

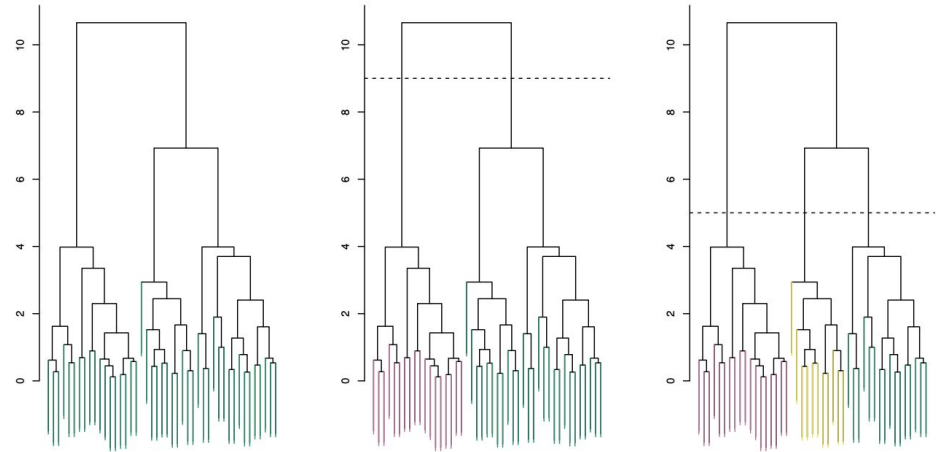
# Hierarchical Clustering

Townson Cocke with David Marcano



# Theory:

- Unlike k-means, hierarchical doesn't require pre-selecting # of clusters
- “Bottom up agglomerative”
- Unsupervised
- Produces visual dendrogram



# Theory:

- Each observation is a “leaf” on the dendrogram
- The lower the “height of fusion” the more similar the observations
- The higher the “height of fusion” the less similar the observations
- Distance matrix generated from observations,
  - Distances:
    - Euclidean
  - Linkage
    - How close/far are the clusters
    - Ward, complete, single

# Motivating Example: Asthma Phenotypes

- Heterogeneous disease:
  - Phenotypes are not very well understood
  - Difficult to precisely define
  - Depends on many factors
- ISAAC: International Study of Asthma and Allergies in Childhood
  - Widely used questionnaire

## Cluster analysis and clinical asthma phenotypes

[P Haldar](#), [ID Pavord](#), [DE Shaw](#), [MA Berry](#)... - American journal of ..., 2008 - [atsjournals.org](#)

Rationale: Heterogeneity in **asthma** expression is multidimensional, including variability in clinical, physiologic, and pathologic parameters. Classification requires consideration of these disparate domains in a unified model. Objectives: To explore the application of a ...

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## Identification of **asthma phenotypes** using **cluster** analysis in the Severe Asthma Research Program

[WC Moore](#), [DA Meyers](#), [SE Wenzel](#)... - American journal of ..., 2010 - [atsjournals.org](#)

Rationale: The Severe **Asthma** Research Program cohort includes subjects with persistent **asthma** who have undergone detailed **phenotypic** characterization. Previous univariate methods compared features of mild, moderate, and severe **asthma**. Objectives: To identify ...

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## Identifying adult **asthma phenotypes** using a **clustering** approach

[V Siroux](#), [X Basagaña](#), [A Boudier](#), [I Pin](#)... - European ..., 2011 - [Eur Respiratory Soc](#)

There is a need to improve **asthma** characterisation by integrating multiple aspects of the disease. The aim of the present study was to identify distinct **asthma phenotypes** by applying latent class analysis (LCA), a model-based **clustering** method, to two large epidemiological ...

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## [HTML] **Cluster analysis of obesity and asthma phenotypes**

, ... [Leung](#)2, 4 for the **Asthma** Clinical Research Network - [PloS one](#), 2012 - [journals.plos.org](#)

Background **Asthma** is a heterogeneous disease with variability among patients in characteristics such as lung function, symptoms and control, body weight, markers of inflammation, and responsiveness to glucocorticoids (GC). **Cluster** analysis of well ...

