JNI 18es Journées Nationales d'Infectiologie
du mercredi 21 au vendredi 23 juin 2017
Palais du Grand Large, Saint-Malo

Saint-Malo
et la région Bretagne

# Best-of : *Neuro-infectieux*

O. Epaulard, Grenoble

**Déclaration de liens d'intérêt avec les industries de santé (loi du 04/03/2002) :**

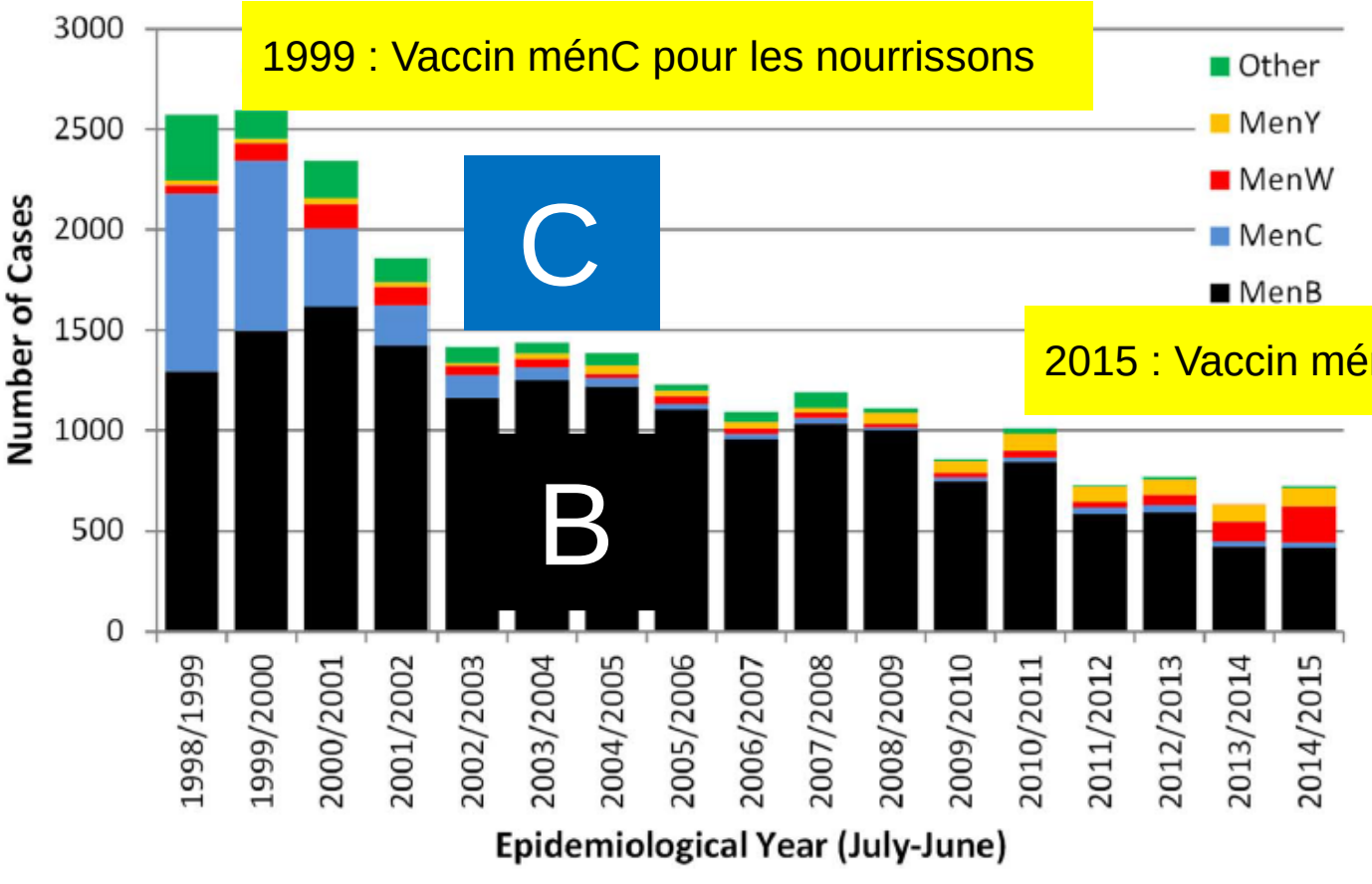
**Intervenant :** Olivier Epaulard

**Titre :** best-of en neuro-infectiologie

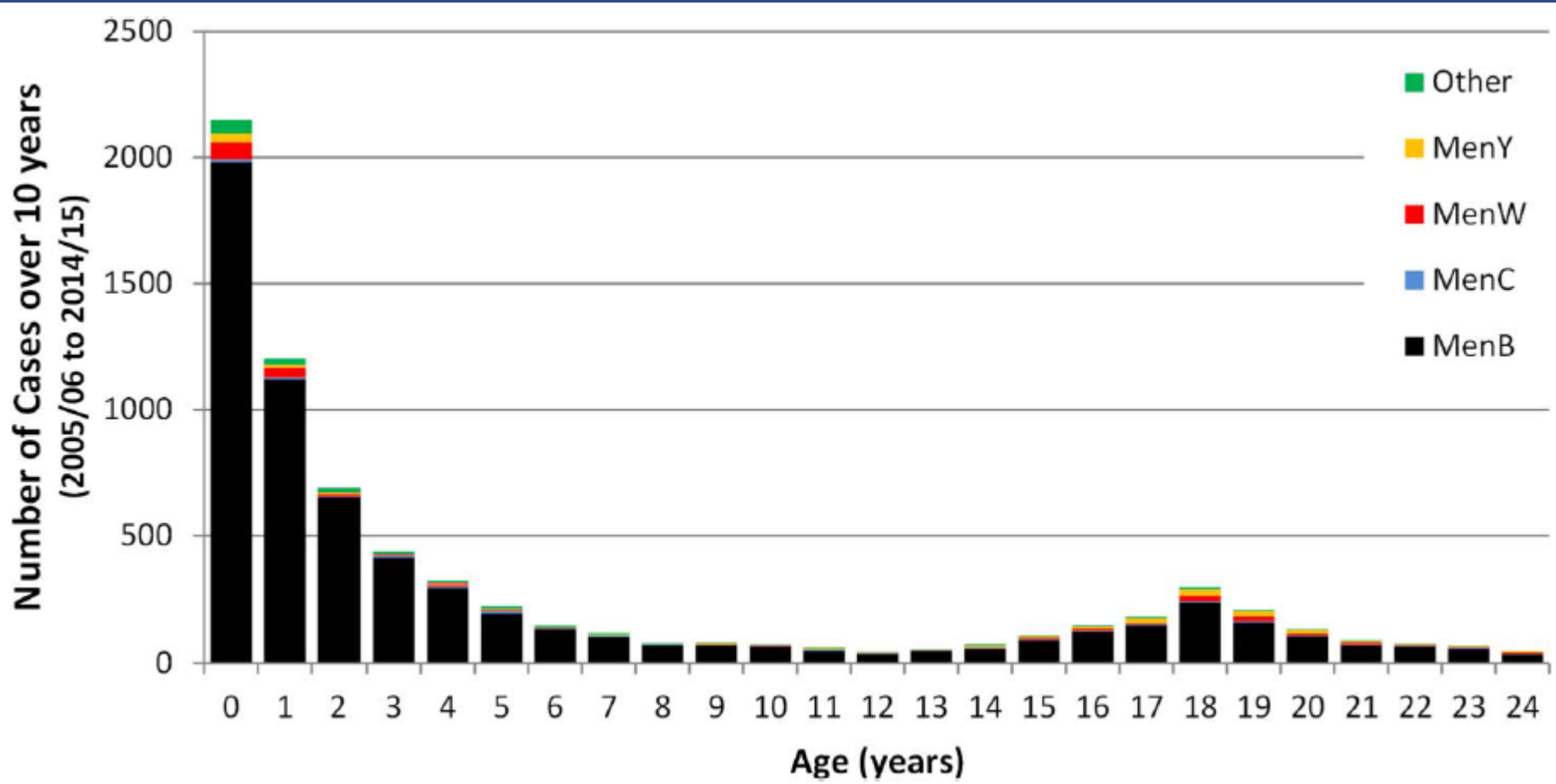
| | | |
|---|---|---|
| Consultant ou membre d'un conseil scientifique | ☐ OUI | ☑ NON |
| Conférencier ou auteur/rédacteur rémunéré d'articles ou documents | ☐ OUI | ☑ NON |
| Prise en charge de frais de voyage, d'hébergement ou d'inscription à des congrès ou autres manifestations | ☑ OUI | ☐ NON |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

# Vaccination anti-méningocoque protéique

# (« anti-méningocoque B »)




Ladhan, *Arch dis child* 2016


Number of Cases over 10 years
(2005/06 to 2014/15)
2500
2000
1500
1000
500
0
0 1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21 22 23 24
Age (years)
Other
MenY
MenW
MenC
MenB

# Introduction du vaccin méningocoque B

- Recommandations JCVI : février 2014
  - 2, 4 et 11 mois
  - Avec coprescription de paracétamol
- Accord avec GSK : mars 2015
- Inscription au CV du Royaume-Uni : septembre 2015
  - Couverture vaccinale à 6 mois pour les enfants nés en décembre : 95,5% et 88,6% pour 1 et 2 dose(s)

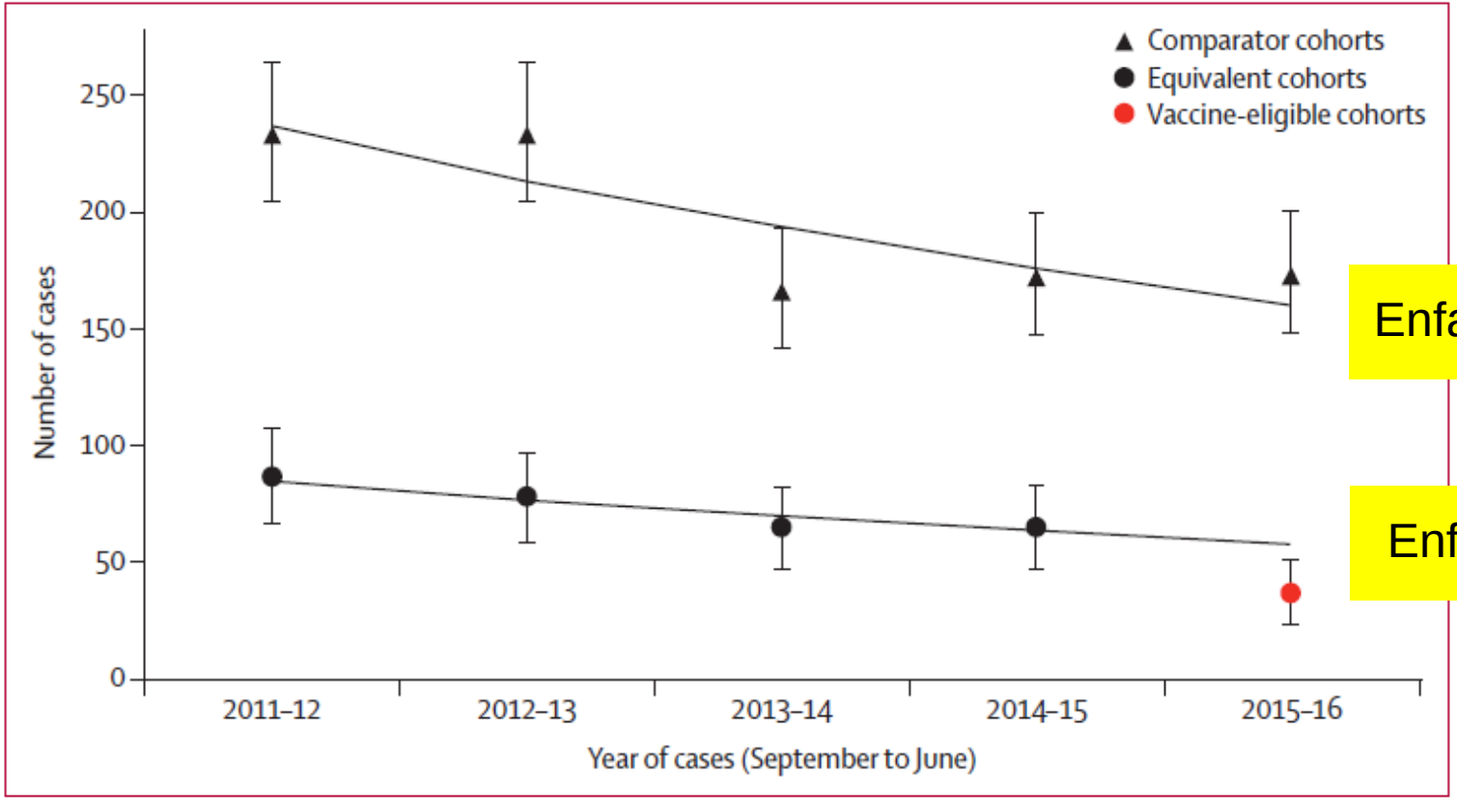
# Effectiveness and impact of a reduced infant schedule of 4CMenB vaccine against group B meningococcal disease in England: a national observational cohort study

*Sydel R Parikh, Nick J Andrews, Kazim Beebeejaun, Helen Campbell, Sonia Ribeiro, Charlotte Ward, Joanne M White, Ray Borrow, Mary E Ramsay, Shamez N Ladhani*

*Lancet* 2016; 388: 2775–82

Published Online
October 27, 2016
http://dx.doi.org/10.1016/
S0140-6736(16)31921-3

