Note:

In December 2012, CR learned by searching in the Cochrane Library that Cochrane was planning to conduct a review on HPV vaccines. She researched the review authors' background and realized that the majority of them had several conflicts of interest (COIs).

Catherine Riva, Jean-Pierre Spinosa, Abby Lippman, Neil Arya, Pierre Biron, Geneviève Rail, Lyba Spring, Anne Taillefer and Fernand Turcotte informed the Cochrane Gynaecological, Neuro-oncology & Orphan Cancer Group (CGNOCG), senior editor of the review, of these puzzling findings.

From: Catherine Riva [catherine.riva@bluewin.ch]
To: 'Jo.Morrison@tst.nhs.uk'; 'chrisjhwilliams@btinternet.com'; 'gailquinn1@nhs.net'
Cc: Peter C. Gøtzsche; 'Philippe Foucras'; 'Serena Tinari'; 'peter@healthyskepticism.org'; 'redaktion@arznei-telegramm.de'; 'president@isdbweb.org'; 'contact@prescrire.org'; 'dewaele@cumg.ucl.ac.be'; 'Biollaz Jerome'; 'narya@sympatico.ca'; 'Abby Lippman'; 'Jean Pierre Spinosa'; 'taillefer.anne@courrier.uqam.ca'; 'Fernand.Turcotte@fmed.ulaval.ca'; 'biron.pierre@videotron.ca'; 'Gen.Rail@concordia.ca'; 'lybaspring@sympatico.ca'

Subject: Cochrane Review "Prophylactic vaccination against human papillomaviruses to prevent cervical cancer and its precursors"
Attached: Cochrane_HPV_authorship_20121210.pdf / Letter_Cochrane_20121210.pdf
Sent: 2012-12-10

Dear Mrs Quinn,
Dear Mr Morrison,
Dear Mr Williams,

We are writing to express our concern about your current plans for a review of the HPV vaccine, in particular about the potential biases and serious conflicts of interest of the majority of those who are preparing the protocol for this review.

We have attached here a letter that provides details about our concerns as well as a document that summarizes our research about the biases and conflicts of interest we spell out.

We look forward to hearing from you.

Sincerely,

Catherine Riva
Dr Jean-Pierre Spinosa
Abby Lippman
Neil Arya
Pierre Biron
Geneviève Rail
Lyba Spring
Anne Taillefer B.SC., M.A.
Fernand Turcotte

Attachment: Letter_Cochrane_20121210.pdf

December 10, 2012

Dear Sir or Madam,

We recently learned that a systematic review protocol on HPV vaccine is currently being developed within the framework of the Cochrane Collaboration (http://summaries.cochrane.org/CD009069/prophylactic-vaccination-against-human-papillomaviruses-to-prevent-cervical-cancer-and-its-precursors).

We consider an independent evaluation of this vaccine an important and useful undertaking and will be pleased to see one done. However, we have some concerns about the current plans.

As the Cochrane Collaboration states in its Policy Manual (http://www.cochrane.org/policy-manual/2111-general-principle), "The performance of the review must be free of any real or perceived bias." This principle does not appear to be taken into account for this review: people responsible for the proposed assessment have conflicts of interest that may seriously compromise their work. For example, some have been supported by the pharmaceutical companies that produce HPV vaccines; have already worked as investigators in company-sponsored clinical trials of the vaccines; have already published their conclusions about the effectiveness and safety of vaccines in publications; work for the Authorities that have recommended vaccination, believing that the efficacy and safety of the HPV vaccines are demonstrated and acquired; or have otherwise conveyed support for the vaccines and vaccination programs either through continuing education activities or publications.

Based on these findings, it is clear that the majority of authors responsible for conducting the proposed Cochrane review on the HPV vaccine have serious risks of bias.

More specifically, the panel of reviewers includes two investigators involved in phase III trials on the quadrivalent vaccine (Joakim Dillner and Marc Steben) who have already reported conflicts of interest with manufacturers of vaccines. Another panel member is on the Advisory / Expert Board of GlaxoSmithKline Biologicals and Gen-Probe, and has also reported receiving travel grant honoraria from GlaxoSmithKline Biologicals and Sanofi Pasteur MSD (Andreas Kaufmann).

At least nine of the fourteen potential reviewers (Marc Arby, E. Paraskevaidis, P. Beutels, You-Lin Qiao, Fang-Hui Zhao, Achim Schneider, Andreas Kaufmann, Marc Steben, Joakim Dillner) have signed or co-authored scientific publications concluding that the vaccine was efficacious and safe, or wrote as if these endpoints were established.