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Original Article

# Childhood Allergic Asthma Is Not a Single Phenotype

Jocelyne Just MD, PhD <sup>1</sup>  , Philippe Saint-Pierre PhD <sup>2</sup>, Rahele Gouvis-Echraghi MD <sup>1</sup>, Yacine Laoudi MD <sup>1</sup>, Layde Roufai MD <sup>1</sup>, Isabelle Momas PharmD, PhD <sup>3</sup>, Isabella Annesi Maesano MD, PhD, DSc <sup>4</sup>

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## Phases Introduction

### Phase One

[ISAAC Manual \(pdf\)](#)[Coding and Data](#)[Transfer Manual \(pdf\)](#)[Centre Report \(pdf\)](#)[Centres and Principal  
Collaborators](#)[Phase One Field Work  
Guide](#)[Guidelines For  
Translation of  
Questionnaires](#)[Instructions For Use  
of the Video  
Questionnaire](#)[Phase One Results](#)[Phase One Individual  
Data](#)[Phase One Study  
Group](#)[Phase Two](#)[Phase Three](#)[Phase Four](#)

You are here: [Home](#) > [Phases](#) > [Phase One](#) > Individual data

## ISAAC Phase One Individual Data

Select a Region, Country and Centre from the list boxes to view the data. To select multiple centres, use the shift or ctrl keys or select 'all' to select all centres in a region or country. The data is presented in a zip file containing a csv file for each centre. Please see the [Coding and Data Transfer Manual](#) for detailed information concerning the how the data is presented within these files. To ensure the privacy of the participants, the date of birth has been replaced with age in months in the data. Centre for which we have not yet received permission to display data have been greyed out in selection boxes below.

Alternatively, ISAAC datasets have now been deposited in an openly accessible data archive. Individual- and centre-level data and documentation from ISAAC Phases One, Two and Three are now accessible at the following webpage:

<http://discover.ukdataservice.ac.uk/catalogue?sn=8131>.

Region	Country	Centre
Please select a region Africa Africa (French Speaking) Asia-Pacific Eastern Mediterranean	Please select a region	Please select a region
<input type="button" value="Reset"/>	<input type="button" value="download zip"/>	

