

SEST, May 7th

# Skin modulating genes and child eczema - the benefits of old age and of avoiding cats.

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# Overview

## The setting

A collaboration between statisticians and clinical researchers on the impact of a genetic mutation on childhood eczema.

## The statistical part

Translating the research questions into an objective and robust statistical framework based on the available data. Explaining the statistical results.

## The clinical part

Asking the research questions, gathering the data, interpreting and communicating the results.

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# The background and rationale for this particular work

*"Common loss-of-function variants of the epidermal barrier protein filaggrin are a major predisposing factor for atopic dermatitis"* Palmer et al (2006).

- *"Loss-of-function variants in the gene encoding filaggrin (FLG) are major determinants of eczema. We hypothesized that weakening of the physical barrier in FLG-deficient individuals may potentiate the effect of environmental exposures"* Bisgaard et al (2008).
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# Material

- 379 ethnic danish children from the COPSAC (Copenhagen Studies on Asthma in Childhood) cohort. Followed intensively through childhood.
- Age at first eczema (Atopic Dermatitis) diagnosis if available/present within the first 5 years of follow-up.
- FLG mutation or not
- Exposure to cat at birth (yes/no)





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# Statistical framework

We want to make statements about how fast eczema develops throughout childhood.

## One minus the Kaplan-Meier estimator

Estimates the probability having developed eczema at a given age.

## The hazard ratio

A measure of how much faster eczema develops in one exposure group compared to another exposure group.



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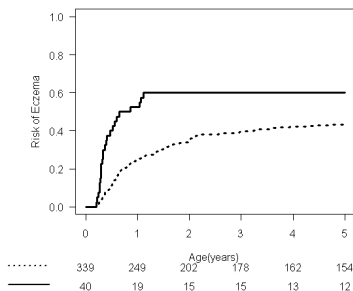
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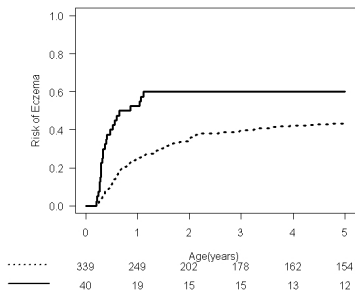
# FLG mutation and age



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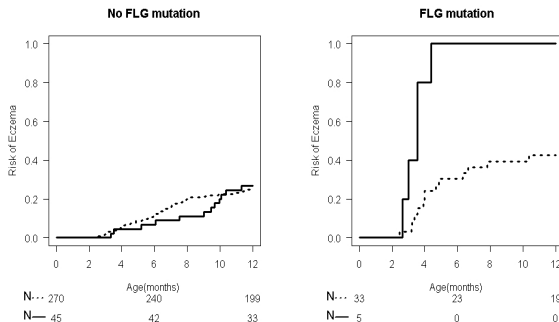


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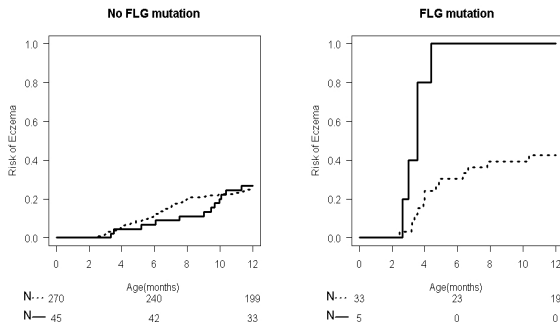
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- More objective than a "do these results make sense" validation (Exploration)

Results validated in the MAAS (Manchester Asthma and Allergy study) cohort.



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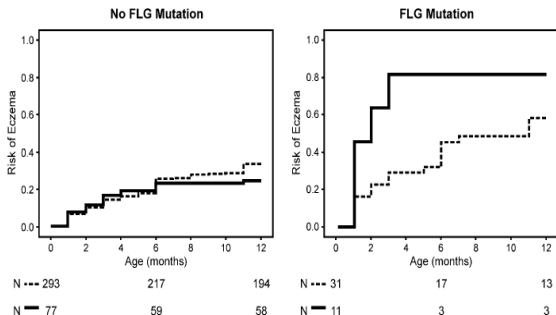
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# Post-script: Delivering the message to the public

The following excerpts are taken from the Daily Mail (June 23rd 2008)

Own a cat and run the risk eczema, researchers warn

By Daily Mail Reporter

Last updated at 10:44 PM on 23rd June 2008

Owning a cat triggers eczema in some babies, a study has found.

The pets can set off the itchy, painful skin disease in the one in ten babies with a certain genetic mutation.

But other infants were not put at extra risk, scientists found.....

Dr Hans Bisgaard, who led the research published in the Public Library of Science journal, said:

'The message isn't to kill the cat.

'If you haven't got the mutation it doesn't matter if you have a cat.

But if you have the mutation, a cat has an effect.'.....

Read more: <http://www.dailymail.co.uk/news/worldnews/article-1028886/>

## One of the reader comments

Oh great!

Now naive parents are going to get rid of their cats because of a new "study"!

- Alison, Milwaukee, Wisconsin USA, 24/6/2008 05:59



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# References

- Palmer, C.N.A, Irvine, A.D., Kwiatkowski, A.T., Zhao, Y., Liao, H., Lee, S.P., Goudie, D.R, Sandilands, A., Cambell, L.E., Smith, F.J.D, O'Regan, G.M., Watson R.M., Cecil, J.E, Bale, S.J., Compton, J.G., DiGiovanna, J.J., Fleckman, P., Jones, S.L., Arseculeratne, G., Sergeant, A., Munro, C.S. Houate, B.E., McElreavey, K., Halkjaer, L.B., Bisgaard, H., Mukhopadhyay, S., McLean, I. (2006). Common loss-of-function variants of the epidermal barrier protein filaggrin are a major predisposing factor for atopic dermatitis. *NATURE Genetics* **38**, 441–446.
- Bisgaard, H., Simpson, A., Palmer, C.N.A, Bønnelykke, K., Mclean, I., Mukhopadhyay, S., Pipper, C.B., Halkjaer, L.B., Lipworth, B., Hankinson, J., Woodcock, A., Custovic, A. (2008). Gene-Environment Interaction in the Onset of Eczema in Infancy: Filaggrin Loss-of-Function Mutations Enhanced by Neonatal Cat Exposure. *PLoS Medicine* **5(6)**, 934–940.