Finally, one of the authors works for the CDC (Centers for Disease Control and Prevention), which recommends the HPV vaccine, thereby considering it safe and effective. Moreover, the CDC has used safety arguments to get approval to extend its use (Lauri E. Markowitz).

Attached is a detailed summary of our research on these conflicts of interest.
In other words, there is a high risk of bias, which may influence the selection, analysis and weighting of the data, with much of the data actually coming from the previous work some of the authors have done for the manufacturers and regulatory authorities. Thus, the studies that may be reviewed may already reflect bias in the methodological quality of the design of phase III clinical trials (efficacy and safety), placebos chosen for comparison and their definitions, statistical quality of data provided to

regulators, unpublished data, conclusions drawn by the health authorities and professional medical societies from subgroups analyses and ecological studies, etc..

The Cochrane Collaboration is according to its mission statement independent and free from pharmaceutical interests. The reputation and credibility of the Cochrane Collection is at risk when its basic principles are compromised. We think this is the case here and we urge you to immediately reject these authors and allow others without conflicts of interest to do the rigorous evaluation of the HPV vaccine evaluation we all would welcome.

Please do not hesitate to contact us if you have any questions or seek further information.

Sincerely,

Catherine Riva
Journaliste indépendante
Rümikerstrasse 112
CH-8409 Wintetrhur

Dr Jean-Pierre Spinosa
Gynécologue-obstétricien
Rue des Terreaux 2
CH – 1003 Lausanne

Abby Lippman
PhD, Professor Emerita
Department of Epidemiology, Biostatistics. and Occupational Health
McGill University
Montréal, Québec

Neil Arya
BASc MD CCFP FCFP D. Litt
Adjunct Professor Environmental Studies University of Waterloo
Assistant Clinical Professor Family Medicine McMaster University
Director Global Health Office Western University

Pierre Biron
Professeur honoraire
Faculté de médecine
Université de Montréal
Canada

Geneviève Rail
Ph.D. Concordia University and CIHR recipient of a research grant on HPV vaccination (2012-2015)

Lyba Spring
Sexual Health Education and Consulting Services
414 Rushton Rd.
Toronto, Ontario
M6C 2Y3

Anne Taillefer B.SC., M.A.
Sociologue de la santé
Université du Québec à Montréal

Fernand Turcotte, MD. MPH. FRCPC
Professeur émérite de santé publique,
Université Laval
Québec, Canada

Attachment: Cochrane_HPV_authorship_20121210.pdf

Conflicts of interests:

Marc Steben, quadrivalent vaccine investigator: "Dr. Steben, consulting fees, advisory board fees, and lecture fees from Digene, Merck Frosst, GlaxoSmithKline, and Roche Diagnostics and grant support from Merck Frosst and GlaxoSmithKline." http://www.ncbi.nlm.nih.gov/pubmed/21491420

Joakim Dillner, quadrivalent vaccine investigator: "J. Dillner has received consultancy fees, lecture fees, and research grants from Merck and Co, Inc, and Sanofi Pasteur MSD." http://www.ncbi.nlm.nih.gov/pubmed/20139221

Andreas Kaufmann: "A. M. Kaufmann is a member of the Advisory/Expert Board at GlaxoSmithKline Biologicals and Gen-Probe. He received travel grant honoraria from GlaxoSmithKline Biologicals and Sanofi Pasteur MSD." http://www.hu.ufsc.br/projeto_hpv/HPV%20vaccination%20against%20cervical%20cancer%20in%20women%20above%2025%20years%20of%20age.pdf

Statements:

Marc Steben, quadrivalent vaccine investigator.
Author of an editorial in CMAJ, where he strongly advocates HPV vaccination. Although he admits: "I may be perceived as biased, being an investigator of the quadrivalent vaccine", he speaks of the quadrivalent vaccine as a "super vaccine" and says: "The success rate was 100% against intraepithelial lesions of the cervix, vagina and vulva and condyloma" and "serious adverse events have been reported more rarely than with other vaccines." http://www.ncbi.nlm.nih.gov/pmc/articles/PMC2278298/
On the issue of the higher risk for girls already carriers of HPV 16 or 18, he concluded: "These data suggest HPV vaccination neither reduces nor enhances progression to HPV16/18-related high grade cervical lesions, and cervical cytology screening and corresponding management should continue as per local recommendations." http://www.ncbi.nlm.nih.gov/pubmed/21491420

