Neuroscience

NOVARTIS

Kristiansand
16.01.2018

NOVARTIS

Neuroscience

NOVARTIS

Frank E. Sørgaard
Medisinsk rådgiver

«Hvordan kan MS medikamentenes effekt og sikkerhet sammenlignes»?

NOVARTIS

Neuroscience

Når det ikke finne head to head studier – Hva da?

- Gjøre en head-head studie
- Indirekte sammenligning av studier
- Databaser - Real World Evidence

NOVARTIS

Neuroscience

Når det ikke finne head to head studier – Hva da?

- Gjøre en head-head studie
- **Indirekte sammenligning av studier**
- Databaser - Real World Evidence

NOVARTIS

Sammenligninger av studier

Kan man sammenligne to forskjellige **studier** gjort på to forskjellige **populasjoner**, ved to forskjellige **tidspunkter** og med to forskjellige **medikamenter**?

NOVARTIS

Sammenligninger av studier

Kan man sammenligne to forskjellige **studier** gjort på to forskjellige **populasjoner**, ved to forskjellige **tidspunkter** og med to forskjellige **medikamenter**?

NOVARTIS

…and what do we need to consider?

Naive indirect comparison

Comparison of the results of individual arms from different trials as if they were from the same trial

Bucher HC, Guyatt GH, Griffith LE, Walter SD: The results of direct and indirect treatment comparisons in meta-analysis of randomized controlled trials. J Clin Epidemiol. 1997 Jun;50(6):683-91.

NOVARTIS

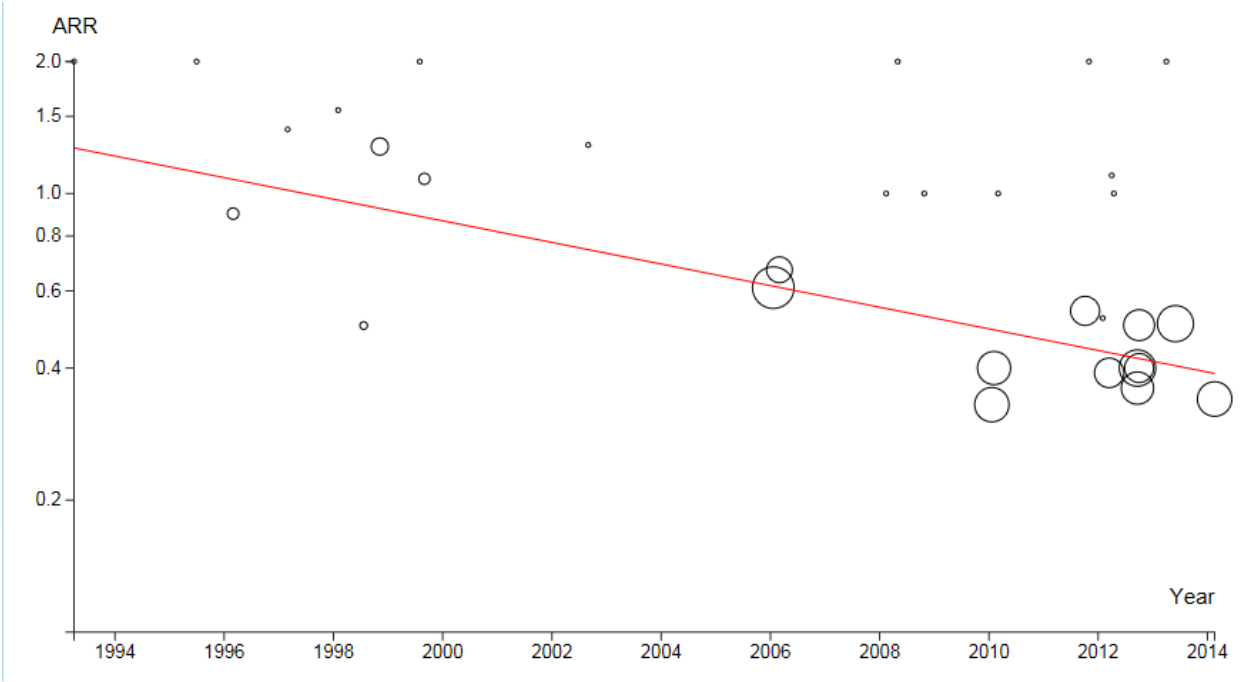
Naiv (enkel) sammenligning

	Placebo ARR 2 år	Aktiv behandling ARR 2 år	RRR
Affirm Tysabri[1]	0,73	0,23	68,5 %
Freedoms Gilenya[2]	0,40	0,16	55 %
	45 %		

