



III Curso de Reumatologia Pediátrica

para Médicos Internos



Vacinação em Reumatologia Pediátrica

Patrícia Costa Reis

Unidade de Reumatologia Pediátrica do Hospital de Santa Maria
Comissão Técnica de Vacinação da Direção-Geral da Saúde

18 de Setembro de 2020



Vacinação num mundo de contrastes

Taxa de cobertura vacinal VAS em Madagáscar 2017: 58%



A military hospital in Antsiranana, Madagascar. The country has seen tens of thousands of cases of measles, with more than 900 dead. Mamyrael/Agence France-Presse — Getty Images

Vacinação num mundo de contrastes

The New York Times



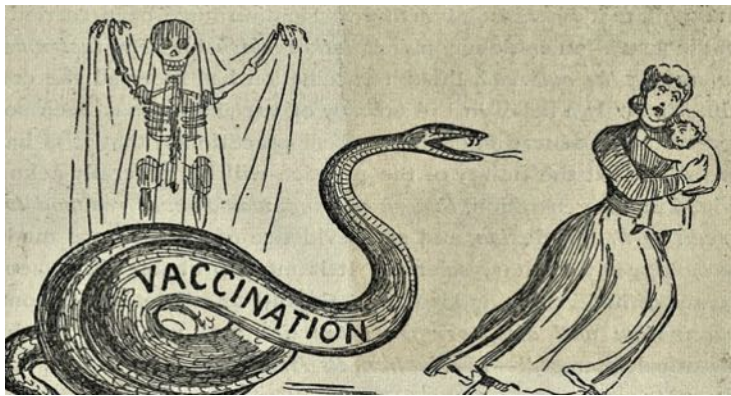
A policeman guarded health workers as they administered polio vaccine in Karachi, Pakistan, in 2016.



Campanhas de vacinação contra a poliomielite no Afeganistão, Paquistão e Nigéria



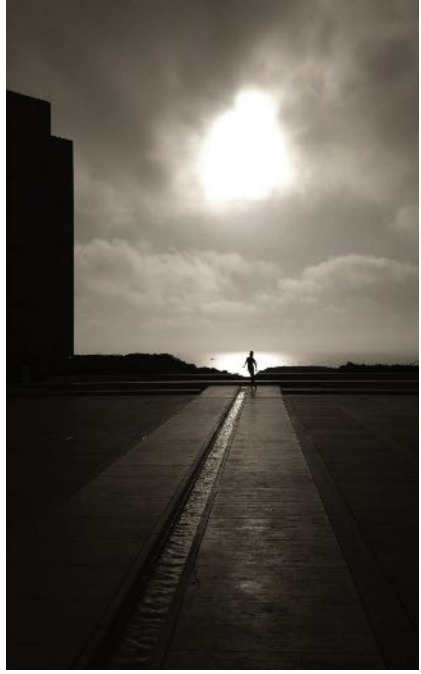
Vacinação num mundo de contrastes



Vacinação contra o Vírus da Poliomielite



1952 – EUA – 58 000 casos de poliomielite; 3 200 mortes



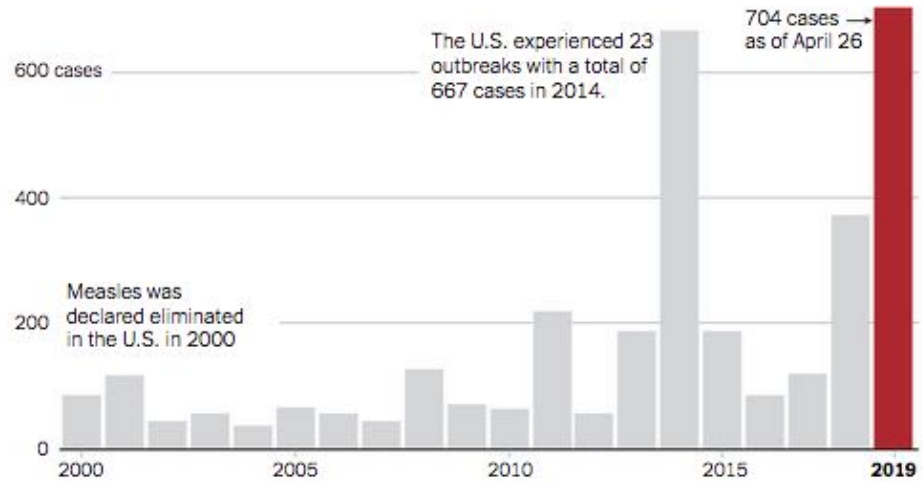
1955 - 260 casos de paralisia e 10 mortes (Cutter Lab)

1957 – EUA – 5 600 casos de poliomielite

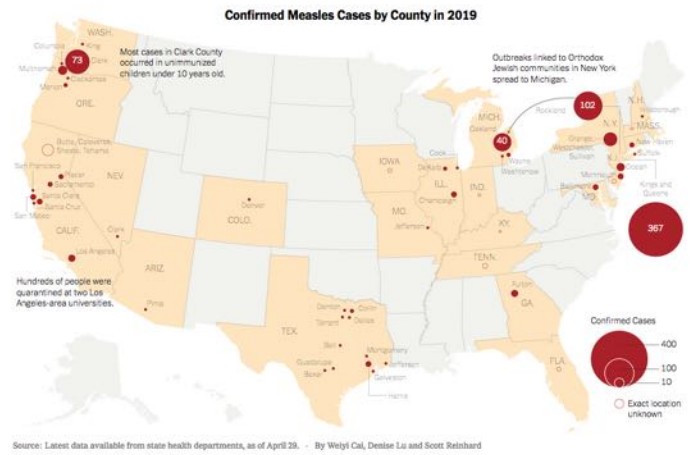
Vacinação num mundo de contrastes

The New York Times

Casos de Sarampo nos EUA

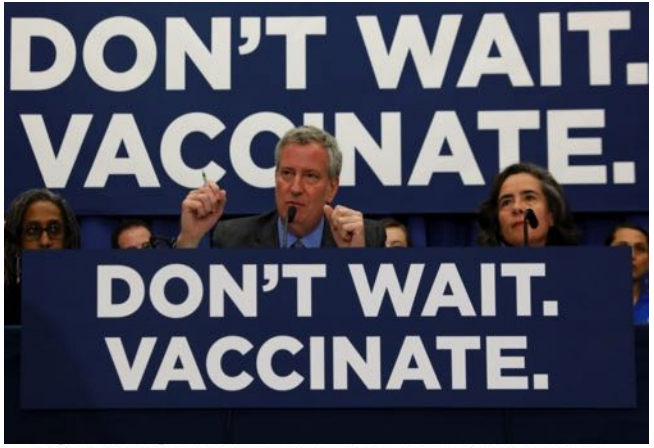


Source: Centers for Disease Control and Prevention - By The New York Times



Source: Latest data available from state health departments, as of April 26. - By Weiyi Cai, Denise Lu and Scott Reinhard

Measles Cases Reach Highest Level in More Than 25 Years, C.D.C. Says



Brian Snyder/Reuters

Measles Outbreak: N.Y. Eliminates Religious Exemptions for Vaccinations

New York, where measles has spread in ultra-Orthodox Jewish communities, joins California and a handful of other states in revoking religious exemptions.

Vacinação num mundo de contrastes



SAÚDE

Mais de 13.400 casos de sarampo na Europa num ano

Em Portugal, entre Outubro do ano passado e deste ano, houve 126 casos de sarampo confirmados laboratorialmente. A maioria registou-se em Março, aquando do surto no hospital de Santo António, no Porto.

24 de Novembro de 2018,

SAÚDE

Quase quatro mil casos de sarampo na Europa no primeiro trimestre deste ano

A maioria dos casos portugueses diz respeito aos três surtos verificados no final do ano passado, que, entretanto, a Direcção-geral da Saúde já declarou como extintos.



