

CURSO BÁSICO DE COLPOSCOPIA

20 e 21 de outubro de 2016

Centro de Formação
Hospital Prof. Doutor Fernando Fonseca
Amadora

HPV em ORL

Filipe M. Freire

Serviço de ORL

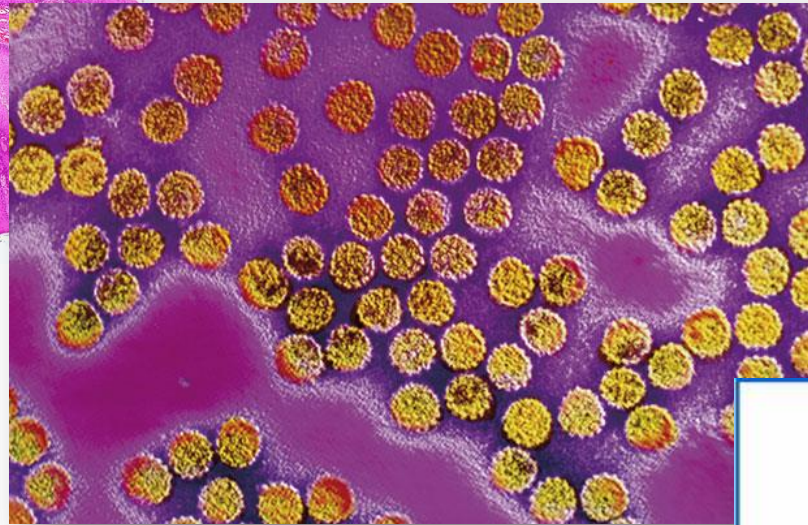


Ears, Nose & Throat (ENT)

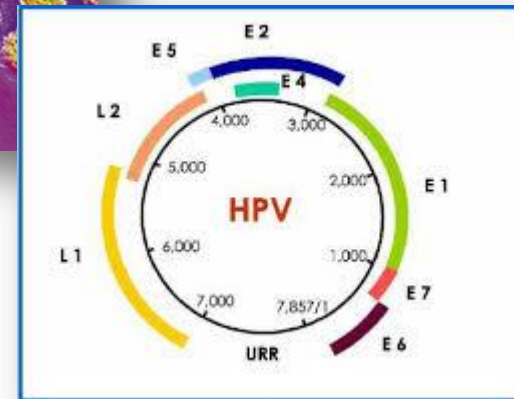




HPV



oncovirus dsDNA epiteliotropico > 180 sub tipos



6 11

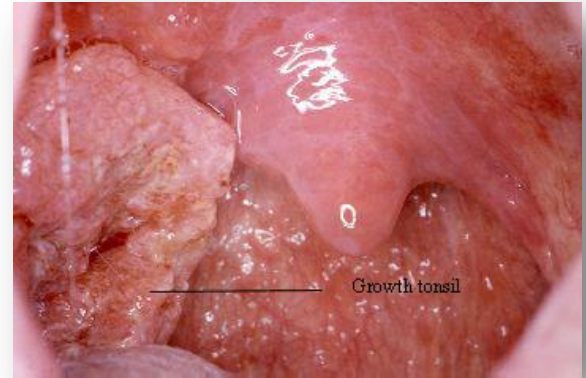
16 18

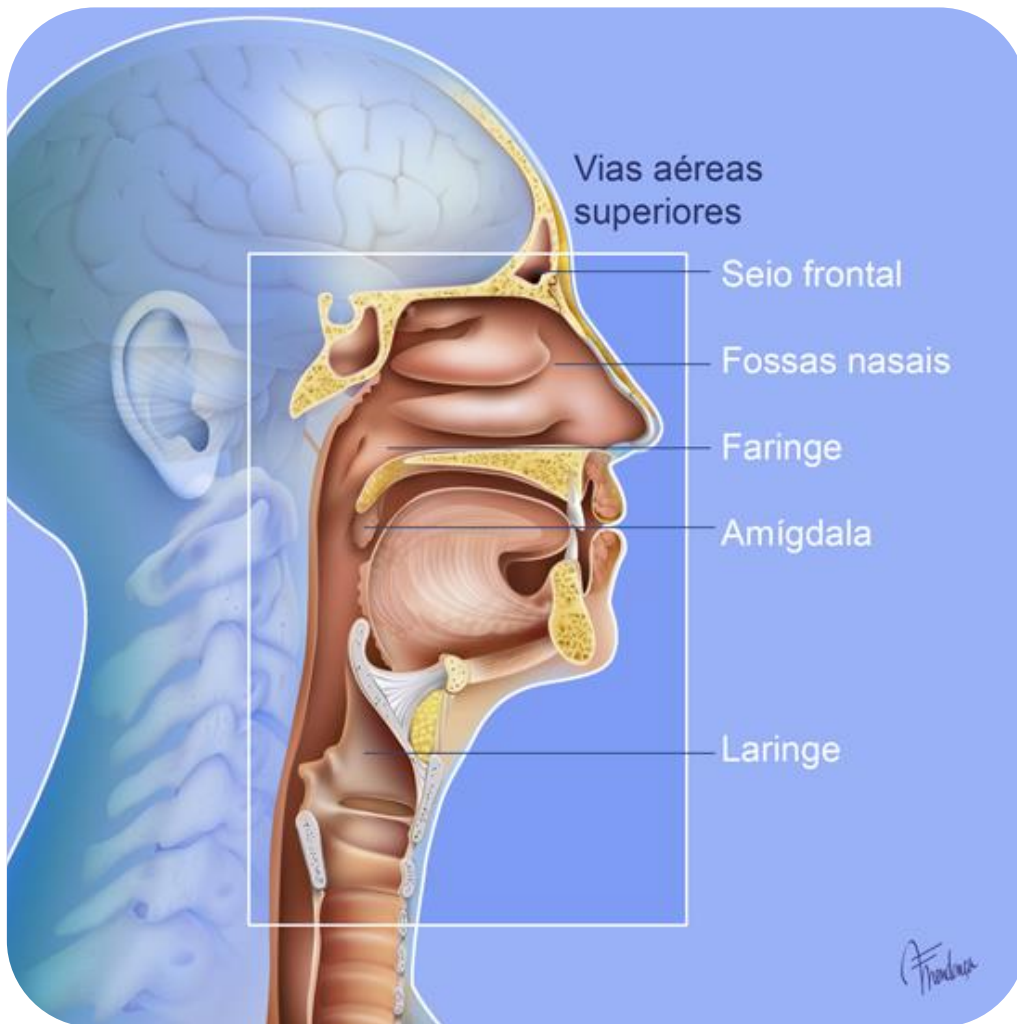
HPV em ORL

- Papilomas benignos das mucosas
- Papilomatose respiratória / laríngea
- Carcinoma pavimento-celular da cabeça e pescoço