Joakim Dillner, quadrivalent vaccine investigator.
Co-author of the Munoz N study (2010) on vaccine efficacy in women HPV negative 14 (subgroup analysis): "High-coverage HPV vaccination programs among adolescents and young women may result in a rapid reduction of genital warts, cervical cytological abnormalities, and diagnostic and therapeutic procedures. In the longer term, substantial reductions in the rates of cervical, vulvar, and vaginal cancers may follow." http://www.ncbi.nlm.nih.gov/pubmed/20139221

Marc Arbyn: "HPV vaccination will reduce the burden of cervical precancer and probably also of invasive cervical and other HPV-related disease in women." http://www.ncbi.nlm.nih.gov/pubmed/22623137

Marc Arbyn and Philippe Beutels: “Well-planned introduction of vaccination combined with an organized screening program and active surveillance are crucial for the program to achieve and monitor its desired aims. Such surveillance should include linkage between vaccination, screening and cancer registries.” http://www.ncbi.nlm.nih.gov/pubmed/21051840

Evangelos Paraskevaidis: “In this context expanding the indications for HPV vaccination to include women who have been treated for CIN should be considered.”
http://www.ncbi.nlm.nih.gov/pubmed/23016771

You-Lin Qia and Fang-Hui Zhao: “Aggressive education is necessary to increase knowledge of HPV and its vaccine. Further proof of vaccine safety and efficacy and government subsidies combined with increased awareness could facilitate development and implementation of HPV vaccination in China.”
http://www.ncbi.nlm.nih.gov/pubmed/22901224

Achim Schneider and Andreas Kaufmann: “HPV vaccination is likely to be beneficial to sexually active women due to their continuous risk of acquiring new HPV infections and of developing cervical intraepithelial neoplasia (CIN) and cervical cancer. Clinical trial data show that the HPV-16/18 AS04-adjuvanted vaccine is safe and immunogenic in women up to the age of 55 years, whilst preliminary data with the quadrivalent vaccine demonstrated evidence of safety, immunogenicity and high-level efficacy in women 24 to 45 years of age. HPV vaccination in women over 25 years of age is already approved in several countries, and these women are individually seeking advice on vaccination from healthcare professionals. The predicted reduction in cost benefit of vaccination with increasing age, however, is likely to limit the implementation of routine vaccination beyond the late 20s.”
http://www.ncbi.nlm.nih.gov/pubmed/19819540

Member of CDC

Lauri E. Markowitz, Team Lead, Centers for Disease Control and Prevention (Atlanta, Georgia): “The CDC has approved these vaccines as safe and effective. Both vaccines were studied in thousands of people around the world, and these studies showed no serious safety concerns. Side effects reported in these studies were mild, including pain where the shot was given, fever, dizziness, and nausea. Vaccine safety continues to be monitored by CDC and the FDA. More than 46 million doses of HPV vaccine have been distributed in the United States as of June 2012.”
http://www.cdc.gov/std/hpv/stdfact-hpv-vaccine-young-women.htm.
L. E. Markowitz also transmits his conclusions in the context of events like this (http://www.medscape.org/viewarticle/768633_sidebar2), sponsored by the manufacturer of the quadrivalent vaccine (“supported by an independent educational grant from Merck”).

From: Quinn Gail (ROYAL UNITED HOSPITAL BATH NHS TRUST - RD1) [gailquinn1@nhs.net]
To: catherine.riva@bluewin.ch

Subject: Prophylactic vaccination against human papillomaviruses to prevent cervical cancer and its precursors
Sent: 2013-01-22

Dear Ms Riva

Thank you for your recent letter regarding our Cochrane review protocol entitled 'Prophylactic vaccination against human papillomaviruses' by Dr Arbyn and co-workers. You raised a number of concerns, which we are currently investigating and taking advice on from the Cochrane Steering Committee.

In the Cochrane Collaboration, we are anxious that work is performed to the highest standard, is open and transparent and that our vigorous review process, at title, protocol and review stages, ensures a balanced assessment of the available evidence.

We will conduct our internal review and respond to you shortly.