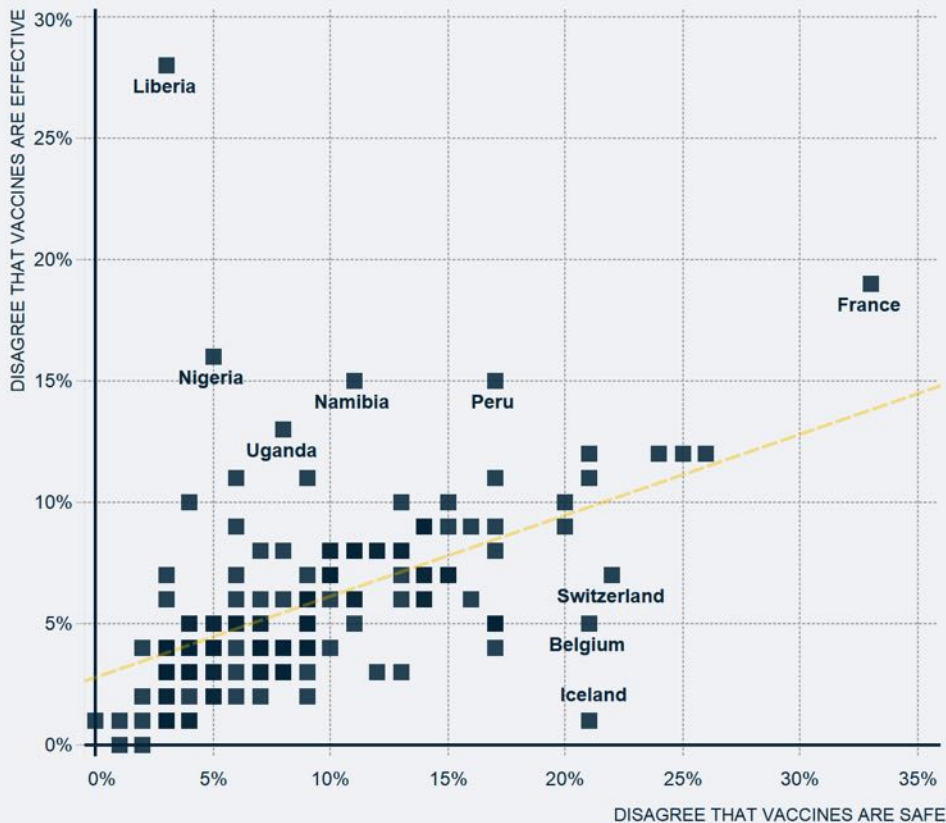
País	2017	2018	Aumento
Ucrânia	4782	53 218	1013%
Madagascar	85	23 558	27615%
Yemen	2101	13 622	548%
Venezuela	727	5668	680%
França	518	2913	462%



Confiança na Vacinação

Chart 5.4: Scatterplot exploring people's perceptions of vaccine safety and vaccine effectiveness

Percentage of people who answered 'disagree'
Do you agree, disagree, or neither agree nor disagree with the following statements? Vaccines are effective. Vaccines are safe



Country
Trend



Source: Wellcome Global Monitor, part of the Gallup World Poll 2018

Em França:

- 1/3 não concorda que as vacinas sejam seguras
- 20% não concorda que as vacinas sejam eficazes
- 10% não considera ser importante vacinar as crianças

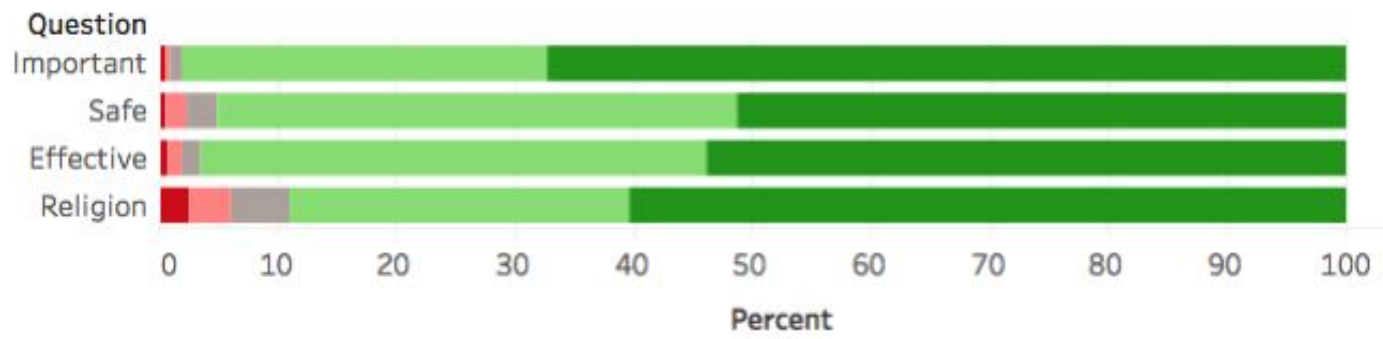
Confiança na Vacinação



2018



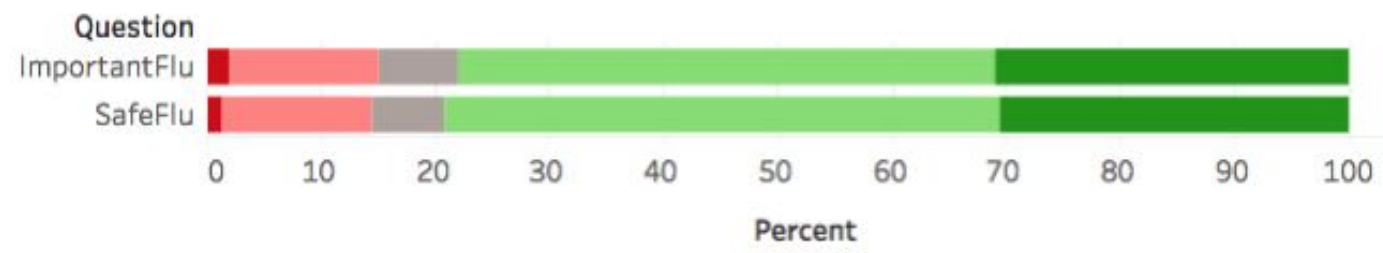
Portugal



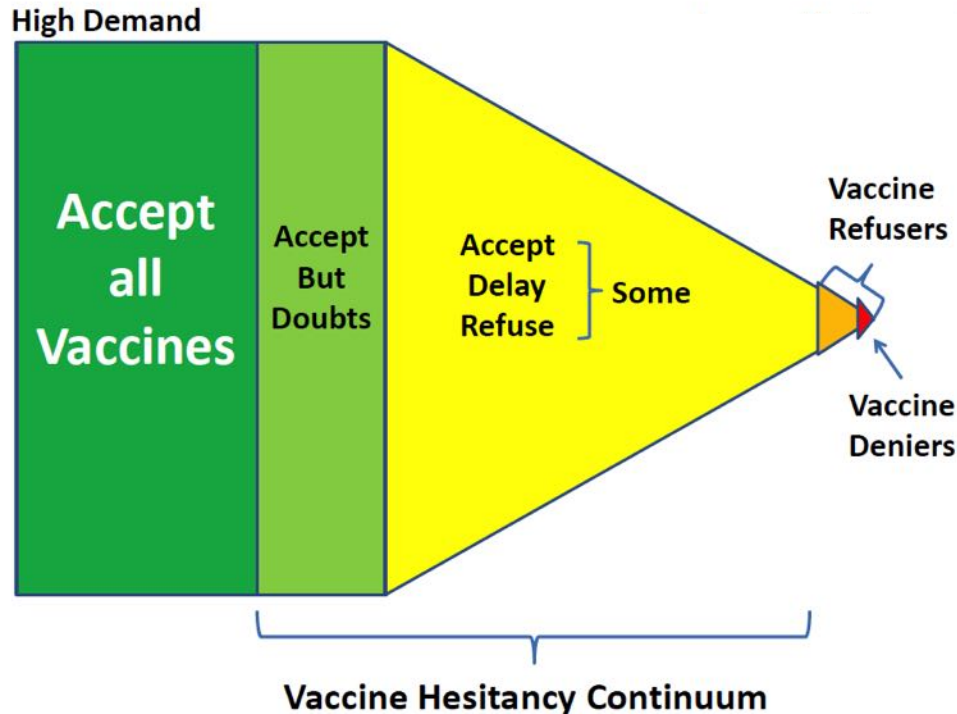
MMR



Seasonal Influenza



Hesitação em Vacinar



Estudo Italiano 2018 sobre hesitação em vacinar:

- Os **pediatras** são a fonte de informação preferencial da maioria dos pais pró-vacinas e dos pais hesitantes em vacinar

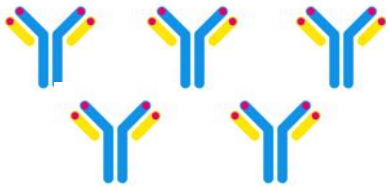
Factores associados à hesitação em vacinar:

- Não receberem informação sobre vacinas do pediatra (OR 3,21; 95% CI: 2,14-4,79)
- Receberem informações discordantes sobre vacinação (OR 1,64; 95% CI: 1,11-2,43)
- Usarem tratamentos de medicina não convencional (OR 2,05; 95% CI: 1,31-3,19)

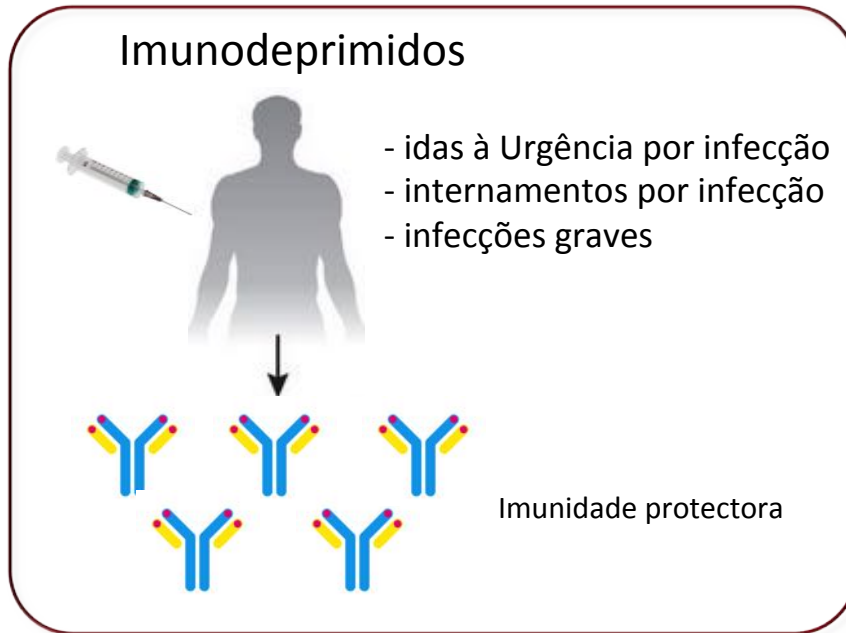
Imunodeprimidos



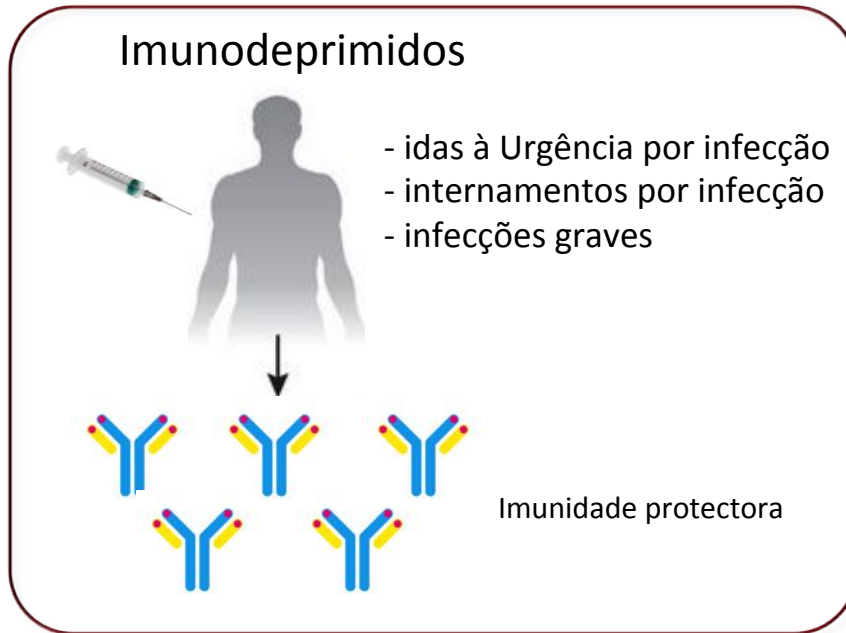
- idas à Urgência por infecção
- internamentos por infecção
- infecções graves



Imunidade protectora

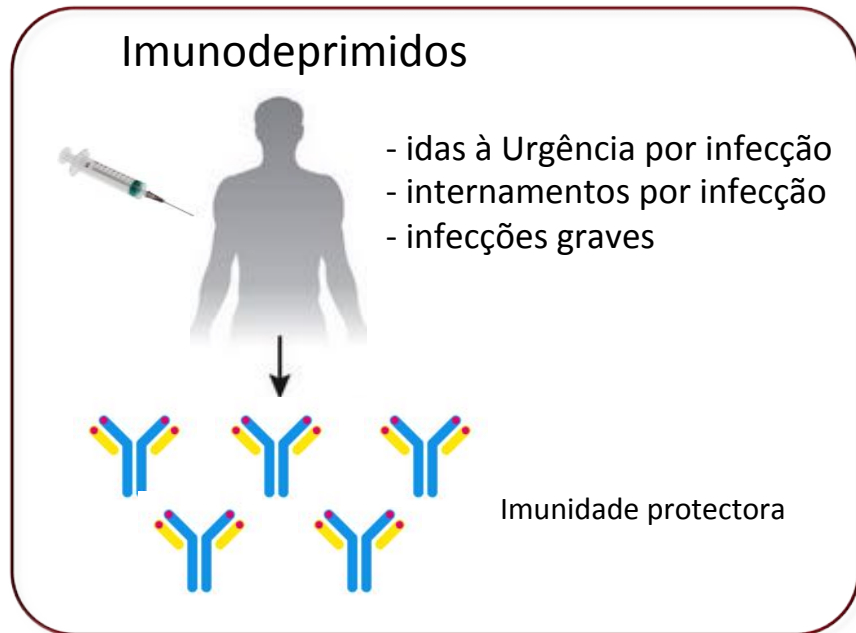


Muito baixa cobertura vacinal
nos imunodeprimidos



Muito baixa cobertura vacinal
nos imunodeprimidos

- Devido à doença crónica as vacinas já não são vistas como prioritárias
- Não há consultas regulares de pediatria/ saúde infantil



Muito baixa cobertura vacinal nos imunodeprimidos

Baixa recomendação das vacinas por parte dos profissionais de saúde

Dúvidas sobre a segurança e eficácia das vacinas nos imunodeprimidos
Preocupação com possível activação da doença imunomediada

- Devido à doença crónica as vacinas já não são vistas como prioritárias
- Não há consultas regulares de pediatria/saúde infantil

PLoS One. 2016 Apr 20;11(4):e0153848. doi: 10.1371/journal.pone.0153848. eCollection 2016.

Influenza and Pneumococcal Vaccination Uptake in Patients with Rheumatoid Arthritis Treated with Immunosuppressive Therapy in the UK: A Retrospective Cohort Study Using Data from the Clinical Practice Research Datalink.

Costello R¹, Winthrop KL², Pye SR¹, Brown B³, Dixon WG^{1,3}.