Tumores da Cabeça e Pescoço

Cavidade Oral

Orofaringe

Hipofaringe

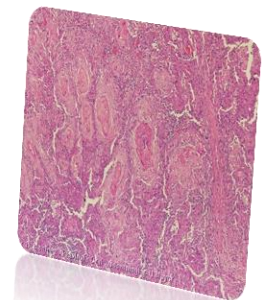
Laringe

Cavidades naso-sinusais

Pele

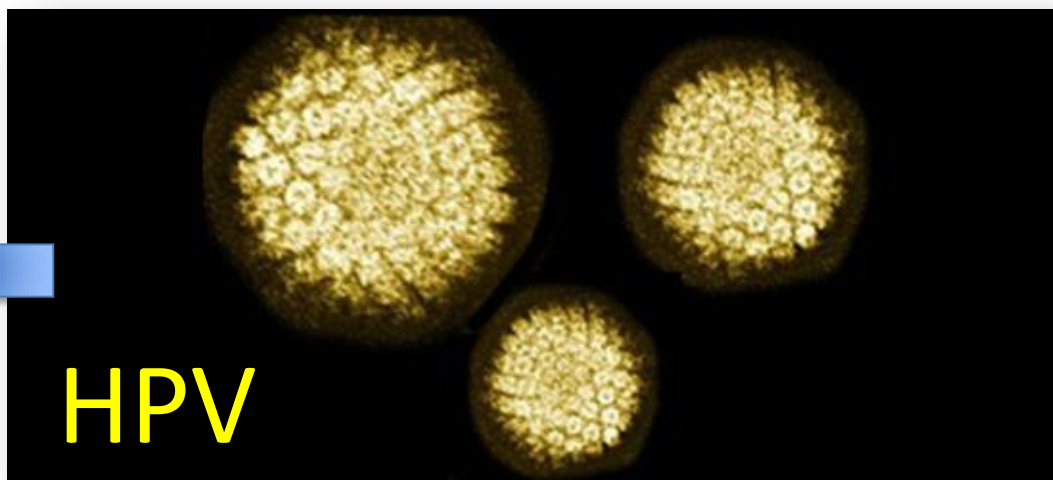
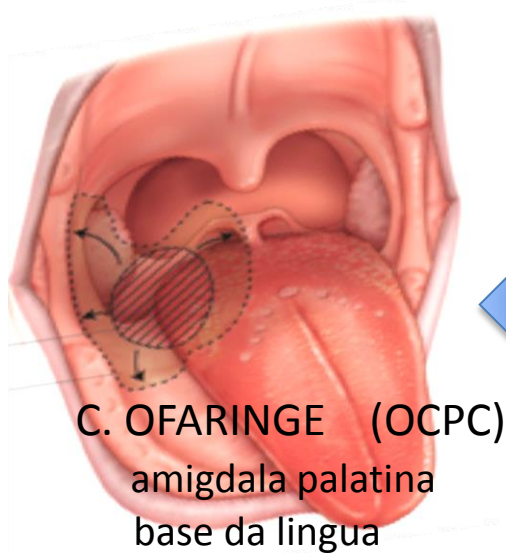
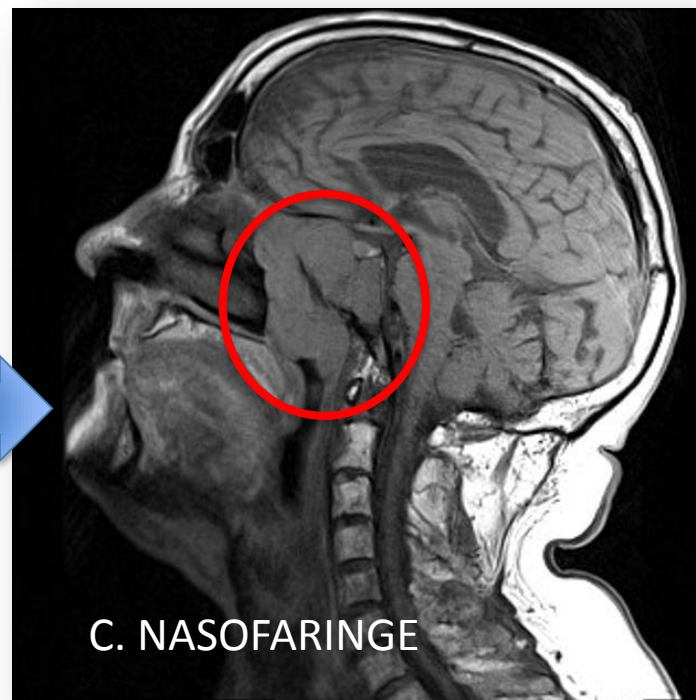
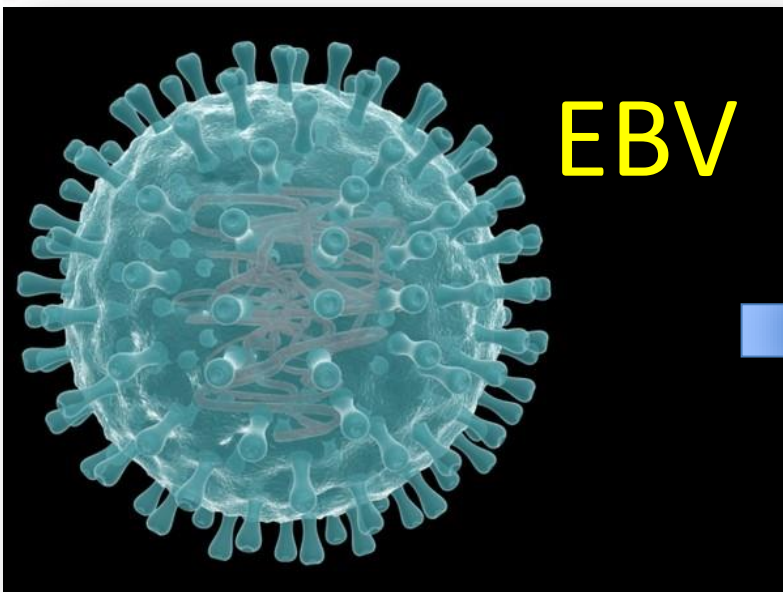
6º grupo de tumores + frequente
500 000 novos casos / ano
\$3,6 bilhões em 2014 nos EUA

90% são CPC



FATORES DE RISCO





HPV e TUMORES DA CABEÇA E PESCOÇO

Int J Oral Surg. 1983 Dec;12(6):418-24.

Morphological and immunohistochemical evidence suggesting human papillomavirus (HPV) involvement in oral squamous cell carcinogenesis.

Syrjänen K, Syrjänen S, Lamberg M, Pyrhönen S, Nuutinen J.

Evidence for a Causal Association Between Human Papillomavirus and a Subset of Head and Neck Cancers

Maura L. Gillison, Wayne M. Koch, Randolph B. Capone, Michael Spafford, William H. Westra, Li Wu, Marianna L. Zahurak, Richard W. Daniel, Michael Viglione, David E. Symer, Keerti V. Shah, David Sidransky

Journal of the National Cancer Institute, Vol. 92, No. 9, May 3, 2000

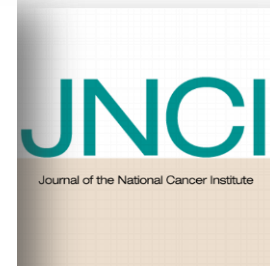
Semin Oncol. 2004 Dec;31(6):744-54.

