La sécurité de la vaccination

Jack Levy
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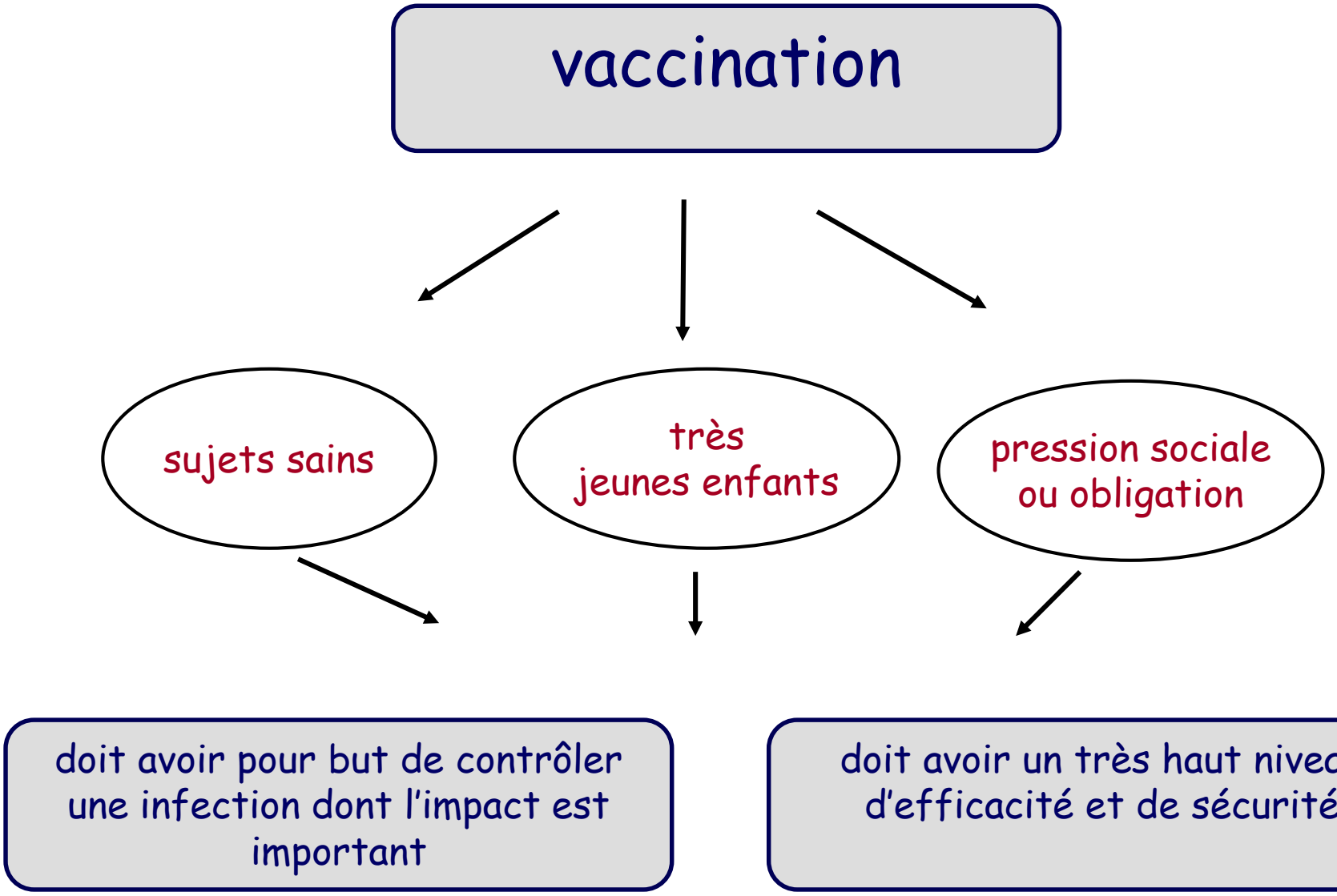
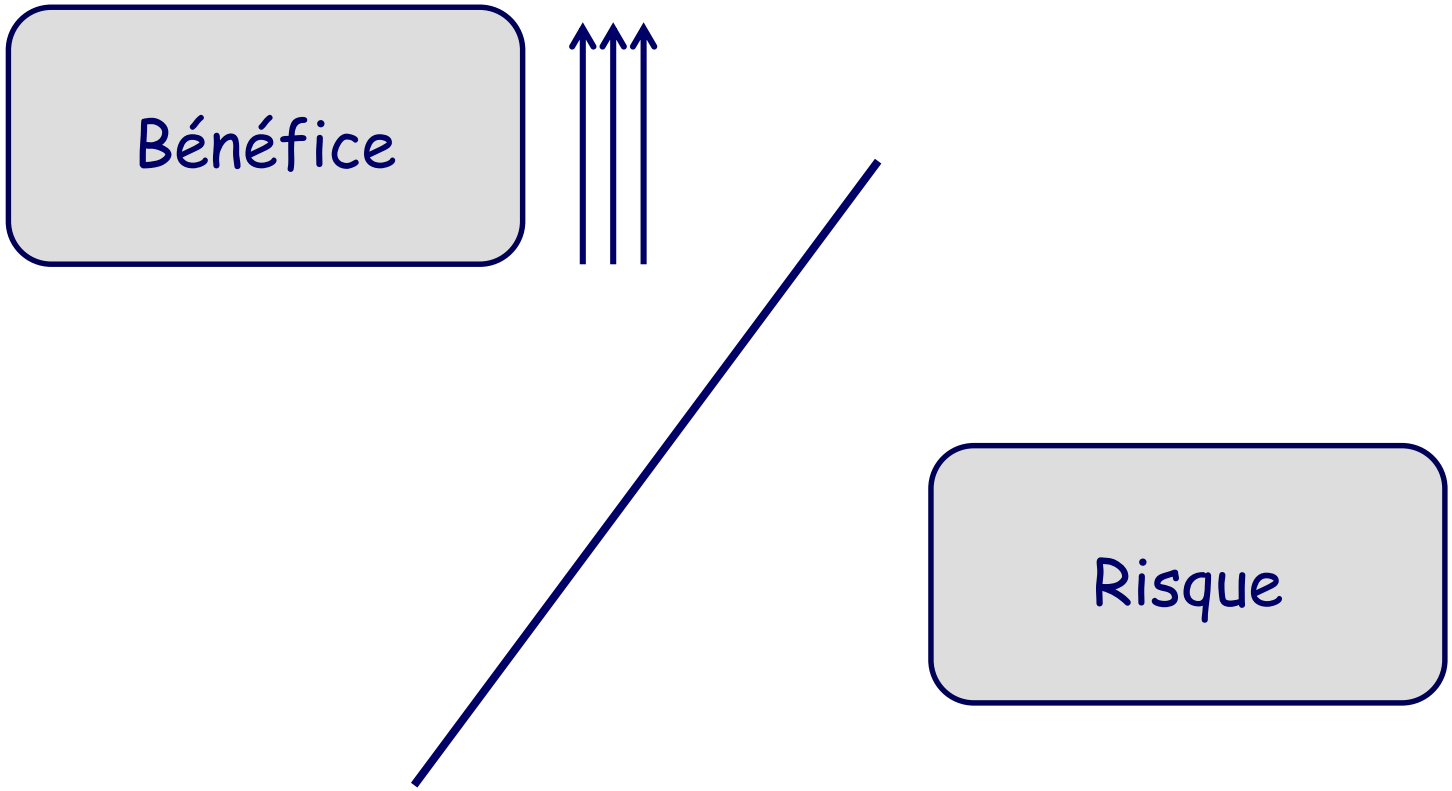
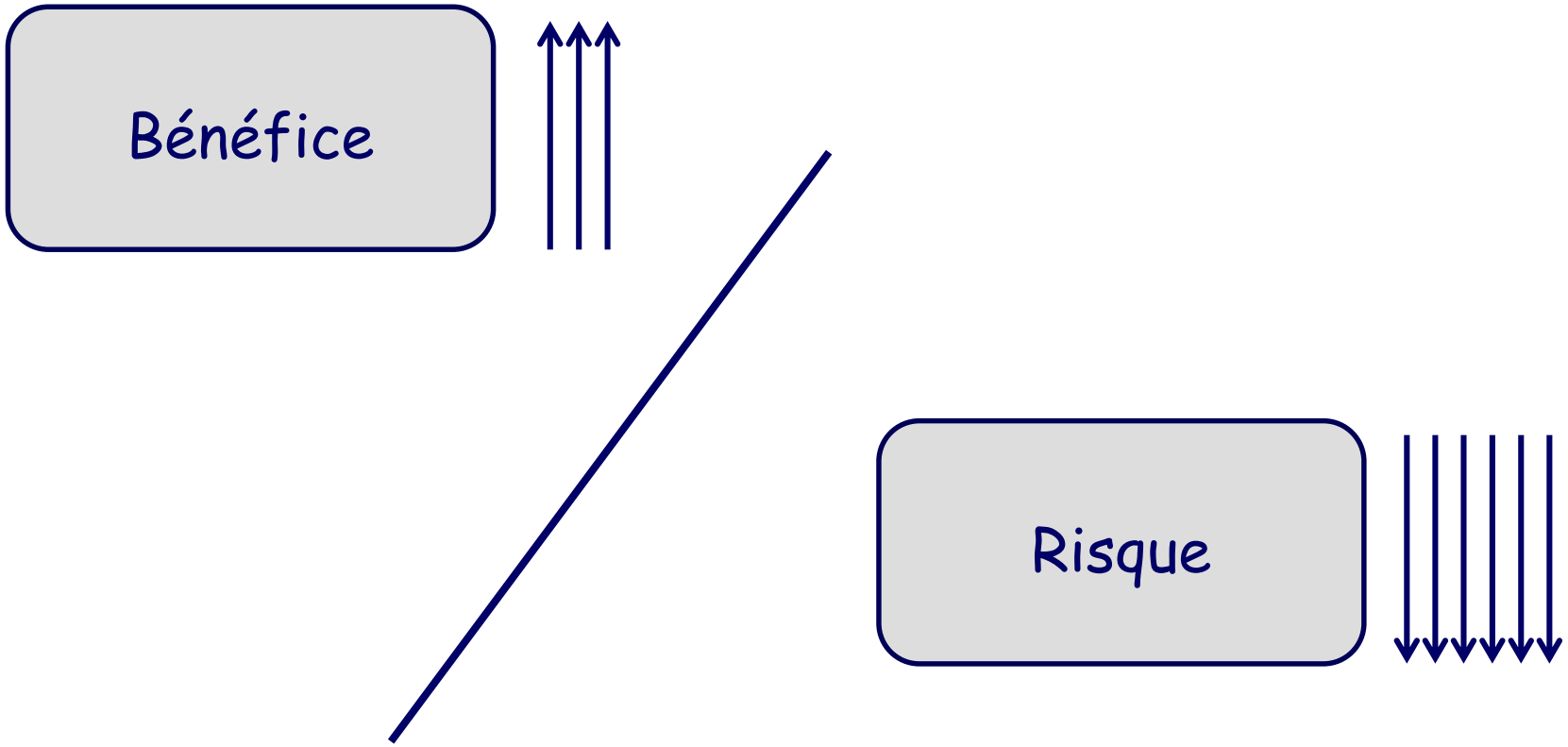

vaccination
sujets sains
très
jeunes enfants
pression sociale
ou obligation
doit avoir pour but de contrôler une infection dont l'impact est important
doit avoir un très haut niveau d'efficacité et de sécurité


Bénéfice
Risque


Bénéfice
Risque

1945-1960: développement et introduction de vaccins pédiatriques qui constituent le socle des programmes de vaccination

Poliomyélite

Coqueluche

Diphtérie

Tétanos

35e ANNEE. HEBDOMADAIRE N° 40. — 2 OCTOBRE 1955.