- Registos electrónicos do Reino Unido
- N=15 724 doentes com **artrite reumatóide**, sem tratamento com biológicos
- Tempo médio de seguimento 5 anos
- **1/5** dos doentes nunca receberam a vacina da gripe
- Apenas **50%** foram vacinados com a vacina antipneumocócica polissacarídica 23 valente

Vaccination coverage in children with juvenile idiopathic arthritis followed at a paediatric tertiary care centre

Marie-Paule Morin¹, Caroline Quach², Élise Fortin² and Gaëlle Chédeville¹

200 crianças com artrite idiopática juvenil
 PNV Canadá completo na última consulta: 61%
 Cobertura vacinal no Quebec: 85%

Variable	Value
Sex, girls, %	69
Mean age, years	11.4
Median age at diagnosis (range), years	4.8 (0.5–16.5)
Diagnosis at onset, %	
Oligoarthritis	51.5
Polyarthritis RF ⁻	20.5
Polyarthritis RF ⁺	1.5
Systemic arthritis	6
Psoriatic arthritis	6
Enthesitis related	7.5
Undifferentiated	7
Medication over time, %	
NSAID	99
MTX	51
Steroids	10.5
Biologic agents	7.5

	At 2.5 years		At 10.5 years		Last clinic visit	
	N	n (%)	N	n (%)	N	n (%)
Measles	198	114 (58)	118	91 (77)	200	165 (83)
Polio	198	193 (97)	118	116 (98)	200	198 (99)
Diphtheria/tetanus	198	197 (99)	118	94 (80)	200	160 (80)
Pertussis	198	197 (99)	118	94 (80)	200	155 (78)
Meningococcus C	47	40 (85)	-	-	49	45 (92)
Hepatitis B	-	-	-	-	98	80 (82)
<i>Haemophilus influenzae</i> type B	198	172 (87)	-	-	-	-
Pneumococcus	31	27 (87)	-	-	-	-
Varicella ^a	12	11 (92)	-	-	14	12 (86)
Complete vaccination status	198	103 (52)	118	80 (68)	200	121 (61)

Paediatric rheumatology

Vaccination coverage in children with rheumatic diseases

M. Bizjak¹, Š. Blazina^{1,2}, M. Zajc Avramovič^{1,2}, G. Markelj^{1,2}, T. Avčin^{1,2}, N. Toplak^{1,2}

¹Department of Allergology, Rheumatology and Clinical Immunology, University Children's Hospital, University Medical Centre Ljubljana; ²Faculty of Medicine, University of Ljubljana, Slovenia.

- N=187 crianças seguidas em consulta de Reumatologia Pediátrica
 - Artrite Idiopática Juvenil (N=165)
 - Lúpus Eritematoso Sistémico (N=6)
 - Dermatomiosite Juvenil (N=5)
 - Doença mista do tecido conjuntivo (N=3)
- 35% dos doentes não estavam correctamente vacinados quando avaliados na última consulta

Vacinação e Imunossupressão



P382

VACCINATION COVERAGE IN PORTUGUESE CHILDREN WITH RHEUMATIC DISEASES UNDERGOING IMMUNOSUPPRESSIVE THERAPY

H. Sousa¹, S. Carvalho², M. Rodrigues³, I. Brito⁴, P. Costa Reis⁵, T. Rocha⁶, M. P. Ramos⁶, M. J. Santos⁶, F. O. Ramos⁶, M. Cabral⁷, M. Guedes⁸, H. V. F. Xira, V. F. Xira, ²CHMA, Farnalício, ³H. S. João, Porto, ⁴H. Santa Maria, ⁵H. D. Estefânia, CHLC, ⁶H. Garcia Orta, ⁷H. F. Fonseca, Lisboa, ⁸CMIN, Porto, Portugal

Introduction: Effective and safe vaccination is key to reducing the burden of infections in children with rheumatic diseases (RD). However, data on vaccination status in Portuguese children with RD remains scarce. Portuguese recommendations were updated in 2012.

Objectives: To evaluate the vaccination status of Portuguese children with RD receiving immunosuppressive treatment (IT).

Methods: Multicentre study of consecutive patients with RD undergoing IT observed at a Pediatric Rheumatology Clinic, from January to March of 2018. Patients were evaluated regarding their vaccination status.

Portuguese National Vaccination Program (PNV) - universal access, free

Hep B	Hib
Hib	MMR
IPV	Men C
DTaP	HPV (Fem)
PCV13 (born ≥ 2015)	

HPV for boys, varicella, other meningococcal and flu vaccines are not included. Since 2015, children receiving IT became eligible for free pneumococcal vaccines (PCV13 and PPV23).

High dose IT - definitions

Glucocorticoids (GCs)
• High dose pulse therapy
• High dose (≥2 mg/kg/day or ≥20 mg/day for 2 weeks)
DMARDs
• Methotrexate: ≥15 mg/m ² /week
• Cyclosporine: > 2.5 mg/kg/day
• Acetaminophen: > 1.3 mg/kg/day
• Cyclophosphamide: 0.5-2.0 mg/kg/day
• Mycophenolate mofetil: ≥ 2 g/m ² /day
Biological agents (any dose)

Results: 120 patients from 7 units were studied.

Patient characteristics	n (%) or mean (n-200)
Age, years	12.5 (2-19)
Sex, female	79 (66%)
Age at diagnosis, years	8.1 (1-18)
Diagnosis	
JIA	n = 82 (68%)
Uveitis	n = 10 (8%)
JSD	n = 10 (8%)
Other connective tissue disease	n = 3 (2%)
Vasculitis	n = 5 (4%)
Autoinflammatory diseases	n = 2 (2%)
Medications	
MTX	n = 98 (82%)
Biologics	n = 41 (34%)
GCs	n = 62 (52%)
AZA	n = 10 (8%)
Cyclosporin	n = 9 (7%)
Cyclophosphamide	n = 3 (2%)
MMF	n = 4 (3%)
Others	n = 6 (5%)
High dose IT	n = 99 (82%)

Before starting IT:

- 98% had an updated PNV.
- 73% patients received at least one dose of PCV7 or 13.
- VAR was done in 17% of the 75 patients with negative or unknown previous history of varicella.
- Time elapsed between diagnosis and IT (> or < 3 months) was not associated with the prescription of extra vaccines.

During IT:

- Of the 32 children without any pneumococcal vaccine, 50% received at least one does.
- Adequate vaccination (at least one PCV13 plus one PPV23 for children > 2 years-old) was present in 30%.
- 74% received at least one flu shot

- Non-compliance to PNV (9%) was only related to MMR.
- MMR was administered in 6 patients under high dose IT (including biologics in 3). No complications were reported.
- Six cases of varicella in unvaccinated patients were reported, 3 were hospitalized.
- No boys received HPV vaccine

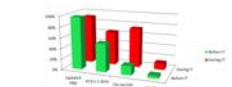


Fig 1 Vaccination rates before and during IT

Conclusion: This was the first national study evaluating immunizations in children with RD. Even though PNV compliance is overall good, extra-PNV vaccination rates are sub-optimal, namely for pneumococcus and varicella. The low prevalence of other extra-PNV recommended safe vaccines can be partially explained by their high cost. It is essential to promote compliance with recommendations about vaccination of children with RD and provide free recommended vaccines to these patients. These results reinforce the need to revisit the item "vaccination" in every routine appointment.

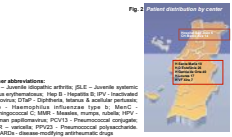


Fig 2 Patient distribution by center

References:
 1. Sousa H, et al. 2015 update of the Portuguese recommendations for the use of biological therapies in children and adolescents with juvenile idiopathic arthritis. Acta Reumatol Port 2015;33(4):219-242.
 2. Kishimoto T, et al. Immunization status and timing of vaccine administration in children with juvenile idiopathic arthritis treated with biologic therapy. Vaccine 30(21):3615-3620 (2012).
 3. Pardo, Maria Valente, 2018 (thesis), and Matthew D. Steiner. "Transmission of the immunosuppressed state." Journal of Allergy and Clinical Immunology 121 (2016): 513-522.
 4. Ministério da Saúde. Centro Nacional de Saúde (CNS). Programa Nacional de Vacinação (PNV). Lisboa: DGS, 2018 (file).

