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Iealth information technology field

Graduate school of natural science and technology
Department of civil engineering and natural science

Also with the collaboration of: Okayama University Hospital, medical center for children

Godest Vincent

Health information technology (en)

Technologies de l'information pour la santé (fr)

Rapport de stage 2018, niveau Master 1
13 semaines de mi-mai à mi-août

Internship report for 2018, 1st Master Course level
13 weeks from mid-May to mid-August

Principal sheet (Version n°1)

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Obesity surveillance in Japan
Statistical study about childhood BMI evolution
first results and future

Aim of the study :

Standard Improvement: Uses of numerical clustering advanced methods and use of machine learning approach on BMI indicator
With the purpose of improving prediction about the childhood BMI evolution, from 0 years old to 15 years old.

Abstract :

In 2017 Okayama hospital doctors haVE explicitly asked the University to define improved statistical methods of Obesity surveillance. They argued that making prognosis by using the actual classic Gaussian normal distribution method, is not appropriate. They wished to use state of art statistical methods.

By using the Gaussian normal approach, Obesity thresholds are likely systematically over- or underestimated. Because obesity is, in the actual standard, just build this way: BMI overpass the 78% up normal interval. (And underweighted the 2% down normal interval).

In our study, we can see that a more precise group can be build up, because hierarchical clustering for example give us 2 robust group in the 1083 child patient database (from 0 to 14 years old). So instead of put an entire confidence on the normal distribution (surely not enough precise) we can adapt and make 2 distinct group. We need then to watch the median and see a likelihood in the curves trace.

Unfortunately, many modern clustering methods are not working on our case: BIRCH algorithm, CLARENS and k-medoids (partitioning around medoids). The problem is that there is so many abnormal BMI curves which give lots of outliers in the cluster we are trying to set-up. So the database need to be clean-up first with a filter, but not so much powerful because we need enough values to have a robust cluster.

Also 2 Dimensional (Age and BMI) make the a huge computer cost (more than 2 hours running without giving any result)

So it's a complex issue that can be not solve until the data-base entrance of data is not under a strict control, in my mind.

Introduction : State of the art :

Clinical concerning : (need to be approved by doctors in Okayama Hospital)

BMI: Body Mass Index: calculate by this formula (Weight/Height^2), is now a standard criteria in public health caring, He is often watching in World Health Organisation covering watching countries and developed countries (Japan, France, America …) as a basic medical check-up standard.

It is an adiposity indicator, he is not showing it directly but can set the direction of a diagnosis. And adiposity abnormal level is a factor of: bad cholesterol, cardiac diseases, diabetes…
It could also be a first step to detect unhealthy sedentary or eating habits.
It also could be an indicator of public health good being (Obama was, for example, caring about it in 2010, for American student life and sports habits in his Health reform program)

(see annex 1.1 for sources)

In our case, for childhood concern, many doctor and nutritionist are according themselves to say that change daily life and food habits at teenage and adult life stage is a tuff task for their patients. So it is surely could be better to take the right habits in the first life moments.

(see annex 1.1 figure 2)

So the main goal here is to precise medical observations with a statistical study, so we want to confirm them and see the importance of separate habits life on the weight group appartenance.

Also, the next step should be to compare the Okayama Obesity prevalence evolution with Japan prevalence evolution, to see if "Westernisation" is becoming an issue for Japan life

habits and good public health maintaining.

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Proposition to improve standard statistical methods for allows prediction of future weight category:

The standard actual Task forces (see figures 1 and 2 annex 1.1) mainely depend on the countries, but they have been calculate with Gaussian method (place in the normal distribution) method applied on a very large scale of clinical data. So doctor can watch their patients BMI and put them in the right cluster.
Then, if BMI is too high: above 75% normal distribution or too low: under 25 % normal distribution, doctors can set the next direction of diagnosis: why the child is evolving to over/under-weighted.

Here, we have tried to find methods which can give a prediction (prognosis in medical terms) of BMI evolution and give the associated error rate. We will try to force data in 4 clusters, representing: under-weighted, normal weight, over-weighted and obese.

For this, after a bibliography of finding best data-mining methods existing for our case (see annex 3.2), We will test it on Python and plotting it thanks to MatplotLib (python module) and compare them thanks to some criteria (see annex 3.1) we set. Then, best methods will be retain.

I also think it could be interesting to automatize the process to avoid to always have to run python files by hand, which are users unfriendly. This is the "machine learning part" I want to introduce in this work (see annex 2 figure 1) but we need to focus on the fact that steps need to be shown and the User can stop the process or choose the method by himself: because doctors must have hands on what append.