**Your selection:**

Region:	Country:	Centre:
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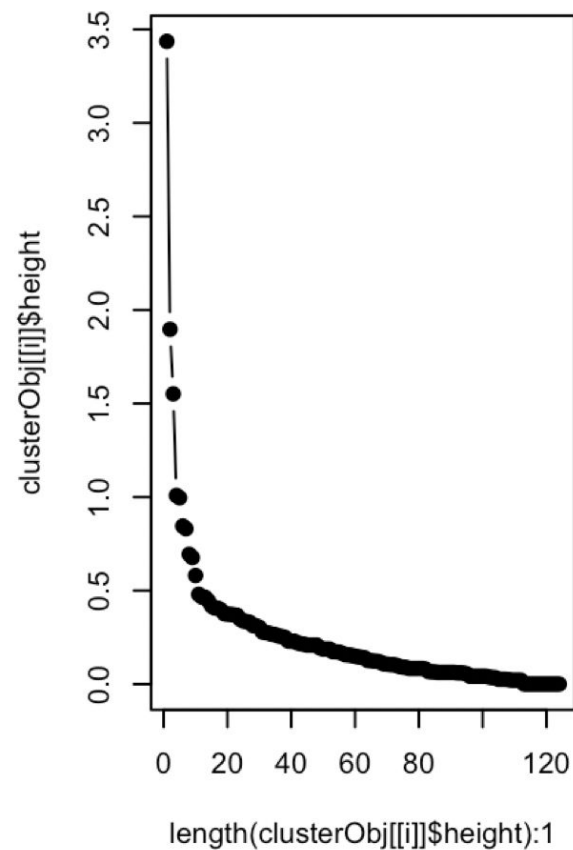
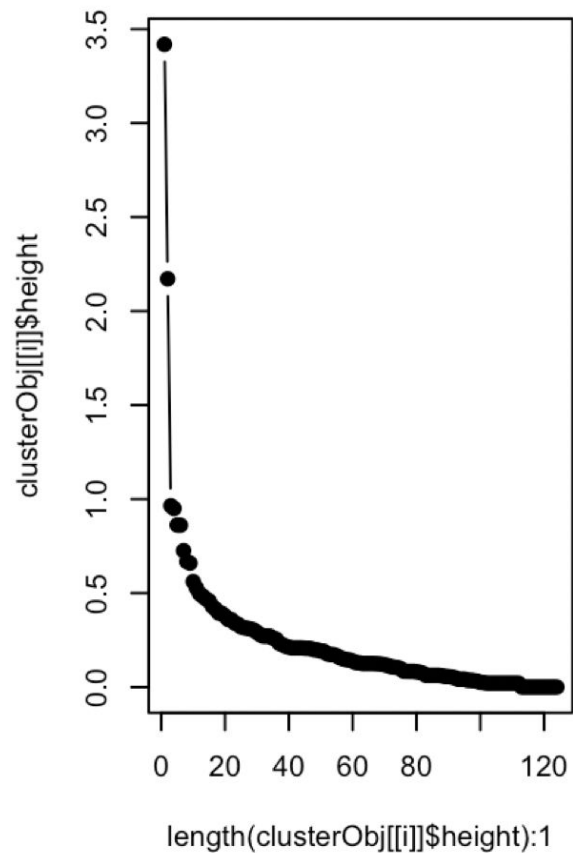
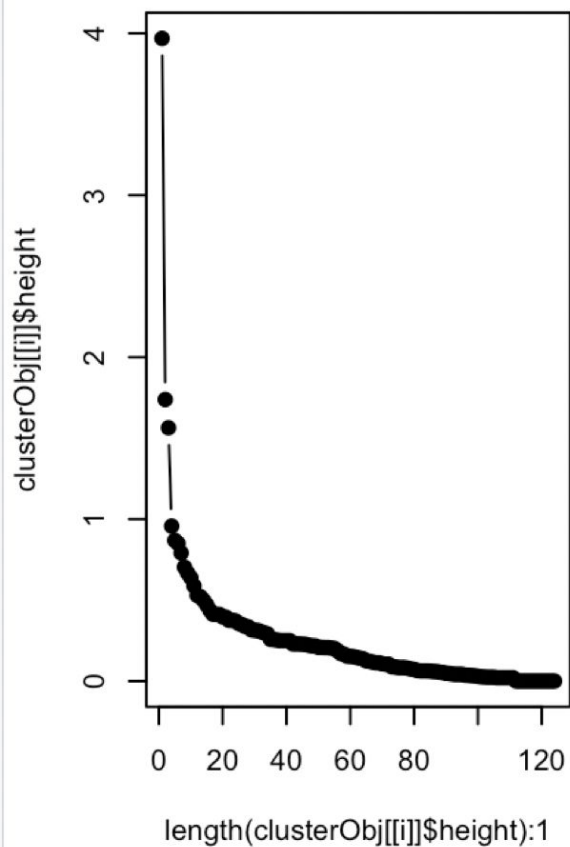
### 7.5.1 Questionnaire

