Long-term survival and causes of death after influenza vaccination in the elderly.

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Influenza is a major cause of morbidity and mortality, especially among elderly individuals. Due to ethical constraints, no randomized controlled trials (RCT) are conducted evaluating serious outcomes such as mortality. Therefore, evidence base...

Ethische beoordeling	Positief advies
Status	Werving gestopt
Type aandoening	-
Onderzoekstype	Observationeel onderzoek, zonder invasieve metingen

Samenvatting

ID

NL-OMON22975

Bron
Nationaal Trial Register

Verkorte titel
N.A.

Aandoening

overall mortality
influenza-related mortality (influenza, pneumonia, respiratory and circulatory causes of death)

Ondersteuning

Primaire sponsor: None
Overige ondersteuning: Maastricht University, department of family medicine, school CAPHRI

Onderzoeksproduct en/of interventie

Uitkomstmaten

Primaire uitkomstmaten

- overall mortality
- cause-specific mortality

Toelichting onderzoek

Achtergrond van het onderzoek

Worldwide, only 3 RCT's on influenza vaccination in community dwelling elderly have been conducted. Among these, we conducted the largest (n=1838) and only randomized double blind trial in the aged, during the 1991-1992 influenza season. This study has shown that in the elderly, influenza vaccination may halve the incidence of serological and clinical influenza.

Now, we set up an observational study based on our randomized trial. In this new study, we explore the effect of influenza vaccination and serologic response to vaccination on short- and long-term survival and cause-specific mortality.

Doel van het onderzoek

Influenza is a major cause of morbidity and mortality, especially among elderly individuals. Due to ethical constraints, no randomized controlled trials (RCT) are conducted evaluating serious outcomes such as mortality.
Therefore, evidence base consists largely of observational studies that are known to be susceptible to bias. These studies often lead to erroneous estimation of the effectiveness of vaccination and even contradictory results.
By adding information on mortality to the data of our previously performed RCT, we aim to counteract some of these methodological limitations and thus examine the influence of vaccination on mortality in an accurate way.
We have formulated four main hypotheses we will address in our manuscript:

1) Influenza vaccination of the elderly reduces overall mortality on short-term and long-term.

2) Influenza vaccination of the elderly reduces influenza-related mortality on short-term and long-term.

3) The degree of serologic response to influenza vaccination in vaccinated elderly is positively related to long-term survival.

4) Occurrence of serologically confirmed influenza in unvaccinated elderly is negatively related to long-term survival.

Onderzoeksopzet

Outcome: overall mortality

Timepoints: 1 year, 2 years, 5 years, 10 years, 25 years (after RCT in 1991/1992)

Outcome: cause-specific mortality

Timepoints: 1 year, 2 years, 5 years, 10 years, 25 years (after RCT in 1991/1992)

Onderzoeksproduct en/of interventie

Since this is an observational study on survival of the two groups mentioned below, no other interventions were carried out apart from the vaccine or placebo administration in November 1991.

Previous interventions (RCT 1991/1992):

- intervention group: purified split-virus vaccine containing A/Singapore/6/68(H1N1), A/Beijing/353/89(H3N2), B/Beijing/1/87 and B/Panama/45/90 all with 15 microgram of hemagglutinin, intramuscular injection in deltoid area

- control group: placebo (physiological saline solution), intramuscular injection in deltoid area.

Contactpersonen

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Wetenschappelijk

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Deelname eisen

Belangrijkste voorwaarden om deel te mogen nemen (Inclusiecriteria)

A randomized clinical trial on the efficacy of influenza vaccination in the elderly, involving 31 general practitioners in 15 practices in the southern region of the Netherlands, was conducted in the winter of 1991-1992. All persons aged 60 years or older were invited to enter the trial if they did not belong to those high-risk groups in which vaccination was recommended. At that time, age was no criterion for recommendation. In total 1838 patients (869 male, 989 female) agreed to participate. Of those who enrolled, 490 patients with heart conditions, lung conditions or diabetes mellitus were not considered to belong to the high-risk group by their general practitioner. In order to perform the new study, we complement the data of the previous trial with present information on mortality of the former participants. In specific, date and causes of death are added.

In order to complete our data with additional mortality statistics the Municipal Personal Records Database (Gemeentelijke Basisadministratie, GBA) is searched by a government official to identify the former participants' "vital status", i.e. whether they had died, and the date of death if applicable. In case of negative findings we contact the participants' family practice to enquire about the vital status. If this cannot be provided by the family practice (e.g. due patients' migration), we request the Netherlands Centre for Family History (Centraal Bureau voor Genealogie, CBG) and – subsequently - an archivist of the Regional Historical Centre of Limburg (Rijksarchief Limburg) to conduct an extensive genealogical search in the national or respectively regional archives. If a search for an individual is not successful, the vital status is checked by the local municipality where the former participant has been living according to our most recent information. Search results of the family practice will be double-checked by the municipalities.

Finally, using the service of Statistics Netherlands (Centraal Bureau voor de Statistiek, CBS) we will verify the dates of death that have been found, and trace back the cause of death of deceased participants up to present time.

The CBS will be asked to perform this search during March 2017.

Belangrijkste redenen om niet deel te kunnen nemen (Exclusiecriteria)

All former trial participants (n=1838) were included. In case of loss to follow-up, the data was censored. No participants were excluded from the analysis.

Onderzoeksopzet

Opzet

Type:	Observationeel onderzoek, zonder invasieve metingen
Onderzoeksmodel:	Parallel
Toewijzing:	Gerandomiseerd
Blindering:	Open / niet geblindeerd
Controle:	Placebo

Deelname

Nederland

Status:	Werving gestopt
(Verwachte) startdatum:	01-03-2017
Aantal proefpersonen:	1838
Type:	Werkelijke startdatum

Ethische beoordeling

Positief advies

Datum:	09-02-2017
Soort:	Eerste indiening

Registraties

Opgevolgd door onderstaande (mogelijk meer actuele) registratie

Geen registraties gevonden.

Andere (mogelijk minder actuele) registraties in dit register

Geen registraties gevonden.

In overige registers

Register	ID
NTR-new	NL5587
NTR-old	NTR6179
Ander register	MEC approval Maastricht : METC 12-4-030

Resultaten

Samenvatting resultaten

Govaert TM, Thijs CT, Masurel N, Sprenger MJ, Dinant GJ, Knottnerus JA. The efficacy of influenza vaccination in elderly individuals. A randomized double-blind placebo-controlled trial. JAMA. 1994 Dec 7;272(21):1661-5.

Cruijff M, Thijs C, Govaert T, Aretz K, Dinant GJ, Knottnerus A. The effect of smoking on influenza, influenza vaccination efficacy and on the antibody response to influenza vaccination. Vaccine. 1999 Feb 5;17(5):426-32

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