Human papillomavirus-associated head and neck cancer is a distinct epidemiologic, clinical, and molecular entity.

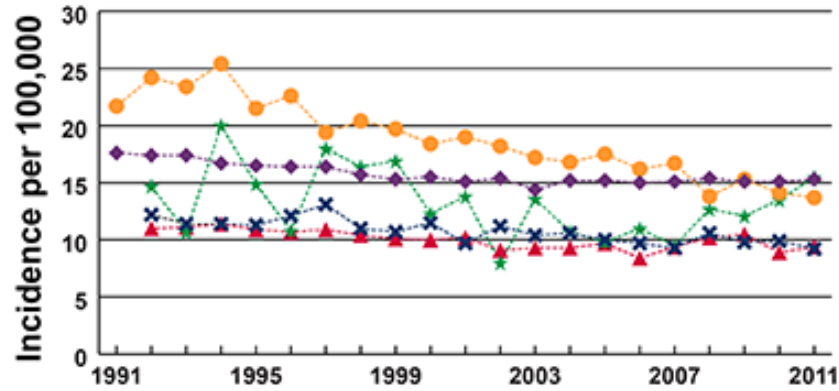
Gillison ML¹.

➔ Author information

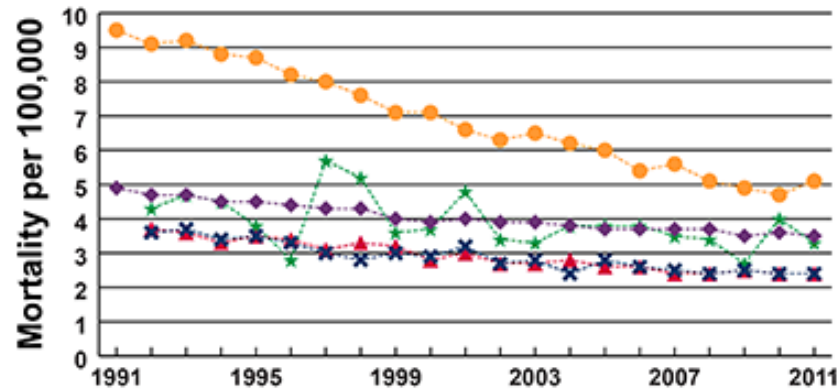
¹Department of Medical Oncology, The Sidney Kimmel Comprehensive Cancer Center at Johns Hopkins, Johns Hopkins School of Medicine, Bunting-Blaustein Cancer Research Building, 1650 Orleans Street, Baltimore, MD 21231, USA.



U.S. Head and Neck Cancer Incidence

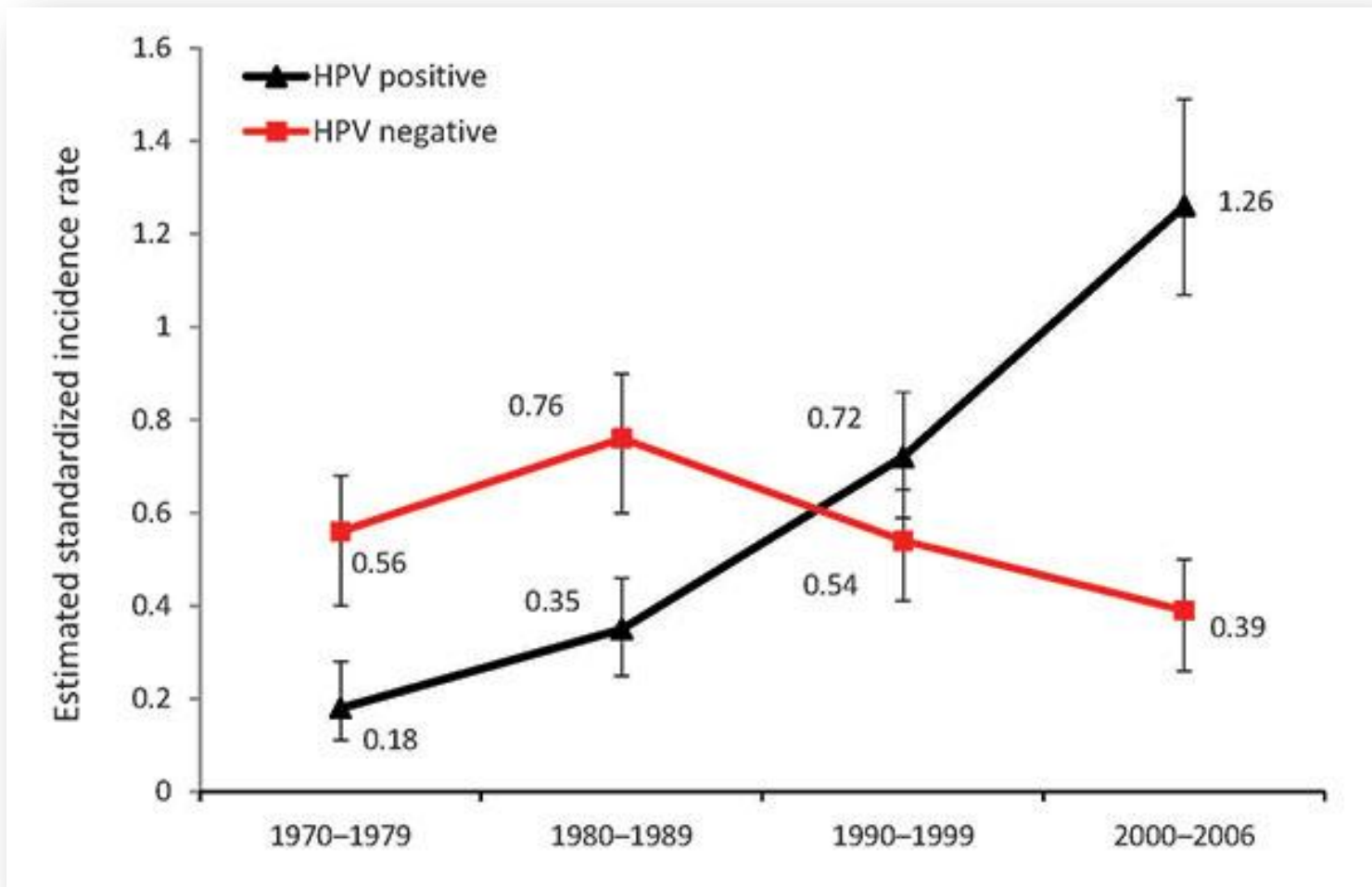


U.S. Head and Neck Cancer Mortality



◆ Whites
 ● African Americans
 ▲ Hispanics*
✕ Asians/Pacific Islanders*
 ★ American Indians/Alaska Natives*

*Incidence and mortality data not available before 1992.



Hammarstedt L, Dahlstrand H, Lindquist D, et al. *The incidence of tonsillar cancer in Sweden is increasing.* Acta Otolaryngol 2007;127:988-92.