BRUXELLES-MÉDICAL

REVUE BELGE DES SCIENCES MÉDICO-CHIRURGICALES

FONDÉ EN 1920 PAR LES DOCTEURS L. MAYER, R. BECKERS ET R. BERNARD.

ECHOS ET NOUVELLES

Bulletin épidémiologique hebdomadaire de la semaine du 4 au 10 septembre 1955.

Fièvre typhoïde : 4 : Anvers, 3; Hainaut, 1.

Fièvres paratyphoïdes : 7 : Hainaut, 1 Liège, 5; Lux., 1.

Diphtérie : 9 : Brabant, 2; Hainaut, 1; Limbourg, 1; Fl. or., 5.

Scarlatine : 12 : Brabant, 2; Anvers, 3; Hainaut, 2; Liège, 2; Namur, 1; Fl. or., 2.

Poliomyélite : 35; Brabant, 7; Anvers, 3; Hainaut, 6; Liège, 2; Lux., 1; Namur, 5 Fl. or., 10; Fl. occ., 1.

Hépatite inject. : 11 : Brabant, 2; Anvers, 1; Liège, 1; Fl. or., 2; Fl. occ., 5.

Tuberculose : 181 : Anvers, 61; Hainaut, 28; Liège, 51; Limbourg, 15; Lux., 1. Namur, 3; Fl. or., 5; Fl. occ., 17.

Syphilis : 5 : Brabant, 2; Hainaut, 1; Namur, 1; Fl. occ., 1.

Blennorragie : 8 : Brabant, 2; Anvers, 1 Hainaut, 1; Liège, 2; Fl. or., 2.

Tétanos : 2 : Liège, 1; Fl. occ., 1.

BELGIQUE :

Situation générale : augmentation sensible des cas de poliomyélite.

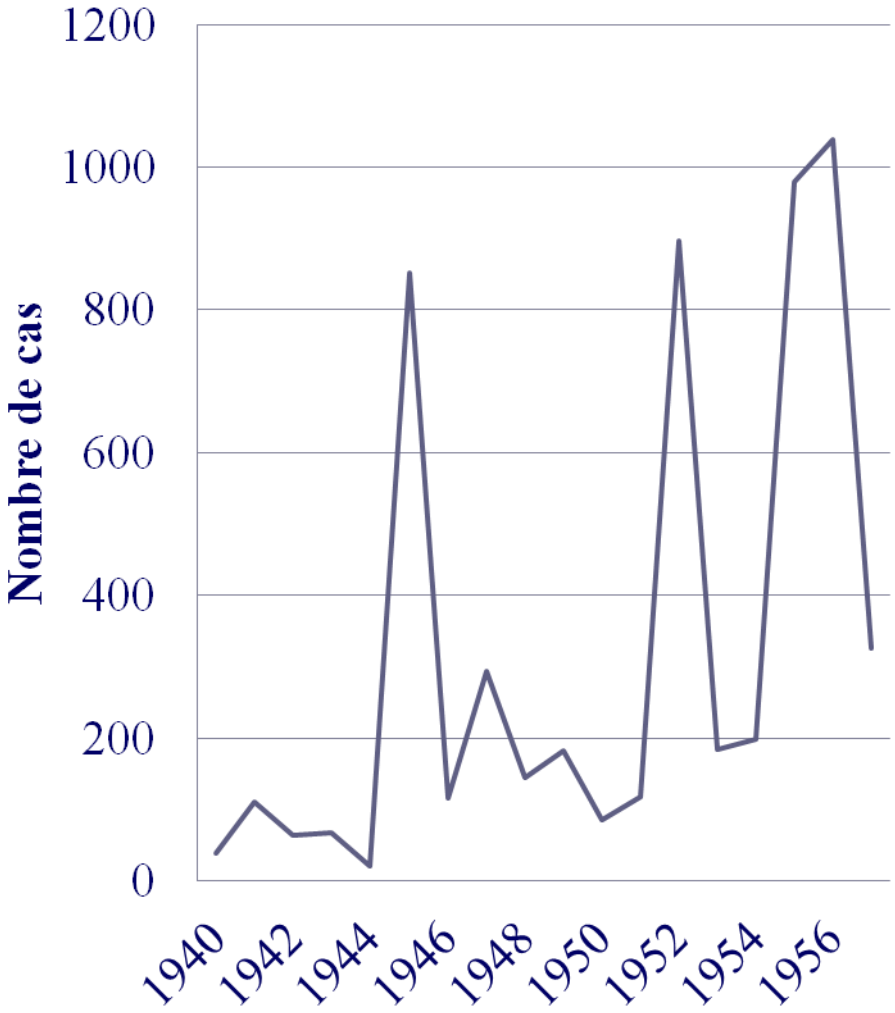
Polio : 35 cas répartis dans 28 communes — 18 cas avec paralysies, 13 cas bénins, 4 formes respiratoires graves dont 3 décès; 19 cas se sont présentés avant l'âge de 5 ans, 7 cas entre 6 et 11 ans et 9 cas chez des adultes (18 à 34 ans).

A Florennes, deux militaires canadiens ont été atteints.

Diphtérie : 9 cas dont aucun vacciné.

La poliomyélite aiguë en Belgique 1940 -1956

1951-1957: 3500 cas (70% de formes paralytiques)




Grimsby Evening Telegraph

I.P. CLOSES 27 SCHOOLS IN LINCS.

arents Told 'Keep Children at Home'

GRIMSBY NEWS

INFANTILE PARALYSIS

NO NEED FOR PANIC

Says Medical Authority

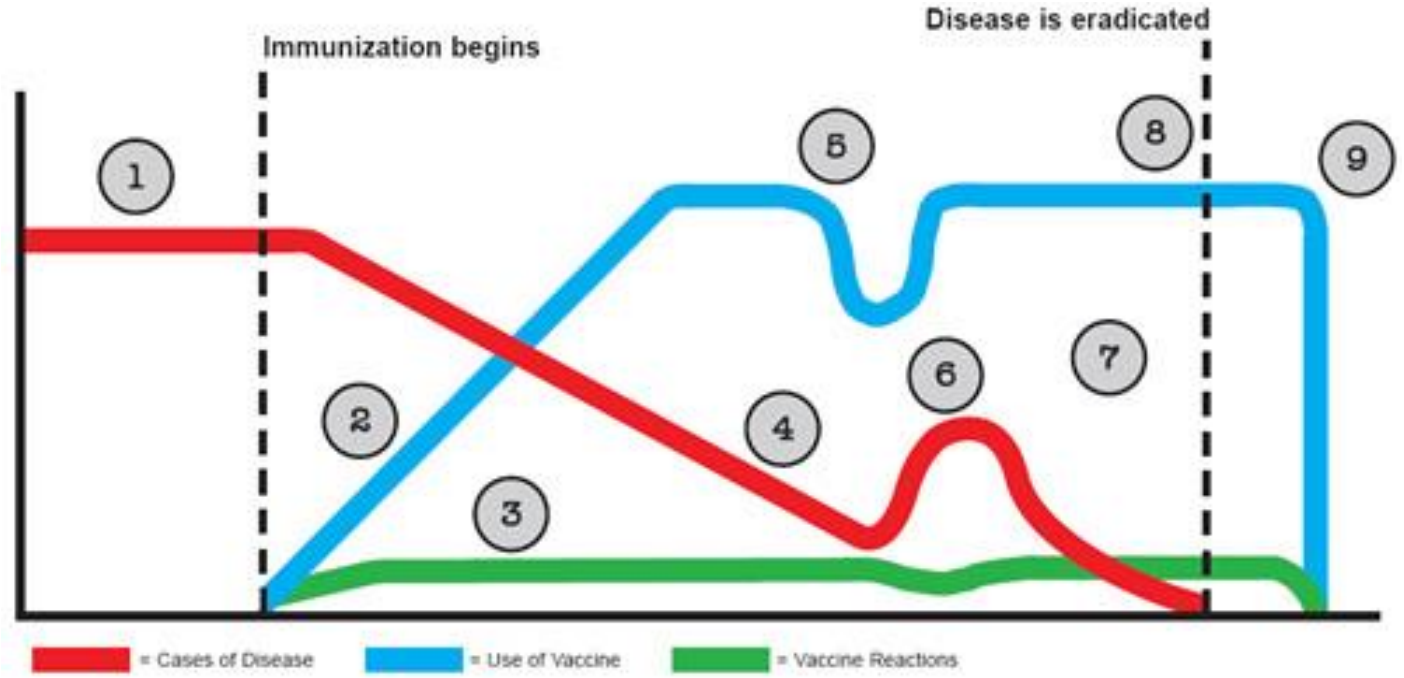
But cases should receive early treatment