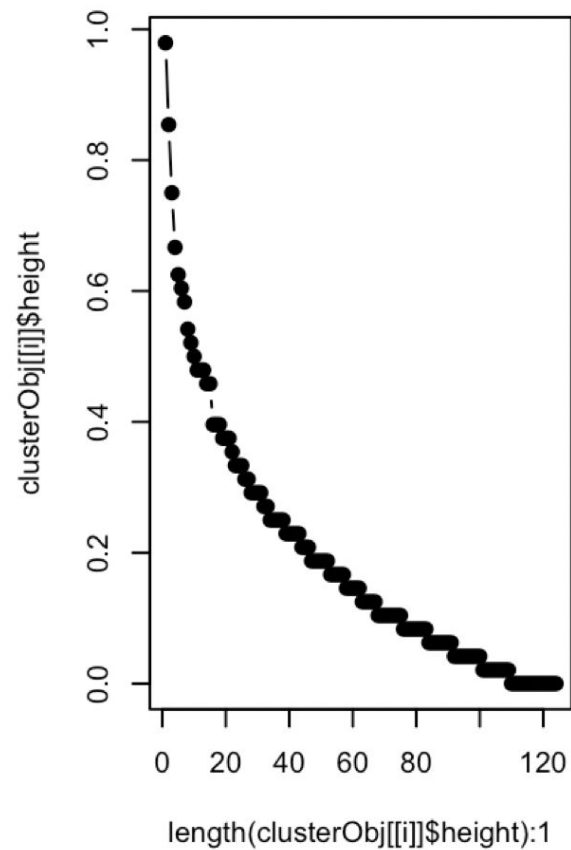
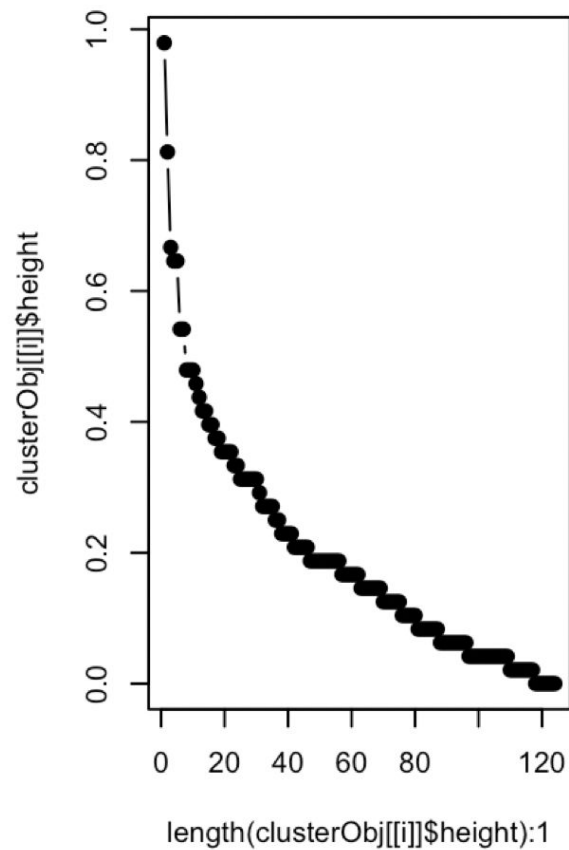
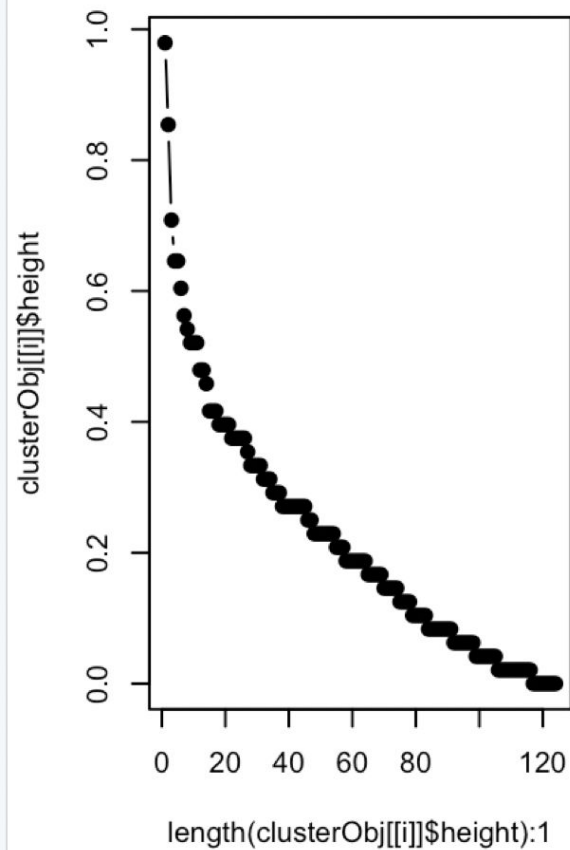
- |    |   |     |                          |    |                          |
|----|---|-----|--------------------------|----|--------------------------|
| 1. | Has your breathing ever been like this?:<br>at any time in your life?                                 | YES | <input type="checkbox"/> | NO | <input type="checkbox"/> |
|    | if YES,; in the last year?  | YES | <input type="checkbox"/> | NO | <input type="checkbox"/> |
|    | if YES,; one or more times a month?   | YES | <input type="checkbox"/> | NO | <input type="checkbox"/> |
| 2. | Has your breathing been like the girl's in the video following exercise?<br>at any time in your life? | YES | <input type="checkbox"/> | NO | <input type="checkbox"/> |
|    | if YES,; in the last year?  | YES | <input type="checkbox"/> | NO | <input type="checkbox"/> |
|    | if YES,; one or more times a month?   | YES | <input type="checkbox"/> | NO | <input type="checkbox"/> |
| 3. | Have you been woken like this at night?:<br>at any time in your life?                                 | YES | <input type="checkbox"/> | NO | <input type="checkbox"/> |
|    | if YES,; in the last year?  | YES | <input type="checkbox"/> | NO | <input type="checkbox"/> |
|    | if YES,; one or more times a month?   | YES | <input type="checkbox"/> | NO | <input type="checkbox"/> |
| 4. | Have you been woken like this at night?:<br>at any time in your life?                                 | YES | <input type="checkbox"/> | NO | <input type="checkbox"/> |
|    | if YES,; in the last year?  | YES | <input type="checkbox"/> | NO | <input type="checkbox"/> |
|    | if YES,; one or more times a month?   | YES | <input type="checkbox"/> | NO | <input type="checkbox"/> |
| 5. | Has your breathing been like this?:<br>at any time in your life?                                      | YES | <input type="checkbox"/> | NO | <input type="checkbox"/> |
|    | if YES,; in the last year?  | YES | <input type="checkbox"/> | NO | <input type="checkbox"/> |
|    | if YES,; one or more times a month?   | YES | <input type="checkbox"/> | NO | <input type="checkbox"/> |