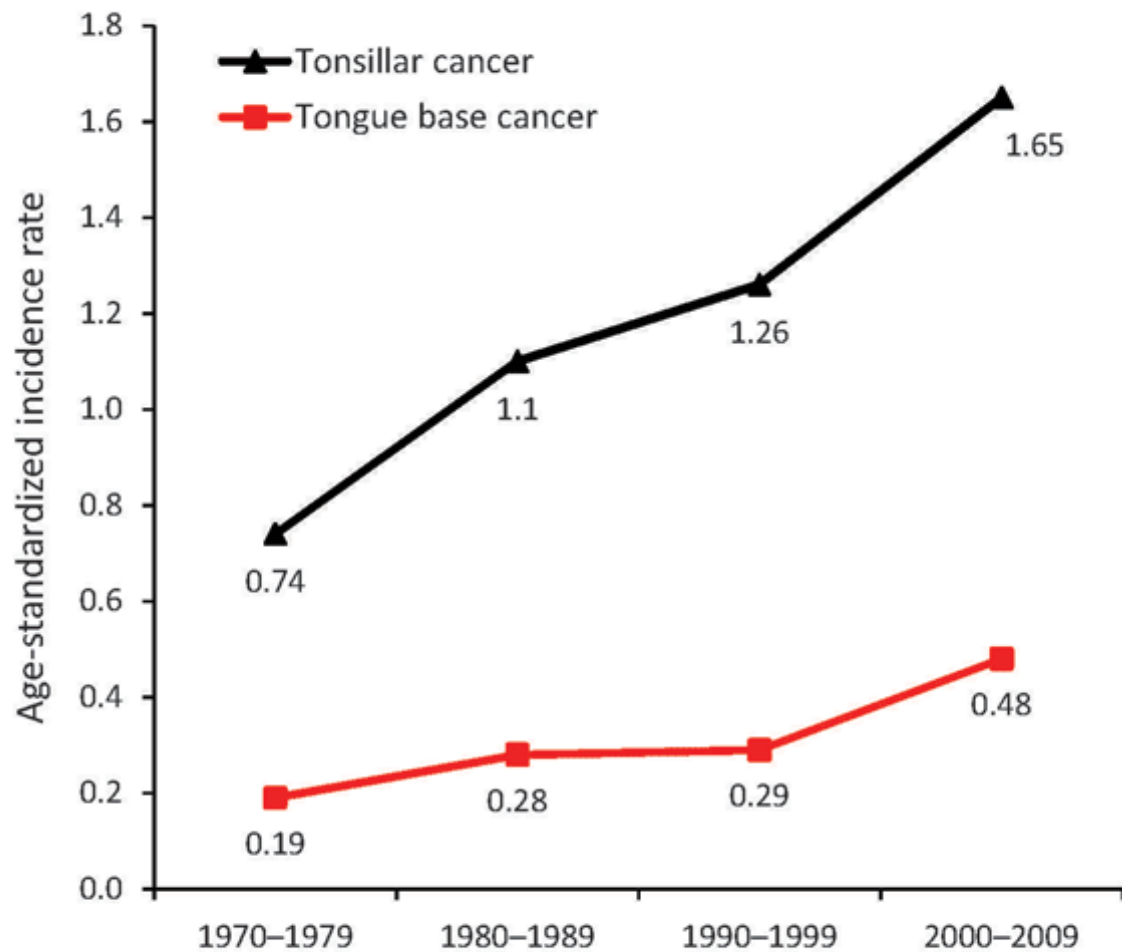
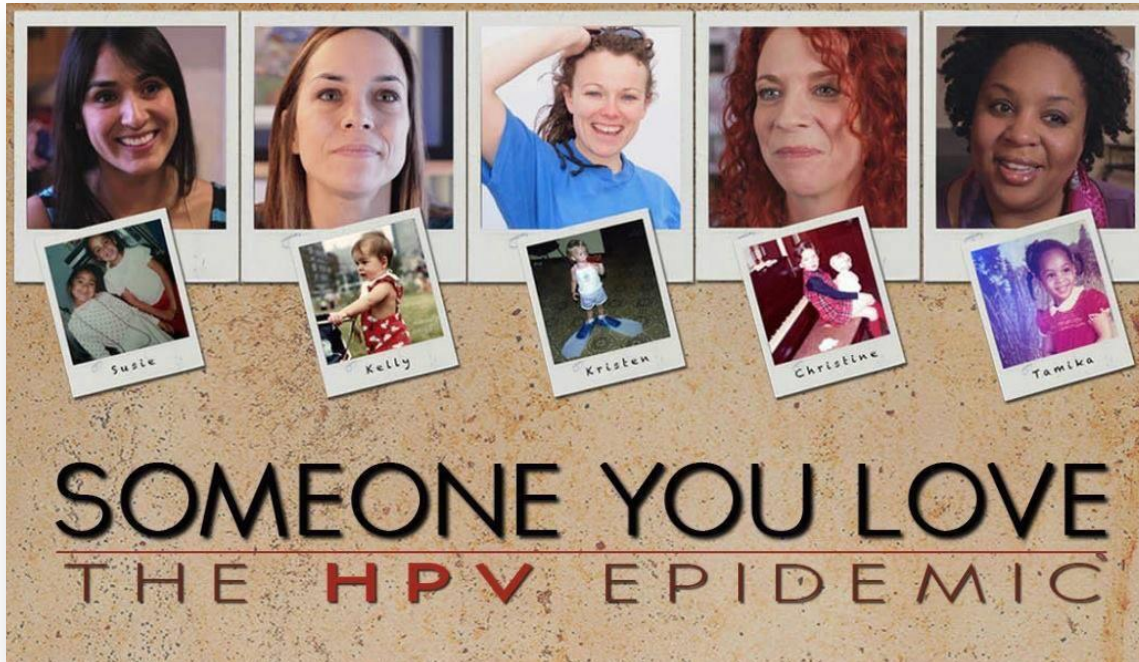
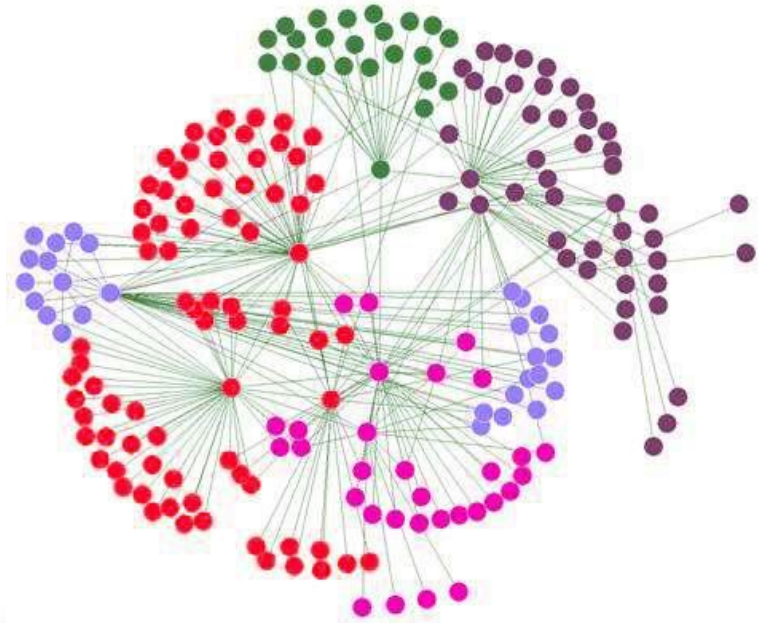


Figure 2. Age-standardized incidence of tonsillar and base of tongue cancers, Stockholm, Sweden, 1970–2006.