DEATH REPORTED

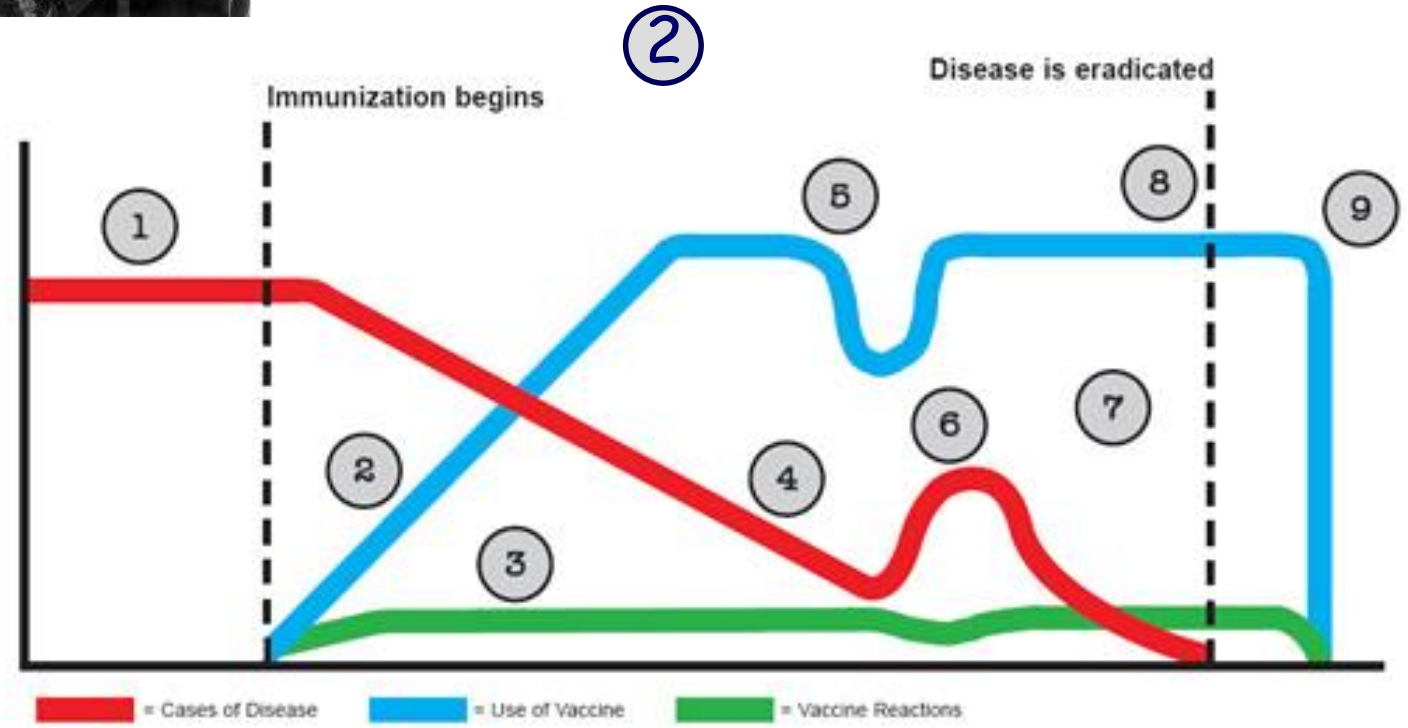
From infantile paralysis

La dynamique de l'interaction infection - vaccination

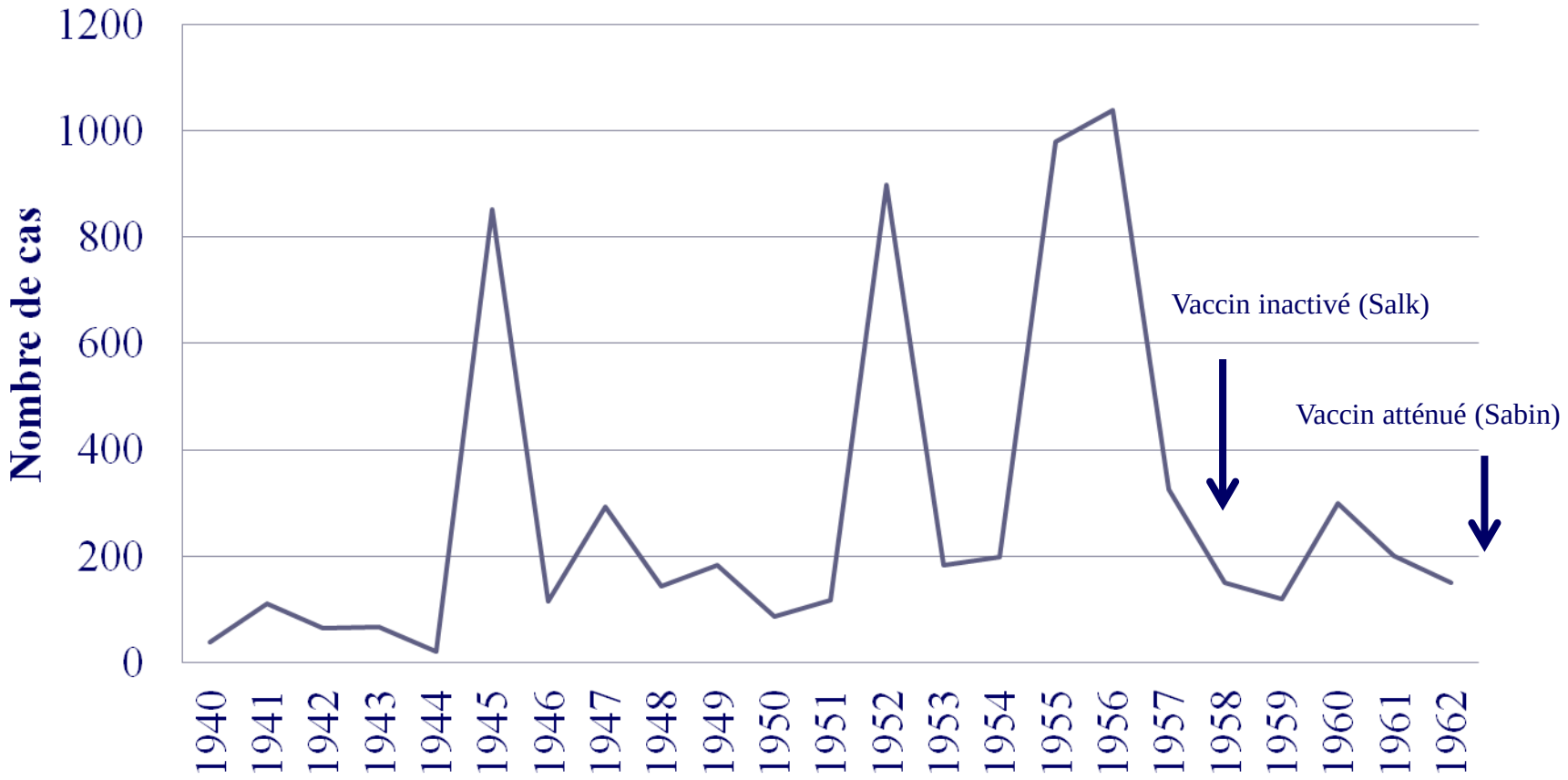
①



La dynamique de l'interaction infection - vaccination

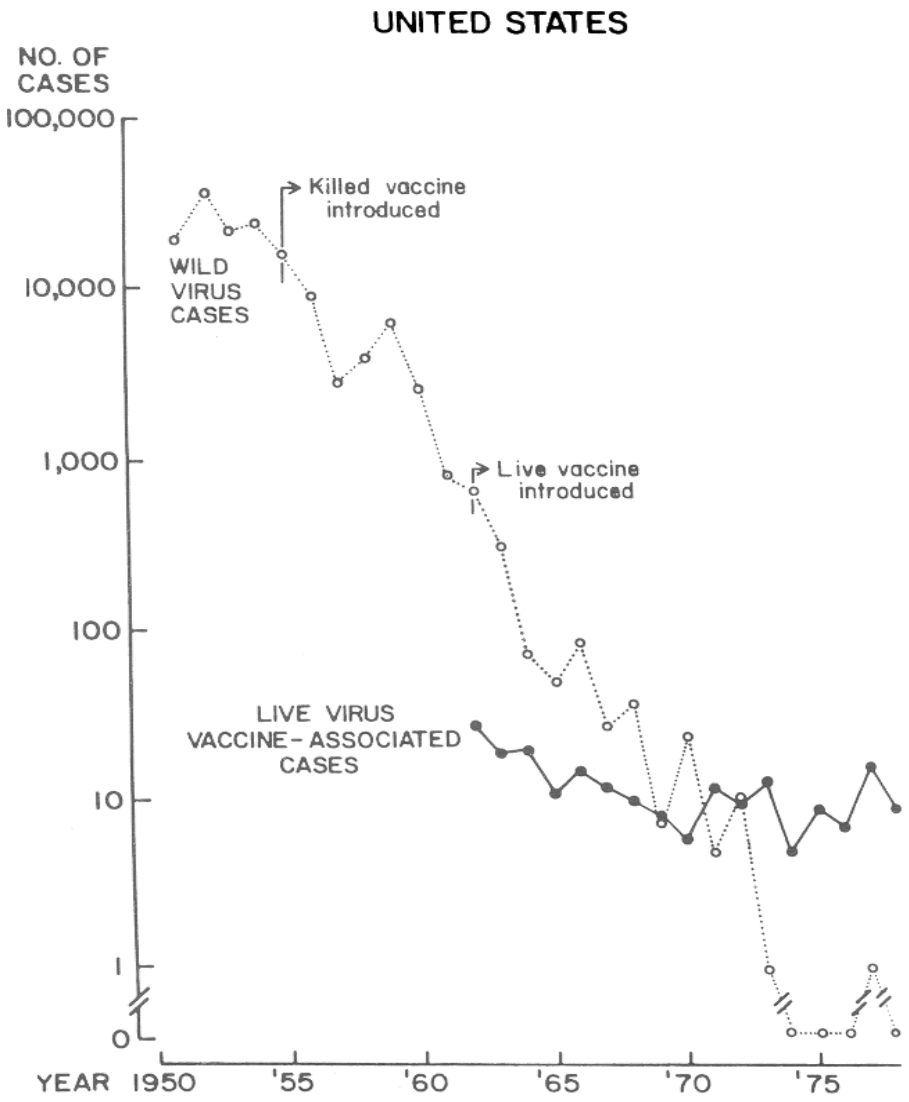


Impact de la vaccination contre la poliomyélite en Belgique



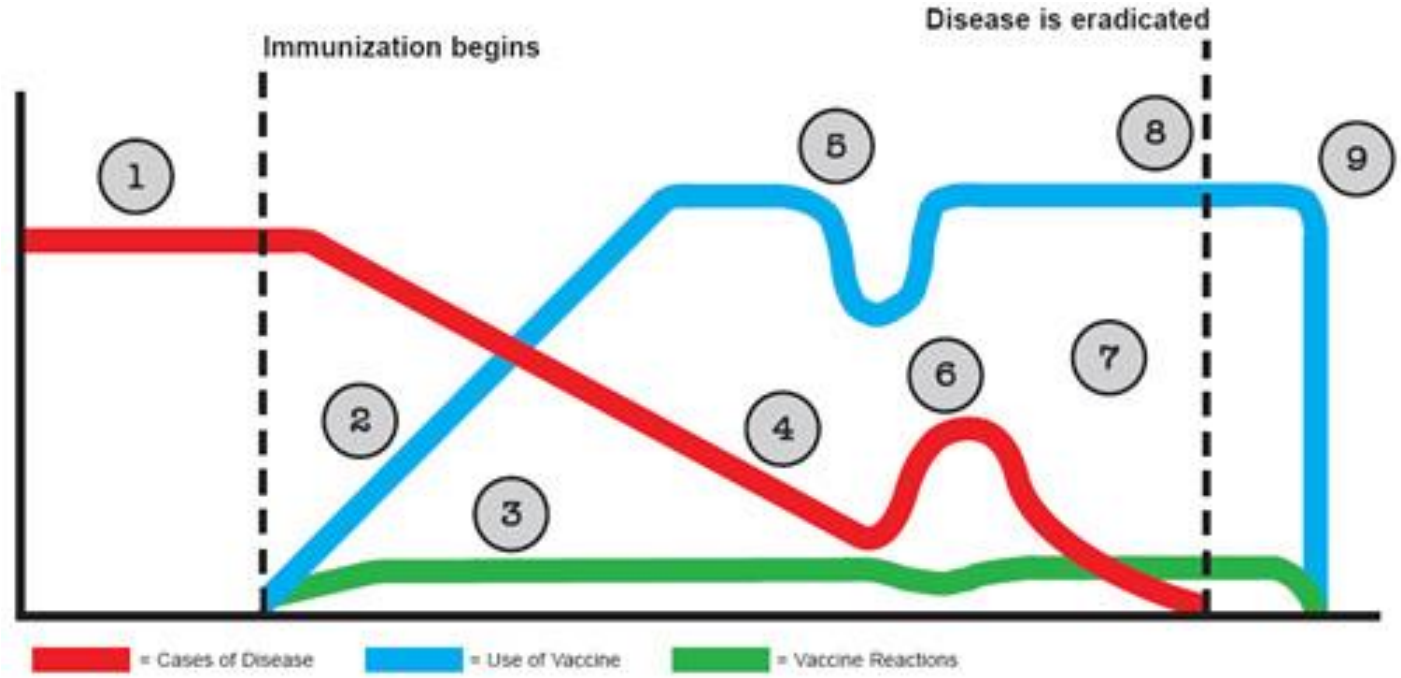
Dernier cas autochtone de poliomyélite: 1979