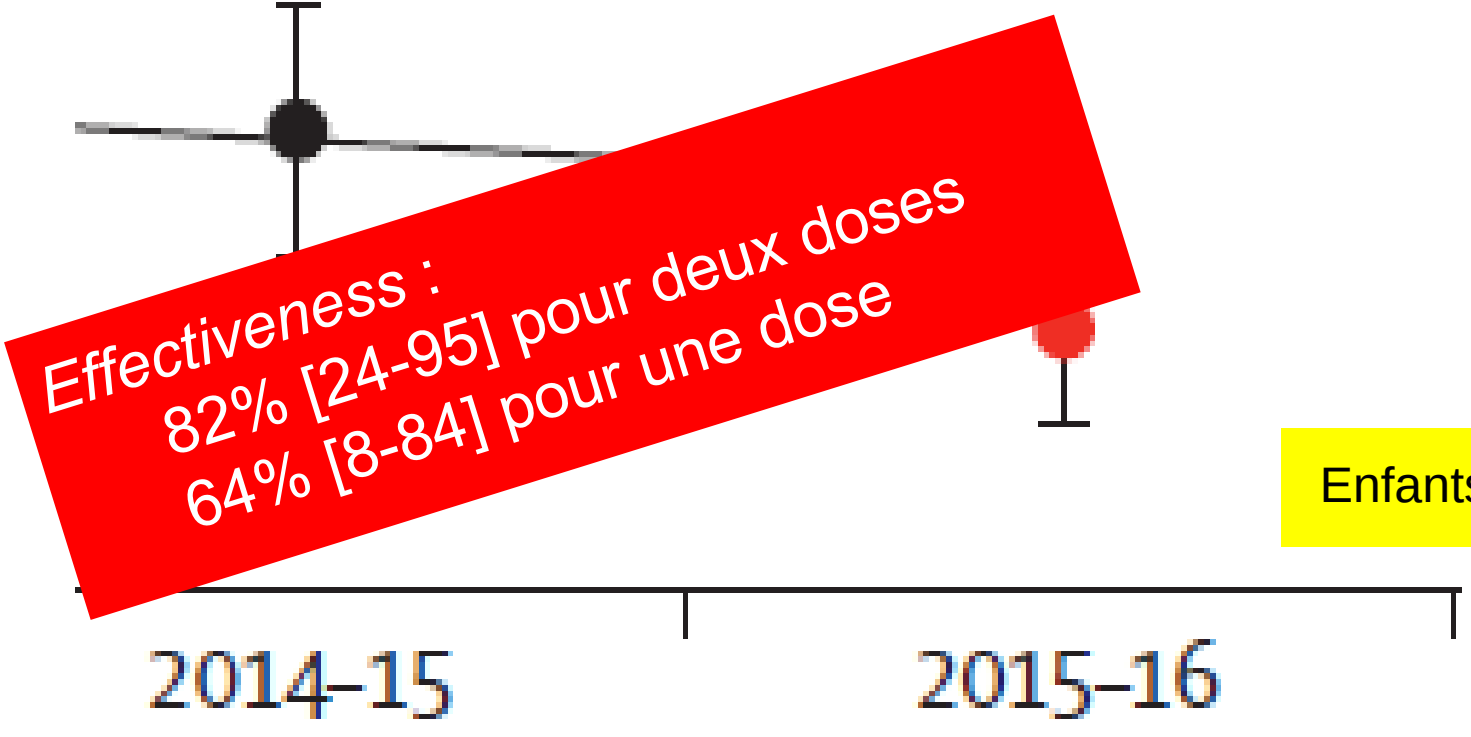
See Comment page 2719




Enfants 1-5 ans

Enfants 0-1 an

*Figure 2:* Numbers of cases of MenB disease in vaccine-eligible and comparator cohorts in England, 2011–16, with Poisson 95% CIs and fitted trend




Enfants 0-1 an

**Petitions**

UK Government and Parliament

Closed petition

# Give the Meningitis B vaccine to ALL children, not just newborn babies.

All children are at risk from this terrible infection, yet the Government plan to only vaccinate 2-5 month olds. There needs to be a rollout programme to vaccinate all children, at least up to age 11. Meningococcal infections can be very serious, causing MENINGITIS, SEPTICAEMIA & DEATH.

▶ More details

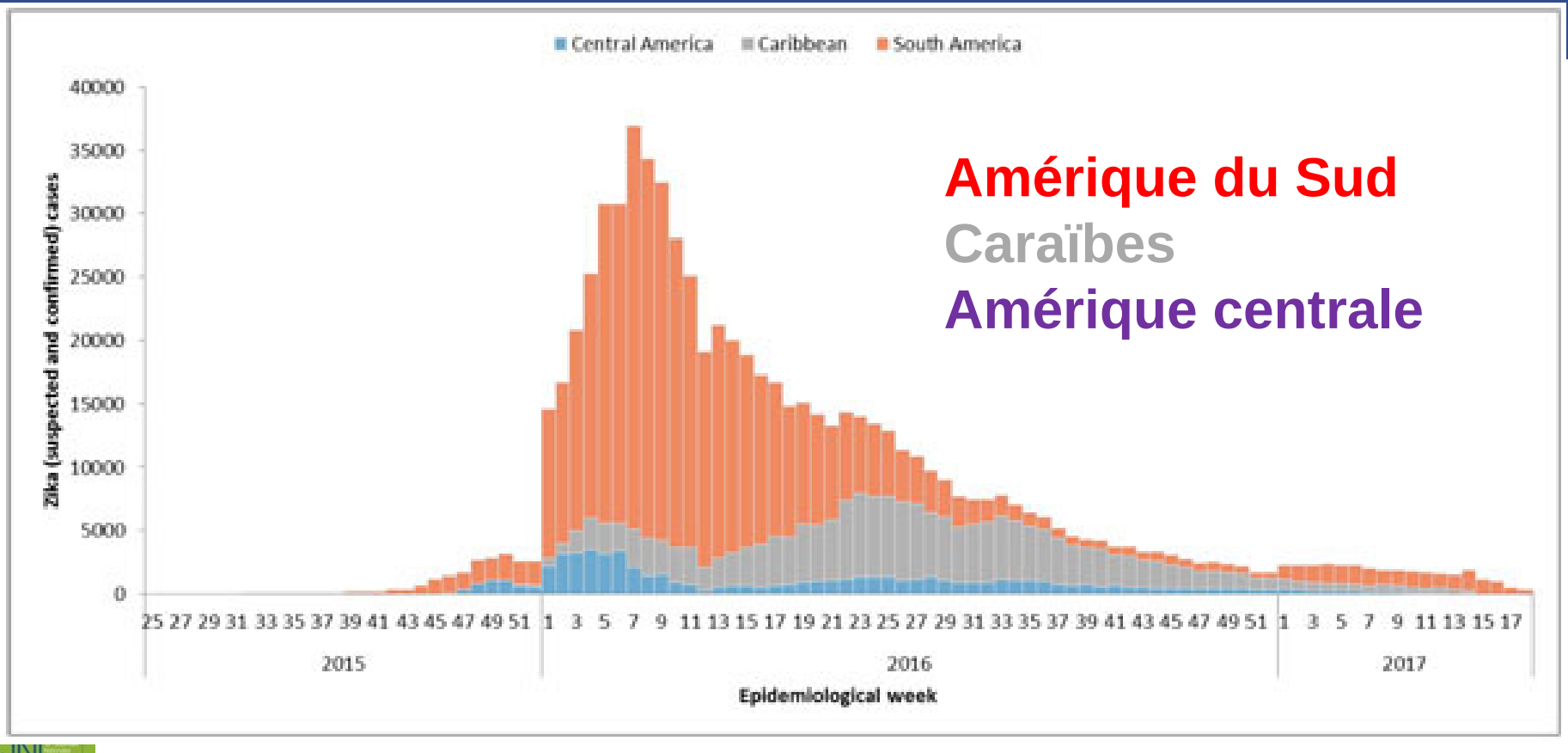
**This petition is closed**

**All petitions run for 6 months**

**823,348 signatures**

100,000

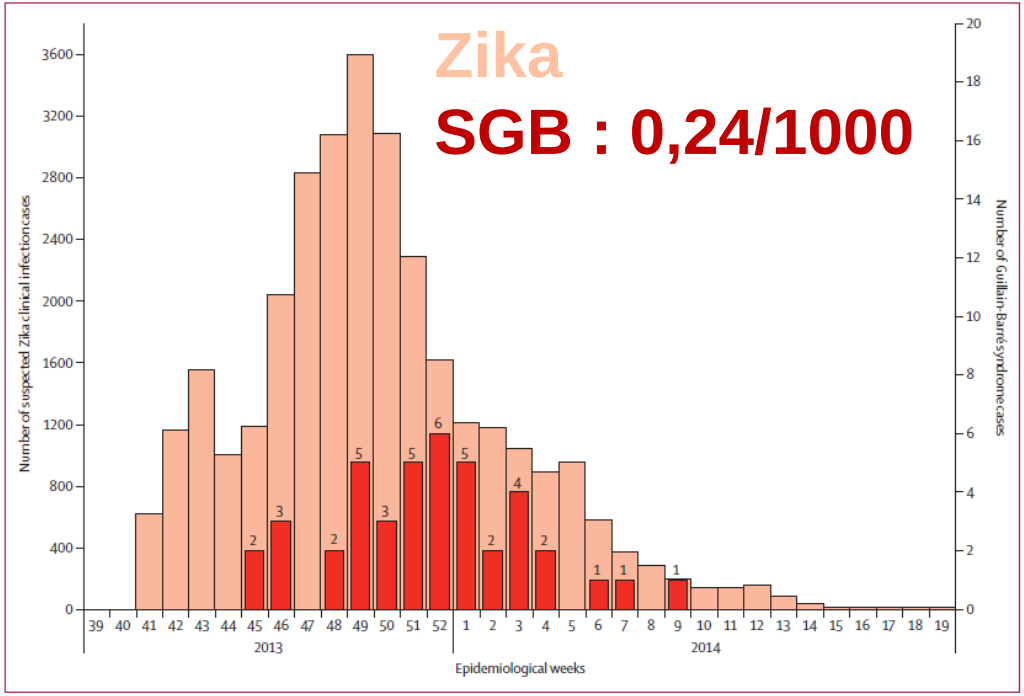
# Neurotropisme du Zika


Central America
Caribbean
South America
Zika (suspected and confirmed) cases
40000
35000
30000
25000
20000
15000
10000
5000
0
25 27 29 31 33 35 37 39 41 43 45 47 49 51 1 3 5 7 9 11 13 15 17 19 21 23 25 27 29 31 33 35 37 39 41 43 45 47 49 51 1 3 5 7 9 11 13 15 17
2015
2016
2017
Epidemiological week
Amérique du Sud
Caraïbes
Amérique centrale

# Guillain-Barré Syndrome outbreak associated with Zika virus infection in French Polynesia: a case-control study

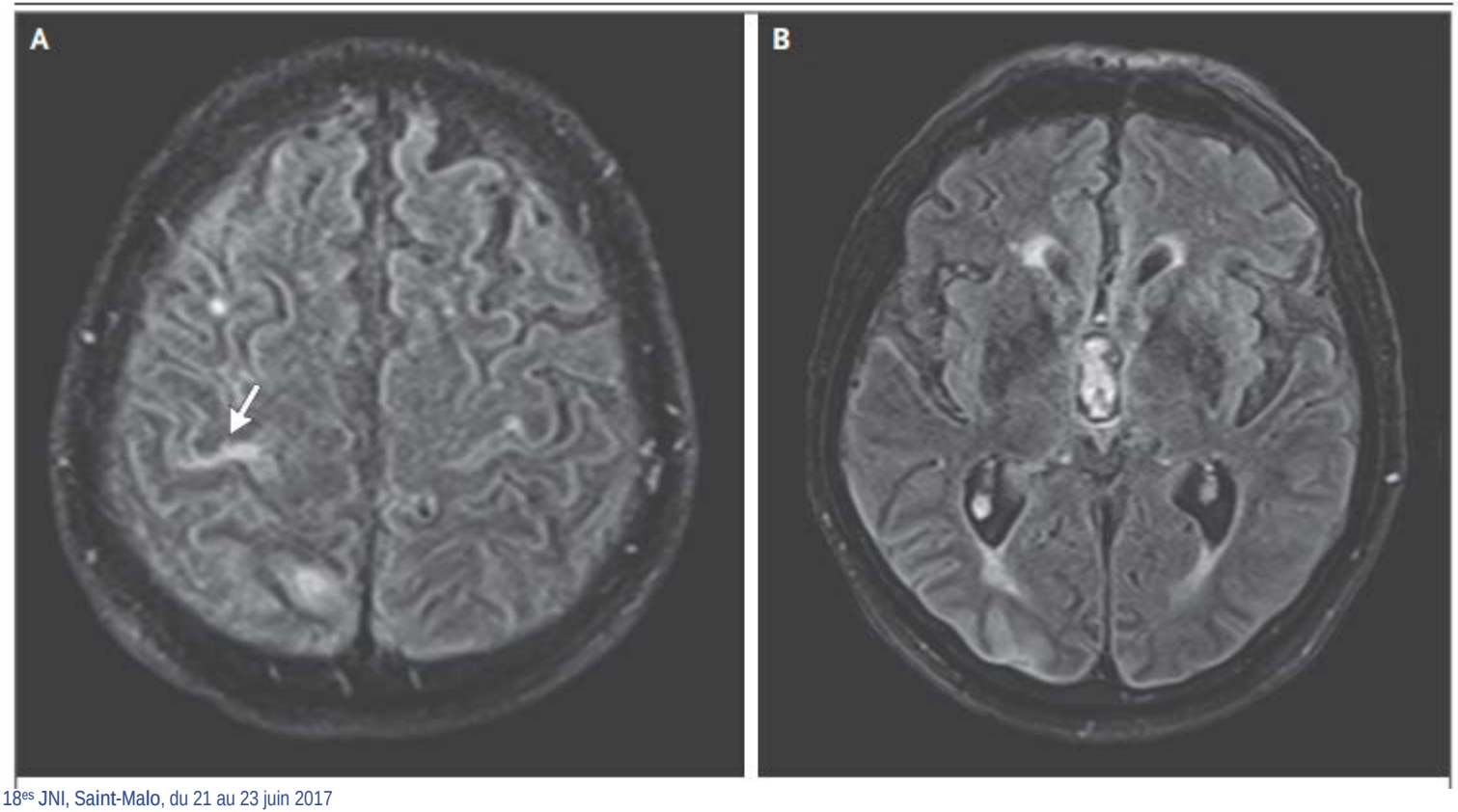
Van-Mai Cao-Lormeau*, Alexandre Blake*, Sandrine Mons, Stéphane Lastère, Claudine Roche, Jessica Vanhomwegen, Timothée Dub, Laure Baudouin, Anita Teissier, Philippe Larre, Anne-Laure Vial, Christophe Decam, Valérie Choumet, Susan K Halstead, Hugh J Willison, Lucile Musset, Jean-Claude Manuguerra, Philippe Despres, Emmanuel Fournier, Henri-Pierre Mallet, Didier Musso, Arnaud Fontanet*, Jean Neil*, Frédéric Ghawché*