Hammarstedt L, Dahlstrand H, Lindquist D, et al. *The incidence of tonsillar cancer in Sweden is increasing.* Acta Otolaryngol 2007;127:988-92

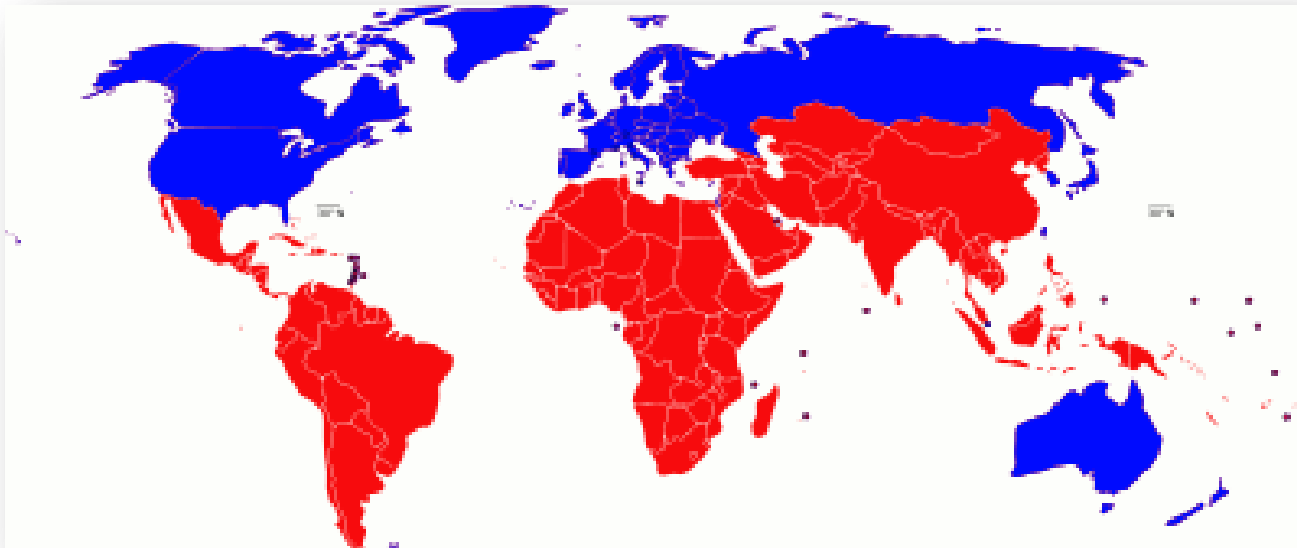
EPIDEMIA?



OCPC
HPV +

≠

OCPC
HPV -



OCPC
HPV +

≠

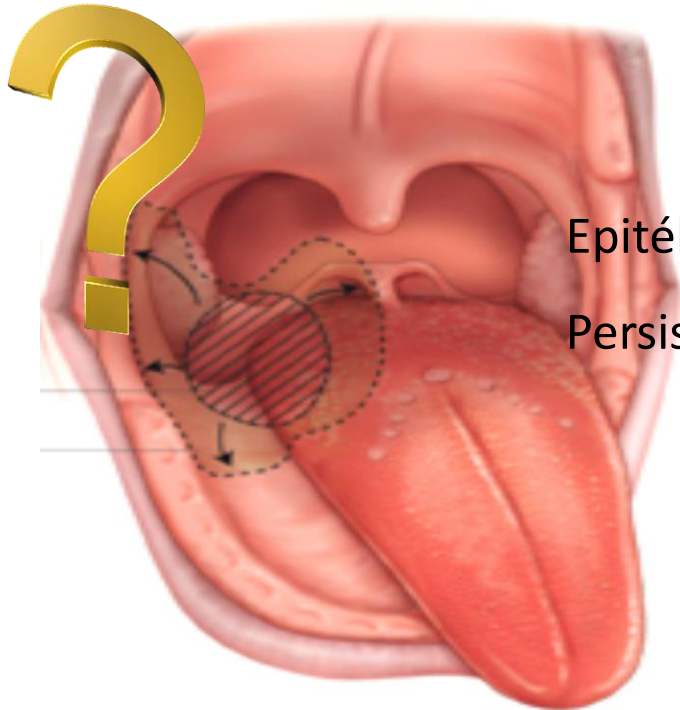
OCPC
HPV -

- DST (?)
- + novos
- > nº de parceiros sexuais
- Início vida sexual + cedo
- > status sócio-económico e educativo
- < associação tabaco e álcool
- > risco de OCPC em mulheres com CPC ano-genitais e seus parceiros
- Papel de outros co-fatores (alcohol, tabaco, susceptibilidade genética, nutrição) e peso relativo?

OCPC
HPV +



OCPC
HPV -



Epitélio de transição

Persistência / quiescência HPV 16 no tecido amigdalino

OCPC
HPV +

≠

OCPC
HPV -

Degradação p53

Up regulation pRB

Down regulation p16

> radiosensibilidade

Mutações p53

Down regulation pRB

Up regulation p16

OCPC
HPV +

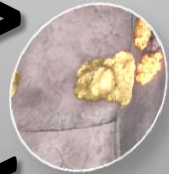
≠

OCPC
HPV -

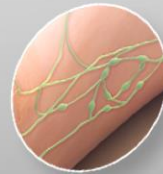
T <

N >

M <



Tumor size



Lymph Nodes



Metastases

OCPC
HPV +

≠

OCPC
HPV -

- < risco de morte (28% menos)
- < risco de recorrência (50% menos)
- < risco de 2º tumor

Melhor resposta a terapia (- alt. genéticas)

> **Sobrevida total e livre de doença**

(ajustado a fatores de melhor prognóstico - idade jovem, menos comorbilidades e menos tabaco)

OCPC
HPV +

≠

OCPC
HPV -



“...suggest that **HPV status** can be used in the clinical decision-making processes to select patients for **less aggressive non-surgical treatment**. Thus, assessing HPV presence is of utmost importance.”