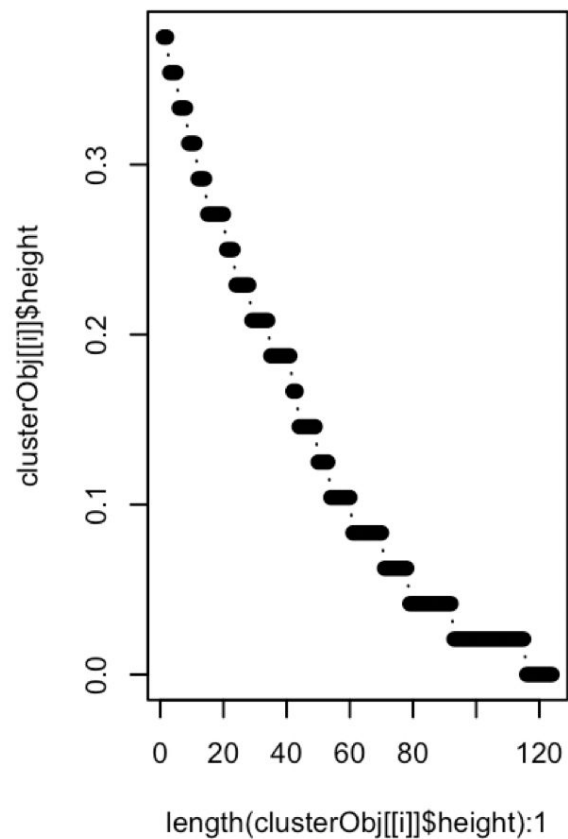
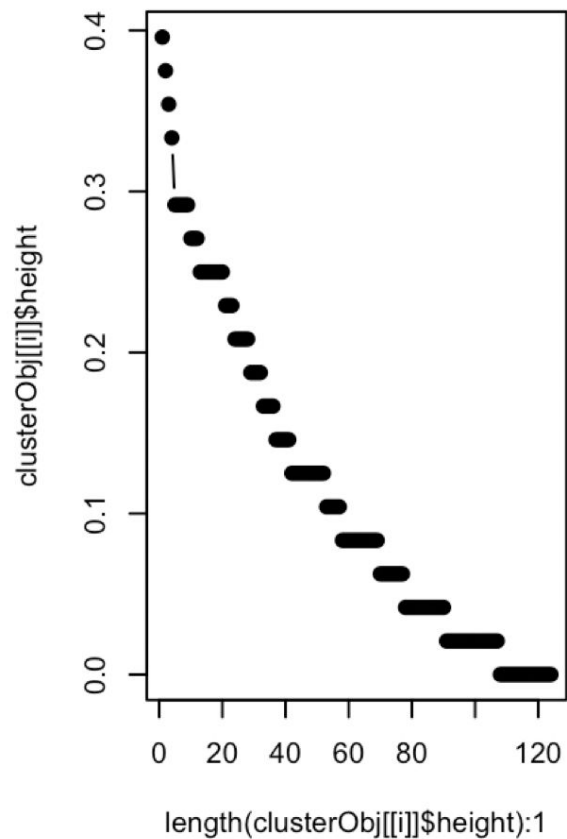
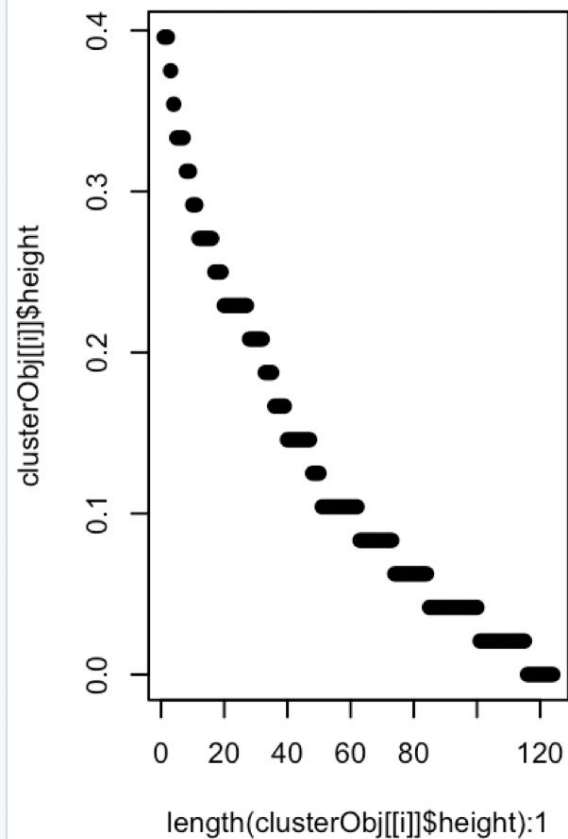