Best wishes,

Gail Quinn on behalf of Jo Morrison, Co-ordinating Editor

Gail Quinn | Managing Editor
Cochrane Gynaecological and Orphan Cancer Group
Education Centre, Royal United Hospital, Bath, BA1 3NG, UK
Tel: +44 (0) 1225 826349|
gailquinn1@nhs.net | www.cochrane.org

Note:

Although in January 2013 Cochrane reassured Catherine Riva, Jean-Pierre Spinosa, Abby Lippman, Neil Arya, Pierre Biron, Geneviève Rail, Lyba Spring, Anne Taillefer and Fernand Turcotte that it would "respond (…) shortly", that never happened. The December 2012 comment on COIs in the HPV vaccines authors panel was not published on the dedicated Cochrane website.

The planned Cochrane HVP vaccines review page (http://summaries.cochrane.org/CD009069/prophylactic-vaccination-against-human-papillomaviruses-to-prevent-cervical-cancer-and-its-precursors) was not modified either; the authors remained the same.

In December 2013, almost a year later, Catherine Riva, Jean-Pierre Spinosa, Abby Lippman, Neil Arya, Pierre Biron, Geneviève Rail, Lyba Spring, Anne Taillefer and Fernand Turcotte sent to Cochrane an email with 3 attachments: a new letter; and again both the December 2012 letter and the analytical comment on the authors COIs.

From: Catherine Riva [catherine.riva@bluewin.ch]
To: 'Quinn Gail (ROYAL UNITED HOSPITAL BATH NHS TRUST - RD1)'; 'Jo.Morrison@tst.nhs.uk'; 'chrisjhwilliams@btinternet.com'
Cc: 'Jean Pierre Spinosa'; 'Abby Lippman'; 'Genevieve Rail'; 'Anne Taillefer'; 'lybaspring@sympatico.ca'; 'Pierre Biron'; 'Neil Arya'; 'Fernand.Turcotte@fmed.ulaval.ca'; p.foucras@wanadoo.fr; 'jbz@bluewin.ch'; 'a.gunn@uq.edu.au'; 'Serena Tinari'; Peter C. Gøtzsche; 'peter@healthyskepticism.org'; 'President ISDB'; 'redaktion@arznei-telegramm.de'; 'contact@prescrire.org'; 'Serena Tinari'; 'jim.wright@ti.ubc.ca'; 'FGodlee@bmj.com'

Subject: AW: Prophylactic vaccination against human papillomaviruses to prevent cervical cancer and its precursors
Attached: 2013-12-08_Letter_Cochrane.pdf / Cochrane_HPV_authorship_20121210.pdf / Letter_Cochrane_20121210.pdf
Sent: 2013-12-09

Dear Mrs Quinn,
Dear Mr Morrison,
Dear Mr Williams,

One year ago, we sent you a letter to express our concern about your plans for a review of the HPV vaccine, in particular about the potential biases and serious conflicts of interest of the majority of those who are preparing the protocol for this review (Letter_Cochrane_20121210.pdf and Cochrane_HPV_autorship_20121210.pdf). However, we haven't hear from you since January.

We have attached here a letter (2013-12-08_Letter_Cochrane.pdf) that provides details about our concerns.

Best regards,

Catherine Riva
Dr Jean-Pierre Spinosa
Abby Lippman
Neil Arya
Pierre Biron
Geneviève Rail
Lyba Spring
Anne Taillefer B.SC., M.A.
Fernand Turcotte

Attachment: 2013-12-08_Letter_Cochrane.pdf

December 8, 2013

Dear Sir, Madam:

Almost a year ago, on December 10, 2012, we sent you a letter informing you of numerous conflicts of interests (some undeclared) involving a majority of the authors expected to conduct the Cochrane Review regarding "Prophylactic vaccination against human papillomaviruses to prevent cervical cancer and its precursors."

On January 22, 2013, Gail Quinn sent us this email response "*You raised a number of concerns, which we are currently investigating and taking advice on from the Cochrane Steering Committee. In the Cochrane Collaboration, we are anxious that work is performed to the highest standard, is open and transparent and that our vigorous review process, at title, protocol and review stages, ensures a balanced assessment of the available evidence. We will conduct our internal review and respond to you shortly."*

Eleven months later, we still have not heard from her or from the Cochrane Gynaecological and Orphan Cancer Group. Moreover, the Internet page devoted to this review (http://summaries.cochrane.org/CD009069/prophylactic-vaccination-against-human-papillomaviruses-to-prevent-cervical-cancer-and-its-precursors) has not been modified and the listed authors remain the same.