- Estudo multicêntrico
- Crianças seguidas em consulta de Reumatologia Pediátrica de Jan a Mar 2018 a fazer imunossupressão (N=120)
- Antes do início da imunossupressão 98% tinha o PNV actualizado
- Das crianças sem vacinação antipneumocócica prévia (32):
 - 50% receberam pelo menos 1 dose
 - 30% vacinação adequada (PCV13+PCV23)
- 74% receberam, pelo menos, uma vez a vacina da gripe

Mensagens chave

1. Os doentes imunodeprimidos estão menos protegidos numa comunidade com menor cobertura vacinal.
2. A opinião do pediatra é fundamental para a confiança na vacinação.
3. Temos de estar informados e informar sobre vacinação em imunodeprimidos.

Recommendations

EULAR recommendations for vaccination in paediatric patients with rheumatic diseases

M W Heijstek,¹ L M Ott de Bruin,¹ M Bijl,² R Borrow,^{3,4} F van der Klis,⁵ I Koné-Paut,⁶ A Fasth,⁷ K Minden,⁸ A Ravelli,⁹ M Abinun,¹⁰ G S Pileggi,¹¹ M Borte,¹² N M Wulffraat¹

ABSTRACT

Evidence-based recommendations for vaccination of paediatric patients with rheumatic diseases (PaedRD) were developed by following the EULAR standardised procedures for guideline development. The EULAR task force consisted of (paediatric) rheumatologists/immunologists, one expert in vaccine evaluation, one expert in public health and infectious disease control, and one epidemiologist. A systematic literature review was conducted in MEDLINE, EMBASE, and abstracts of the EULAR and American College of Rheumatology meetings of 2008/9. The level of evidence and strength of recommendation were based on customary scoring systems. Delphi voting was applied to assess the level of agreement between task force members. 107 papers and eight abstracts were used. The majority of papers considered seasonal influenza (41) or pneumococcal (23) vaccination. 26 studies were performed specifically in paediatric patients, and the majority in adult rheumatoid arthritis and systemic lupus erythematosus patients. Fifteen recommendations were developed with an overall agreement of 91.7%. More research is needed on the safety and immunogenicity of (live-attenuated) vaccination in PaedRD, particularly in those using biologicals, and the effect of vaccination on prevention of infections.

Vaccination has greatly reduced the burden of childhood infections.¹ Paediatric patients with rheumatic diseases (PaedRD) are at increased risk of infections, due to the immunosuppressive effect of the disease or its treatment.²⁻⁴ With current aggressive treatment strategies incorporating the early use of immunosuppressive drugs and biological agents, susceptibility to infections increases further.⁵ In this context, safe vaccination and adequate serological responses to vaccinations are vital. The immunogenicity of vaccinations might be reduced as a result of the immunosuppressed status. In addition, the safety profile might differ from healthy subjects. Moreover, the potential effects of vaccination on the underlying disease must be considered. Generally, recommendations on the immunisation of children with rheumatological diseases follow the recommendations for immunosuppressed patients (patients with solid organ transplantation, haematological malignancy, immunodeficiency), in which live-attenuated vaccines are contraindicated when using high-dose immunosuppressive drugs.^{6,7} However, to what extent antirheumatic treatment actually suppresses the immune system remains unclear.

Our aim was to develop recommendations for vaccinations in PaedRD based on available evidence in the literature.

METHODS

The recommendations were constructed using the European League Against Rheumatism (EULAR) standard operating procedures.⁸ An expert committee was instituted, consisting of eight paediatric rheumatologists/immunologist (IK-P, AF, KM, AR, MA, GSF, MB, NMW), one adult rheumatologist/immunologist (MB), one expert in vaccine evaluation (RB), one expert in public health and infectious disease control (FvdK), one epidemiologist (KM) and two physicians/PhD students in charge of the systematic literature research (MWH, LMOdB).

First, the expert committee defined search terms for the systematic literature review (see supplementary tables 1-5, available online only), which was conducted in MEDLINE in December 2009, in MEDLINE and EMBASE in November 2010 and abstracts from EULAR and American College of Rheumatology meetings in 2008/9. Relevant papers, among others found by searching references from keynote papers, were added by experts. Exclusion criteria were: non-rheumatic autoimmune diseases, malignancies, immunodeficiencies, transplantations, atopic diseases, animal studies, infections rather than vaccinations, vaccine development, phase I-III trials, in-vitro studies, non-English papers. Papers concerning the potential role of vaccinations in inducing rheumatic diseases were excluded, because these recommendations focus on the effect of vaccination on established disease.⁹⁻¹⁵

Experts independently graded literature on methodological quality and level of evidence.⁹ Each paper was evaluated by at least three experts. Abstracts were rated a level of evidence 3 or 4. Data were extracted using predefined criteria. Results of studies on adult patients with rheumatic diseases were extrapolated to juvenile patients. Critical appraisal results were debated, and subsequently the recommendations were formulated. The strength of each recommendation was based on the level of evidence.⁹ Finally, a closed Delphi voting procedure was performed to determine the level of agreement with the recommendation ranging from 0 (no agreement) to 10 (maximal agreement). Recommendations on which the agreement was below 7.5 were removed.

RESULTS

Sixty papers were critically appraised on vaccination versus immunosuppressive drugs and 147 on vaccination versus rheumatic diseases after the first search (figure 1). In the second search (November

Recommendation

2019 update of EULAR recommendations for vaccination in adult patients with autoimmune inflammatory rheumatic diseases

Victoria Furer,^{1,2} Christien Rondaan,^{3,4} Marloes W Heijstek,⁵ Nancy Agmon-Levin,^{2,6} Sander van Assen,⁷ Marc Bijl,⁸ Ferry C Breedveld,⁹ Raffaele D'Amelio,¹⁰ Maxime Dougados,¹¹ Meliha Crnkic Kapetanovic,¹² Jacob M van Laar,¹³ A de Thurah,¹⁴ Robert BM Landewé,^{15,16} Anna Molto,¹¹ Ulf Müller-Ladner,¹⁷ Karen Schreiber,^{18,19} Leo Smolar,²⁰ Jim Walker,²¹ Klaus Wernatz,²² Nico M Wulffraat,²³ Ori Elkayam^{1,2}

Handling editor

Jesper S Smolen

► Additional material is published online only. To view please visit the journal online (<http://dx.doi.org/10.1136/annrheumdis-2019-215882>).

For numbered affiliations see end of article.

Correspondence to

Victoria Furer, Rheumatology, Tel Aviv Sourasky Medical Center, Tel Aviv 62431, Israel; furer.vheum@gmail.com

VF and CR contributed equally.

Received 12 June 2019
Revised 19 July 2019
Accepted 22 July 2019



© Author(s) for their employer(s) 2019. No commercial re-use. See rights and permissions. Published by BMJ.

To cite: Furer V, Rondaan C, Heijstek MW, et al. *Ann Rheum Dis*. Epub ahead of print: [please include Day Month Year]. doi:10.1136/annrheumdis-2019-215882

ABSTRACT

To update the European League Against Rheumatism (EULAR) recommendations for vaccination in adult patients with autoimmune inflammatory rheumatic diseases (AIIRD) published in 2011. Four systematic literature reviews were performed regarding the incidence/prevalence of vaccine-preventable infections among patients with AIIRD; efficacy, immunogenicity and safety of vaccines; effect of anti-rheumatic drugs on the response to vaccines; effect of vaccination of household of AIIRDs patients. Subsequently, recommendations were formulated based on the evidence and expert opinion. The updated recommendations comprise six overarching principles and nine recommendations. The former address the need for an annual vaccination status assessment, shared decision-making and timing of vaccination, favouring vaccination during quiescent disease, preferably prior to the initiation of immunosuppression. Non-live vaccines can be safely provided to AIIRD patients regardless of underlying therapy, whereas live-attenuated vaccines may be considered with caution. Influenza and pneumococcal vaccination should be strongly considered for the majority of patients with AIIRD. Tetanus toxoid and human papilloma virus vaccination should be provided to AIIRD patients as recommended for the general population. Hepatitis A, hepatitis B and herpes zoster vaccination should be administered to AIIRD patients at risk. Immunocompetent household members of patients with AIIRD should receive vaccines according to national guidelines, except for the oral poliovirus vaccine. Live-attenuated vaccines should be avoided during the first 6 months of life in newborns of mothers treated with biologics during the second half of pregnancy. These 2019 EULAR recommendations provide an up-to-date guidance on the management of vaccinations in patients with AIIRD.