Evolution du rapport bénéfice/risque lié à l'utilisation de l'OPV

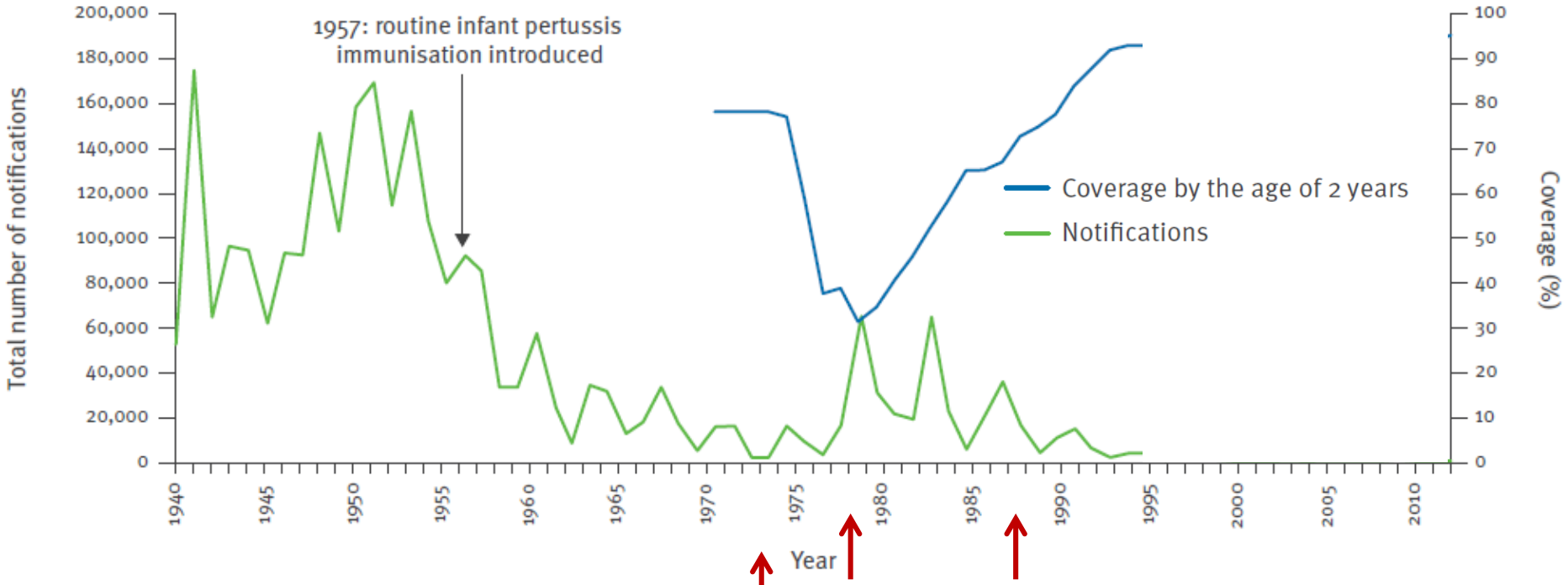


La dynamique de l'interaction infection - vaccination

④



Mise en cause de la sécurité du vaccin contre la coqueluche en Grande Bretagne



Mise en cause de la sécurité du vaccin Pw

3 épidémies: 400.000 cas en excès
- 500 admissions hospitalières
- 200 cas de pneumonie
- 80 cas de convulsions
- 38 décès

Amirthalingham et al , Eurosurveillance 2013

Conditions pour une adhésion du public et des soignants à la vaccination contre une maladie infectieuse

- l'impact maladie doit être significatif en termes
  - de morbidité aiguë
  - ou de séquelles
  - ou de mortalité
  - ou de coût social

- la mémoire collective de cette maladie et de sa gravité doit être présente

1955

Est-ce que la sévérité de cette maladie justifie la vaccination?

Grimsby Evening Telegraph

I.P. CLOSES 27 SCHOOLS IN LINCS.

Parents Told 'Keep Children at Home'

BECAUSE of the serious poliomyelitis outbreak in Lincolnshire the re-opening after the summer holidays of 27 Kesteven schools within six miles radius of Digby has been postponed.

The primary schools in the area were scheduled to re-open on Tuesday, and the grammar schools on Wednesday, September 13. The decision was made by Kesteven Education Committee after consultation with the medical authorities.

Parents living in the areas served by the closed schools whose children attend schools outside those areas have been asked not to send their children to school until further notice.

The epidemic is believed to have started in the Digby district, and the decision to close the schools is stated to be "purely a precautionary measure in view of the cases of infantile paralysis that have occurred during the past few weeks."

No similar action is contemplated, however, in the north of the county.

There is no satisfactory explanation of its geographical distribution, its mode of spread and its tendency in recent years to attack adults. There is no explanation of the immunity conferred by one attack. The virus has been recovered from flies; it has also been found on fruit. Strawberries have shown to be responsible for some small outbreaks —and so have swimming baths.

GRIMSBY NEWS

INFANTILE PARALYSIS

NO NEED FOR PANIC

Says Medical Authority

But cases should receive early treatment

POLIOMYELITIS—a word little known outside the medical profession a couple of months ago—has for thousands of parents thrown a shadow of fear over this holiday time.

For "polio"—or to give it its more popular and rather misleading name, infantile paralysis—has suddenly become a scourge walking in the summer sun and sending up the incidence of reported cases to the highest figure for ten years.

As far as Grimsby is concerned, this outbreak is not nearly so severe in type of case as was that in the summer of 1938.

Erroneously believed to be a disease peculiar to children, poliomyelitis is in reality less discriminating. In Grimsby there are as many cases in adults as children, indeed the only death so far in the district has been that of a woman of 25.

But in past weeks mothers who were unaware of its early symptoms learned of its rising toll and grew anxious.

In the absence of balanced information it is perhaps not surprising that something approaching fear has grown up. Medical authorities everywhere, however, warn against an undue state of panic.

Dr. J. Hepburn, Grimsby's Deputy Medical Officer of Health, is very definite on this point.

NO NEED FOR PANIC

"There is absolutely no need for panic," she told a "News" reporter this week.

"I think that the Press in the past month has so over-emphasised this epidemic as to cause untold alarm," she further declared.

"Polio" should be brought in line with the ordinary ailments common to childhood, such as whooping cough, measles and things of that sort.

"Only in a few cases does the disease leave permanent paralysis or cause death, whereas measles and whooping cough are responsible for more deaths in children under one year."

Really the fear of death or injury from accidents on the road was a thousand times greater than the fear of infantile paralysis, yet mothers failed to look at the matter in that light.

Notifications in Grimsby have slowed down tremendously, she said, adding, however, that the peak has been reached, and the incidence of cases will remain at a steady level until the fine weather breaks, when there will be a rapid fall in the incidence.

THE WORST YEAR YET

While there always has been some infantile paralysis in Britain, the present outbreak will make 1947 the worst year yet. The disturbing fact that the disease has shown but slight sign of abating has been given much publicity, but little has been said about the mild nature of many of the cases.

Since 1912, when statistics were first kept, there have been between 600 and 800 cases a year, except in 1926 (1,150 cases) and 1938 (nearly 1,500 cases).

A safe estimate is that of every 100 cases 50 recover completely, 30 are left with very minor muscular defects which probably will not interfere with normal activities, 15 are permanently disabled and the remaining five die.

DEATH REPORTED

From infantile paralysis

The death of a young Cleethorpes woman from infantile paralysis in the Grimsby Corporation Hospital on Tuesday night was the first fatality in the present outbreak.

Patients in the Hospital now number 22, plus two suspected cases.

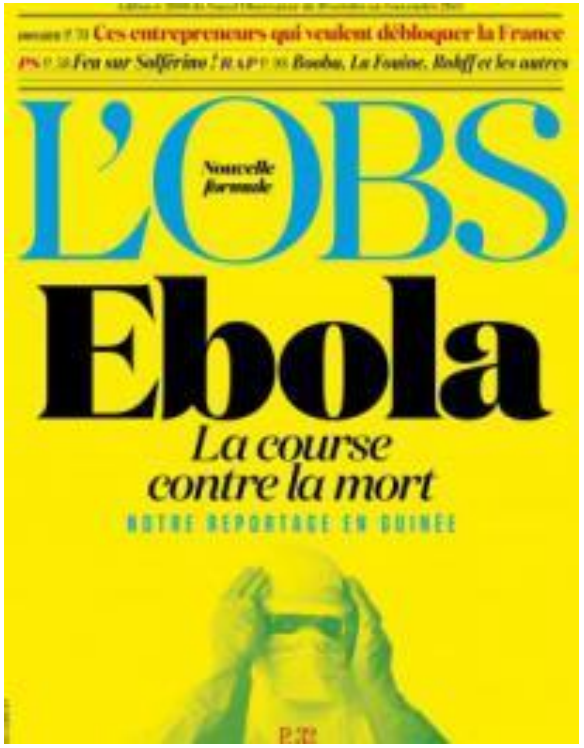
Ten of the cases are from Grimsby, the latest admission being a boy of five years.

The remainder are from Cleethorpes and district.

Some towns have gone so far as to close all cinemas, but this does not find favour with the health authorities in Grimsby at the moment.

2016

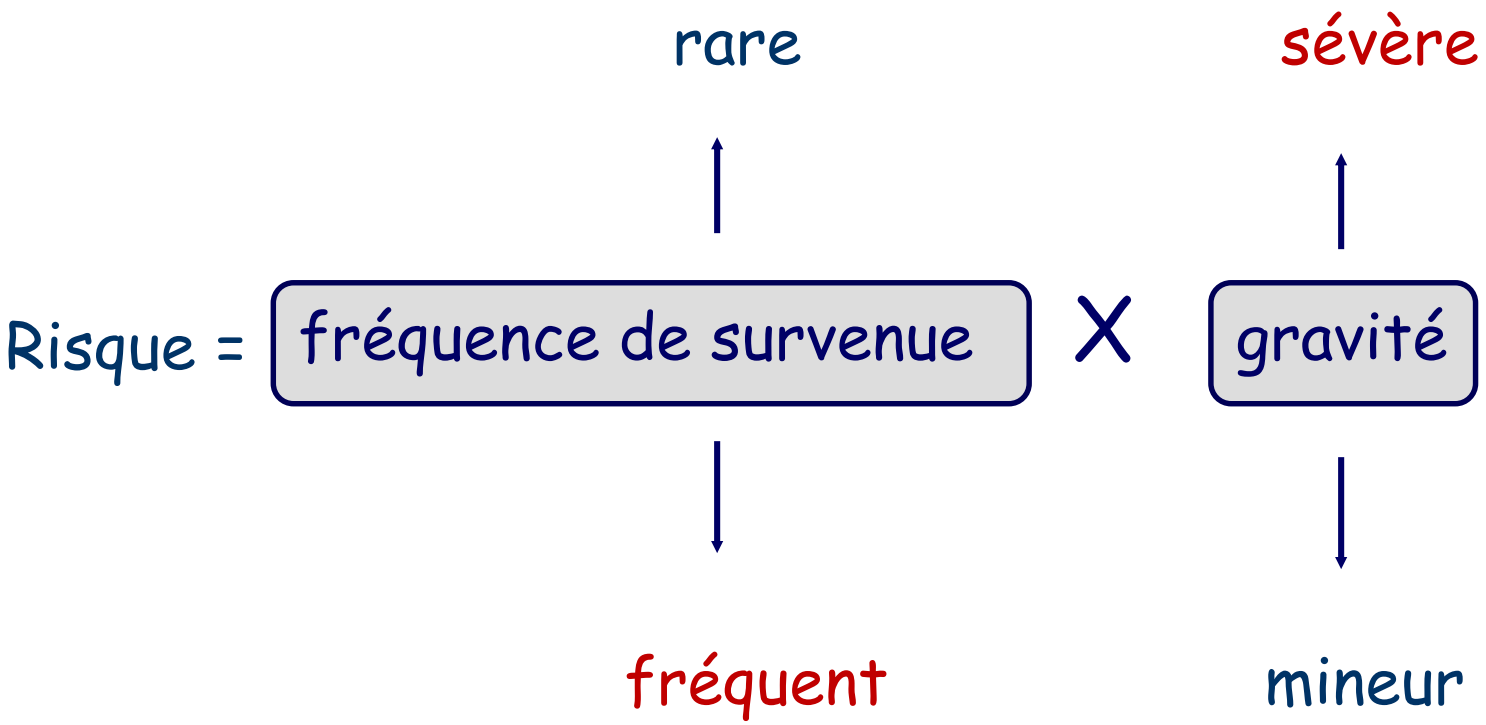
Est-ce que la sévérité de cette maladie justifie la vaccination?