1: Polman CH, O'Connor PW, Havrdova E, et al. A randomized placebo-controlled trial of natalizumab for relapsing multiple sclerosis. N Engl J Med 2006;354:899–910
2: Kappos L, Radue EW, O'Connor Pet al: A placebo-controlled trial of oral fingolimod in relapsing multiple sclerosis.N Engl J Med. 2010 Feb 4;362(5):387-401

NOVARTIS

Placebo relapse rate in different studies between 1993 and 2014



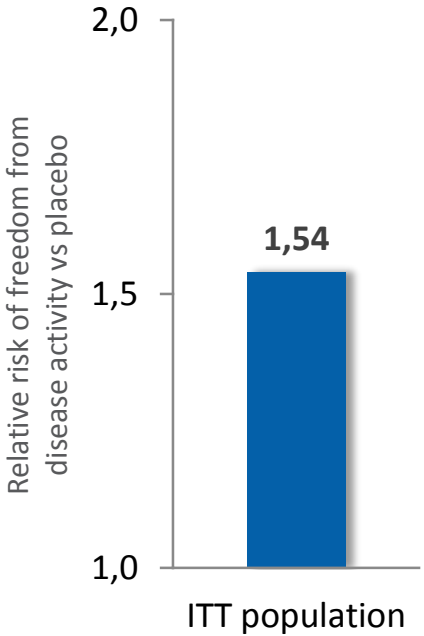
http://www.msdiscovery.org/arr

NOVARTIS

The similarity assumption…

- …can be violated if efficacy depends on patient characteristics

Figure 1. Likelihood (relative risk) of freedom from disease activity for fingolimod 0.5 mg versus placebo by patient characteristics at baseline in pooled analyses of FREEDOMS and FREEDOMS II[a]



The similarity assumption…

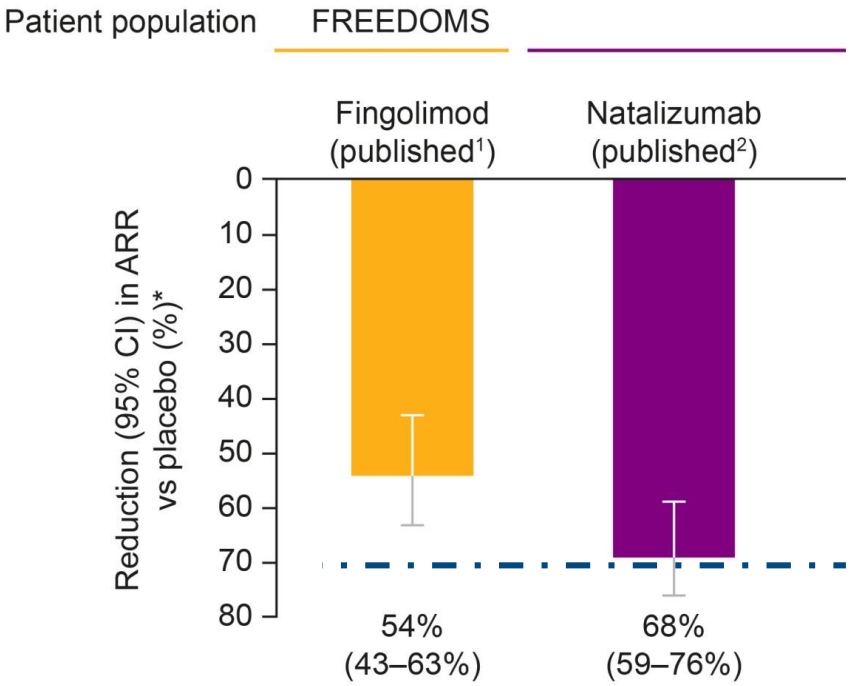
- …can be violated if endpoints are defined differently across trials

a) **In FREEDOMS** confirmed disability progression was considered to be an increase of **1 EDSS** point for patients with a baseline score **of 0–5.0**, and of **0.5** points for patients with a baseline EDSS score of **5.5**

b) **In DEFINE and CONFIRM**, disability progression was defined as an increase of **1** point in patients with an EDSS score of **1.0–5.0,** and of at least **1.5 EDSS** points in patients with a baseline EDSS score of **0**

c) Data modified from Bergvall et al.: Consequences of different definitions of confirmed disability progression across randomized trials of multiple sclerosis therapies Poster presented at ECTRIMS 2012, P1020