So: Setting up clear method and architecture and a clear interface is important in our case, that's one of the reason of the python language choice.

Statistical methods choice :

(see annex 3.2)

Methods rejected: Neural networks (1); Reinforcement learning (2);

Reasons: (1): Too much instable and not enough supported and build yet by scientific community.
(2) Way too much complex (take many memory and time).

Methods which could be interesting: Machine learning (1); Anomaly detection (2); FPDC (3); Noise density measurement & dynamic noise density (4); FDPC (5); Mixed models & expectation maximization(6)

Reasons: (1) (2) Adaptable methods, change way of calculus if we do not have the wanted result. But also take memory and time (not a problem if many software versions are made).
(3) Can be really powerful but also not so reliable.
(4) To erase noise (residual variance), but not a final method (and can amplify error rate), also what it "noise" here, it's difficult to define. **Can be done if we compare variances between our model and World Health Organization model.**
(5) Maybe too much probability-dependent but can sometimes show interesting results.
(6) Need to try some when simple model are not working. But we also need to know the variances part of the model which is difficult. (same problem as (4))

Methods more adapted for our issue in my mind: Hierarchical clustering (1); Medium-link (2); Ward algorithm (3); Multiple Correspondence Analysis (4); k-medoids (partitioning around medoids) (5)

Reasons:
(1)(2)(3) Agglomerative methods are interesting because we can begin with our 4 pre-define groups, define by medical references (Task force), but we need to be careful: this is an artificial group making.
(4) (5) Interesting but maybe not so original.

Discussion:

Interesting algorithm and methods could have been rejected here. (Because I am actually not a statistical expert but just an internship's student)

Also I can have not found interesting methods, I have followed the bibliography method mentioned in the previous document (see annex 3.2) But this is only public area research papers and maybe interesting private method or not well known methods can be interesting.

There is no perfect methods existing, we need to pay attention about the error rate generated, about how significantly they are and their powerfulness.

I could also be a good idea to build-up a "doctor version" which cut-off on statistical details and just directly give important medical information.

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Very important: We also forgive about some of the probabilistic methods for the moment due to the difficulty to characterize a "noise" (error rate, variance). But this can be done with the World health Organization set of data (for japan BMI surveillance), which was unfortunately not available in a good data form when I was doing my work.

So this can be a very interesting next step in BMI study to apply statistical methods to WHO dataset and compare the differences.

Why python?

Here, we found that python is more judicious because he is object oriented and dispose of many libraries adapted for our issue, more than Java for example.
He is also adapted for figure plotting, which is important in a statistic work.
R also permit this, but it maybe begin to be less supported for clustering, machine learning and hierarchical methods. But it is not a bad idea to test R in the future.

The main issue with R is that it is not user friendly, so the choice have been make mainly thinking about the future of the study : user interplay, connection with web-database and code review.
(for example : doctors will never set correction on an R script, but with a good user interplay, it is possible to correct the filter or update the methods)

Also, in a research and development phase, it is important to set a great visibility on the work to facilitate the continuous of research, Matlab has been rejected because of the money fee needed, and we need fully open-source languages. C has been rejected because it is also not enough User friendly.

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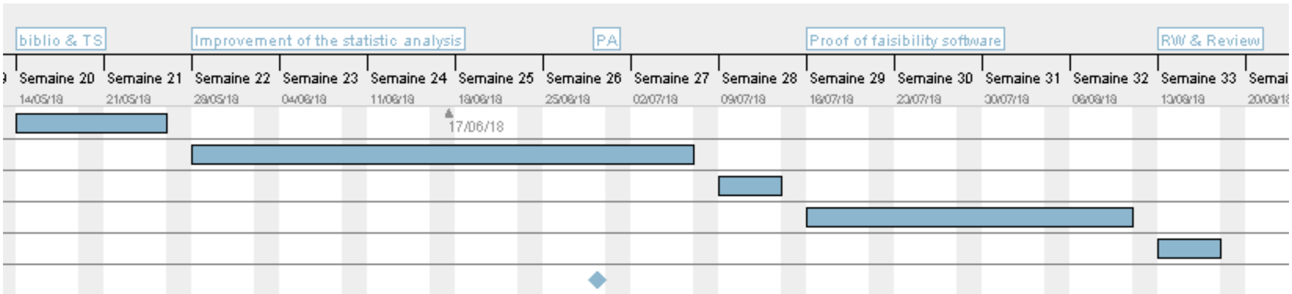
Work organisation:

Gantt diagram: (Wanted schedule)



Legend : biblio : bibliography; TS : technological surveillance ; PA : professional appointments; RW & review : report writing & review of the previous work

Milestones charts (real advancing)

27/05/2018 :

				Time needed		
Milestone		Advancing	Time allowe	Optimistic	Estimated	Pestimistic
Bibliographie & Technological surveillance		80%	+	5 days	0.5 month	1 month
Improvement of the statistic analysis		26%	+++	1 month	1.5 month	2 month
test (comparison)		0%				
finding python libraries		80%				
load values from excel chart		0%				
Proof of faisability (simple software)		30%	++	0.5 month	1 month mir	1 month minus 6 days
Modelisation	Modelisation	100%	(+)			cut here
User Interplay	User Interplay	80%	(-)			
Graphism	Graphism	0%	(++)			cut here
Functionnal core	Functionnal core	0%	(++)			
Database	Database	0%	(-)			cut here (Excel is enough)
Testing	Testing	0%	(++)			
Professional appointments		0%	~	1 day	2 days	3 day
Report		10%	~	0.5 day	2 days	3 days
Total		29%	3 month	›nth and 1.5	3 month	3 month
	Legend	red : not begin				
		blue : static				
		green :advancing or finish				

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08/06/2018 :

					Time needed		
1					Time needed		
2	Milestone		Advancing	Time allowe	Optimistic	Estimated	Pestimistic
3	Bibliographie & Technological survei		80%	+	5 days	0.5 month	1 month
4							
5	Improvement of the statistic analysis		63%	+++	1 month	1.5 month	2 month
6	test (comparison)		10%				
7	finding python libraries		80%				
8	load values from excel chart		100%				
9							
10	Proof of faisability (simple software		41%	++	0.5 month	1 month mir	1 month minus 6 days
11	Modelisation	Modelisatic	100%	(+)			No cut possible
12	User Interplay	User Interpl	80%	(-)			cut here maybe
13	Graphism	Graphism	10%	(++)			cut here
14	Functionnal core	Functionnal	30%	(++)			
15	Database	Database	0%	(-)			cut here (Excel is enough)
16	Testing	Testing	10%	(++)			cut here
17	Implementation	Implementa	60%	(++)			
18							
19	Professional appointments		0%	~	1 day	2 days	3 day
20							
21	Report		20%	~	0.5 day	2 days	3 days
22							
23	Total		41%	3 month	›nth and 1.5	3 month	3 month
24							
25		Legend	red : not begin				
26			blue : static				
27			green :advancing or finish				

22/06/2018 :

				Time needed		
Milestone		Advancing	Time allowed	Optimistic	Estimated	Pestimistic
Bibliographie & Technological surveillance		80%	+	5 days	0.5 month	1 month
Improvement of the statistic analysis		40%	+++	1 month	1.5 month	2 month
test (comparison)		0%				
finding python libraries		80%				
load values from excel chart		40%				
Proof of faisability (simple software)		37%	++	0.5 month	1 month mir	1 month minus 6 days
Modelisation	Modelisation	100%	(+)			No cut possible
User Interplay	User Interplay	80%	(-)			cut here maybe
Graphism	Graphism	0%	(++)			cut here
Functionnal core	Functionnal core	20%	(++)			
Database	Database	0%	(-)			cut here (Excel is enough)
Testing	Testing	0%	(++)			cut here
Implementation	Implementation	60%	(++)			
Professional appointments		0%	~	1 day	2 days	3 day
Report		20%	~	0.5 day	2 days	3 days
Total		35%	3 month	2 month and 1.5 days	3 month	3 month
	Legend	red : not begin				
		blue : static				
		green :advancing or finish				

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09/07/2018 :

					Time needed		
Milestone			Advancing	Time allowed	Optimistic	Estimated	Pestimistic
Bibliographie & Technological surveillance			90%	+	5 days	0.5 month	1 month
Improvement of the statistic analysis			87%	+++	1 month	1.5 month	2 month
test (comparison)			60%				
finding python libraries			100%				
load values from excel chart			100%				
Proof of faisability (simple software)			50%	++	0.5 month	1 month minus 4 days	1 month minus 6 days
Modelisation		Modelisation	100%	(+)			No cut possible
User Interplay		User Interplay	80%	(-)			cut here maybe
Graphism		Graphism	40%	(++)			cut here
Functionnal core		Functionnal core	40%	(++)			
Database		Database	0%	(-)			cut here (Excel is eno
Testing		Testing	30%	(++)			cut here
Implementation		Implementation	60%	(++)			
Professional appointments			0%	~	1 day	2 days	3 day
Report			60%	~	0.5 day	2 days	3 days
Total			57%	3 month	2 month and 1.5 days	3 month	3 month
		Legend	red : not begin				
			blue : static				
			green :advancing or finish				