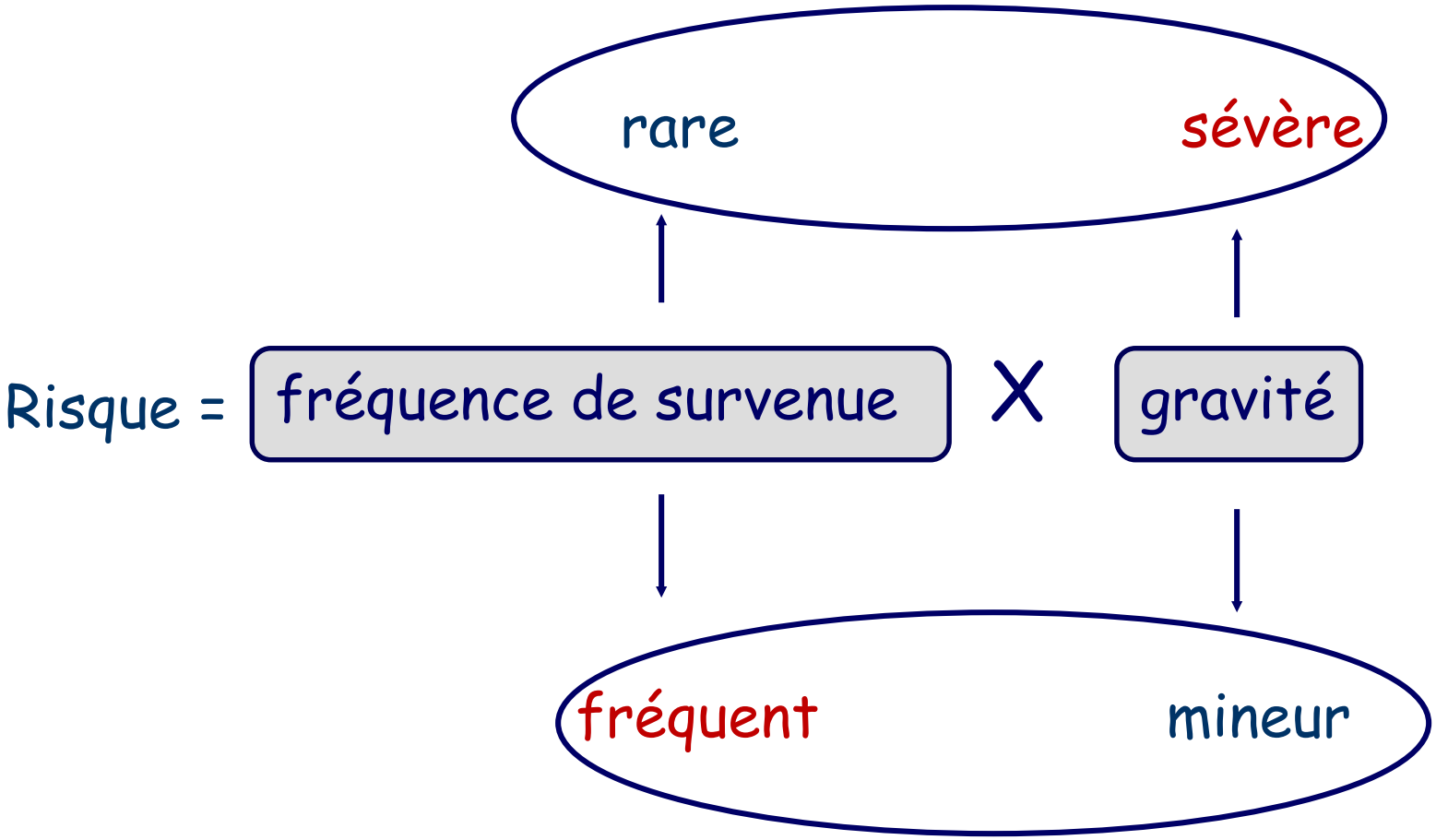
Conditions pour une adhésion du public et des soignants à la vaccination contre une maladie infectieuse

- l'impact maladie doit être significatif en termes
  - de morbidité aiguë
  - ou de séquelles
  - ou de mortalité
  - ou de coût social
- la mémoire collective de cette maladie et de sa gravité doit être présente
- la sécurité du vaccin doit être élevée

Evaluation du risque lié à un événement indésirable



Evaluation du risque lié à un événement indésirable lors d'une intervention médicale



Effets indésirables fréquents et mineurs des vaccins

généraux:
- fièvre
- irritabilité
- malaise

locaux:
- rougeur
- gonflement
- douleur

- surviennent habituellement endéans les 48 h, limités dans le temps
- aspécifiques
- mais fréquence variable en fonction du vaccin (>1%)

- peu d'impact en termes de morbidité
-impact modéré en termes d'acceptation

Effets indésirables peu fréquents et modérément sévères des vaccins

tableau clinique
aigu de sévérité variable
($<1/10^2$ à $1/10^5$)

morbidité peu importante, absence de séquelles

- fièvre > 40°c
- convulsions fébriles
- épisodes d'hypotension et d'aréactivité
- méningite après vaccination antiourlienne

- peu d'impact en termes de morbidité
-impact significatif en termes d'acceptation

Risque de convulsions après DTPw et RRO

- étude de cohorte aux USA:
  - 679 949 enfants
  - 340 386 vaccinations DTPw
  - 137 457 vaccinations RRO
- évaluation du risque de convulsions fébriles et non fébriles attribuable à la vaccination:
  - risque accru de convulsions fébriles

    DTPw: 6 à 9/100 000

    RRO: 25 à 34/100 000
  - pas d'excès de convulsions non fébriles

Barlow et al NEJM 2001

Effets indésirables rares mais sévères des vaccins

tableau clinique
aigu de sévérité variable
(<1/10^4 à 1/10^7)

morbidité importante, conduisant parfois des séquelles ou au décès

- Poliomyélite vaccinale
- Invagination après vaccin rotavirus
- Narcolepsie après vaccin H1N1-ASO3
- Choc anaphylactique

- impact important en termes de morbidité
-impact majeur en termes d'acceptation

Mécanismes responsables des effets indésirables des vaccins

- effet pathogène direct de la préparation antigénique

  - poliomyélite vaccinale
  - méningite causée par le vaccin ourlien souche Urabe
  - BCGite

- effet médié par la réaction immune à l'antigène

  - syndrome de Guillain-Barré après anti-rougeoleux
  - narcolepsie après vaccin H1N1-ASO3

- réaction inflammatoire

  - locale et systémique après DPTw
  - médiée par l'adjuvant ou la préparation antigénique

Mécanismes responsables des effets indésirables des vaccins

- erreur dans le processus de production du vaccin

  Incident Cutter en 1955 aux USA: inactivation incomplète d'un lot de vaccin polio Salk: 200 cas de polio vaccinale

- faille dans les procédures de distribution ou d'administration

  - contaminations bactériennes de flacons multidoses
  - transmission de virus par aiguilles non stériles

Mécanismes responsables des effets indésirables des vaccins

- susceptibilité individuelle

  - susceptibilité génétique à certains effets secondaires (au niveau individuel ou à celui des populations)

  - réactions anaphylactiques, exceptionnelles, causée par les composants autres que l'antigène vaccinal

L'évaluation de la sécurité est au centre des préoccupations dans le développement des nouveaux vaccins

Evaluation de la sécurité des vaccins: dans le cadre du développement du produit

- avant l'autorisation de mise sur le marché:
  - études de phase 1: < 20 sujets

    effets indésirables fréquents et sévères, tolérance
  - études de phase 2 et 3: plusieurs centaines à des milliers de sujets

    profil de tolérance: effets secondaires mineurs systémiques et locaux fréquents
- après l'autorisation de mise sur le marché
  - études de phase 4: jusqu'à 100 000 sujets

    effets secondaires rares et sévères

Evaluation de la sécurité des vaccins: après la phase de développement

- programmes de surveillance passive
  - intégrés dans les programmes de pharmacovigilance
  - spécifiques à la vaccination
- programmes de surveillance active pour confirmer ou caractériser un événement indésirable dont la liaison à la vaccination est suspectée

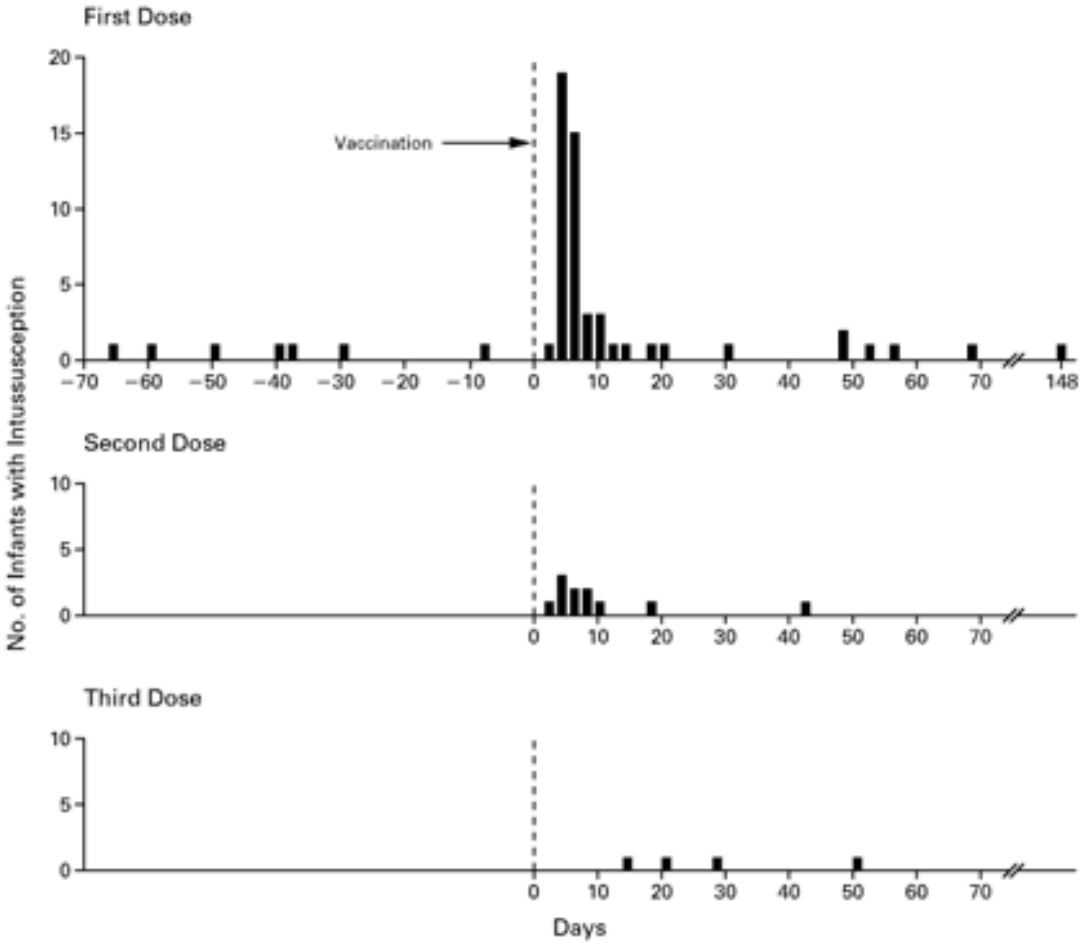
L'évaluation de la sécurité : la saga des vaccins contre le Rotavirus