2016

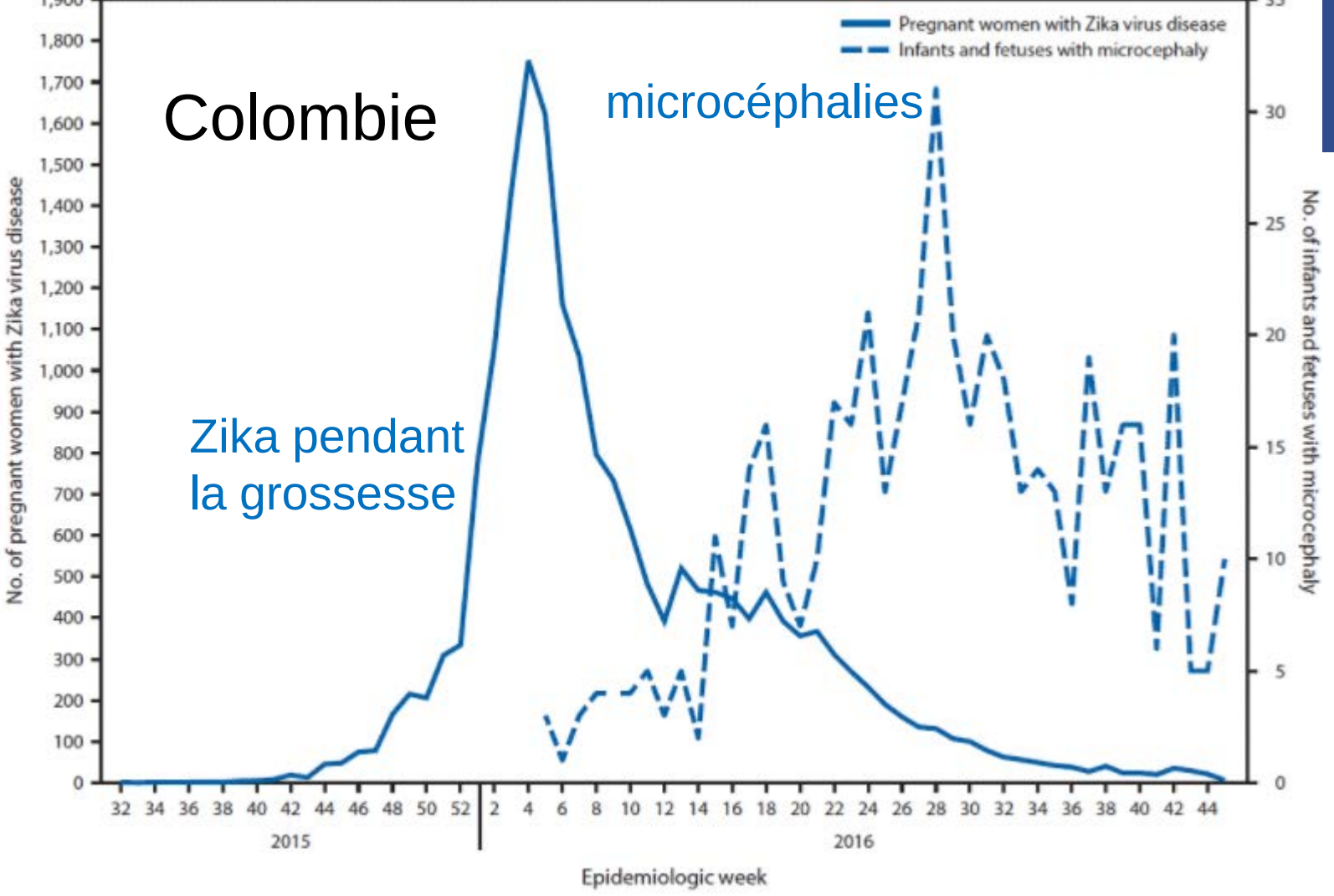


# Zika Virus Associated with Meningoencephalitis

Carteaux, *NEJM* 2016



# Colombie




microcéphalies

Zika pendant
la grossesse

The NEW ENGLAND JOURNAL of MEDICINE

BRIEF REPORT

# Zika Virus Associated with Microcephaly

Jernej Mlakar, M.D., Misa Korva, Ph.D., Nataša Tul, M.D., Ph.D., Mara Popović, M.D., Ph.D., Mateja Poljšak-Prijatelj, Ph.D., Jerica Mraz, M.Sc., Marko Kolenc, M.Sc., Katarina Resman Rus, M.Sc., Tina Vesnaver Vipotnik, M.D., Vesna Fabjan Vodušek, M.D., Alenka Vizjak, Ph.D., Jože Pižem, M.D., Ph.D., Miroslav Petrovec, M.D., Ph.D., and Tatjana Avšič Županc, Ph.D.

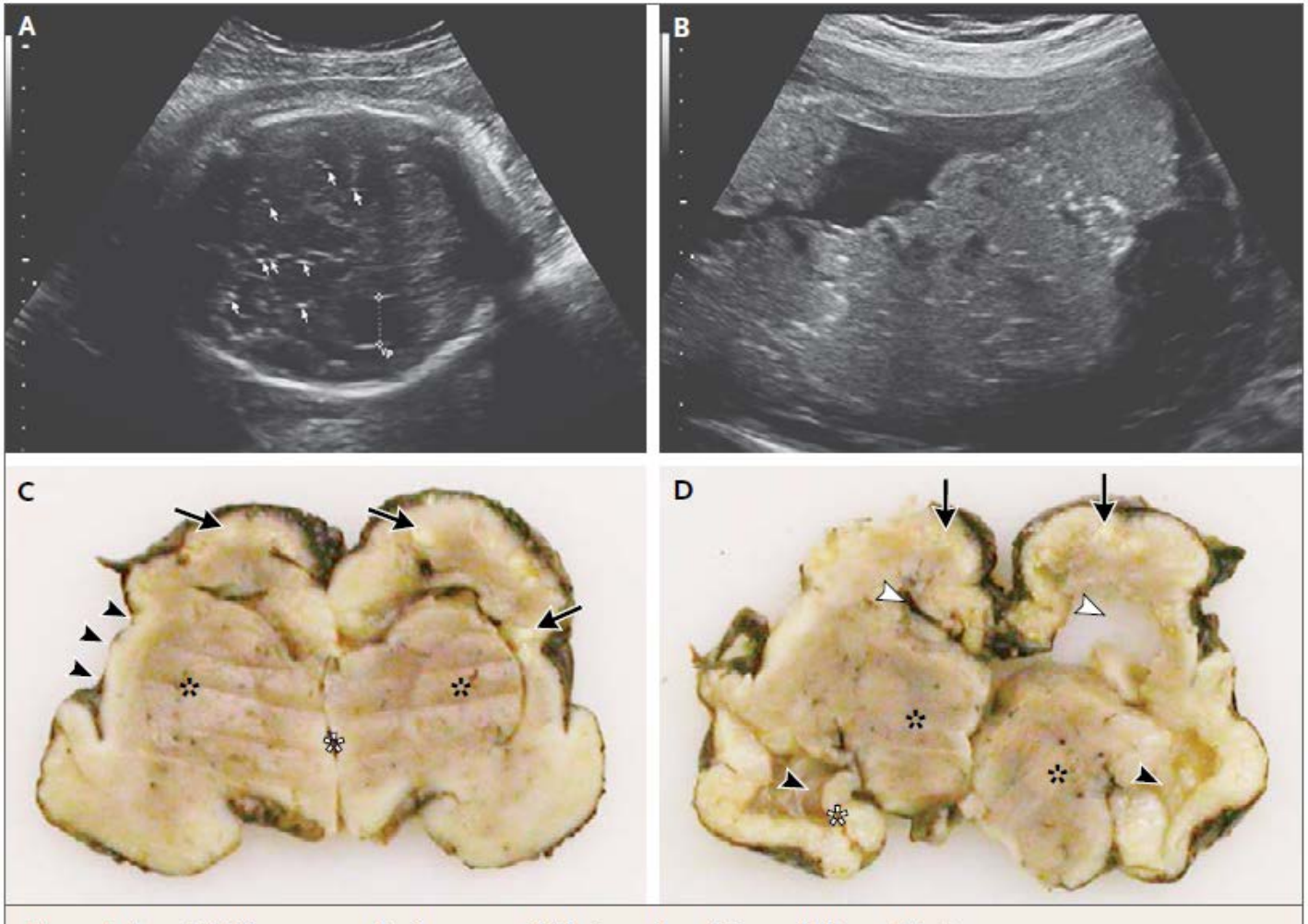
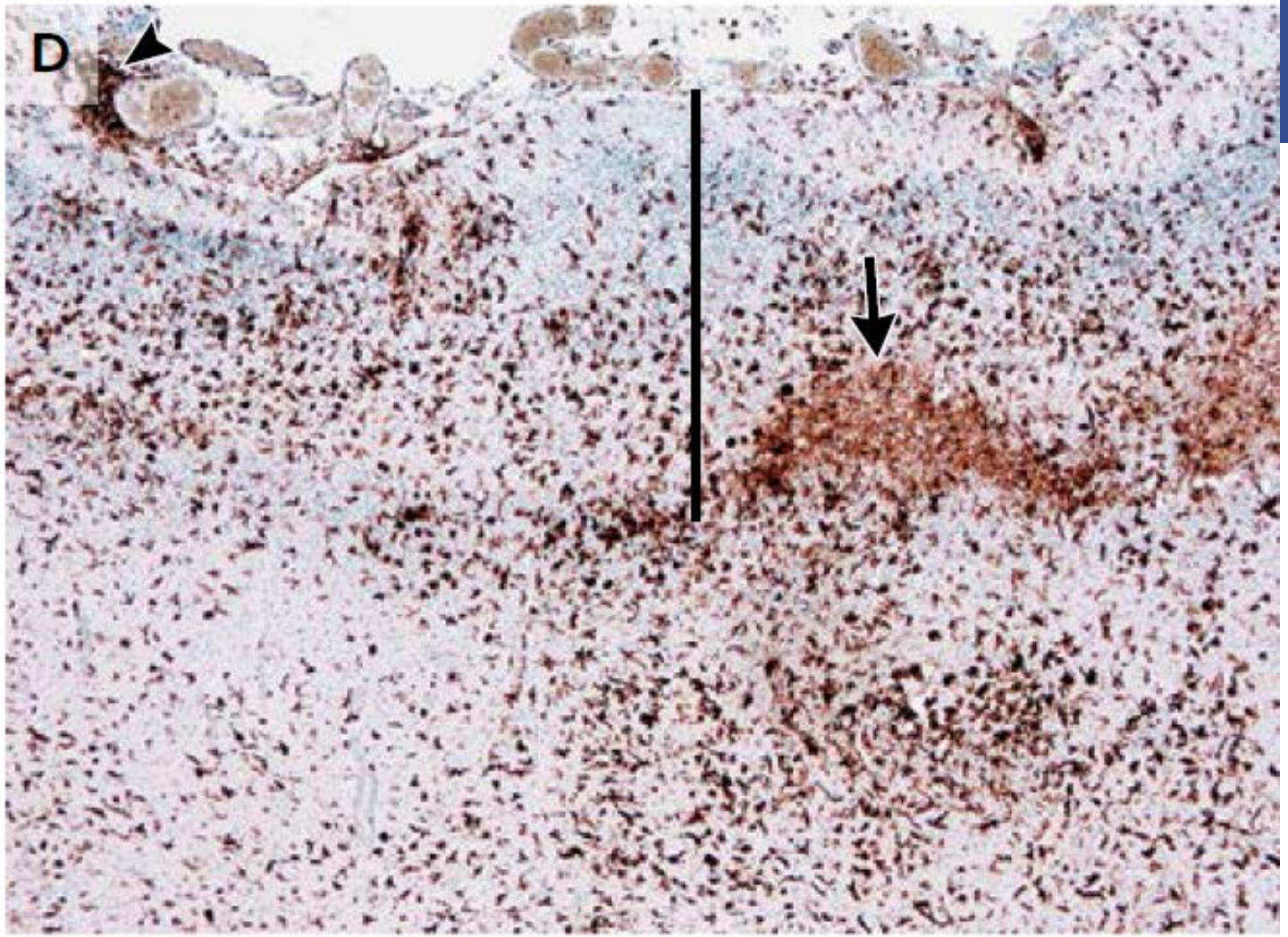