# Data Analysis

- Using the `hclust()` function in R, we created a distance matrix using the gower distance metric
  - Gower allows for a mixture of categorical and continuous data
- Used three linkages: ward, complete, single
- Bootstrapping
  - Useful for testing stability (how similar are scree plots in next slide for each of the samples of 125 individuals)







# Interpretation

- 4 clusters seem to work best (using the “elbow method” visual check of the scree plot)
  - Past this point of four clusters, there are diminishing returns in terms of cluster robustness

descriptive statistics by group													group: 1															
vars	n	mean	sd	median	trimmed	mad	min	max	range	skew	kurtosis	se	vars	n	mean	sd	median	trimmed	mad	min	max	range	skew	kurtosis	se			
age*	1	95	2.77	1.34	3	2.65	1.48	1	6	5	-0.66	0.00	0.14	age*	1	16	2.75	1.44	2	2	64	0.00	1	6	5	1.29	0.48	0.36
sex*	2	95	1.63	0.53	2	1.64	0.00	1	3	2	-0.10	-1.10	0.05	sex*	2	16	1.50	0.52	1.5	1.50	0.74	1	2	1	0.00	-2.12	0.13	
whzeev*	3	95	1.86	0.52	2	1.86	0.00	1	3	2	-0.18	0.34	0.05	whzeev*	3	16	1.31	0.48	1	1.29	0.00	1	2	1	0.73	-1.55	0.12	
rwhezi2*	4	95	2.51	0.71	3	2.62	0.00	1	3	2	-1.07	-0.28	0.07	rwhezi2*	4	16	1.81	0.98	1	1.79	0.00	1	3	2	0.35	-1.24	0.15	
rwhezi1*	5	95	4.03	1.63	4	4.27	0.00	1	5	4	-1.14	-0.61	0.17	rwhezi2*	5	16	1.88	1.20	4	3.93	1.48	2	5	3	-0.42	-1.51	0.30	
awakei2*	6	95	1.27	1.31	4	3.32	0.00	1	4	3	-0.96	-1.03	0.13	awakei2*	6	16	2.81	1.22	3	2.86	1.48	1	4	3	-0.28	-1.66	0.31	
speedch2*	7	95	2.67	0.55	3	2.77	0.00	1	3	2	-1.45	1.11	0.06	speedch2*	7	16	2.22	0.77	2	2.23	1.48	3	2	-0.40	-1.24	0.19		
asthmaev*	8	95	1.93	0.40	1	1.99	0.00	1	2	-0.35	3.08	0.04	asthmaev*	8	16	1.50	0.52	1.5	1.50	0.74	1	2	1	0.00	-2.12	0.13		
exwhezi2*	9	95	1.88	0.48	2	1.90	0.00	1	3	2	-0.31	0.88	0.05	exwhezi2*	9	16	1.44	0.51	1	1.43	0.00	1	2	1	0.23	-2.07	0.13	
coughi2*	10	95	1.92	0.52	2	1.90	0.00	1	3	2	-0.12	0.54	0.05	coughi2*	10	16	1.56	0.63	1.5	1.50	0.74	1	3	2	0.54	-0.87	0.16	
ieyes12*	11	95	1.89	0.31	2	1.99	0.00	1	2	-2.53	4.46	0.03	ieyes12*	11	16	1.00	0.00	1	1.00	0.00	1	1	0	NAN	NAN	0.00		