INTRODUCTION

Patients with autoimmune inflammatory rheumatic diseases (AIIRD) have an increased burden of infections, attributed to the underlying autoimmune disease,¹⁻⁴ comorbidities⁵ and immunosuppressive therapy, including glucocorticoids (GCs), disease-modifying antirheumatic drugs (DMARDs): conventional synthetic (csDMARDs), biological

(bDMARDs) and targeted synthetic DMARDs (tsDMARDs).^{2,6,7} As the 'treat to target' principle currently guides an intensive immunosuppressive therapy aimed at remission in most rheumatic diseases,⁸⁻¹⁰ these therapies are commonly applied, in particular at early disease stages. Thus, prevention of infections is crucial in the management of patients with AIIRD.

Vaccination prevents infections by inducing and/or enhancing protective immunity. Vaccination is particularly important in AIIRD patients, potentially translating into a lower rate of hospital admissions due to infections, emergency room visits and the rate of invasive infectious diseases.¹¹ Yet, the AIIRD population universally suffers from a suboptimal uptake of vaccinations,¹²⁻¹⁹ in part due to a low rate of referral for vaccination by rheumatologists,²⁰ and other treating physicians,²¹ indicating that further interventions are needed to raise the awareness for vaccination among the rheumatology community and involved healthcare professionals. Another important factor for a low vaccination rate relates to concerns about efficacy, immunogenicity and safety of vaccinations,¹⁵ an important issue to be addressed by upcoming evidence.

Our aim was to update the present European League Against Rheumatism (EULAR) recommendations for vaccination in patients with AIIRD published in 2011 and to incorporate the new evidence on the incidence/prevalence of vaccine preventable infections (European League) among AIIRD patients, along with efficacy, immunogenicity and safety of vaccines provided to AIIRD patients under a wide range of immunosuppressive therapies. The update was conducted in line with the standard operating procedures (SOP) of the EULAR,²² combining evidence from clinical studies and expert opinion. Our recommendations target all healthcare professionals involved in the care for patients with AIIRD.

METHODS

Development of recommendations

The present update of the EULAR recommendations for vaccination in patients with AIIRD was a combined project for the adult and paediatric AIIRD populations. Following the 2014 updated EULAR SOP,²² the convenor (OE) first formed the

2011

Vacinação em Reumatologia Pediátrica

Princípios Gerais

Deve-se avaliar anualmente o estado vacinal e a necessidade de administrar novas vacinas

- Registo da história vacinal, dos efeitos adversos da vacinação e se houve ou não agravamento da doença imunomediada
- O médico assistente deve informar o doente e a família sobre os benefícios e os riscos das vacinas



+ Avaliar o estado vacinal e programar vacinas na primeira consulta de Reumatologia Pediátrica e antes de iniciar imunossupressão de altas doses

- PDS – Plataforma de Dados da Saúde
- eVacinas

Vacinação em Reumatologia Pediátrica

Princípios Gerais

As vacinas devem ser administradas preferencialmente antes do início da imunossupressão.

- Esta estratégia aumenta a resposta óptima às vacinas.
- É particularmente importante antes da administração de rituximab.
 - A vacinação pode ser realizada 4 semanas antes e 6 meses depois da terapêutica com rituximab.
 - Se não for possível, a vacinação com vacinas não vivas deverá ser realizada, tendo em consideração que existe o potencial para uma resposta sub-óptima.
- Nunca se deve adiar o início da terapêutica imunossupressora em casos graves. Nestes casos a prioridade será sempre controlar a doença e não a administração da vacina.

Vacinação em Reumatologia Pediátrica

Princípios Gerais

Deve-se vacinar quando a doença se encontra em remissão.

- A maioria dos estudos sobre a imunogenicidade das vacinas foram realizados em doentes em remissão. Há poucos dados sobre a utilização de vacinas em doentes com doença activa.
- Quando os doentes se encontram com doença activa, não se deve adiar a vacinação. O estado vacinal deve ser avaliado posteriormente.

Vacinação em Reumatologia Pediátrica

Princípios Gerais

As vacinas não vivas podem ser administradas com segurança a crianças e adolescentes com doenças autoimunes ou autoinflamatórias.

- Há inúmeros estudos a confirmarem a eficácia e segurança das vacinas não vivas neste grupo de doentes.

Vacinação em Reumatologia Pediátrica

Princípios Gerais

As vacinas vivas atenuadas podem ser consideradas com precaução.

Contra-indicadas (2011) \longrightarrow Consideradas com precaução (2019)

Recommendation

Table 1 Overarching principles for vaccination in adult patients with AIIRD

Overarching principles	Level of Agreement (%)
1. The vaccination status and indications for further vaccination in patients with AIIRD should be assessed yearly by the rheumatology team.	100%
2. The individualised vaccination programme should be explained to the patient by the rheumatology team, providing a basis for shared decision-making, and be jointly implemented by the primary care physician, the rheumatology team and the patient.	94%
3. Vaccination in patients with AIIRD should preferably be administered during quiescent disease.	94%
4. Vaccines should preferably be administered prior to planned immunosuppression, in particular B cell depleting therapy.	100%
5. Non-live vaccines can be administered to patients with AIIRD also while treated with systemic glucocorticoids and DMARDs.	100%
6. Live-attenuated vaccines may be considered with caution in patients with AIIRD.	53%

AIIRD, autoimmune inflammatory rheumatic diseases; DMARDs, disease-modifying antirheumatic drugs.

Vacinação em Reumatologia Pediátrica

Princípios Gerais

As vacinas vivas atenuadas podem ser consideradas com precaução.

- Devem ser administradas 4 semanas antes do início da imunossupressão
- Usar com especial cuidado se imunossupressão de alta dose:
 - Prednisolona ≥ 2 semanas com doses $\geq 2\text{mg/Kg/dia}$ ou $\geq 20\text{mg/dia}$
 - Metotrexato $\geq 15\text{mg/m}^2/\text{semana}$
 - Azatioprina $\geq 3,0\text{ mg/Kg/dia}$
 - Outros DMARDs e biológicos
- Alguma evidência de que o reforço da vacina do sarampo e a vacina da varicela poderão ser imunogênicos e seguros em alguns subgrupos de doentes