2008



“HPV testing is recommended for all oropharyngeal tumors”

2013



NORMA I

da Direção-Geral da Saúde

NÚMERO: 020/2013
DATA: 06/12/2013
ATUALIZAÇÃO 27/04/2015

Francisco
Henrique
Moura
George

Digitally signed by Francisco
Henrique Moura George
DN: c=PT, o=Ministério da
Saúde, ou=Direção-Geral da
Saúde, cn=Francisco
Henrique Moura George
Date: 2015.04.27 09:58:15
+01'00'

ASSUNTO: Tratamento do Cancro da Orofaringe no Adulto
PALAVRAS-CHAVE: Cancro da orofaringe, tratamento
PARA Médicos do Sistema de Saúde
CONTACTOS: Departamento da Qualidade na Saúde (dqs@dgs.pt)



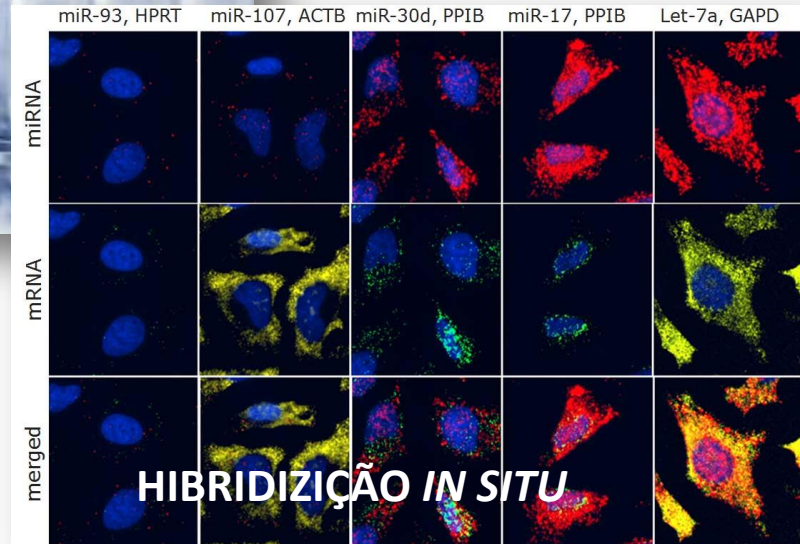
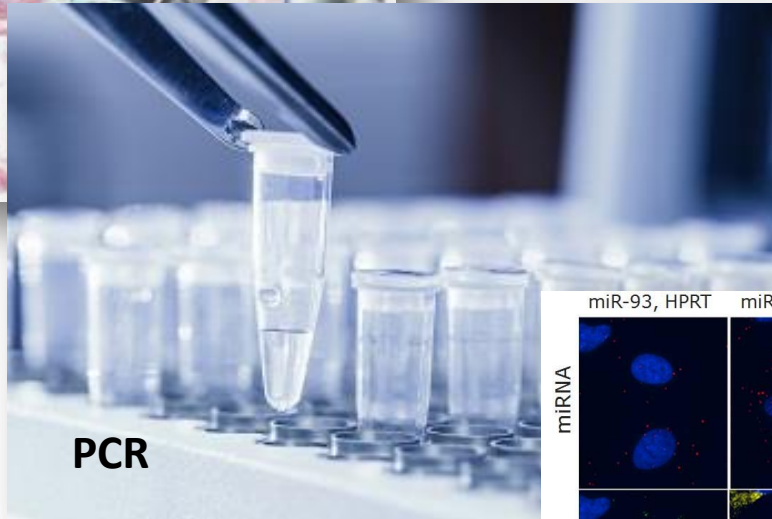
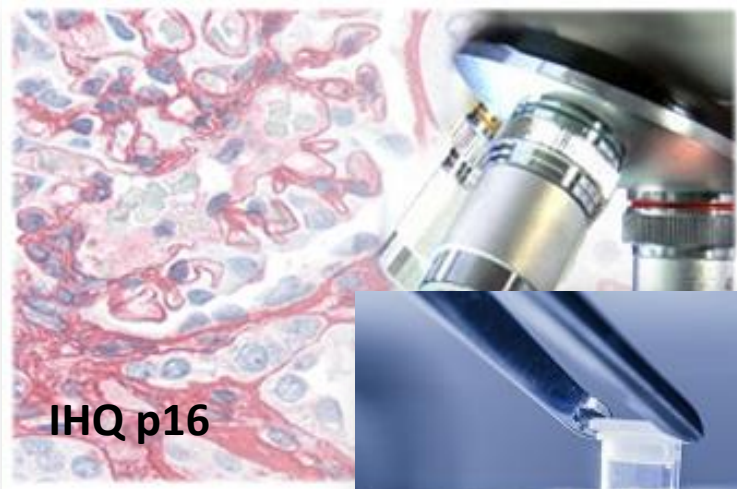
DGS desde
1899
Direção-Geral da Saúde



NORMA |

da Direção-Geral da Saúde

7. O diagnóstico deve ser confirmado por biópsia efetuada no centro de tratamento especializado (ou por revisão efetuada no centro de tratamento especializado) de exame histológico efetuada no exterior e o seu resultado disponibilizado em oito dias úteis (Nível de Evidência C, Grau de Recomendação I)¹⁻⁵.
8. A determinação do HPV deve ser efetuada em todos os tumores da orofaringe (Nível de Evidência B, Grau de Recomendação I)^{1-4,27,28}.
9. O primeiro tratamento, se for cirúrgico, deve realizar-se até 15 dias seguidos após a decisão terapêutica, conforme tempo máximo de resposta garantida na Portaria 1529/2008 de 26 de dezembro que define os tempos máximos de resposta garantidos (TMRG)⁵.
10. Se o primeiro tratamento não for cirúrgico devem ser observados os tempos de resposta considerados clinicamente adequados segundo o melhor julgamento clínico (Nível de Evidência C, Grau de Recomendação I)⁵.



HPV DNA Teste
Anti E6 HPV 16 ?



**YOU ARE THE KEY TO
CANCER PREVENTION**



Centers for Disease Control and Prevention
CDC 24/7: Saving Lives, Protecting People™

HUMAN PAPILLOMAVIRUS (HPV)



APPROXIMATELY
20 MILLION
AMERICANS

ARE CURRENTLY INFECTED WITH HPV,
AND ANOTHER

6.2 MILLION
PEOPLE BECOME NEWLY INFECTED
EACH YEAR.

Learn more about the diseases
that can be prevented by vaccines at
vaccinateyourbaby.org/eBook.pdf

ECBT
EST. 1991

2006



9-26

2011



11-21

PROTECT them from **CANCER**
get them the **HPV VACCINE**



27,000

people get cancer
caused by HPV
each year in the
United States



That's **1 person**
every **20 minutes**

HUMAN PAPILLOMAVIRUS (HPV)

12 strains

of human papillomavirus (HPV)
caused ~30% of new cancer
cases attributed to infection
globally in 2008.

IN THE UNITED STATES, HPV CAUSES:

- 96% of cervical cancer cases.
- 51% of vulvar cancers.
- 64% of vaginal cancers.
- 36% of penile cancers.
- 93% of anal cancers.
- 63% of oropharyngeal
head and neck cancers.



PREVENTING INFECTION

Two FDA-approved vaccines can protect
against infection with HPV16 and HPV18.

Both vaccines are highly effective at
preventing precancerous cervical lesions.

One of the vaccines, Gardasil, was also
found to prevent precancerous anal,
vulvar, and vaginal lesions.

