

Impact of fever and antipyretic use on influenza vaccine immunogenicity in children

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Background

- Flu burden high in children
- Flu vaccine only moderately effective esp in young children
- Factors affecting immunogenicity unclear
- Reactogenicity (eg. fever) and immunogenicity related?
- Treating fever with antipyretics can dampen immunogenicity of multiple childhood vaccines (Prymula et al. Lancet. 2009;374(9698):1339-50.)

Aims and methods

- Pilot study: fever/antipyretics effect on immunogenicity
- Received individual level clinical trial data from GSK

Study	Age	n	Study groups
Pavia-Ruz (2013)	6-35 m	3317	1. GSK Fluorix TIV 0.25mL 2. GSK Fluorix TIV 0.5mL 3. Sanofi Fluzone TIV 0.25mL
Domachowski (2012)	3-17y	2128	1. GSK Flulaval TIV 2. Comparator TIV
Baxter (2010)	6m-5y immunogenicity subset	871	1. GSK Fluorix TIV 2. Sanofi Fluzone TIV

Fever & Antipyretic use and Immunogenicity

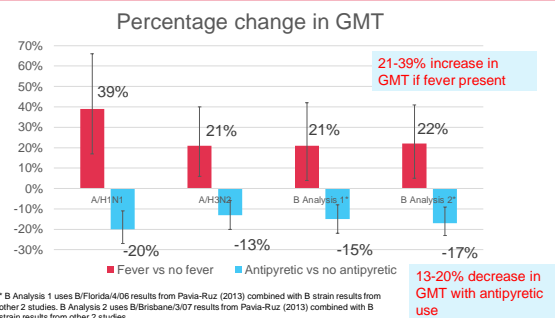
- Multivariate General Linear Model.
 - Dependent variable: post-vaccination titre
 - Predictor variables:
 - age
 - pre-vaccination titre
 - fever Y/N
 - antipyretic Y/N
 - number of vaccine doses (1 or 2)
 - Assessed relationship of each predictor adjusting for other variables in the model.

Fever and antipyretic use

	Pavia-Ruz	Domachowski	Baxter
Fever (any dose)	5.4%	3.5%	5.0%
Antipyretic use (any dose)	17.0%	13.2%	27.1%
Antipyretic use with Fever	61.2%	73.9%	84.1%
Antipyretic use without Fever	14.5%	11.0%	24.1%

- Fever rates are generally low
- High rates of antipyretic use when fever present
- Substantial antipyretic use even without fever

Multivariable pooled analysis of 3 studies. n=5902



Conclusions



- Fever (day 0-3):
 - independently associated \uparrow **immunogenicity**
- Antipyretics (day 0-3):
 - associated with \downarrow **immunogenicity**
- QIV analysis and prospective confirmation needed
- Implications:
 - understanding factors affecting immunogenicity
 - optimising immunogenicity
 - guidance re post-vaccination antipyretic use

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Impact of Fever and Antipyretic Use on Influenza Vaccine Immune Responses in Children

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Abstract Author Information

Background: Comparing post-vaccination fever rates in pediatric influenza vaccine clinical trials is difficult due to variability in how fever is reported. The impact of vaccine-related fever and antipyretic use on trivalent influenza vaccine (TIV) immunogenicity in children is also unclear.

Methods: In this pilot study, we obtained individual-level data provided by GlaxoSmithKline (GSK) from three pediatric clinical trials of GSK versus comparator TIV. We explored a crossover study (NCT00764790), the largest

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