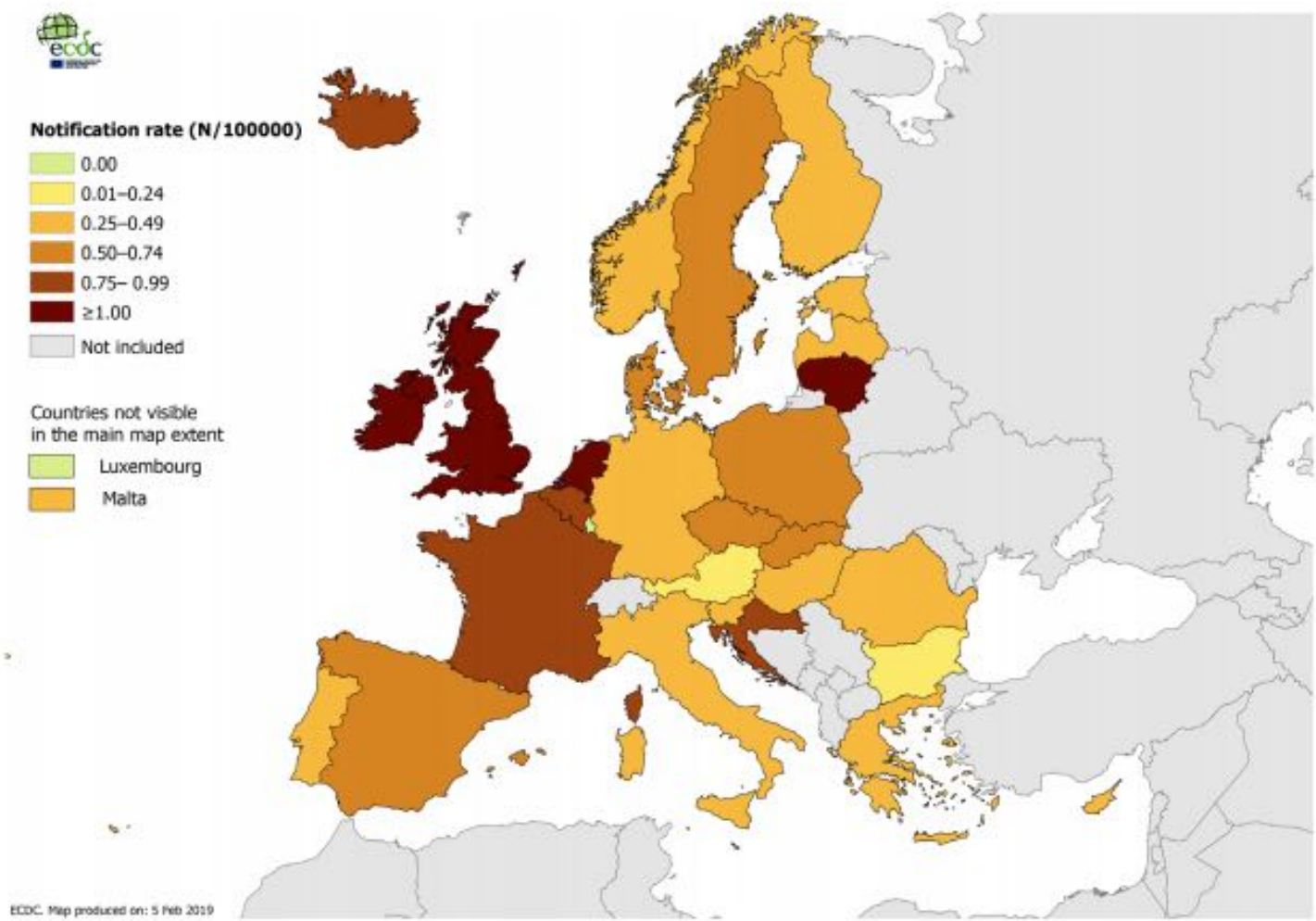
Vacinação em Reumatologia Pediátrica

Qualquer recomendação sobre vacinas em crianças e adolescentes com doenças autoimunes e autoinflamatórias implica saber:

1. Incidência e as complicações neste grupo de doentes da doença que é prevenida pela vacina
 - De acordo com a gravidade da doença
 - De acordo com a terapêutica
2. Eficácia da vacina
3. Imunogenicidade humoral e/ou celular da vacina
4. Segurança da vacina
 - Efeitos adversos
 - Activação da doença autoimune ou autoinflamatória

Doença Meningocócica

Doença Invasiva Meningocócica na Europa

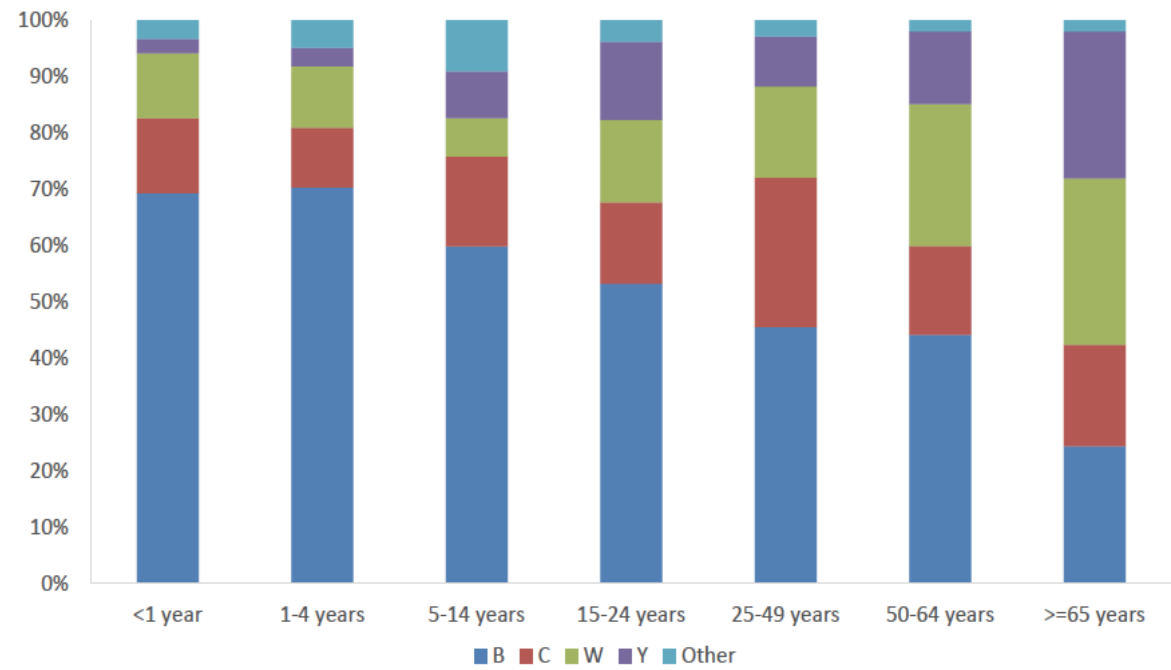


Número de casos confirmados de DIM/100.000 por país, na EU/EEA, 2017. ECDC. *Annual epidemiological report for 2017*. Stockholm: ECDC; 2019