These facts are of tremendous concern to us as they appear to demonstrate that the thorough investigation promised by Gail Quinn has not been conducted. This lack of diligence, transparency and responsiveness seems to be in direct contradiction with the standards espoused by the Cochrane Collaboration. We would expect the Cochrane Gynaecological and Orphan Cancer Group to ensure that all reviews, including this one, are carried out in ways that are compatible with the mission and principles of the Cochrane Collaboration, with this including *"a balanced assessment of the available evidence"*.

We are copying this letter to the ISDB, as well as to some selected independent journals, the Healthy Skepticism network, the Nordic Cochrane, the Cochrane Hypertension Group, the Cochrane Acute Respiratory Infections Group, and the Editors of the British Medical Journal. We will also attach our prior correspondence related to the above concerns.

Best regards,

Catherine Riva
Journaliste indépendante
Rümikerstrasse 112
CH-8409 Wintetrhur

Dr Jean-Pierre Spinosa
Gynécologue-obstétricien
Rue des Terreaux 2
CH – 1003 Lausanne

Abby Lippman
PhD, Professor Emerita
Department of Epidemiology, Biostatistics. and Occupational Health
McGill University
Montréal, Québec

Neil Arya
BASc MD CCFP FCFP D. Litt
Adjunct Professor Environmental Studies University of Waterloo
Assistant Clinical Professor Family Medicine McMaster University
Director Global Health Office Western University

Pierre Biron
Professeur honoraire
Faculté de médecine
Université de Montréal
Canada

Geneviève Rail
Ph.D. Concordia University and CIHR recipient of a research grant on HPV vaccination (2012-2015)

Lyba Spring
Sexual Health Education and Consulting Services
414 Rushton Rd.
Toronto, Ontario
M6C 2Y3

Anne Taillefer B.SC., M.A.
Sociologue de la santé
Université du Québec à Montréal

Fernand Turcotte, MD. MPH. FRCPC
Professeur émérite de santé publique,
Université Laval
Québec, Canada

Attachment: Letter_Cochrane_20121210.pdf

December 10, 2012

Dear Sir or Madam,

We recently learned that a systematic review protocol on HPV vaccine is currently being developed within the framework of the Cochrane Collaboration (http://summaries.cochrane.org/CD009069/prophylactic-vaccination-against-human-papillomaviruses-to-prevent-cervical-cancer-and-its-precursors).

We consider an independent evaluation of this vaccine an important and useful undertaking and will be pleased to see one done. However, we have some concerns about the current plans.

As the Cochrane Collaboration states in its Policy Manual (http://www.cochrane.org/policy-manual/2111-general-principle), "The performance of the review must be free of any real or perceived bias." This principle does not appear to be taken into account for this review: people responsible for the proposed assessment have conflicts of interest that may seriously compromise their work. For example, some have been supported by the pharmaceutical companies that produce HPV vaccines; have already worked as investigators in company-sponsored clinical trials of the vaccines; have already published their conclusions about the effectiveness and safety of vaccines in publications; work for the Authorities that have recommended vaccination, believing that the efficacy and safety of the HPV vaccines are demonstrated and acquired; or have otherwise conveyed support for the vaccines and vaccination programs either through continuing education activities or publications.

Based on these findings, it is clear that the majority of authors responsible for conducting the proposed Cochrane review on the HPV vaccine have serious risks of bias.

More specifically, the panel of reviewers includes two investigators involved in phase III trials on the quadrivalent vaccine (Joakim Dillner and Marc Steben) who have already reported conflicts of interest with manufacturers of vaccines. Another panel member is on the Advisory / Expert Board of GlaxoSmithKline Biologicals and Gen-Probe, and has also reported receiving travel grant honoraria from GlaxoSmithKline Biologicals and Sanofi Pasteur MSD (Andreas Kaufmann).

At least nine of the fourteen potential reviewers (Marc Arby, E. Paraskevaidis, P. Beutels, You-Lin Qiao, Fang-Hui Zhao, Achim Schneider, Andreas Kaufmann, Marc Steben, Joakim Dillner) have signed or co-authored scientific publications concluding that the vaccine was efficacious and safe, or wrote as if these endpoints were established.

Finally, one of the authors works for the CDC (Centers for Disease Control and Prevention), which recommends the HPV vaccine, thereby considering it safe and effective. Moreover, the CDC has used safety arguments to get approval to extend its use (Lauri E. Markowitz).