**Figure 1.** Prenatal Ultrasonographic Images and Photographs of Coronal Slices of Brain.


D

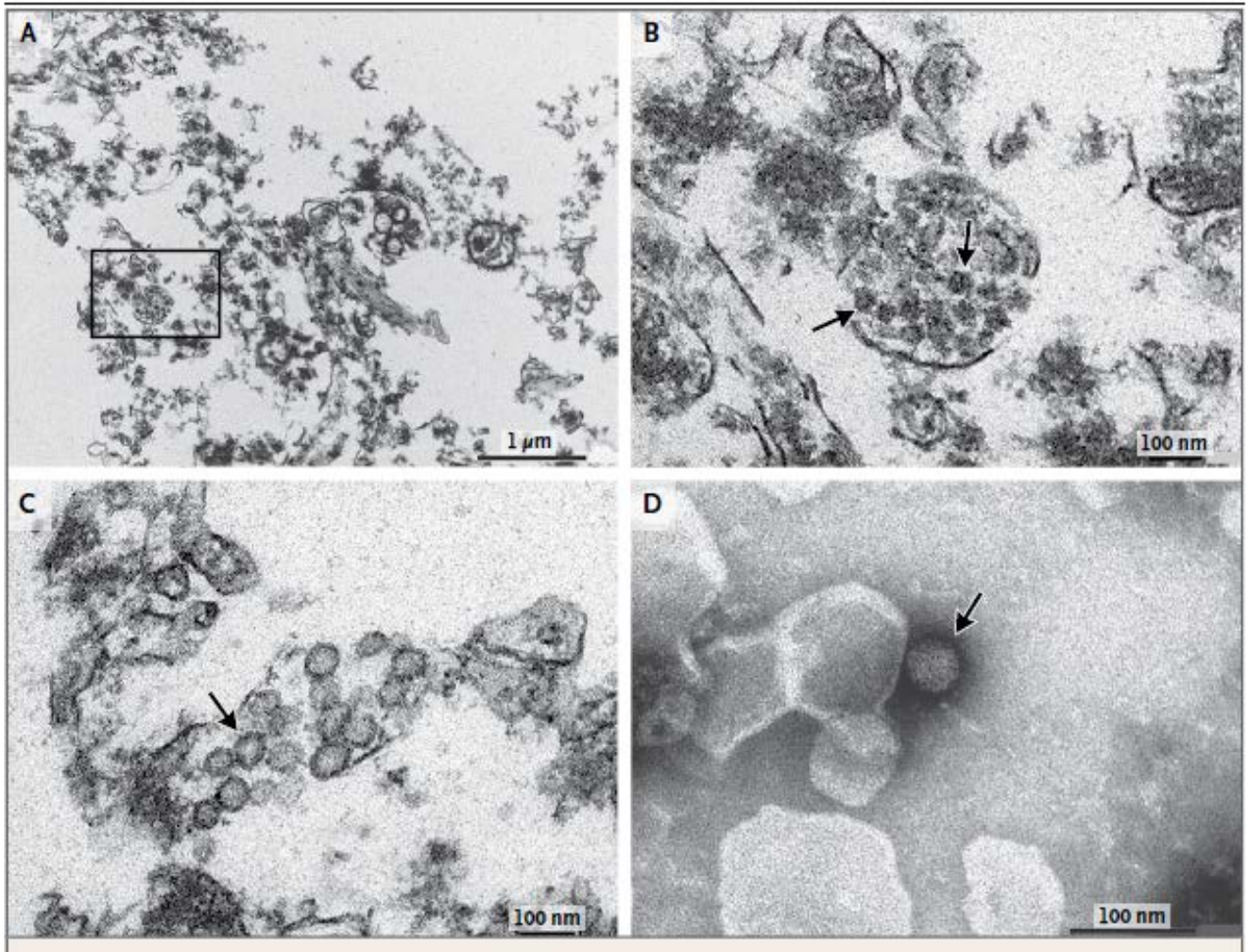
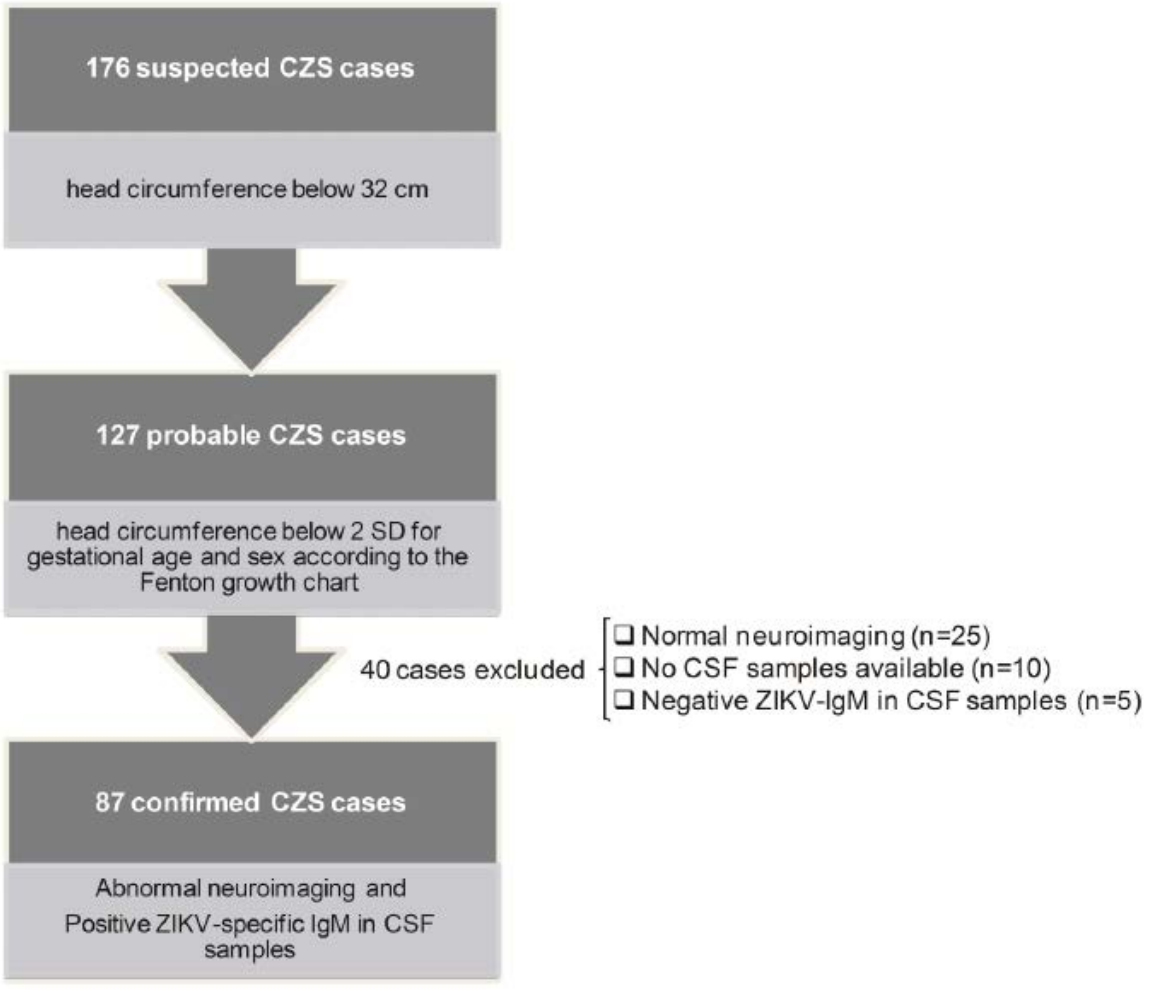
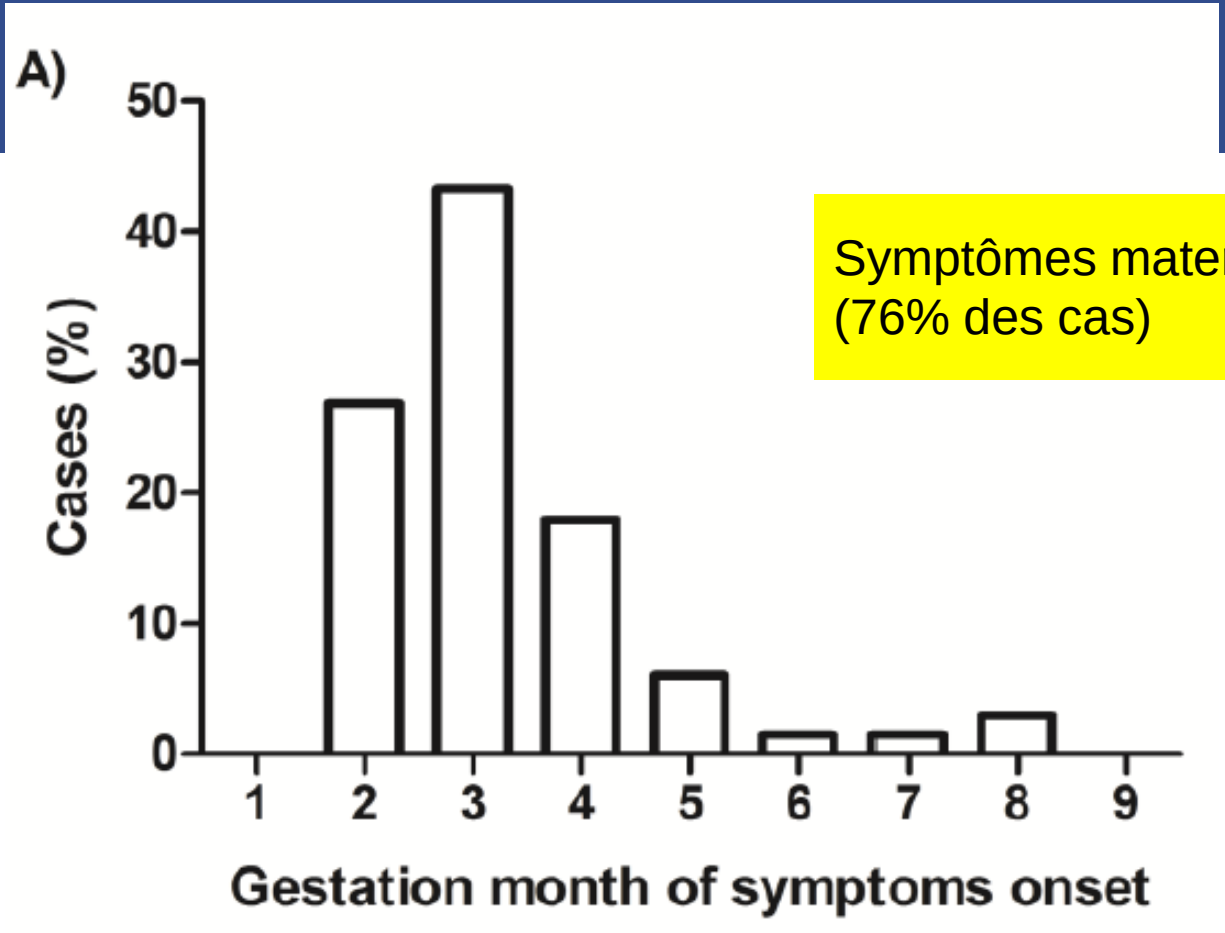



**Figure 3.** Electron Microscopy of Ultrathin Sections of Fetal Brain and Staining of a Flavivirus-like Particle.

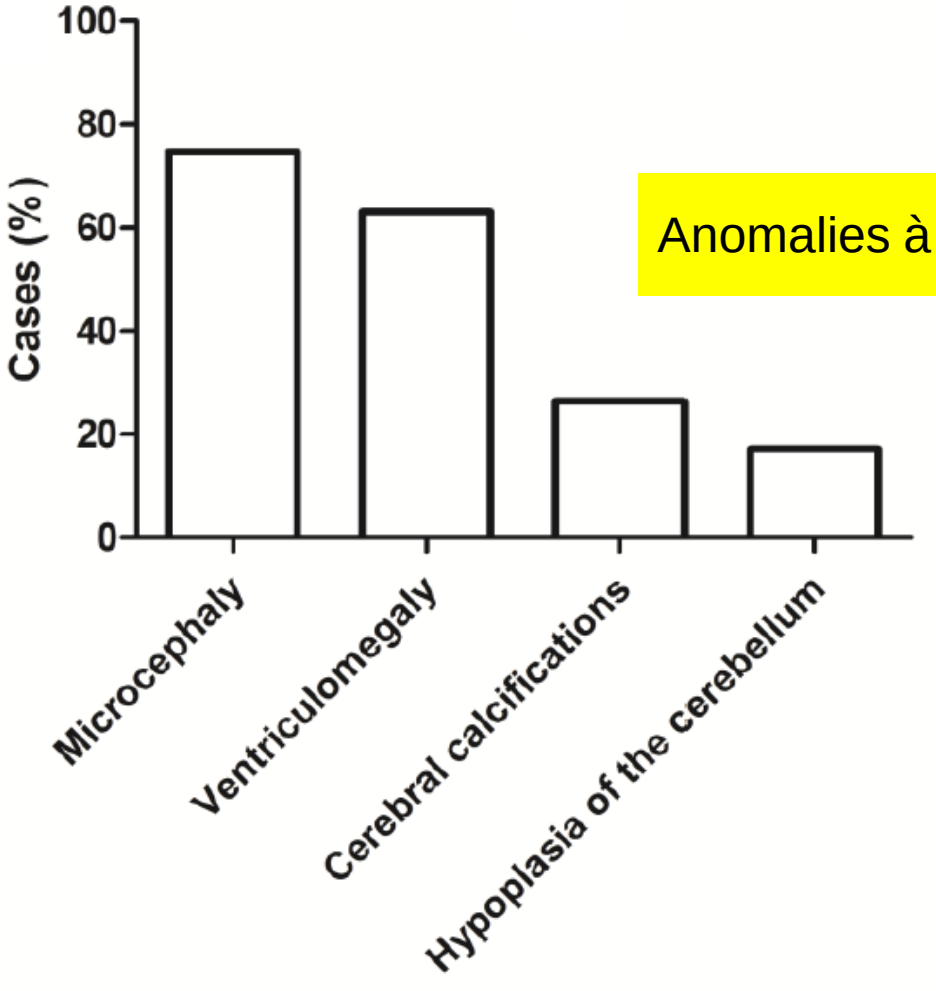
# Lessons Learned at the Epicenter of Brazil's Congenital Zika Epidemic: evidence from 87 Confirmed Cases

