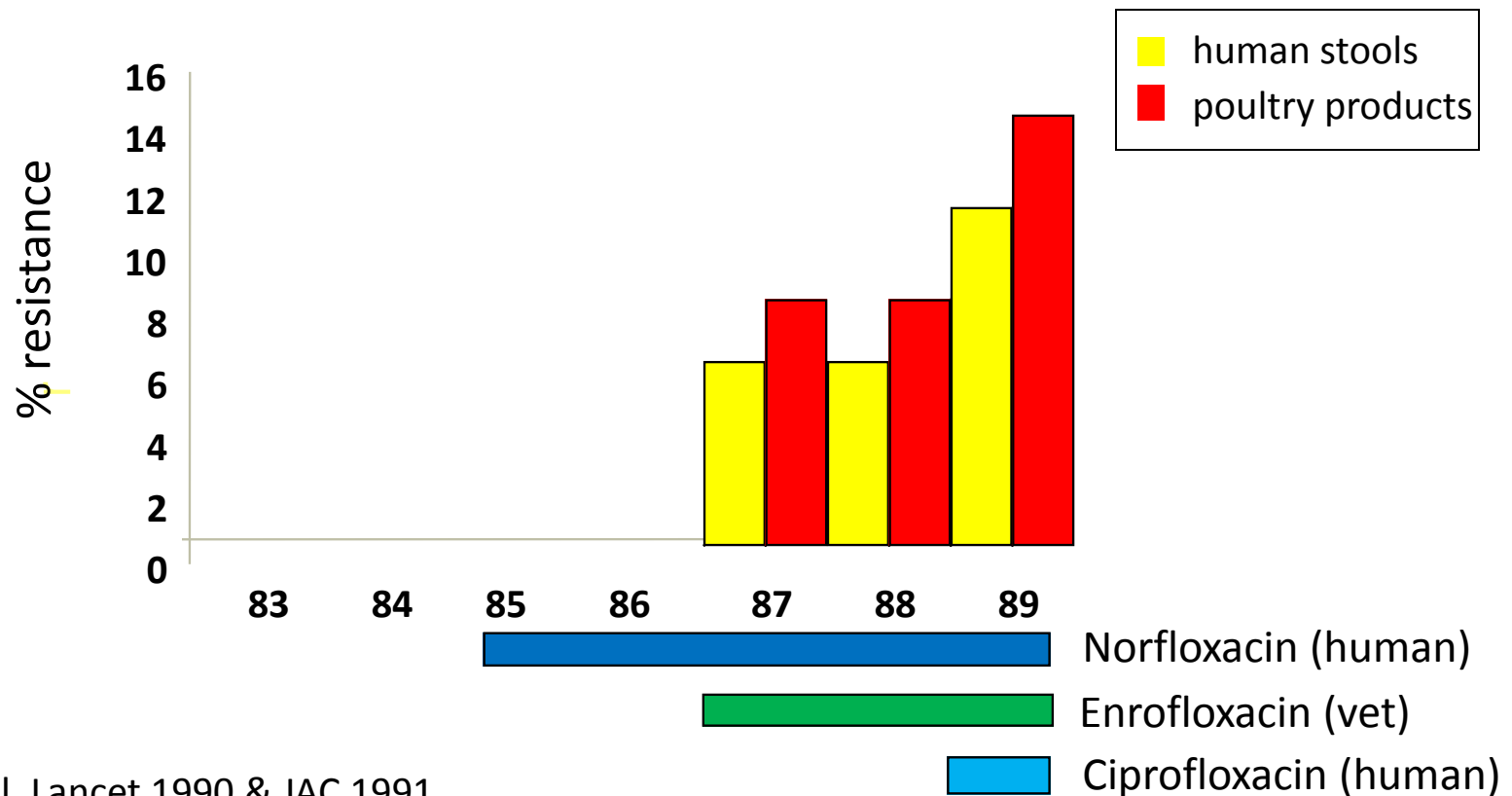


Hubert Endtz 0677221882 ou Glaucia Baccala 0619672388

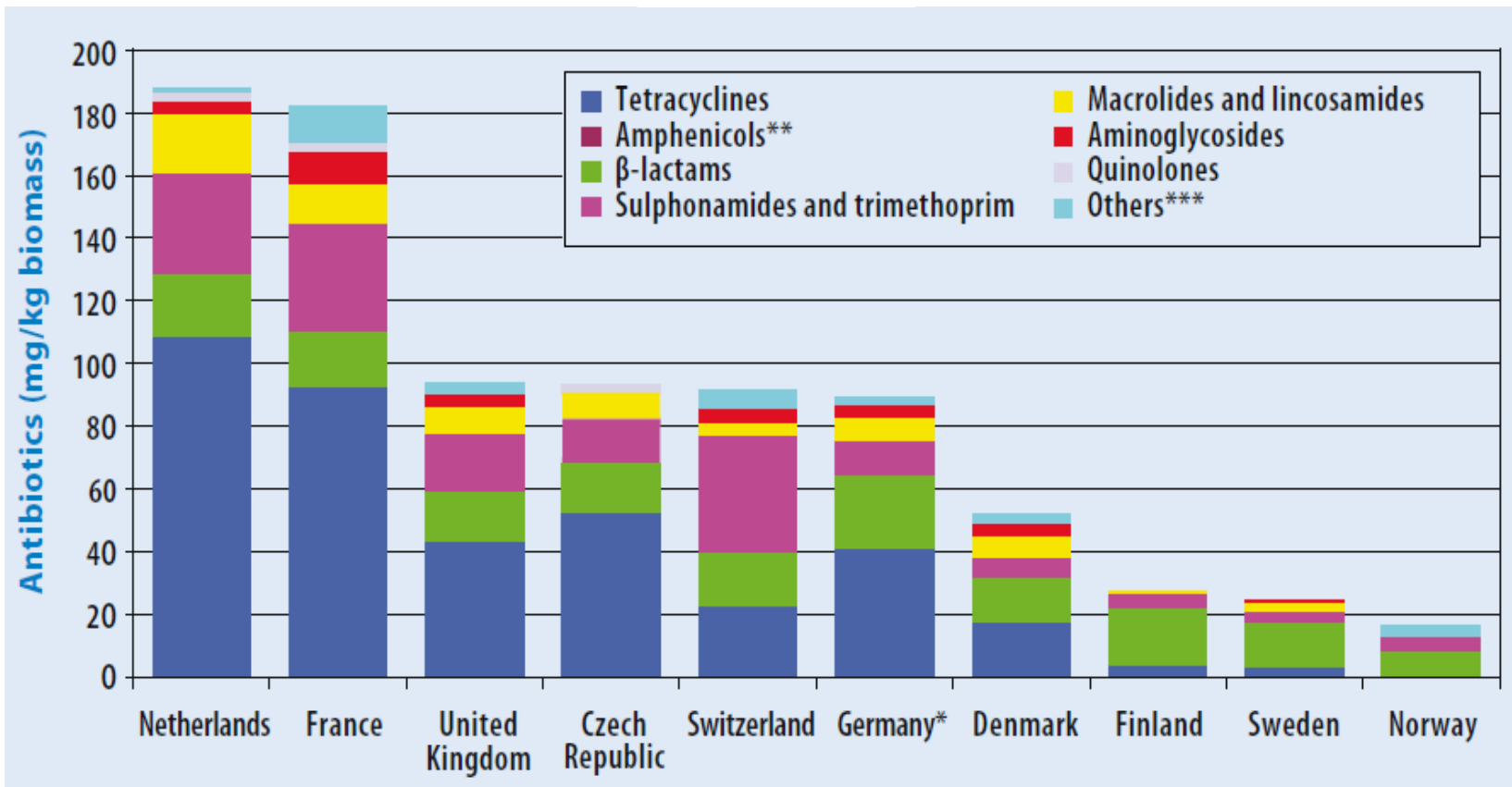


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Introduction of fluoroquinolone resistance in *Campylobacter jejuni* after its introduction on the market



Veterinary antibiotics sold per kg of biomass of pig, poultry and cattle meat, plus estimated live weight of dairy cattle



AMR in *Campylobacter jejuni*

USA		erythromycin	tetracyclin	ciprofloxacin	year
human	<i>C. jejuni</i>	1	43	22	2010
chicken	<i>C. jejuni</i>	1	36	22	2010

EU		erythromycin	tetracyclin	ciprofloxacin	year
human	<i>C. jejuni</i>	2	21	52	2010
chicken	<i>C. jejuni</i>	1	22	50	2010



AMR and Campylobacter knowledge gaps

- Few data on incidence and clinical importance of campylobacter in LIDC
- Few data on public health impact of resistance
- Few data on sources of resistant organisms
- Absence of clinical validation of resistance breakpoints

WHO 2013: Global view on campylobacteriosis