Evaluation de la sécurité du vaccin recombinant rhésus-humain contre le rotavirus (RotaShield)

- Études cliniques : 5 invaginations parmis 10.054 vaccinés
- AMM (FDA) en 1998: invagination = effet adverse possible
- 9 mois plus tard (1.2×10^6 doses chez 6×10^5 nourrissons): vaccin retiré du marché car 1/4670 à 1/9474 cas d'invagination en excès parmis les vaccinés

Evaluation de la sécurité du vaccin RotaShield après sa mise sur le marché aux USA

Murphy et al NEJM 2001



Interval between RRV-TV vaccination and intussusception in 74 infants

Depuis lors, 2 vaccins vivants ont été développés

- **Rotarix™** (**RV1**, GlaxoSmithKline Biologicals, Rixensart, Belgium)
- **RotaTeq™** (**RV5**, Merck and Co, Pennsylvania, USA)

Childhood Intussusception: A Literature Review

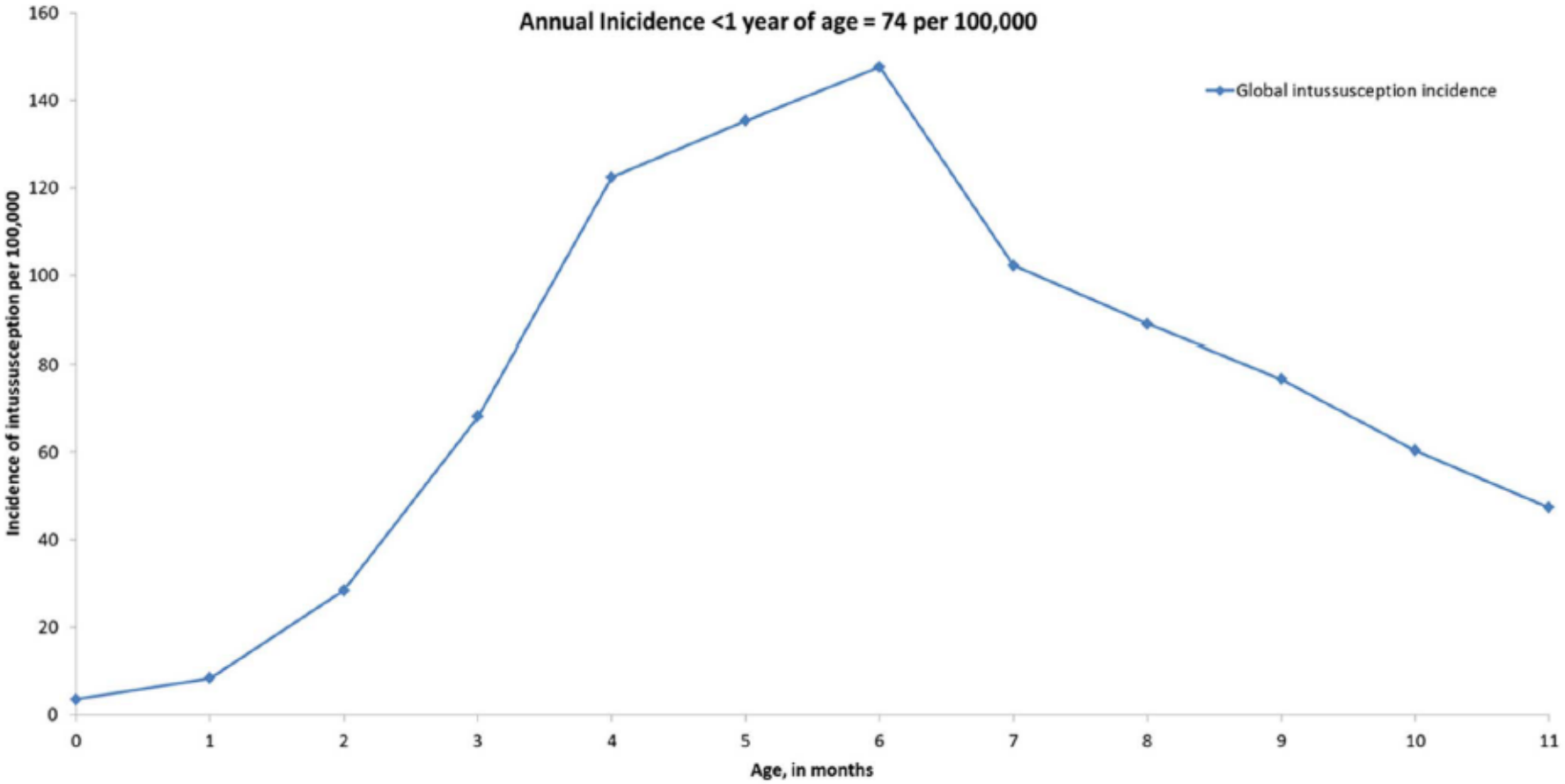


Figure 3. Incidence of intussusception by month of life during first year of life. Intussusception incidence or number of cases by month of life from 22 studies extrapolated to remaining 13 studies that only presented data on rates for infants <1 year (as displayed in Table 2).
doi:10.1371/journal.pone.0068482.g003

Citation: Jiang J, Jiang B, Parashar U, Nguyen T, Bines J, et al. (2013) Childhood Intussusception: A Literature Review. PLoS ONE 8(7): e68482. doi:10.1371/journal.pone.0068482

Evaluation de la sécurité des vaccins contre le Rotavirus dans les études cliniques

- Les 2 vaccins ont bénéficié d'études de sécurité extensives (>130.000 sujets) avant leur mise sur le marché. Aucune association avec l'invagination n' a été détectée au cours de ces études.

  - Ruiz-Palacios GM, et al. N Engl J Med 2006;354:11

  - Vesikari T, et al. N Engl J Med 2006;354:23

- Ces études cliniques n'avaient néanmoins probablement pas le pouvoir statistique de détecter des effets indésirables survenant à une fréquence inférieure à 1/50.000

Rotarix: pas de risque accru d'invagination après vaccination

- Phase III trial involving over 60,000 subjects showed no increased risk of IS between Rix4414 & placebo[1]

Timing of IS	Rix4414 n ~ 31,000	Placebo n ~ 31,000	Relative risk IS Rix4414 vs Placebo (95% CI)
IS cases within 31-day window	6	7	0.85 (0.30;2.42)
IS cases between dose 1 and 30-90 days post dose 2	9	16	0.56 (0.25;1.24)

[1]Ruiz-Palacios GM et al. New Engl J Med 2006;354(1):11-22

2007: Introduction des vaccins contre le rotavirus dans le calendrier de vaccination en Belgique

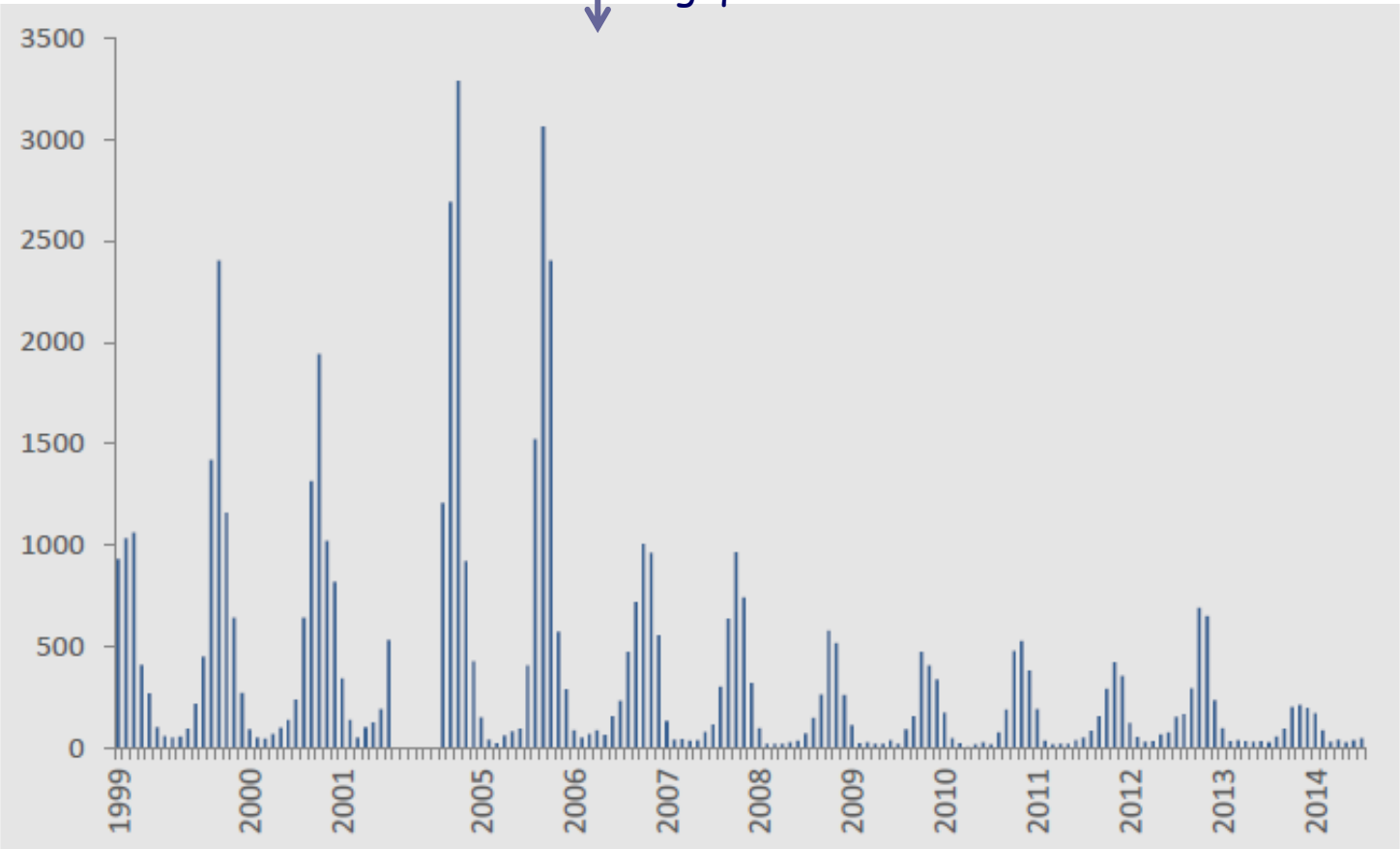


Figure 15 | Nombre de cas d'infections par le rotavirus par mois, 1999-2001 et 2005-2014, Belgique (Source: Réseau des Laboratoires vigies, WIV-ISP)

Intussusception Risk after Rotavirus Vaccination in U.S. Infants

W. Katherine Yih, Ph.D., M.P.H., Tracy A. Lieu, M.D., M.P.H., Martin Kulldorff, Ph.D., David Martin, M.D., M.P.H., Cheryl N. McMahill-Walraven, M.S.W., Ph.D., Richard Platt, M.D., Nandini Selvam, Ph.D., M.P.H., Mano Selvan, Ph.D., Grace M. Lee, M.D., M.P.H., and Michael Nguyen, M.D.