Indirect comparison model results:
predicted efficacy for reducing relapse rates



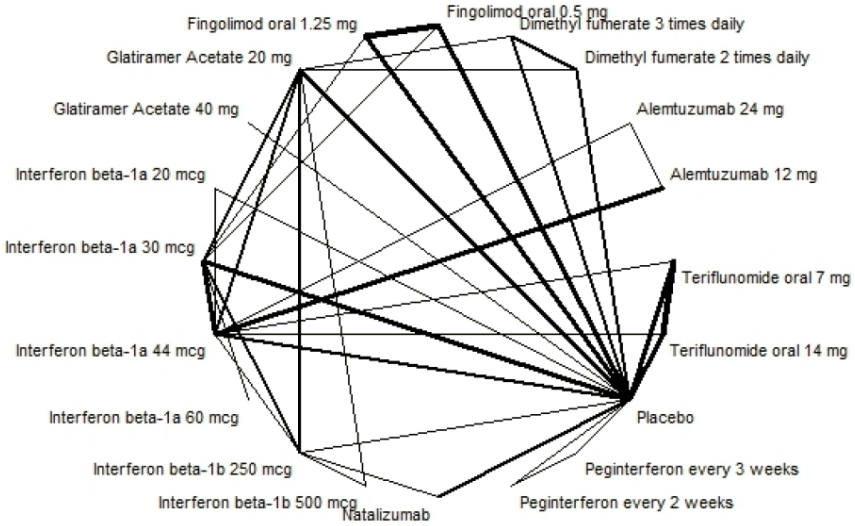
Final model covariates: **age, previous DMT use, number of Gd-enhancing T1 lesions.**
ARR, annualized relapse rate; CI, confidence interval; DMT, disease-modifying therapy; Gd, gadolinium.

Nettverkanalyser

2016

Medicines used for Multiple Sclerosis – A Health Technology Assessment

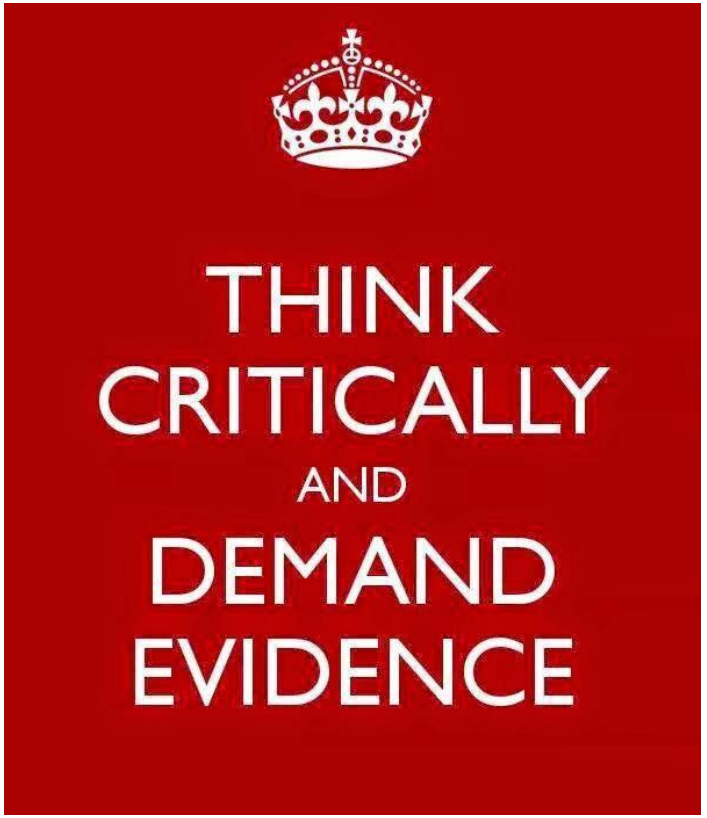
Norwegian Institute of Public Health



NOVARTIS

https://nyemetoder.no/Documents/Rapporter/Rapport_2016_MS%20legemidlerV5.pdf

Så...Kan man.....



NOVARTIS