- Meneses et al, CID 2017


176 suspected CZS cases
head circumference below 32 cm
127 probable CZS cases
head circumference below 2 SD for gestational age and sex according to the Fenton growth chart
40 cases excluded
❑ Normal neuroimaging (n=25)
❑ No CSF samples available (n=10)
❑ Negative ZIKV-IgM in CSF samples (n=5)
87 confirmed CZS cases
Abnormal neuroimaging and
Positive ZIKV-specific IgM in CSF samples




Symptômes maternels
(76% des cas)




Anomalies à l'imagerie

Arthrogrypose : 20,6%

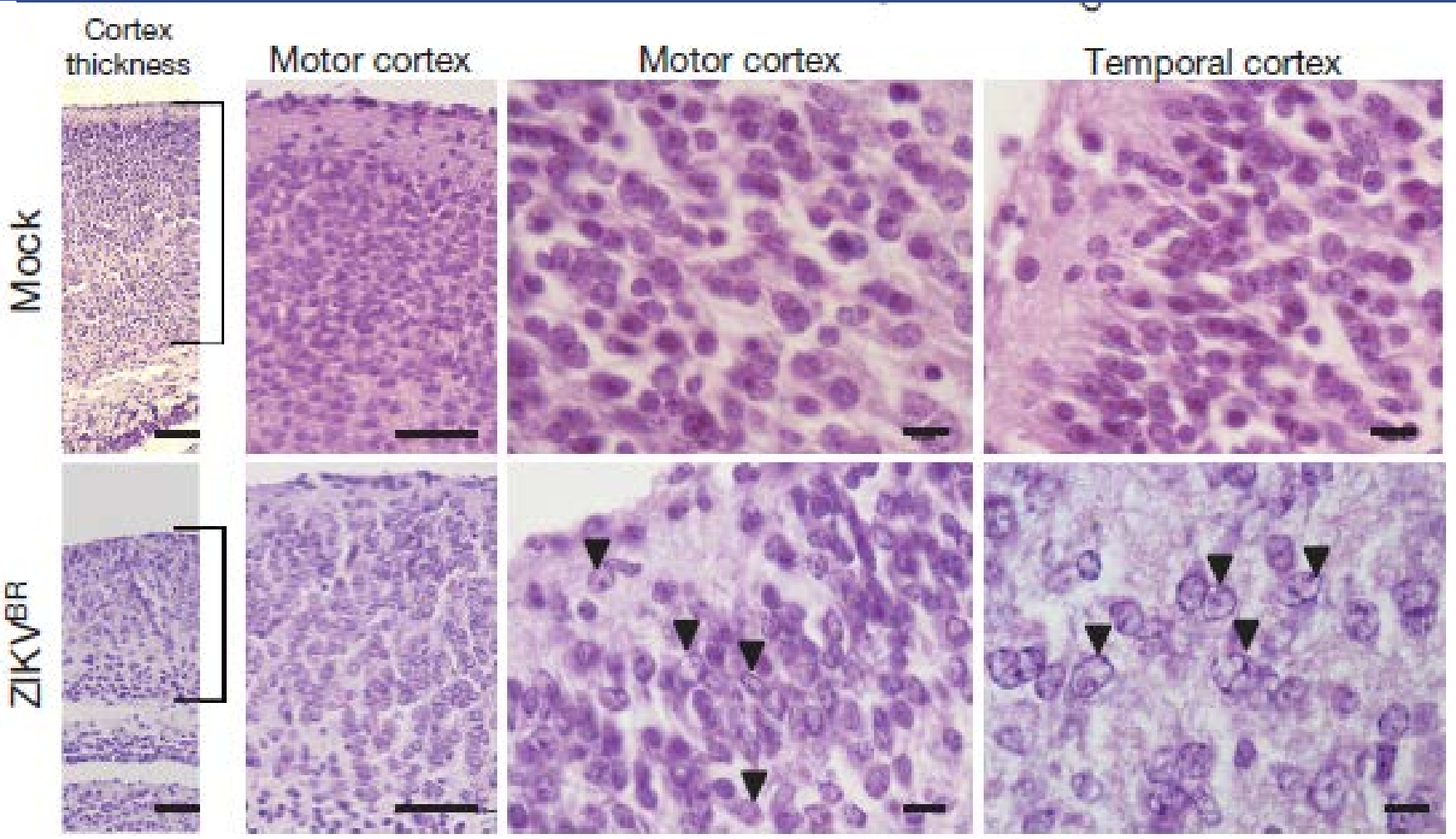
LETTER

doi:10.1038/nature18296

# The Brazilian Zika virus strain causes birth defects in experimental models

Fernanda R. Cugola[1]*, Isabella R. Fernandes[1,2]*, Fabiele B. Russo[1,3]*, Beatriz C. Freitas[2], João L. M. Dias[1], Katia P. Guimarães[1], Cecília Benazzato[1], Nathalia Almeida[1], Graciela C. Pignatari[1,3], Sarah Romero[2], Carolina M. Polonio[4], Isabela Cunha[4], Carla L. Freitas[4], Wesley N. Brandão[4], Cristiano Rossato[4], David G. Andrade[4], Daniele de P. Faria[5], Alexandre T. Garcez[5], Carlos A. Buchpigel[5], Carla T. Braconi[6], Erica Mendes[6], Amadou A. Sall[7], Paolo M. de A. Zanotto[6], Jean Pierre S. Peron[4], Alysson R. Muotri[2] & Patricia C. B. Beltrão-Braga[1,8]

2017

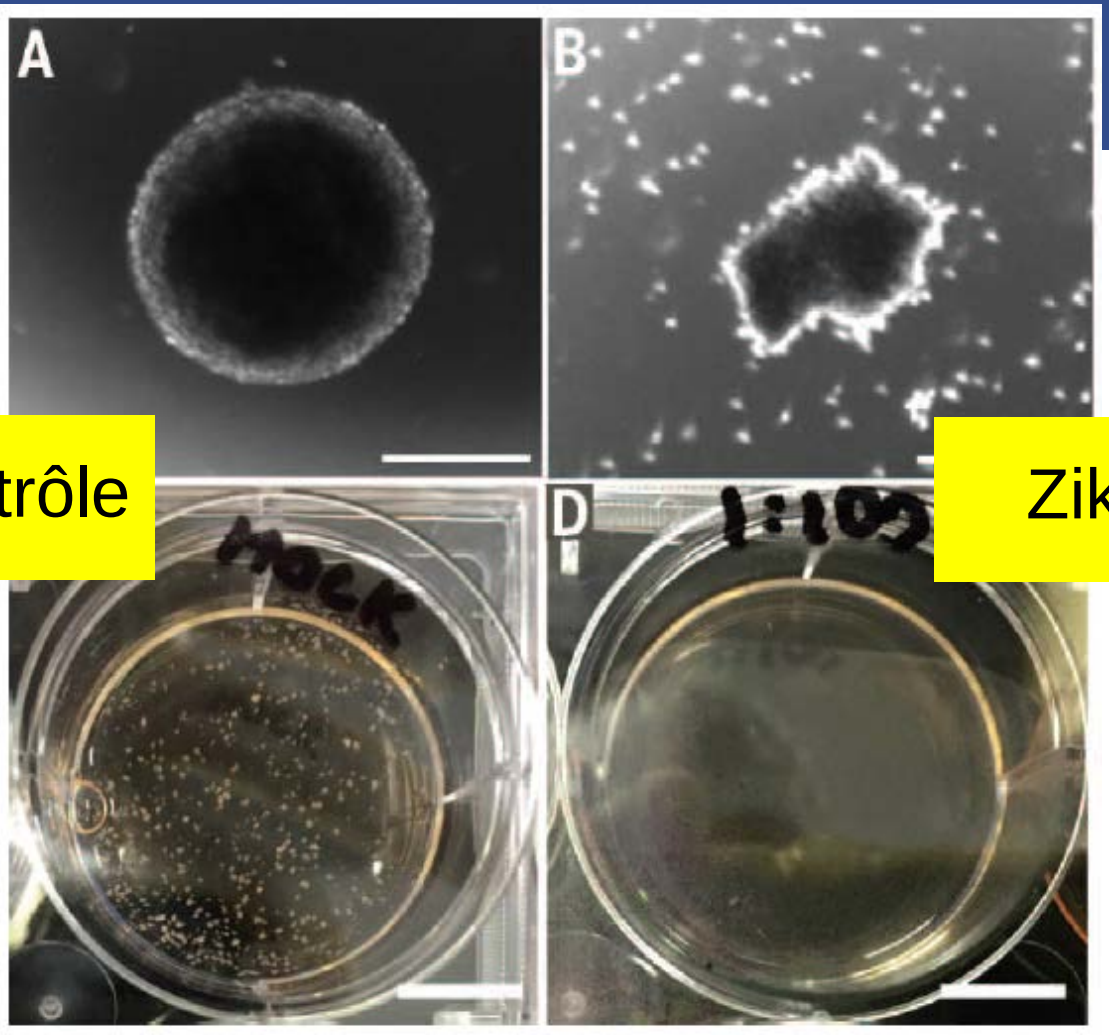

Cortex thickness
Motor cortex
Motor cortex
Temporal cortex
Mock
ZIKV^BR

# Zika virus impairs growth in human neurospheres and brain organoids

Patricia P. Garcez,[2,1*] Erick Correia Loiola,[1†] Rodrigo Madeiro da Costa,[1†]
Luiza M. Higa,[3†] Pablo Trindade,[1†] Rodrigo Delvecchio,[3]
Juliana Minardi Nascimento,[1,4] Rodrigo Brindeiro,[3]
Amilcar Tanuri,[3] Stevens K. Rehen[1,2*]

Science 2017


Contrôle




Contrôle

Zika

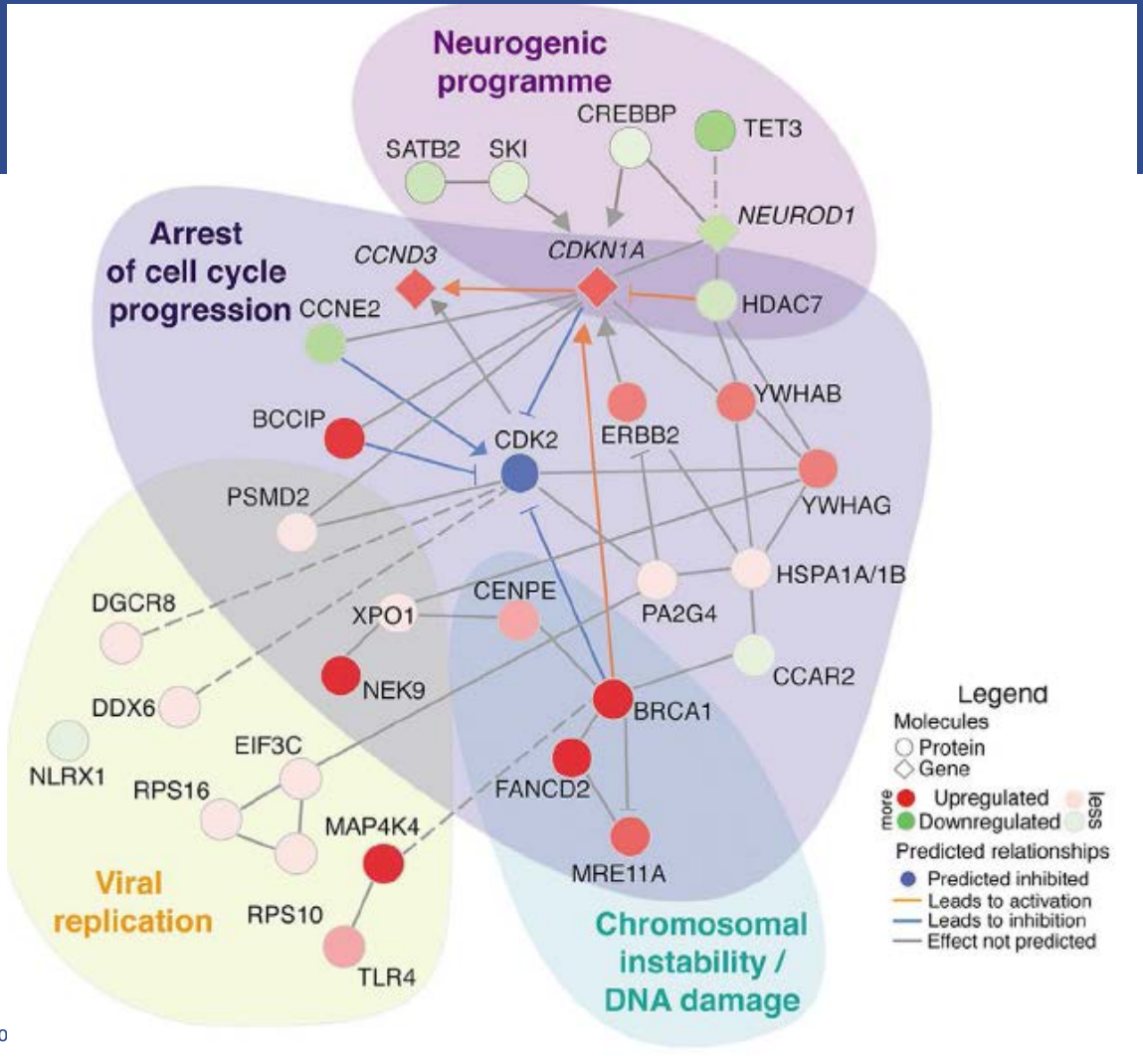
SCIENTIFIC REPORTS

OPEN

# Zika virus disrupts molecular fingerprinting of human neurospheres

Received: 01 August 2016
Accepted: 09 December 2016
Published: 23 January 2017

Patricia P. Garcez[1,2], Juliana Minardi Nascimento[1,3], Janaina Mota de Vasconcelos[4], Rodrigo Madeiro da Costa[1], Rodrigo Delvecchio[5], Pablo Trindade[1], Erick Correia Loiola[1], Luiza M. Higa[5], Juliana S. Cassoli[3], Gabriela Vitória[1], Patricia C. Sequeira[6], Jaroslaw Sochacki[1], Renato S. Aguiar[5], Hellen Thais Fuzii[7], Ana M. Bispo de Filippis[6], João Lídio da Silva Gonçalves Vianez Júnior[4], Amilcar Tanuri[5], Daniel Martins-de-Souza[3] & Stevens K. Rehen[1,2]