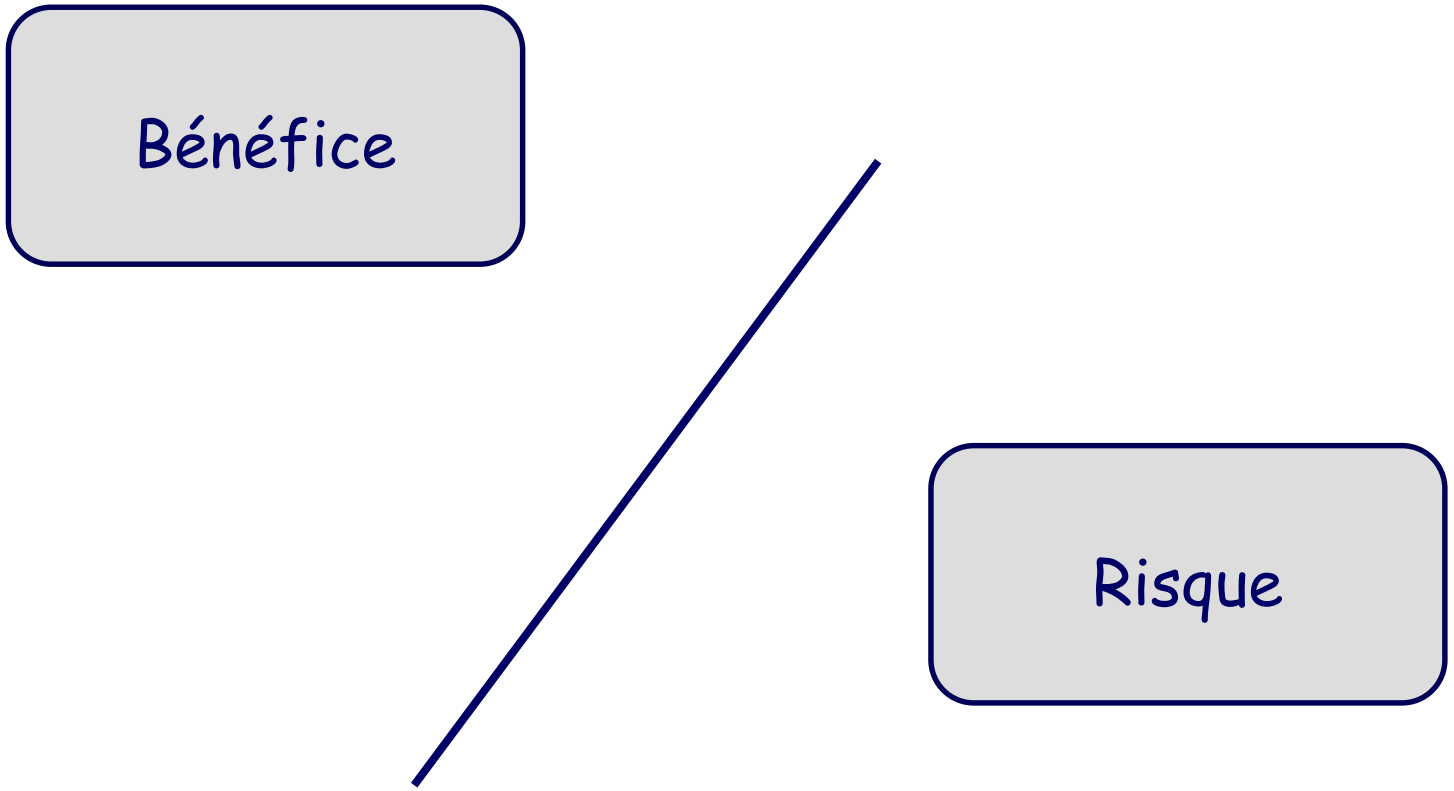
CONCLUSIONS

RV5 was associated with approximately 1.5 (95% CI, 0.2 to 3.2) excess cases of intussusception per 100,000 recipients of the first dose. The secondary analysis of RV1 suggested a potential risk, although the study of RV1 was underpowered. These risks must be considered in light of the demonstrated benefits of rotavirus vaccination. (Funded by the Food and Drug Administration.)

Intussusception Risk and Disease Prevention Associated With Rotavirus Vaccines in Australia's National Immunization Program

CID 2013:57 (15 November) • Carlin et al

- Vaccination contre le rotavirus introduit en 2007
  - RV1 ou RV5 selon les états/territoires
  - Cohortes de naissances d'environ 300.000 enfants
- Evaluation du risque d'invagination au cours des 3 premières années d'utilisation
- Incidence relative d'invagination dans les 7 jours après vaccination:
  - 6,8 (IC 95% 2.4-19, p<.001) pour RV1
  - 9,9 (IC 95% 3.7-26.4, p<.001) pour RV5


Bénéfice
Risque

Intussusception Risk and Disease Prevention Associated With Rotavirus Vaccines in Australia's National Immunization Program

Table 4. Effect of a Rotavirus Vaccination Program, Compared With No Program, on Hospitalizations Associated With Rotavirus-Attributable Gastroenteritis or Intussusception in Australia[a]

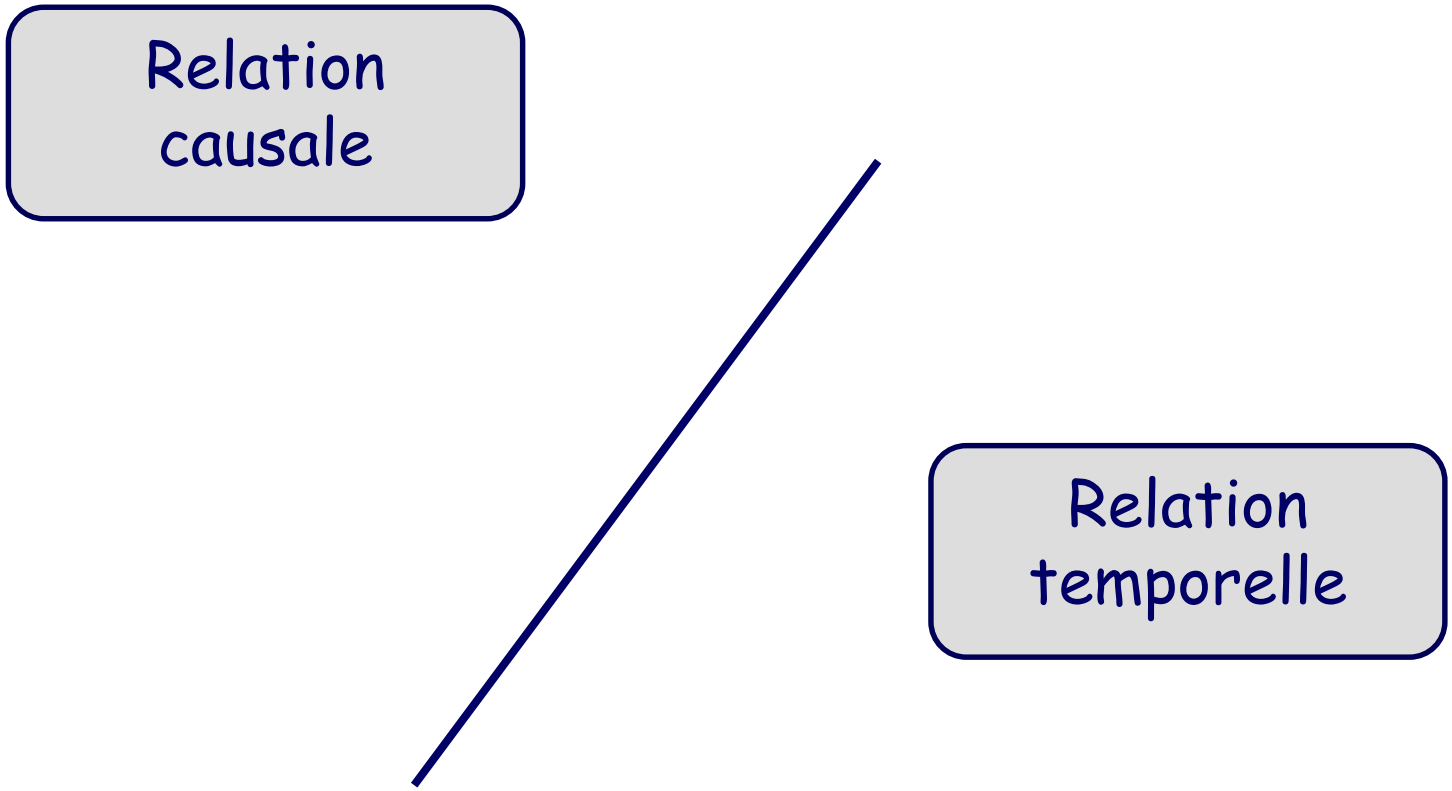
Reason for Hospitalization	Annual Hospitalizations in Children <5 y of Age, No.		
	Without Vaccination Program	With Vaccination Program	Events Averted or Caused, No.
Rotavirus-attributable gastroenteritis	11 073	4545	–6528
Intussusception[b]	144	158	+14

Controverses concernant la sécurité vaccinale

- existence d'une association entre
  - RRO, Hg ou timerosal et autisme
  - vaccination Hépatite B et maladies démyélinisantes
  - vaccins contenant de l'hydroxyde d'alumine et myofasciite nécrosante
  - ……

Circonstances conduisant au développement des controverses vaccinales

- maladie ou syndrome
  - d'étiologie inconnue
  - mécanisme immun
- rapports de cas en association temporelle avec la vaccination publiés dans la littérature médicale


Relation causale
Relation temporelle

Evaluation du lien de causalité

- aisée si:
  - syndrome clinique proche de la maladie sauvage
  - examen de laboratoire impliquant un composant du vaccin
- difficile si:
  - événement clinique dont les causes sont multiples ou encore inconnues

- lien de causalité impossible à établir sur base individuelle
- association entre vaccin et événement, et risque attribuable établis par des études épidémiologiques
- absence de conclusions probantes pour événements très rares ($1/10^5$ à $1/10^6$)

Facteurs alimentant les polémiques vaccinales

- délais requis pour réaliser les études scientifiques
- interprétation des « résultats négatifs »
- émotion provoquées par les témoignages
- images fortes utilisées par les media
- confusion entretenue par les scientifiques
- interventions de soignants opposés à la vaccination

Vaccin RRO, autisme et maladie inflammatoire du tube digestif

- Wakefield et al, Lancet 1998:
  - 12 enfants avec une entérocolite non spécifique et des désordres neurologiques dont 9 autismes
  - à 8 reprises parents établissent le lien entre le début des symptômes neurologiques et la vaccination RRO (délai précisé dans 5 cas: 1 à 14 jours)
  - conclusions prudentes quant à la causalité
  - éditorial mettant en évidence les faiblesses de l'étude
- aucune étude épidémiologique à large échelle publiée depuis lors n'a pu montrer montrer d'association entre ces entités

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A POPULATION-BASED STUDY OF MEASLES, MUMPS, AND RUBELLA VACCINATION AND AUTISM

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TABLE 2. ADJUSTED RELATIVE RISK OF AUTISTIC DISORDER AND OF OTHER AUTISTIC-SPECTRUM DISORDERS IN VACCINATED AND UNVACCINATED CHILDREN.*

VACCINATION	PERSON-YEARS†	AUTISTIC DISORDER		OTHER AUTISTIC-SPECTRUM DISORDERS	
		NO. OF CASES	ADJUSTED RELATIVE RISK (95% CI)	NO. OF CASES	ADJUSTED RELATIVE RISK (95% CI)
Total	2,129,864	316		422	
Vaccination					
No	482,360	53	1.00	77	1.00
Yes	1,647,504	263	0.92 (0.68–1.24)	345	0.83 (0.65–1.07)