Attached is a detailed summary of our research on these conflicts of interest.
In other words, there is a high risk of bias, which may influence the selection, analysis and weighting of the data, with much of the data actually coming from the previous work some of the authors have done for the manufacturers and regulatory authorities. Thus, the studies that may be reviewed may already reflect bias in the methodological quality of the design of phase III clinical trials (efficacy and safety), placebos chosen for comparison and their definitions, statistical quality of data provided to

regulators, unpublished data, conclusions drawn by the health authorities and professional medical societies from subgroups analyses and ecological studies, etc..

The Cochrane Collaboration is according to its mission statement independent and free from pharmaceutical interests. The reputation and credibility of the Cochrane Collection is at risk when its basic principles are compromised. We think this is the case here and we urge you to immediately reject these authors and allow others without conflicts of interest to do the rigorous evaluation of the HPV vaccine evaluation we all would welcome.

Please do not hesitate to contact us if you have any questions or seek further information.

Sincerely,

Catherine Riva
Journaliste indépendante
Rümikerstrasse 112
CH-8409 Wintetrhur

Dr Jean-Pierre Spinosa
Gynécologue-obstétricien
Rue des Terreaux 2
CH – 1003 Lausanne

Abby Lippman
PhD, Professor Emerita
Department of Epidemiology, Biostatistics. and Occupational Health
McGill University
Montréal, Québec

Neil Arya
BASc MD CCFP FCFP D. Litt
Adjunct Professor Environmental Studies University of Waterloo
Assistant Clinical Professor Family Medicine McMaster University
Director Global Health Office Western University

Pierre Biron
Professeur honoraire
Faculté de médecine
Université de Montréal
Canada

Geneviève Rail
Ph.D. Concordia University and CIHR recipient of a research grant on HPV vaccination (2012-2015)

Lyba Spring
Sexual Health Education and Consulting Services
414 Rushton Rd.
Toronto, Ontario
M6C 2Y3

Anne Taillefer B.SC., M.A.
Sociologue de la santé
Université du Québec à Montréal

Fernand Turcotte, MD. MPH. FRCPC
Professeur émérite de santé publique,
Université Laval
Québec, Canada

Attachment: Cochrane_HPV_authorship_20121210.pdf

Conflicts of interests:

Marc Steben, quadrivalent vaccine investigator: "Dr. Steben, consulting fees, advisory board fees, and lecture fees from Digene, Merck Frosst, GlaxoSmithKline, and Roche Diagnostics and grant support from Merck Frosst and GlaxoSmithKline." http://www.ncbi.nlm.nih.gov/pubmed/21491420

Joakim Dillner, quadrivalent vaccine investigator: "J. Dillner has received consultancy fees, lecture fees, and research grants from Merck and Co, Inc, and Sanofi Pasteur MSD." http://www.ncbi.nlm.nih.gov/pubmed/20139221

Andreas Kaufmann: "A. M. Kaufmann is a member of the Advisory/Expert Board at GlaxoSmithKline Biologicals and Gen-Probe. He received travel grant honoraria from GlaxoSmithKline Biologicals and Sanofi Pasteur MSD." http://www.hu.ufsc.br/projeto_hpv/HPV%20vaccination%20against%20cervical%20cancer%20in%20women%20above%2025%20years%20of%20age.pdf

Statements:
Marc Steben, quadrivalent vaccine investigator.
Author of an editorial in CMAJ, where he strongly advocates HPV vaccination. Although he admits: "I may be perceived as biased, being an investigator of the quadrivalent vaccine", he speaks of the quadrivalent vaccine as a "super vaccine" and says: "The success rate was 100% against intraepithelial lesions of the cervix, vagina and vulva and condyloma" and "serious adverse events have been reported more rarely than with other vaccines." http://www.ncbi.nlm.nih.gov/pmc/articles/PMC2278298/
On the issue of the higher risk for girls already carriers of HPV 16 or 18, he concluded: "These data suggest HPV vaccination neither reduces nor enhances progression to HPV16/18-related high grade cervical lesions, and cervical cytology screening and corresponding management should continue as per local recommendations." http://www.ncbi.nlm.nih.gov/pubmed/21491420

Joakim Dillner, quadrivalent vaccine investigator.
Co-author of the Munoz N study (2010) on vaccine efficacy in women HPV negative 14 (subgroup analysis): "High-coverage HPV vaccination programs among adolescents and young women may result in a rapid reduction of genital warts, cervical cytological abnormalities, and diagnostic and therapeutic procedures. In the longer term, substantial reductions in the rates of cervical, vulvar, and vaginal cancers may follow." http://www.ncbi.nlm.nih.gov/pubmed/20139221