Doença Meningocócica

Doença Invasiva Meningocócica na Europa

Letalidade 5% a 10%
Sequelas em 10% a 20%

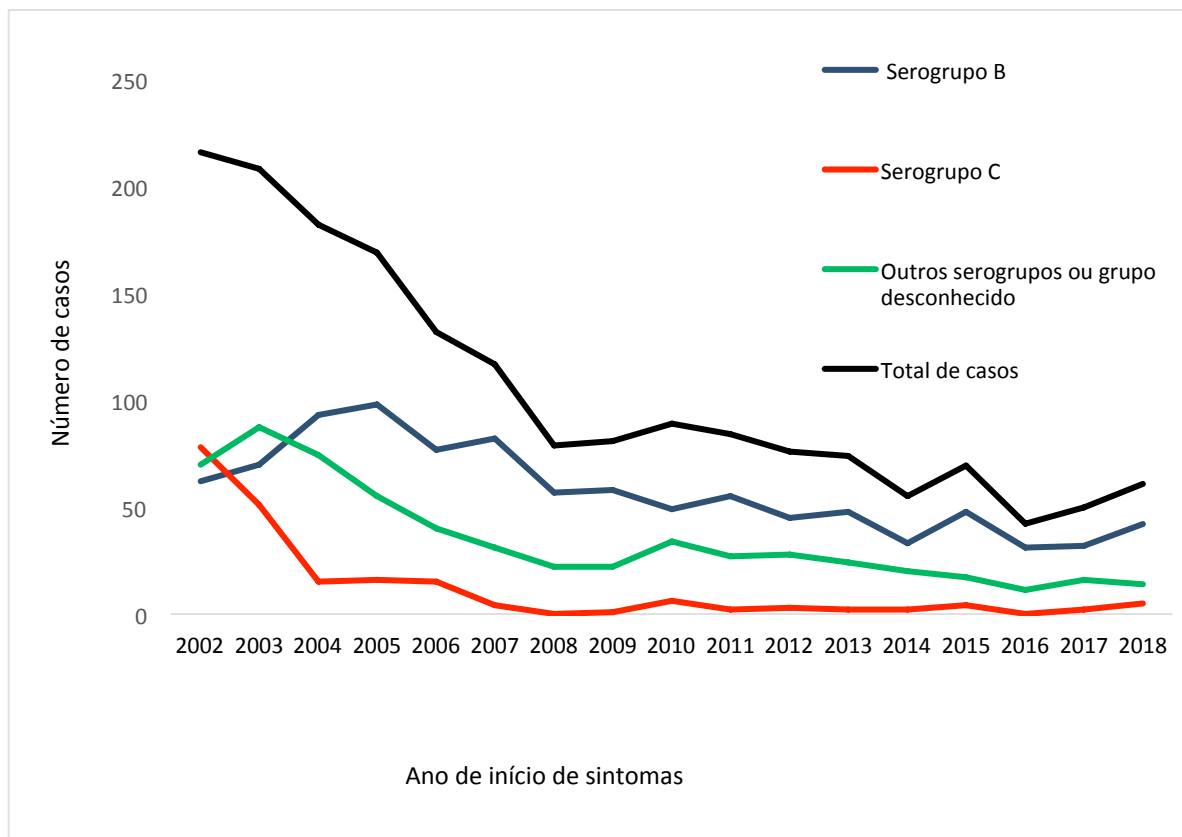


Distribuição percentual dos grupos de *N. meningitidis* nos casos confirmados de DIM, por grupo etário EU/EEA, 2017. Annual epidemiological report for 2017. Stockholm: ECDC; 2019

Doença Meningocócica

Doença Invasiva Meningocócica em Portugal

Vacina antimeningococica C no PNV desde 2006
Cobertura vacina 96%



Número total de casos de DIM por serogrupo, Portugal 2002-2018. Fonte: INSA - Vigilância Epidemiológica Integrada da Doença Meningocócica

Doença Meningocócica

Vacinação anti-Meningocócica B

Cobertura 56,7% (2018)

Classes etárias (anos)	2002	2003	2004	2005	2006	2007	2008	2009	2010	2011	2012	2013	2014	2015	2016	2017	2018	Total
0 anos	11	25	34	33	26	21	18	17	13	19	12	21	10	8	6	9	17	300
1-4 anos	31	29	37	24	35	37	23	21	13	12	21	10	9	11	9	8	12	342
5-9 anos	7	9	9	13	6	9	9	6	9	5	4	5	5	6	4	4	2	112
10-14	0	1	3	9	0	4	1	1	0	3	0	0	1	2	0	1	1	27
15-19	1	0	2	7	2	1	2	4	4	2	3	3	2	5	1	0	2	41
20-24	1	1	1	1	1	2	0	1	1	4	0	2	0	1	0	1	1	18
25-44	2	1	3	5	3	2	1	3	2	2	3	1	4	4	2	1	3	42
≥45	5	3	4	6	4	6	3	4	7	8	2	6	2	11	9	8	4	92
Desconhecida	4	1	0	0	0	0	0	1	0	0	0	0	0	0	0	0	0	6
Total	62	70	93	98	77	82	57	58	49	55	45	48	33	48	31	32	42	980

INSA

A vacinação anti-meningocócica B é segura e eficaz nos doentes com doenças autoimunes ou autoinflamatórias

Vacina Doença	Idade											
	Nasci-mento	2 meses	4 meses	6 meses	12 meses	18 meses	5 anos	10 anos	25 anos	45 anos	65 anos	10/10 anos
Hepatite B	VHB 1	VHB 2		VHB 3								
<i>Haemophilus influenzae b</i>		Hib 1	Hib 2	Hib 3		Hib 4						
Difteria, tétano, tosse convulsa		DTPa 1	DTPa 2	DTPa 3		DTPa 4	DTPa 5					
Poliomielite		VIP 1	VIP 2	VIP 3		VIP 4	VIP 5					
<i>Streptococcus pneumoniae</i>		Pn ₁₃ 1	Pn ₁₃ 2		Pn ₁₃ 3							
<i>Neisseria meningitidis B</i>		MenB 1	MenB 2		MenB 3							
<i>Neisseria meningitidis C</i>					MenC							
Sarampo, parotidite epidémica, rubéola					VASPR 1		VASPR 2					
Vírus Papiloma humano								HPV 1,2				
Tétano, difteria e tosse convulsa									Tdpa - Grávidas			
Tétano e difteria									Td	Td	Td	Td

MenB

Aplicável aos nascidos ≥ 2019 . As crianças que iniciaram a vacinação por prescrição médica podem completar o esquema no âmbito do PNV, até aos 5 anos de idade, respeitando o esquema recomendado para a sua idade (Quadros I, IIIc ou VIII).

Vacina Anti-Meningocócica B

Idade de início ¹	Primovacinação (intervalo: 8 semanas entre doses)	Idade do reforço único (intervalo: 8 semanas desde a dose anterior)
2 - 11 meses	2 doses	≥12 meses
12 - 23 meses	2 doses	< 5 anos
24 meses - 4 anos	2 doses (intervalo: 4-8 semanas)	-----

Doença Meningocócica

Vacinação anti-Meningocócica ACWY

Y

Classes etárias (anos)	2002	2003	2004	2005	2006	2007	2008	2009	2010	2011	2012	2013	2014	2015	2016	2017	2018	Total
0 anos	0	0	1	1	1	1	0	0	0	0	0	0	0	1	1	1	1	8
1-4 anos	2	0	2	1	1	1	2	0	0	2	0	0	2	0	0	3	1	17
5-9 anos	0	0	1	0	0	1	1	2	0	2	0	1	1	1	1	0	0	11
10-14 anos	0	0	0	0	0	0	0	0	0	0	0	0	0	2	1	0	1	4
15-19 anos	0	0	0	0	0	0	0	0	0	2	0	0	0	1	0	0	1	4
20-24 anos	0	0	0	0	0	0	0	0	0	1	1	1	0	0	0	0	0	3
25-44 anos	0	0	0	0	0	0	0	0	0	1	3	0	0	0	1	0	1	6
≥45 anos	0	0	0	0	3	0	0	0	0	1	0	1	2	2	2	0	1	12
Desconhecida	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0	1
Total	2	0	4	2	5	3	3	2	0	10	4	3	5	7	6	4	6	66

C

Classes etárias (anos)	2002*	2003	2004	2005	2006	2007	2008	2009	2010	2011	2012	2013	2014	2015	2016	2017	2018	Total
0	11	9	5	4	0	0	0	0	0	0	0	0	1	0	0	0	0	30
1-4	28	17	5	2	3	1	0	0	0	0	0	0	0	0	0	0	0	56
5-9	11	9	1	5	2	1	0	0	2	0	0	0	0	0	0	0	0	31
10-14	8	4	2	2	2	0	0	0	0	1	0	0	0	0	0	0	0	19
15-19	9	5	1	1	2	0	0	0	0	0	0	0	0	0	0	1	0	19
20-24	2	0	0	1	3	1	0	0	0	0	1	1	0	2	0	0	0	11
25-44	1	5	1	1	2	0	0	1	1	0	2	0	0	0	0	0	3	17
≥45	3	2	0	0	1	1	0	0	3	1	0	1	1	2	0	1	2	18
Total	73	51	15	16	15	4	0	1	6	2	3	2	2	4	0	2	5	201

W

Classes etárias (anos)	2002	2003	2004	2005	2006	2007	2008	2009	2010	2011	2012	2013	2014	2015	2016	2017	2018	Total
0 anos	0	2	1	0	0	0	0	0	0	0	0	0	0	0	0	0	1	4
1-4 anos	1	2	2	1	1	0	0	0	0	0	0	0	0	0	0	0	0	7
5-9 anos	1	0	1	0	0	0	0	0	0	0	0	0	0	0	1	0	0	3
10-14 anos	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
15-19 anos	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1
20-24 anos	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
25-44 anos	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
≥45 anos	0	1	0	1	0	1	0	0	0	0	1	1	0	0	0	2	4	11
Desconhecida	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1
Total	3	6	4	2	1	1	0	0	0	0	1	1	0	0	1	2	5	27

Vacina antimeningococica C no PNV desde 2006
Cobertura vacina 96%

A vacinação anti-meningocócica ACWY é segura e eficaz em doentes com doenças autoimunes ou autoinflamatórias