Vaccines are not associated with autism: An evidence-based meta-analysis of case-control and cohort studies

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Vaccine 32 (2014) 3623–3629

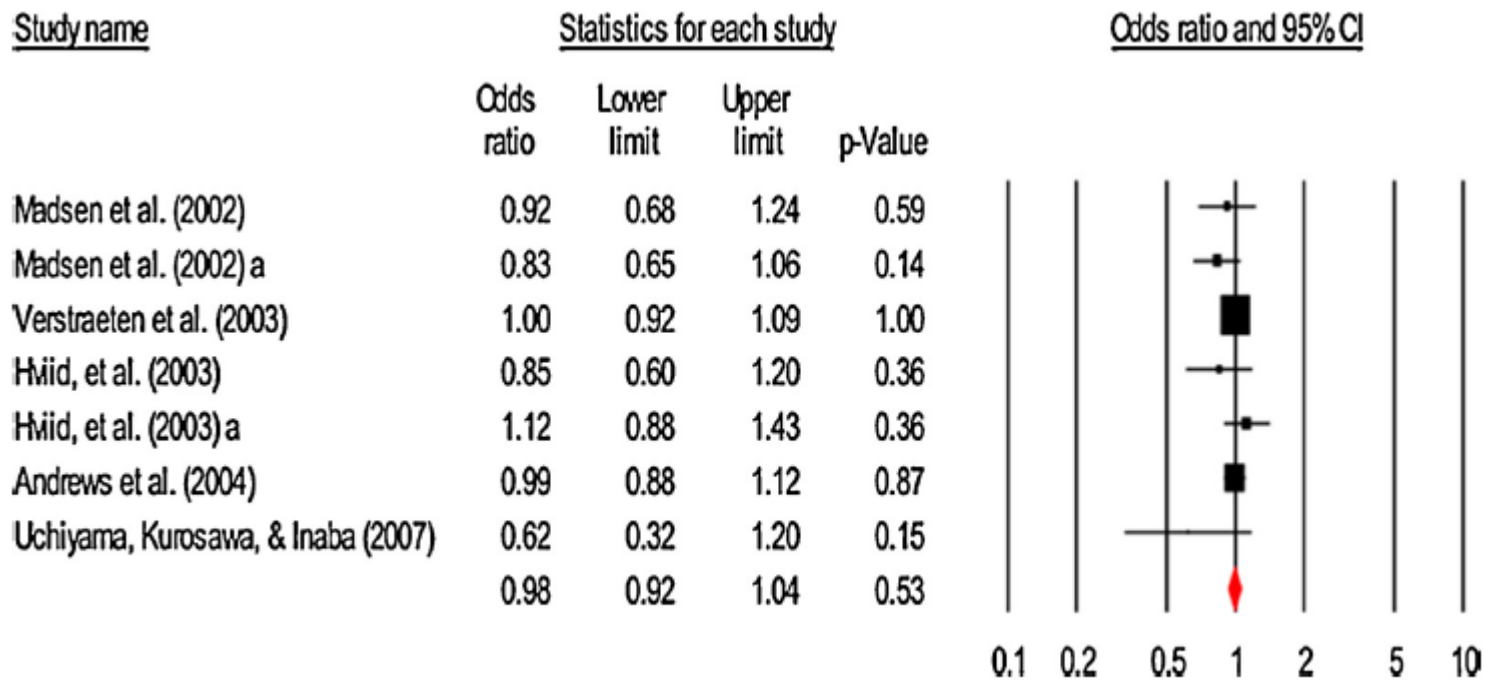

Fig. 2. Combined estimate for vaccines and autism or ASD.

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Group by Condition	Study name	Odds ratio	Lower limit	Upper limit	p-Value
ASD	Madsen et al. (2002) a	0.83	0.65	1.06	0.14
ASD	Hviid, et al. (2003) a	1.12	0.88	1.43	0.36
ASD	Uchiyama, Kurosawa, & Inaba (2007)	0.62	0.32	1.20	0.15
ASD		0.91	0.68	1.20	0.49
Autism	Madsen et al. (2002)	0.92	0.68	1.24	0.59
Autism	Verstraeten et al. (2003)	1.00	0.92	1.09	1.00
Autism	Hviid, et al. (2003)	0.85	0.60	1.20	0.36
Autism	Andrews et al. (2004)	0.99	0.88	1.12	0.87
Autism		0.99	0.92	1.06	0.70

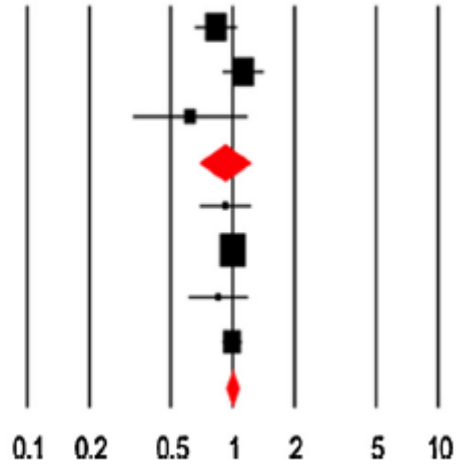

Fig. 3. Pooled estimate for vaccines and autism and ASD.

Vaccines are not associated with autism: An evidence-based meta-analysis of case-control and cohort studies

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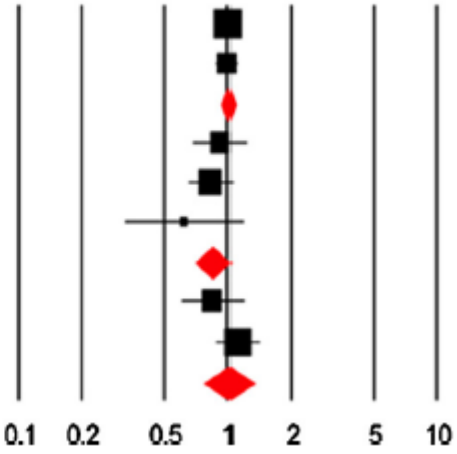
Group by Vaccine Type	Study name	Odds ratio	Lower limit	Upper limit	p-Value
Hg	Verstraeten et al. (2003)	1.00	0.92	1.09	1.00
Hg	Andrews et al. (2004)	0.99	0.88	1.12	0.87
Hg		1.00	0.93	1.07	0.92
MMR	Madsen et al. (2002)	0.92	0.68	1.24	0.59
MMR	Madsen et al. (2002) a	0.83	0.65	1.06	0.14
MMR	Uchiyama, Kurosawa, & Inaba (2007)	0.62	0.32	1.20	0.15
MMR		0.84	0.70	1.01	0.07
Thimerosal	Hviid, et al. (2003)	0.85	0.60	1.20	0.36
Thimerosal	Hviid, et al. (2003) a	1.12	0.88	1.43	0.36
Thimerosal		1.00	0.77	1.31	0.97



Early report

Ileal-lymphoid-nodular hyperplasia, non-specific colitis, and pervasive developmental disorder in children

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Summary

Background We investigated a consecutive series of children with chronic enterocolitis and regressive developmental disorder.

Methods 12 children (mean age 6 years [range 3–10], 11 boys) were referred to a paediatric gastroenterology unit with a history of normal development followed by loss of acquired skills, including language, together with diarrhoea and abdominal pain. Children underwent gastroenterological, neurological, and developmental assessment and review of developmental records. Ileocolonoscopy and biopsy sampling, magnetic-resonance imaging (MRI), electroencephalography (EEG), and lumbar puncture were done under sedation. Barium follow-through radiography was done where possible. Biochemical, haematological, and immunological profiles were examined.

Findings Onset of behavioural symptoms was associated by the parents, with measles, mumps, and rubella vaccination in eight of the 12 children, with measles infection in one child, and otitis media in another. All 12 children had intestinal abnormalities, ranging from lymphoid nodular hyperplasia to aphthoid ulceration. Histology showed patchy chronic inflammation in 11 children and reactive ileal lymphoid hyperplasia in seven, but no granulomas. Behavioural disorders included autism (nine), disintegrative psychosis (one), and possible postviral or vaccinal encephalitis (two). There were no focal neurological abnormalities and MRI and EEG tests were normal. Abnormal laboratory results were significantly raised urinary methylmalonic acid compared with age-matched controls ($p=0.003$), low haemoglobin in four children, and low serum IgA in four children.

Interpretation We identified associated gastrointestinal disease and developmental regression in a group of previously normal children, which was generally associated in time with possible environmental triggers.

Lancet 1998; **351:** 637–41
See Commentary page

Inflammatory Bowel Disease Study Group, University Departments of Medicine and Histopathology (A J Wakefield FRCS, A Anthony MB,

Introduction

We saw several children who, after a period of apparent normality, lost acquired skills, including communication. They all had gastrointestinal symptoms, including abdominal pain, diarrhoea, and bloating and, in some cases, food intolerance. We describe the clinical findings, and gastrointestinal features of these children.

Patients and methods

12 children, consecutively referred to the department of paediatric gastroenterology with a history of a pervasive developmental disorder with loss of acquired skills and intestinal symptoms (diarrhoea, abdominal pain, bloating and food intolerance), were investigated. All children were admitted to the ward for 1 week, accompanied by their parents.

Clinical investigations

We took histories including details of immunisations and exposure to infectious diseases, and assessed the children. In 11 cases the history was obtained by the senior clinician (JW-S). Neurological and psychiatric assessments were done by consultant staff (PH, MB) with HMS-4 criteria.[1] Developmental assessment included a review of prospective developmental records from parents, health visitors, and general practitioners. Four children did not undergo psychiatric assessment in hospital; all had been assessed professionally elsewhere, so these assessments were used as the basis for their behavioural diagnosis.

After bowel preparation, ileocolonoscopy was performed by SHM or MAT under sedation with midazolam and pethidine. Paired frozen and formalin-fixed mucosal biopsy samples were taken from the terminal ileum; ascending, transverse, descending, and sigmoid colons, and from the rectum. The procedure was recorded by video or still images, and were compared with images of the previous seven consecutive paediatric colonoscopies (four normal colonoscopies and three on children with ulcerative colitis), in which the physician reported normal appearances in the terminal ileum. Barium follow-through radiography was possible in some cases.

Also under sedation, cerebral magnetic-resonance imaging (MRI), electroencephalography (EEG) including visual, brain stem auditory, and sensory evoked potentials (where compliance made these possible), and lumbar puncture were done.

Laboratory investigations

Thyroid function, serum long-chain fatty acids, and cerebrospinal-fluid lactate were measured to exclude known causes of childhood neurodegenerative disease. Urinary methylmalonic acid was measured in random urine samples from eight of the 12 children and 14 age-matched and sex-matched

Conclusions

- Le profil de sécurité et la balance bénéfices/risques des vaccins actuellement utilisés dans le programme de vaccination de base sont excellents.

- Les effets secondaires des vaccins, rares ou fréquents, démontrés scientifiquement ou non, peuvent affecter l'attitude du public et des soignants envers la vaccination.

- Le refus de la vaccination est le résultat de nombreux facteurs, dont la diminution d'incidence des infections, les incertitudes scientifiques, mais aussi le désir d'autonomie individuel.

Conclusions

- Pour maintenir la confiance du public dans la vaccination, il faut que les autorités de santé:
  - considèrent les aspects de sécurité vaccinale avec autant de sérieux et de vigilance que les aspects d'efficacité
  - si il ya lieu, prennent toutes les mesures nécessaires, en temps utiles, pour réduire les risques
  - informent le public à propos de cette attitude