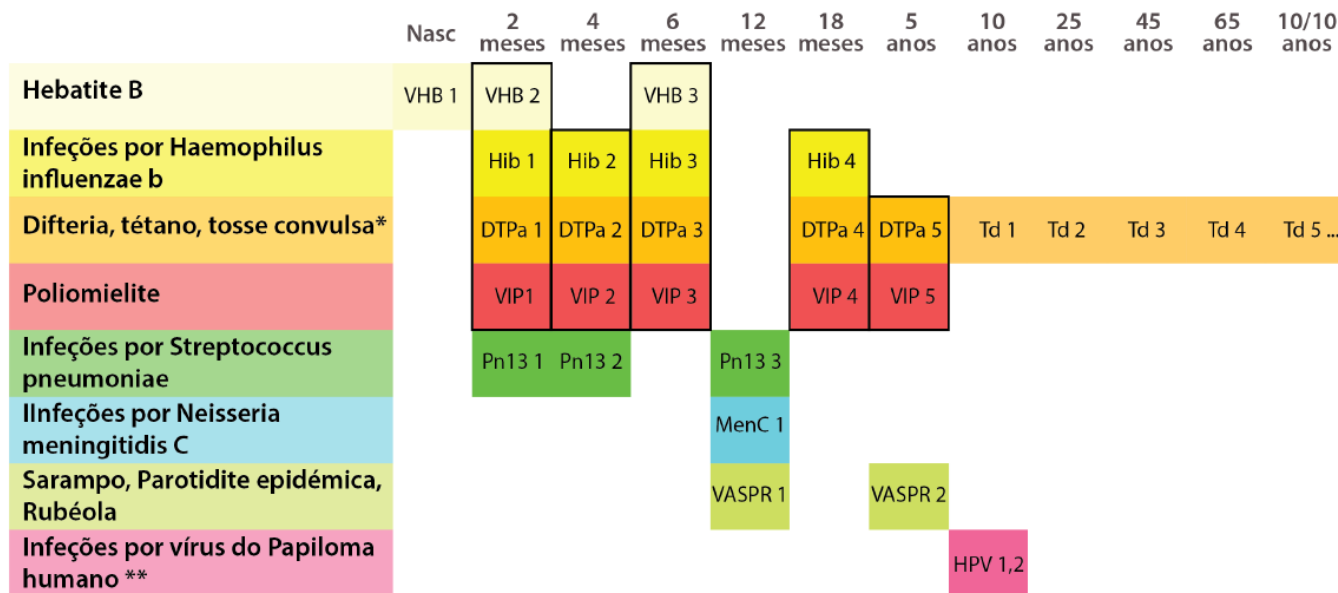
According to the CDC, safe sex practices
may lower the risk of, but may not fully
protect against, HPV infection.



Desde 2008



PNV 2017 – ESQUEMA RECOMENDADO



* As grávidas serão vacinadas contra a tosse convulsa, o tétano e a difteria (Tdpa) em cada gravidez

** Aplicável apenas a raparigas, com o esquema 0, 6 meses

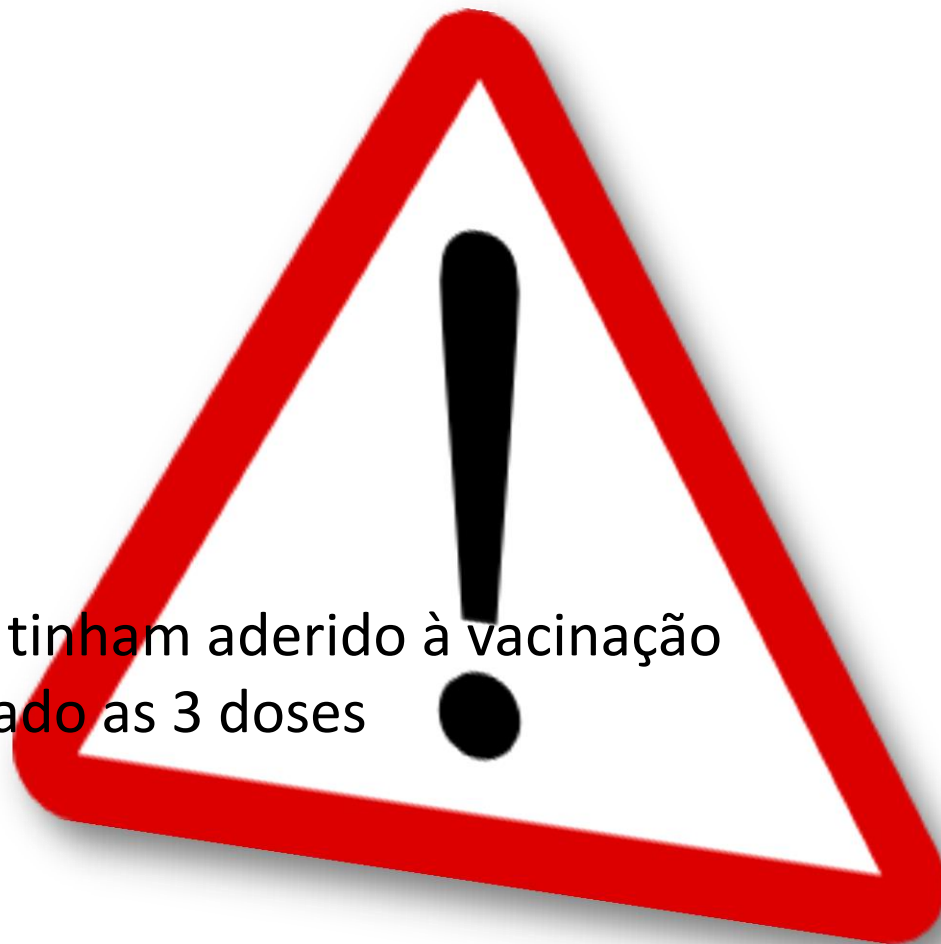
EUA 2013



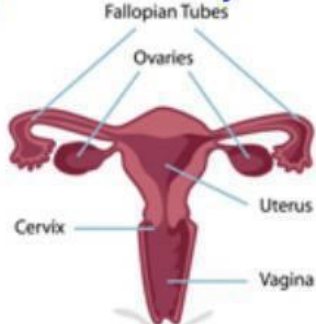
53% das raparigas tinham aderido à vacinação
1/3 tinha completado as 3 doses



34,6%



New Study: HPV Vaccines (Gardasil, Cervarix) Induce Primary Ovarian Failure



Am J Reprod Immunol. 2013 Jul 31. Conclusion: We document evidence of the potential of the HPV vaccine to trigger a life-disabling autoimmune condition. The increasing number of similar reports HPV vaccine-linked autoimmunity and the uncertainty of long-term benefits of HPV vaccination are a matter of public health that warrants further rigorous inquiry.

TheHealthyHomeEco

THE HPV VACCINE

TORONTO STAR

WEATHER HIGH-71C | PARTLY SUNNY | MAP S12

THURSDAY, FEBRUARY 5, 2015

> STAR INVESTIGATION

A wonder drug's dark side

Hundreds of thousands of teen girls in Canada have safely taken Gardasil, a vaccine shown to prevent HPV. But a Star investigation has found that since 2008, at least 60 Canadians experienced debilitating illnesses after inoculation. Patients and parents say the incidents point to the importance of full disclosure of risks

DAVID BRUSER AND JESSE MCLEAN

By the time Kaitlyn Armstrong received her third and final injection of the popular HPV vaccine Gardasil, pain had spread through the Whitney teen's body, migrating from her back to her knees to her hips.