Neurogenic programme
CREBBP
TET3
SATB2
SKI
NEUROD1
Arrest of cell cycle progression
CCND3
CDKN1A
CCNE2
HDAC7
YWHAB
BCCIP
CDK2
ERBB2
PSMD2
YWHAG
HSPA1A/1B
CENPE
DGCR8
XPO1
PA2G4
CCAR2
NEK9
DDX6
BRCA1
NLRX1
EIF3C
FANCD2
RPS16
MAP4K4
MRE11A
Viral replication
RPS10
TLR4
Chromosomal instability / DNA damage
Legend
Molecules
Protein
Gene
more
Upregulated
Downregulated
less
Predicted relationships
Predicted inhibited
Leads to activation
Leads to inhibition
Effect not predicted


Expert Review of Vaccines

ISSN: 1476-0584 (Print) 1744-8395 (Online) Journal homepage: http://www.tandfonline.com/loi/ierv20

# An update on Zika vaccine developments

Anna Durbin & Annelies Wilder-Smith

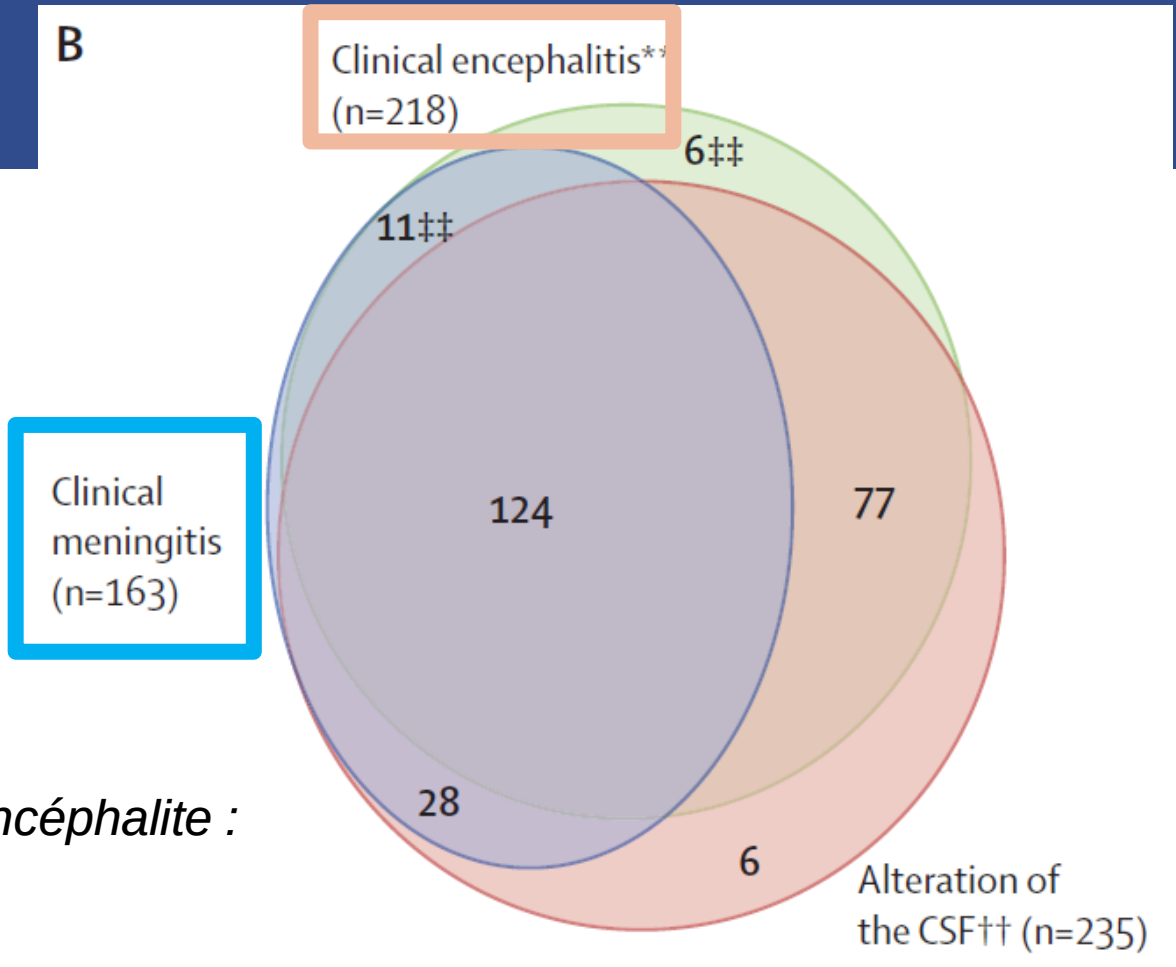
| Platform | Trial Status | Sponsor Type | Phase | Study Start date | Sample Size, Enrollment | Location |
|---|---|---|---|---|---|---|
| DNA | Open, not recruiting | Industry | Phase 1 | 01/07/2016 | 40 | United States of America \| Canada |
| DNA | Open, recruiting | Industry | Phase 1 | 01/08/2016 | 160 | Puerto Rico |
| Peptide | Open, recruiting | Government | Phase 1 | 09/02/2017 | 60 | United States of America |
| Recombinant viral vector | Open, recruiting | Industry | Phase 1 | 04/04/2017 | 48 | Austria |
| mRNA | Open, recruiting | Industry | Phase 2 | 01/12/2016 | 90 | United States of America |
| DNA | Open, not recruiting | Government | Phase 1 | 11/07/2016 | 120 | United States of America |
| DNA | Open, recruiting | Government | Phase 1 | 08/12/2016 | 50 | United States of America |
| DNA | Open, recruiting | Government | Phase 2 | 29/03/2017 | 2500 | United States of America \| Puerto Rico |
| Inactivated whole target organism | Open, recruiting | Government | Phase 1 | 01/11/2016 | 75 | United States of America |
| Inactivated whole target organism | Open, recruiting | Government | Phase 1 | 14/10/2016 | 90 | United States of America |
| Inactivated whole target organism | Open, recruiting | Academic | Phase 1 | 01/10/2016 | 48 | United States of America |
| Inactivated whole target organism | Open, recruiting | Government | Phase 1 | 24/02/2017 | 90 | Puerto Rico |

Listériose
Tuberculose
Herpès
Rougeole

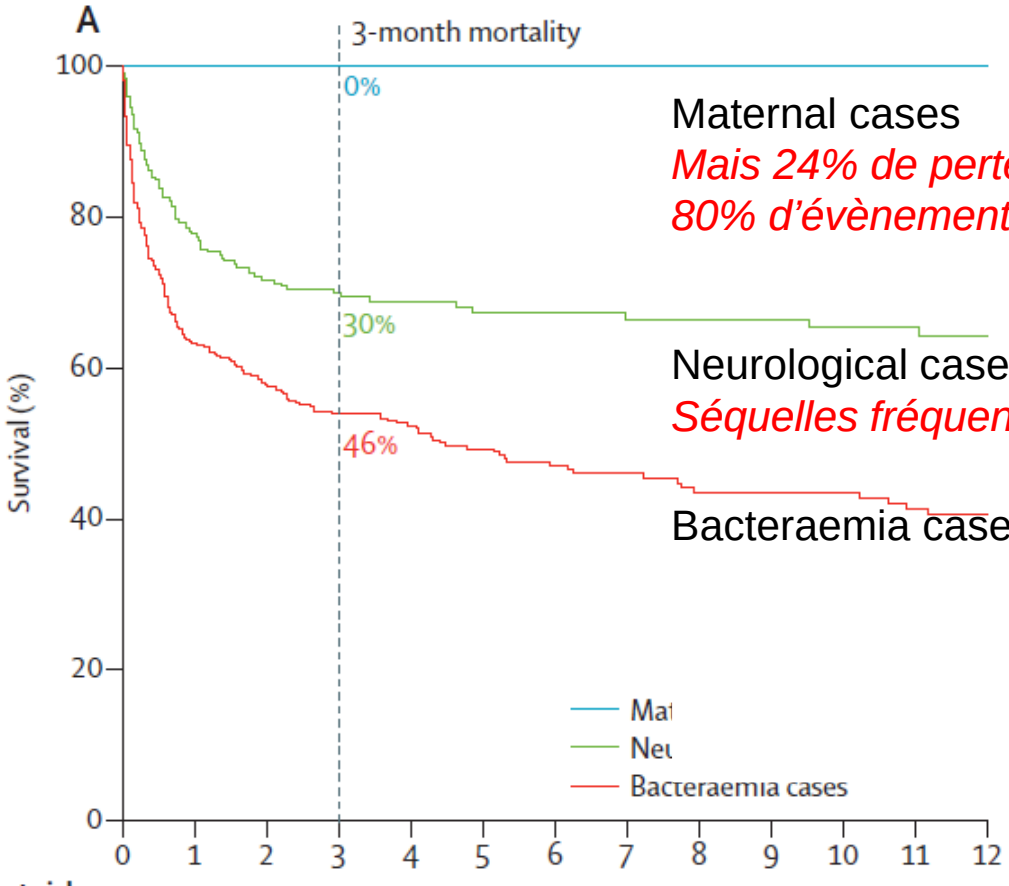
# Clinical features and prognostic factors of listeriosis: the MONALISA national prospective cohort study

*Caroline Charlier, Élodie Perrodeau, Alexandre Leclercq, Benoît Cazenave, Benoît Pilmis, Benoît Henry, Amanda Lopes, Mylène M Maury, Alexandra Moura, François Goffinet, Hélène Bracq Dieye, Pierre Thouvenot, Marie-Noëlle Ungeheuer, Mathieu Tourdjman, Véronique Goulet, Henriette de Valk, Olivier Lortholary, Philippe Ravaud, Marc Lecuit, on behalf of the MONALISA study group*

- 2009-2013
- 818 cas de 372 centres
  - 107 infections pendant la grossesse
  - 427 bactériémies
  - 252 neurolistérioses




*Rhombencéphalite : 17%*




Maternal cases

*Mais 24% de perte fœtale*

*80% d'évènements fœtaux graves*

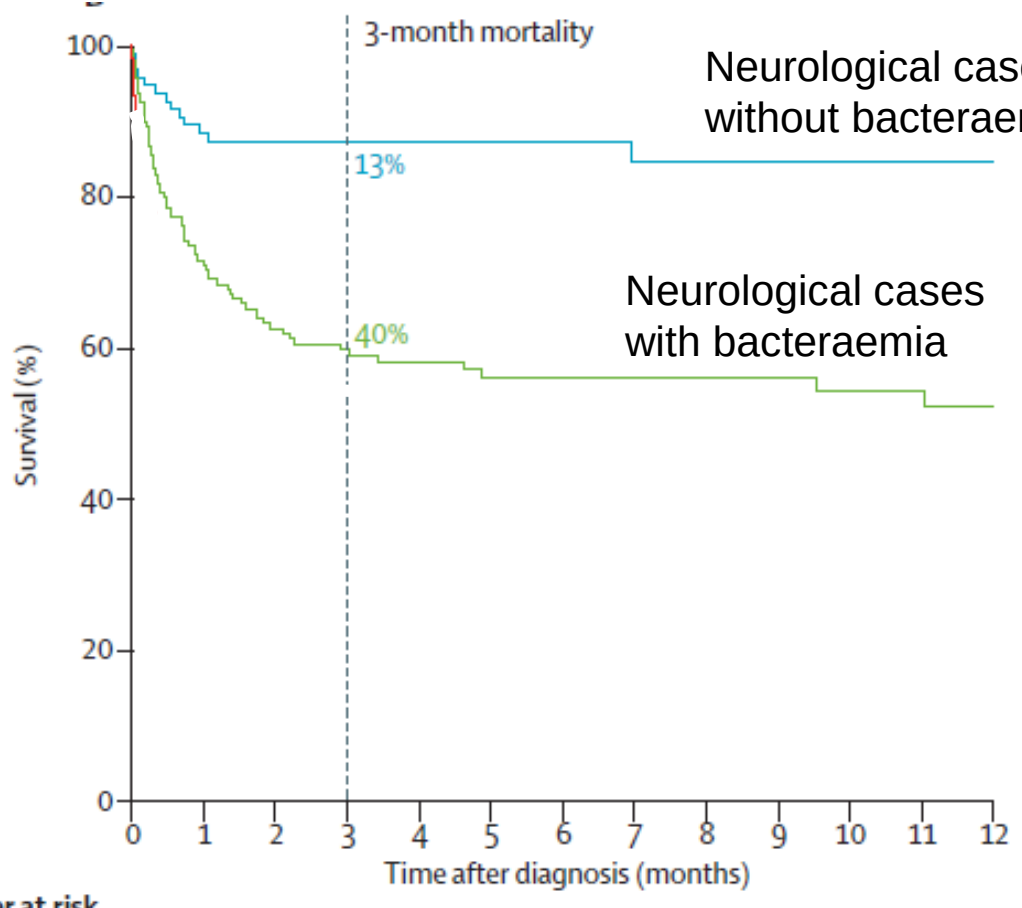
Neurological cases

*Séquelles fréquentes par ailleurs*

Bacteraemia cases

| Number at risk | | | | | | | |
|---|---|---|---|---|---|---|---|
| Maternal cases | 104 | 100 | 65 | 45 | 28 | 14 | 8 |
| Neurolisteriosis cases | 252 | 169 | 108 | 76 | 65 | 55 | 48 |
| Bacteraemia cases | 423 | 235 | 149 | 94 | 68 | 59 | 53 |