Marc Arbyn: "HPV vaccination will reduce the burden of cervical precancer and probably also of invasive cervical and other HPV-related disease in women." http://www.ncbi.nlm.nih.gov/pubmed/22623137

Marc Arbyn and Philippe Beutels: “Well-planned introduction of vaccination combined with an organized screening program and active surveillance are crucial for the program to achieve and monitor its desired aims. Such surveillance should include linkage between vaccination, screening and cancer registries.” http://www.ncbi.nlm.nih.gov/pubmed/21051840

Evangelos Paraskevaidis: “In this context expanding the indications for HPV vaccination to include women who have been treated for CIN should be considered.”
http://www.ncbi.nlm.nih.gov/pubmed/23016771

You-Lin Qia and Fang-Hui Zhao: “Aggressive education is necessary to increase knowledge of HPV and its vaccine. Further proof of vaccine safety and efficacy and government subsidies combined with increased awareness could facilitate development and implementation of HPV vaccination in China.”
http://www.ncbi.nlm.nih.gov/pubmed/22901224

Achim Schneider and Andreas Kaufmann: “HPV vaccination is likely to be beneficial to sexually active women due to their continuous risk of acquiring new HPV infections and of developing cervical intraepithelial neoplasia (CIN) and cervical cancer. Clinical trial data show that the HPV-16/18 AS04-adjuvanted vaccine is safe and immunogenic in women up to the age of 55 years, whilst preliminary data with the quadrivalent vaccine demonstrated evidence of safety, immunogenicity and high-level efficacy in women 24 to 45 years of age. HPV vaccination in women over 25 years of age is already approved in several countries, and these women are individually seeking advice on vaccination from healthcare professionals. The predicted reduction in cost benefit of vaccination with increasing age, however, is likely to limit the implementation of routine vaccination beyond the late 20s.”
http://www.ncbi.nlm.nih.gov/pubmed/19819540

Member of CDC

Lauri E. Markowitz, Team Lead, Centers for Disease Control and Prevention (Atlanta, Georgia): “The CDC has approved these vaccines as safe and effective. Both vaccines were studied in thousands of people around the world, and these studies showed no serious safety concerns. Side effects reported in these studies were mild, including pain where the shot was given, fever, dizziness, and nausea. Vaccine safety continues to be monitored by CDC and the FDA. More than 46 million doses of HPV vaccine have been distributed in the United States as of June 2012.”
http://www.cdc.gov/std/hpv/stdfact-hpv-vaccine-young-women.htm.
L. E. Markowitz also transmits his conclusions in the context of events like this (http://www.medscape.org/viewarticle/768633_sidebar2), sponsored by the manufacturer of the quadrivalent vaccine (“supported by an independent educational grant from Merck”).

From: Quinn Gail (ROYAL UNITED HOSPITAL BATH NHS TRUST - RD1) [gailquinn1@nhs.net]
To: Catherine Riva
Cc: jo.morrison@obs-gyn.ox.ac.uk; Toby Lasserson (TLasserson@cochrane.org)

Subject: Prophylactic vaccination against human papillomaviruses to prevent cervical cancer and its precursors
Sent: 2013-12-12

Dear Catherine

Thank you for your email regarding this protocol first published in 2011. As per our correspondence from earlier this year, we referred this matter to the funding arbiter and the Cochrane Editorial Unit and have been in discussion with the main authors since then to find a satisfactory resolution. We ascertained that a number of the authors with potentially conflicting interests had been involved as clinical topic advisers, since they were well respected experts in the field. Following these discussions, authors with significant CoI have withdrawn from the review process and we are in the process of amending the protocol accordingly. The revised protocol will be published on the Cochrane Library by the end of 2013. No significant work has taken place on the review during this time and with a new junior epidemiologist on board, we hope that the review will now proceed quickly, given its importance to millions of women worldwide who are at significant risk of cervical cancer, often without the benefit of co-ordinated screening programmes.