After her first dose, Natalie Kenzie of London developed egg-size lumps on the soles of her feet, her joints swelled and her limbs twitched uncontrollably.

Before getting the shots, both 15-year-old girls were told the vaccine had no significant risks. And as they struggled to learn what ailed them, and began to believe Gardasil played a role, doctors dismissed their concerns.

Hundreds of thousands of teenage girls in Canada have received the vaccine's three doses, the vast majority without incident.

Regulators, including Health Canada and the FDA in the United States, cite comprehensive clinical trials and other data that show the vaccine's well-studied safety and efficacy.

But since 2008 at least 60 girls and women in Canada have convulsed or developed disabling joint and muscle pain and other debilitating conditions after receiving Gardasil.

One needed a wheelchair, another a feeding tube. A 14-year-old Quebec girl, Annabelle Morin, died two weeks after receiving the second injection of the vaccine.

It was 7:30 p.m. on the night of Dec. 9, 2008, when her mother, Linda, found her in the tub, her head underwater and turned to the side.

"The paramedics lifted Annabelle's body on to a stretcher. I put a blanket on her, saying, 'She's going to freeze,'" Linda recalled. "I did not know she was already dead."

The Quebec coroner's office said the cause of death was drowning, yet also said that any role Gardasil might have played should be further investigated.

In the cases discussed in this article, it is the opinion of a patient or doctor that a particular drug has caused a side-effect.

There is no conclusive evidence showing the vaccine caused a death or illness.

Like Kenzie and Armstrong, many of the girls say the vaccine was pushed on them by school officials, nurses or doctors who understated the risks, sometimes



BANDY BELLING/TORONTO STAR

Kaitlyn Armstrong says the nurses giving her the HPV vaccine Gardasil ignored her when she said she was allergic to metal.

claiming zero significant side effects despite the existence of a list of rare but serious vaccine-related reactions published by the drug's maker.

The Star has found the girls' concerns are not isolated, that in Canada important safety information about the vaccine has not been communicated to many young patients and their parents.

As part of its ongoing investigation into drug safety, the newspaper analyzed side-effect reports from a Health Canada data-

base, and interviewed regulators, a doctor closely involved in the vaccine's clinical trial and, in 12 cases, young women and parents who believe the vaccine caused considerable suffering.

Some of the girls have, after several years, made partial recoveries and are trying to live normal lives. Others are still bouncing from doctor to doctor, looking for answers.

GARDASIL continued on A10



STOP! Go back to the safety of properly this

libertycampaign.org



> WHAT IS GARDASIL?

A vaccine delivered in a series of shots. The \$400-\$500 cost paid by province. Public health nurses administer the inoculations in schools.

Approved in more than 100 countries, the vaccine protects against strains of human papillomavirus (HPV) that cause 70 per cent of cervical cancer cases. Roughly 400 Canadian women die of cervical cancer each year.

LE KNOWN

RISKS OF THE HPV VACCINE





Reduced Prevalence of Oral Human Papillomavirus (HPV) 4 Years after Bivalent HPV Vaccination in a Randomized Clinical Trial in Costa Rica

Rolando Herrero^{1*}, Wim Quint², Allan Hildesheim³, Paula Gonzalez⁴, Linda Struijk², Hormuzd A. Katki³, Carolina Porras⁴, Mark Schiffman³, Ana Cecilia Rodriguez⁴, Diane Solomon⁵, Silvia Jimenez⁴, John T. Schiller⁶, Douglas R. Lowy⁶, Leen-Jan van Doorn², Sholom Wacholder³, Aimée R. Kreimer³ for the CVT Vaccine Group[†]

1 Prevention and Implementation Group, International Agency for Research on Cancer, Lyon, France, **2**DDL Diagnostic Laboratory, Rijswijk, The Netherlands, **3** Division of Cancer Epidemiology and Genetics, National Cancer Institute, Bethesda, Maryland, United States of America, **4** Proyecto Epidemiológico Guanacaste, Fundación INCIENSA, Guanacaste, Costa Rica, **5** Division of Cancer Prevention, National Cancer Institute, Bethesda, Maryland, United States of America, **6** Laboratory of Cellular Oncology, National Cancer Institute, Bethesda, Maryland, United States of America

2013 n= 7 466 DB



**KEEP
CALM
AND
GET YOUR
HPV VACCINE**

Bibliografia

Reduced Prevalence of Oral Human Papillomavirus (HPV) 4 Years after Bivalent HPV Vaccination in a Randomized Clinical Trial in Costa Rica. Rolando Herrero, Wim Quint, Allan Hildesheim, Paula Gonzalez, Linda Struijk, Hormuzd A. Katki, Carolina Porras, Mark Schiffman, Ana Cecilia Rodriguez, Diane Solomon, Silvia Jimenez, John T. Schiller, Douglas R. Lowy, Leen-Jan van Doorn, Sholom Wacholder, Aime'e R. Kreimer for the CVT Vaccine Group.

HPV in oropharyngeal cancer: the basics to know in clinical practice. S. Elrefaey, M.A. Massaro, S. Chiocca, F. Chiesa, M. Ansarin. *ACTA OTORHINOLARYNGOLOGICA ITALICA* 2014;34:299-309.

Human papillomavirus-associated cancers: a survey on otorhinolaryngologists' knowledge and attitudes on prevention. A. Odone, S Visciarelli, T. Lalic, F. Pezzetti, F. Spagnoli, C. Pasquarella, G. Ferrari, C Signorelli. *ACTA OTORHINOLARYNGOLOGICA ITALICA* 2015;35:379-385; doi: 10.14639/0392-100X-621

Human papillomavirus-mediated carcinogenesis and HPV-associated oral and oropharyngeal squamous cell carcinoma. Part 2: Human papillomavirus associated oral and oropharyngeal squamous cell carcinoma. Feller et al. *Head & Face Medicine* 2010, 6:15

Recent Progress in Therapeutic Treatments and Screening Strategies for the Prevention and Treatment of HPV-Associated Head and Neck Cancer. Sonia N. Whang, Maria Filippova and Penelope Duerksen-Hughes. *Viruses* 2015, 7, 5040–5065

Human Papilloma Virus (HPV) in head and neck region: review of literature. L. Mannarini, v. Kratochvil, I. Calabrese, I. Gomes silva, p. Morbini, j. Betka, m. Benazzo. *ACTA OTORHINOLARYNGOLOGICA ITALICA* 2009;29:119-126

Age, sexual behavior and human papillomavirus infection in oral cavity and oropharyngeal cancers. Elaine m. Smith, justine m. Ritchie, kurt f. Summersgill, jens p. Klussmann, john h. Lee, donghong wang, thomas h. Haugen and lubomir p. Turek

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Epidemiology of Head and neck cancer. Rettig EM, D'Souza G. *Surg Oncol Clin N Am.* 2015 Jul; 24(3): 379-96

International Trends in Head and Neck cancer incidence rates: differences by country, sex and anatomic site. Simard EP, Torre LA, Jemal A. *Oral Oncol.* 2014 May; 50(5) : 387-403.