Parmi les facteurs de risque de mortalité des neurolistérioses : **corticoïdes pour la méningite**




**Number at risk**

| | | | | | | | |
|---|---|---|---|---|---|---|---|
| Neurolisteriosis cases without bacteraemia | 94 | 76 | 49 | 35 | 30 | 26 | 25 |
| Neurolisteriosis cases with bacteraemia | 158 | 93 | 59 | 41 | 35 | 29 | 23 |
| Bacteraemia cases | 423 | 235 | 149 | 94 | 68 | 59 | 53 |

The NEW ENGLAND JOURNAL of MEDICINE

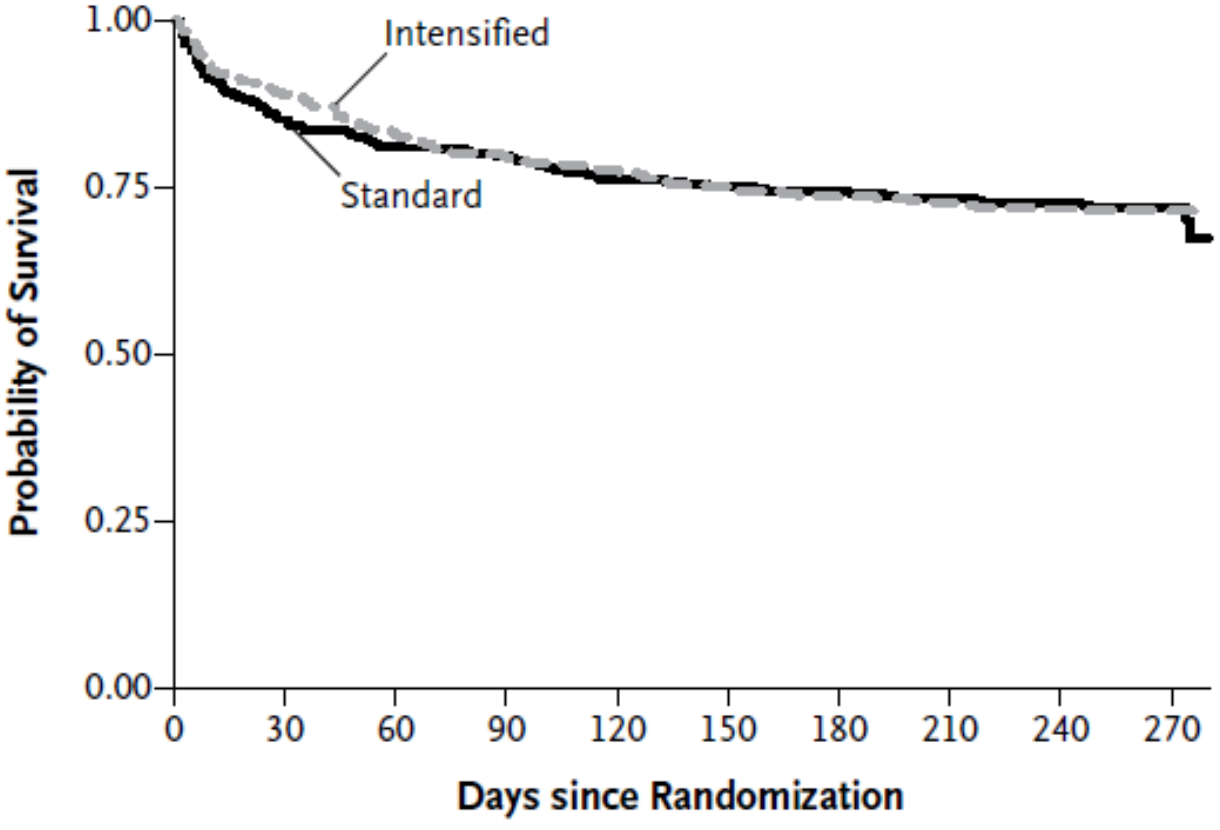
ORIGINAL ARTICLE

# Intensified Antituberculosis Therapy in Adults with Tuberculous Meningitis

2016

A. Dorothee Heemskerk, M.D., Nguyen D. Bang, Ph.D., Nguyen T.H. Mai, Ph.D., Tran T.H. Chau, Ph.D., Nguyen H. Phu, Ph.D., Pham P. Loc, M.D., Nguyen V.V. Chau, Ph.D., Tran T. Hien, Ph.D., Nguyen H. Dung, Ph.D., Nguyen T.N. Lan, Ph.D., Nguyen H. Lan, M.D., Nguyen N. Lan, M.D., Le T. Phong, M.D., Nguyen N. Vien, M.D., Nguyen Q. Hien, M.D., Nguyen T.B. Yen, M.D., Dang T.M. Ha, Ph.D., Jeremy N. Day, F.R.C.P., Maxine Caws, Ph.D., Laura Merson, B.S., Tran T.V. Thinh, M.D, Marcel Wolbers, Ph.D., Guy E. Thwaites, F.R.C.P., and Jeremy J. Farrar, F.R.C.P.

- 817 patients randomisés
  - I + R 10mg/kg + E + P  3 mois puis IR 6 mois
  - I + R 15mg/kg + E + P + LéFlox  2 mois puis poursuite idem




| No. at Risk | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| Standard | 409 | 342 | 322 | 315 | 298 | 293 | 290 | 286 | 284 | 222 |
| Intensified | 408 | 353 | 328 | 313 | 305 | 295 | 288 | 283 | 379 | 225 |

*Clinical Infectious Diseases*

MAJOR ARTICLE

# Clinical Outcomes of Patients With Drug-Resistant Tuberculous Meningitis Treated With an Intensified Antituberculosis Regimen

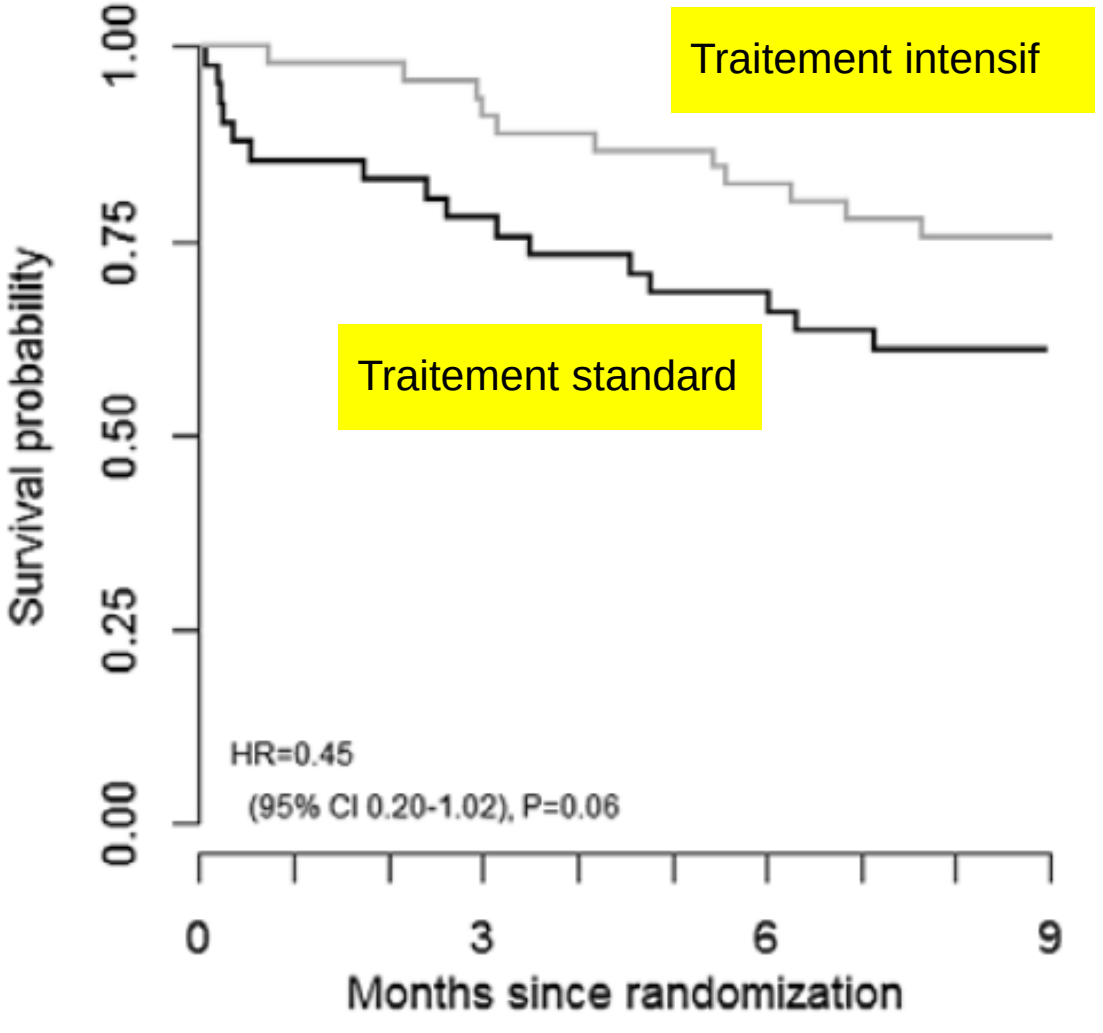
2017

**A. Dorothee Heemskerk,[1,2] Mai Thi Hoang Nguyen,[1] Ha Thi Minh Dang,[1,3] Chau Van Vinh Nguyen,[1,4] Lan Huu Nguyen,[3] Thu Dang Anh Do,[1] Thuong Thuy Thuong Nguyen,[1] Marcel Wolbers,[1,2] Jeremy Day,[1,2] Thao Thi Phuong Le,[1] Bang Duc Nguyen,[1,3] Maxine Caws,[1,5] and Guy E. Thwaites[1,2]**

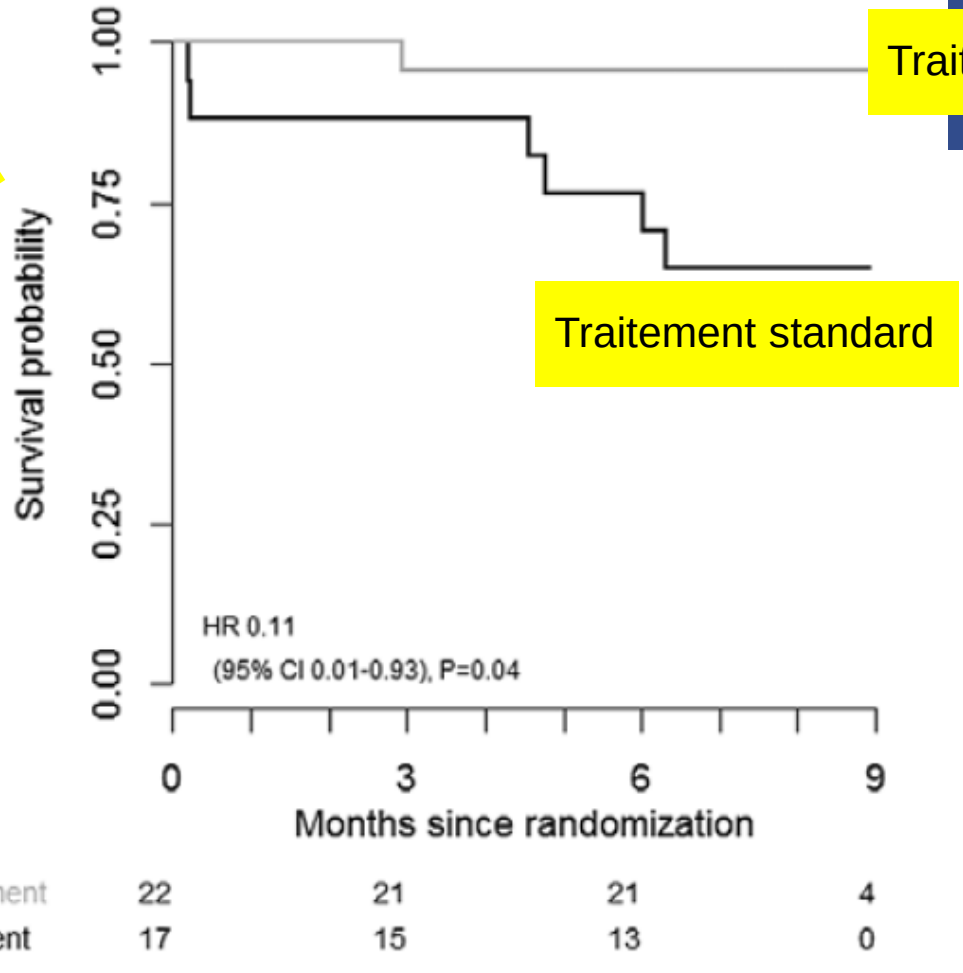
[1]Oxford University Clinical Research Unit, Ho Chi Minh City, Vietnam; [2]Nuffield Department of Medicine, University of Oxford, United Kingdom; [3]Pham Ngoc Thach Hospital for Tuberculosis and Lung Disease, and [4]Hospital for Tropical Diseases, Ho Chi Minh City, Vietnam; and [5]Liverpool School of Tropical Medicine, United Kingdom