Best wishes,

Gail

Gail Quinn | Managing Editor
Cochrane Gynaecological and Orphan Cancer Group
Education Centre, Royal United Hospital, Bath, BA1 3NG, UK
Tel: +44 (0) 1225 826349|
gailquinn1@nhs.net | www.cochrane.org

From: Catherine Riva [catherine.riva@bluewin.ch]
To: Quinn Gail (ROYAL UNITED HOSPITAL BATH NHS TRUST - RD1)
Cc: jo.morrison@obs-gyn.ox.ac.uk; 'Toby Lasserson'; 'Jean Pierre Spinosa'; 'Abby Lippman'; 'Genevieve Rail'; 'Anne Taillefer'; lybaspring@sympatico.ca; 'Pierre Biron'; 'Neil Arya'; Fernand.Turcotte@fmed.ulaval.ca; p.foucras@wanadoo.fr; jbz@bluewin.ch; a.gunn@uq.edu.au; 'Serena Tinari'; Peter C. Gøtzsche; peter@healthyskepticism.org; 'President ISDB'; redaktion@arznei-telegramm.de; contact@prescrire.org; 'Serena Tinari'; jim.wright@ti.ubc.ca; FGodlee@bmj.com

Subject: AW: Prophylactic vaccination against human papillomaviruses to prevent cervical cancer and its precursors
Attached: 2013-12-23_Letter_Cochrane.pdf
Sent: 2013-12-09

Dear Mrs Quinn,
Thank you very much for your answer.
Please find an attached letter (2013-12-23_Letter_Cochrane.pdf) that provides some questions.
Best regards,

Catherine Riva
Dr Jean-Pierre Spinosa
Abby Lippman
Neil Arya
Pierre Biron
Geneviève Rail
Lyba Spring
Anne Taillefer B.SC., M.A.
Fernand Turcotte

Attachment: 2013-12-23_Letter_Cochrane.pdf

December 23, 2013

Dear Madam Quinn:

Thank you for your response to our letter. We are pleased to learn that the Cochrane Gynaecological and Orphan Cancer Group took action following our inquiry of December 2012.
However, we would still like some further clarification of a few points in your response that remain vague and hope you can provide some details. Specifically.

- What criteria will be used to select authors of future reviews: or have they already been chosen?
- What conflicts of interest criteria/processes has the Cochrane Gynaecological and Orphan Cancer Group established that would exclude an author?
- Does the Cochrane Gynaecological and Orphan Cancer Group itself verify the accuracy of declarations of conflicts of interest of potential or current authors and, if so, how is this done?

We look forward to your responses to these few questions, and thank you in advance for your help.

Sincerely,

Catherine Riva
Journaliste indépendante
Rümikerstrasse 112
CH-8409 Wintetrhur

Dr Jean-Pierre Spinosa
Gynécologue-obstétricien
Rue des Terreaux 2
CH – 1003 Lausanne

Abby Lippman
PhD, Professor Emerita
Department of Epidemiology, Biostatistics. and Occupational Health
McGill University
Montréal, Québec

Neil Arya
BASc MD CCFP FCFP D. Litt
Adjunct Professor Environmental Studies University of Waterloo
Assistant Clinical Professor Family Medicine McMaster University

Pierre Biron
Professeur honoraire
Faculté de médecine
Université de Montréal
Canada

Geneviève Rail
Ph.D. Concordia University and CIHR recipient of a research grant on HPV vaccination (2012-2015)

Lyba Spring
Sexual Health Education and Consulting Services
414 Rushton Rd.
Toronto, Ontario
M6C 2Y3

Anne Taillefer B.SC., M.A.
Sociologue de la santé
Université du Québec à Montréal

Fernand Turcotte, MD. MPH. FRCPC
Professeur émérite de santé publique,
Université Laval
Québec, Canada

From: Quinn Gail (ROYAL UNITED HOSPITAL BATH NHS TRUST - RD1) [gailquinn1@nhs.net]
To: Catherine Riva

Subject: Prophylactic vaccination against human papillomaviruses to prevent cervical cancer and its precursors
Sent: 2013-12-23

Dear Catherine

As with all our systematic reviews we have abided by the current Cochrane Collaboration policies regarding conflict of interest and we have respected and implemented the funding arbiters' decision. We are aware that these policies are currently being revised and are expected to be ratified in early 2014.

We have revised our list of authors and the protocol will be republished when the license for publication forms have been collected.

Seasons' Greetings,

Gail

Gail Quinn | Managing Editor
Cochrane Gynaecological and Orphan Cancer Group
Education Centre, Royal United Hospital, Bath, BA1 3NG, UK
Tel: +44 (0) 1225 826349|
gailquinn1@nhs.net | www.cochrane.org