prosej12*	12	95	2.00	0.00	2	2.00	0.00	2	2	0	NAN	NAN	0.00	prosej12*	12	16	1.00	0.00	1	1.00	0.00	1	1	0	NAN	NAN	0.00	
prosejan*	13	95	1.00	0.00	3	1.00	0.00	3	3	0	NAN	NAN	0.00	prosejan*	13	16	1.12	0.34	1	1.07	0.00	1	2	1	2.06	2.40	0.09	
prosefeb*	14	95	1.00	0.00	3	1.00	0.00	3	3	0	NAN	NAN	0.00	prosejan*	14	16	1.00	0.51	2	1.57	0.00	1	2	-0.23	-2.07	0.13		
prosema*	15	95	1.00	0.00	3	1.00	0.00	3	3	0	NAN	NAN	0.00	prosefeb*	15	16	1.75	0.45	2	1.79	0.00	1	2	1	-1.05	-0.95	0.11	
prosema*	16	95	1.00	0.00	3	1.00	0.00	3	3	0	NAN	NAN	0.00	prosema*	16	16	1.94	0.25	2	2.00	0.00	1	2	1	-3.28	9.36	0.06	
prosema*	17	95	1.00	0.00	3	1.00	0.00	3	3	0	NAN	NAN	0.00	prosema*	17	16	1.94	0.25	2	2.00	0.00	1	2	1	-3.28	9.36	0.06	
prosema*	18	95	1.00	0.00	3	1.00	0.00	3	3	0	NAN	NAN	0.00	prosema*	18	16	1.81	0.40	2	1.86	0.00	1	2	1	-1.45	0.13	0.10	
prosejan*	19	95	1.00	0.00	3	1.00	0.00	3	3	0	NAN	NAN	0.00	prosejan*	19	16	1.94	0.25	2	2.00	0.00	1	2	1	-3.28	9.36	0.06	
prosej*	20	95	1.00	0.00	3	1.00	0.00	3	3	0	NAN	NAN	0.00	prosejan*	20	16	1.88	0.34	2	1.93	0.00	1	2	1	-2.06	2.40	0.09	
proseaug*	21	95	1.00	0.00	3	1.00	0.00	3	3	0	NAN	NAN	0.00	proseaug*	21	16	1.94	0.25	2	2.00	0.00	1	2	1	-3.28	9.36	0.06	
prosefeb*	22	95	1.00	0.00	3	1.00	0.00	3	3	0	NAN	NAN	0.00	proseaug*	22	16	1.94	0.25	2	2.00	0.00	1	2	1	-3.28	9.36	0.06	
prosema*	23	95	1.00	0.00	3	1.00	0.00	3	3	0	NAN	NAN	0.00	prosefeb*	23	16	1.69	0.48	2	1.71	0.00	1	2	1	-0.73	-1.55	0.12	
prosema*	24	95	1.00	0.00	3	1.00	0.00	3	3	0	NAN	NAN	0.00	prosema*	24	16	1.75	0.45	2	1.79	0.00	1	2	1	-1.05	-0.95	0.11	
prosej*	25	95	1.00	0.00	3	1.00	0.00	3	3	0	NAN	NAN	0.00	prosema*	25	16	1.69	0.48	2	1.71	0.00	1	2	1	-0.73	-1.55	0.12	
proseoct*	26	95	1.00	0.00	3	1.00	0.00	3	3	0	NAN	NAN	0.00	proseoct*	26	16	2.12	0.96	2	2.07	1.48	1	4	3	-0.73	-1.55	0.12	
prosenov*	27	95	1.00	0.00	3	1.00	0.00	3	3	0	NAN	NAN	0.00	prosenov*	27	16	1.31	0.48	1	1.29	0.00	1	2	1	0.73	-1.55	0.12	
proseoct*	28	95	1.00	0.00	3	1.00	0.00	3	3	0	NAN	NAN	0.00	proseoct*	28	16	1.56	0.51	2	1.57	0.00	1	2	1	-0.23	-2.07	0.13	
prosenov*	29	95	1.00	0.00	3	1.00	0.00	3	3	0	NAN	NAN	0.00	prosenov*	29	16	1.62	0.50	2	1.64	0.00	1	2	1	-0.87	-1.89	0.12	
proseoct*	30	95	1.00	0.00	3	1.00	0.00	3	3	0	NAN	NAN	0.00	proseoct*	30	16	2.44	0.81	3	2.50	0.00	1	3	2	-0.86	-1.02	0.20	