Sous-analyse de 86 cas résistants à l'isoniazide

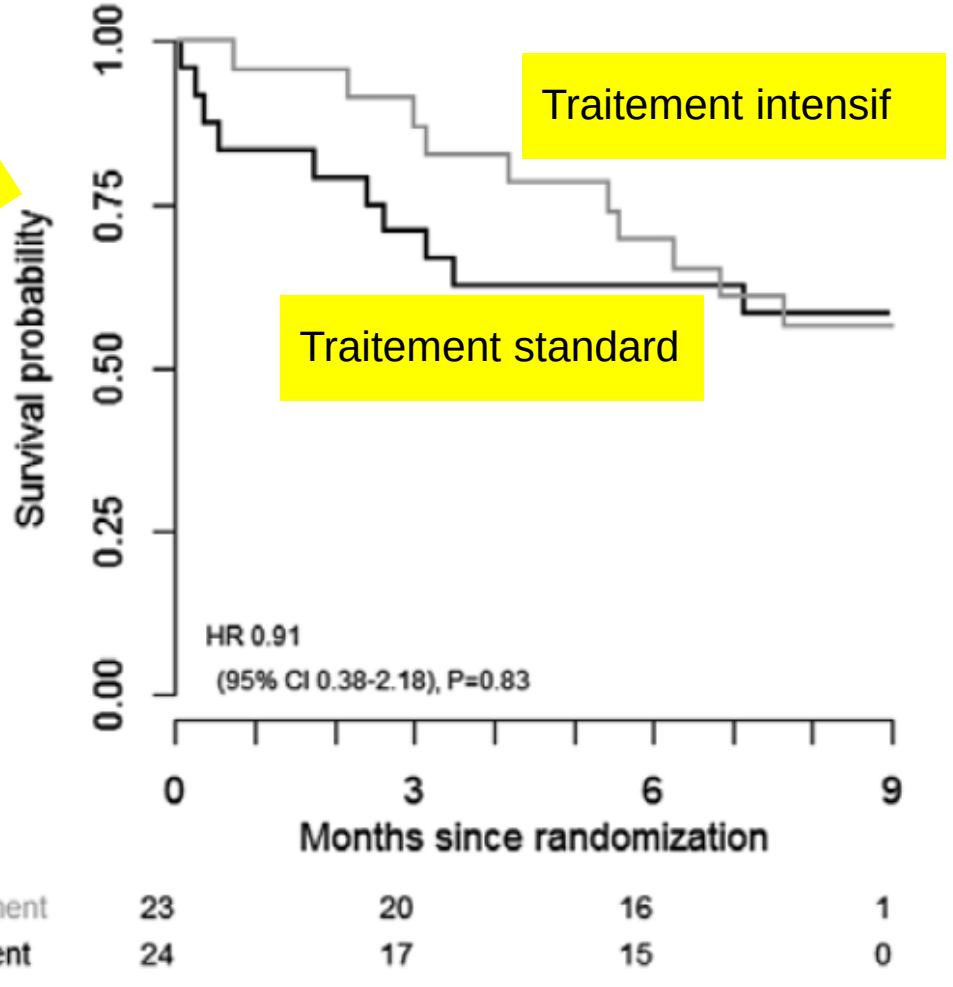
**All patients**



**HIV-uninfected**



**HIV-infected**



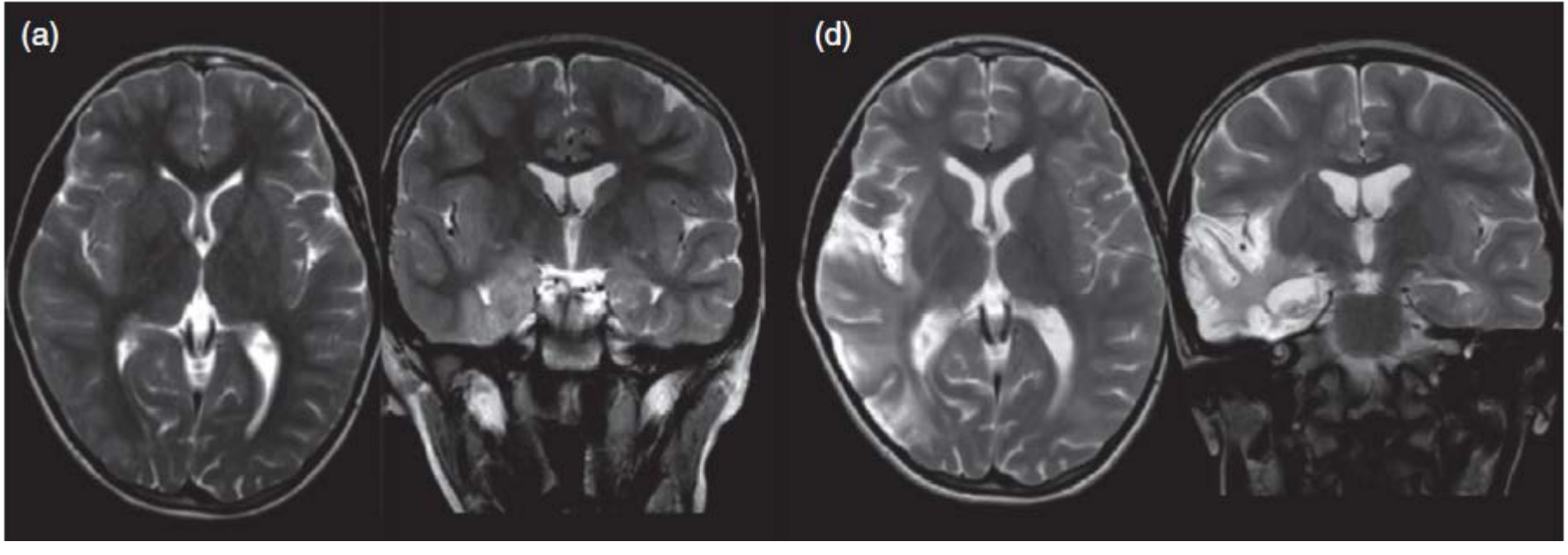
DEVELOPMENTAL MEDICINE & CHILD NEUROLOGY SYSTEMATIC REVIEW

# Herpes simplex virus-induced anti-*N*-methyl-D-aspartate receptor encephalitis: a systematic literature review with analysis of 43 cases

MARGHERITA NOSADINI[1] | SHEKEEB S MOHAMMAD[2] | FRANCESCO CORAZZA[1] | EZIA MARIA RUGA[3] | KAVITHA KOTHUR[2] | GIORGIO PERILONGO[3] | ANNA CHIARA FRIGO[4] | IRENE TOLDO[1] | RUSSELL C DALE[2] | STEFANO SARTORI[1]

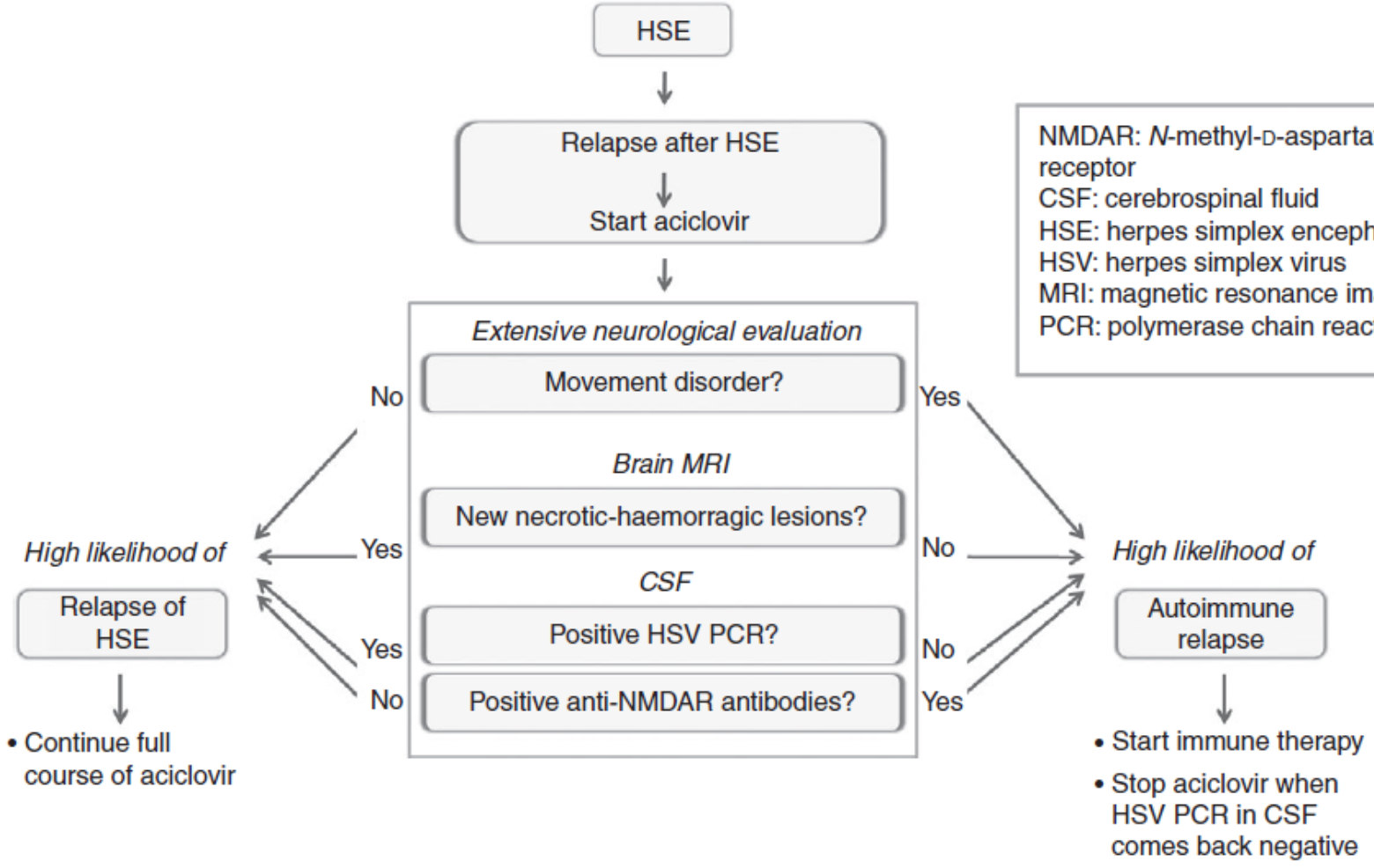
**1** Paediatric Neurology and Neurophysiology Unit, Department of Women's and Children's Health, University Hospital of Padua, Padua, Italy. **2** Neuroimmunology Group, Institute for Neuroscience and Muscle Research, Kids Research Institute at the Children's Hospital at Westmead, University of Sydney, Sydney, Australia. **3** Department of Paediatrics, University of Padua, Padua; **4** Department of Cardiac, Thoracic and Vascular Sciences, Biostatistics, Epidemiology and Public Health Unit, University of Padua, Padua, Italy.

Correspondence to Margherita Nosadini at Neurologia Pediatrica, Pediatria, Via Giustiniani 3, 35128 Padova, Italy. E-mail: margherita.nosadini@gmail.com


(a)
(d)

# Principales caractéristiques

- Délai moyen entre MEH et EAI
  - Enfants : 27,4 jours
  - Adultes : 44,8 jours
- Comitialité
  - 70% MEH, 30% 30 EAI
- Troubles du mouvement
  - 3% MEH, 75% EAI


HSE
Relapse after HSE
Start aciclovir
NMDAR: N-methyl-D-aspartate receptor
CSF: cerebrospinal fluid
HSE: herpes simplex encephalitis
HSV: herpes simplex virus
MRI: magnetic resonance imaging
PCR: polymerase chain reaction
Extensive neurological evaluation
Movement disorder?
No
Yes
Brain MRI
New necrotic-haemorragic lesions?
Yes
No
CSF
Positive HSV PCR?
Yes
No
Positive anti-NMDAR antibodies?
No
Yes
High likelihood of
Relapse of HSE
• Continue full course of aciclovir
High likelihood of
Autoimmune relapse
• Start immune therapy
• Stop aciclovir when HSV PCR in CSF comes back negative

+Model
MEDMAL-3801; No. of Pages 16
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Médecine et maladies infectieuses

Médecine et maladies infectieuses xxx (2017) xxx–xxx

Recommendations/Recommandations

# Guidelines on the management of infectious encephalitis in adults

## *Recommandations de prise en charge des encéphalites infectieuses de l'adulte*

J.P. Stahl [a,*,1], P. Azouvi [b], F. Bruneel [c], T. De Broucker [d], X. Duval [e], B. Fantin [f], N. Girard [g], J.L. Herrmann [h], J. Honnorat [i], M. Lecuit [j,k], A. Mailles [l,1], L. Martinez-Almoyna [m], P. Morand [n], L. Piroth [o], P. Tattevin [p,1], The reviewing group[2]

# Subacute Sclerosing Panencephalitis: More Common than Previously Estimated?

- 17 cas californiens, 1998-2015
- 12 rougeoles cliniques
  - Toutes avant 15 mois
  - Délai : 9 ans (25-34)
- Incidence :
  - 1/607 si rougeole <12mois

**Wendorf, CID 2017**