prosenov*	31	95	1.00	0.00	3	1.00	0.00	3	3	0	NAN	NAN	0.00	prosenov*	31	16	1.00	0.00	1	1.00	0.00	1	1	0	NAN	NAN	0.00	
proseoct*	32	95	1.00	0.00	3	1.00	0.00	3	3	0	NAN	NAN	0.00	proseoct*	32	16	2.00	0.73	3	2.57	0.00	1	3	2	-0.96	-0.58	0.18	
prosenov*	33	95	1.00	0.00	3	1.00	0.00	3	3	0	NAN	NAN	0.00	prosenov*	33	16	2.00	1.34	4	3.14	0.00	1	4	3	-0.73	-1.42	0.34	
proseoct*	34	95	1.00	0.00	3	1.00	0.00	3	3	0	NAN	NAN	0.00	proseoct*	34	16	1.50	0.52	1.5	1.50	0.74	1	2	1	0.00	-2.12	0.13	
prosenov*	35	95	1.00	0.00	3	1.00	0.00	3	3	0	NAN	NAN	0.00	prosenov*	35	16	1.25	0.45	1	1.21	0.00	1	2	1	1.05	-0.95	0.11	
proseoct*	36	95	1.00	0.00	3	1.00	0.00	3	3	0	NAN	NAN	0.00	proseoct*	36	16	1.44	0.51	1	1.43	0.00	1	2	1	0.23	-2.07	0.13	
prosenov*	37	95	1.00	0.00	3	1.00	0.00	3	3	0	NAN	NAN	0.00	prosenov*	37	16	1.50	0.51	2	1.57	0.00	1	2	1	-0.23	-2.07	0.13	
proseoct*	38	95	1.00	0.00	3	1.00	0.00	3	3	0	NAN	NAN	0.00	proseoct*	38	16	1.19	0.40	1	1.14	0.00	1	2	1	1.45	0.13	0.10	
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prosenov*	43	95	1.00	0.00	3	1.00	0.00	3	3	0	NAN	NAN	0.00	prosenov*	43	16	1.88	0.50	2	1.86	0.00	1	3	2	-0.28	0.36	0.12	
proseoct*	44	95	1.00	0.00	3	1.00	0.00	3	3	0	NAN	NAN	0.00	proseoct*	44	16	1.25	0.45	1	1.21	0.00	1	2	1	1.05	-0.95	0.11	
prosenov*	45	95	1.00	0.00	3	1.00	0.00	3	3	0	NAN	NAN	0.00	prosenov*	45	16	1.50	0.52	1.5	1.50	0.74	1	2	1	0.00	-2.12	0.13	
proseoct*	46	95	1.00	0.00	3	1.00	0.00	3	3	0	NAN	NAN	0.00	proseoct*	46	16	1.75	0.45	2	1.79	0.00	1	2	1	-1.05	-0.95	0.11	
prosenov*	47	95	1.00	0.00	3	1.00	0.00	3	3	0	NAN	NAN	0.00	prosenov*	47	16	1.31	0.48	1	1.29	0.00	1	2	1	0.73	-1.55	0.12	
proseoct*	48	95	1.00	0.00	3	1.00	0.00	3	3	0	NAN	NAN	0.00	proseoct*	48	16	1.44	0.51	1	1.43	0.00	1	2	1	0.23	-2.07	0.13	
prosenov*	49	95	1.00	0.00	3	1.00	0.00	3	3	0	NAN	NAN	0.00	prosenov*	49	16	1.56	0.51	2	1.57	0.00	1	2	1	-0.23	-2.07	0.13	
proseoct*	50	95	1.00	0.00	3	1.00	0.00	3	3	0	NAN	NAN	0.00	proseoct*	50	16	2.00	0.00	2	2.00	0.00	2	2	0	NAN	NAN	0.00	
cluster_num*	50	95	1.00	0.00	1	1.00	0.00	1	1	0	NAN	NAN	0.00	cluster_num*	50	16	2.00	0.00	2	2.00	0.00	2	2	0	NAN	NAN	0.00	