23/07/2018 :

	A	B	C	D	E	F	G	H	I
1						Time needed			
2	Milestone			Advancing	Time allowed	Optimistic	Estimated	Pestimistic	
3	Bibliographie & Technological surveillance			100%	+	5 days	0.5 month	1 month	
4									
5	Improvement of the statistic analysis			87%	+++	1 month	1.5 month	2 month	
6	test (comparison)			60%					
7	finding python libraries			100%					
8	load values from excel chart			100%					
9									
10	Proof of faisability (simple software)			77%	++	0.5 month	1 month minus 4 days	1 month minus 6 days	
11	Modelisation		Modelisation	100%	(+)			No cut possible	
12	User Interplay		User Interplay	100%	(-)			cut here maybe	
13	Graphism		Graphism	60%	(++)			cut here	
14	Functionnal core		Functionnal core	60%	(++)				
15	Database		Database	80%	(-)			cut here (Excel is enough)	
16	Testing		Testing	60%	(++)			cut here	
17	Implementation		Implementation	60%	(++)				
18									
19	Professional appointments			0%	~	1 day	2 days	3 day	
20									
21	Report			70%	~	0.5 day	2 days	3 days	
22									
23	Total			67%	3 month	2 month and 1.5 days	3 month	3 month	
24									
25			Legend	red : not begin					
26				blue : static					
27				green :advancing or finish					

06/08/2018 :

	A	B	C	D	E	F	G	H
1						Time needed		
2	Milestone			Advancing	Time allowed	Optimistic	Estimated	Pestimistic
3	Bibliographie & Technological surveillance			100%	+	5 days	0.5 month	1 month
4								
5	Improvement of the statistic analysis			93%	+++	1 month	1.5 month	2 month
6	test (comparison)			80%				
7	finding python libraries			100%				
8	load values from excel chart			100%				
9								
10	Proof of faisability (simple software)			91%	++	0.5 month	1 month minus 4 days	1 month minus 6 days
11	Modelisation		Modelisation	100%	(+)			No cut possible
12	User Interplay		User Interplay	100%	(-)			cut here maybe
13	Graphic		Graphic	80%	(++)			cut here
14	Functionnal core		Functionnal core	100%	(++)			
15	Database		Database	100%	(-)			cut here (Excel is enough)
16	Testing		Testing	80%	(++)			cut here
17	Implementation		Implementation	80%	(++)			
18								
19	Professional appointments			Dismiss	~	1 day	2 days	3 day
20								
21	Report			80%	~	0.5 day	2 days	3 days
22								
23	Total			91%	3 month	2 month and 1.5 days	3 month	3 month
24								
25			Legend	red : not begin				
26				blue : static				
27				green :advancing or finish				
28								

Improvement of the statistical analysis, results found at the end of imparted time :

After the test phase of all the methods found in the library, I set some conclusion on each methods Some could be wrong because of the limited time I had, I will now explain in detail :

Dismissed methods :

Probabilistic methods: Not tested, but don't seem adapted.

If we set some probabilistic based link between the cluster, we will have different kind of link in our model: stronger and weaker. (Correlation and regression)

But we want the same strength in clustering link: the distance from the model center (average or median or leader) should be the same a not based on probability. If it is too much sparse, the error rate will be not satisfying.

So finally we choose to work with Bayesian approach in priority. The strength of the model is Watch at the final step and there is no curve elimination during the process.

We also do not want to reduce data or dimension of the model in a first step, because we want to have the weight of every daily habits.

Multiple-correspondence analysis and correspondence analysis : Maybe not adapted

(Maybe the most adapted probabilistic method)
This methods are close to Principal component analysis, the aim is to reduce data to find the leading daily habits link to all the main clusters we can found.

This seem very powerful because of the twice benefit.

But, this is about test all possible combination of daily habits and erase the non-significant ones.
This could be interesting, but we are not searching for supervised method in the first step. We first want unsupervised find of likelihood.

So it is taking a lot's of coding time and memory for having maximum 2 leading habits in final (Source: https://github.com/esafak/mca/blob/master/docs/usage.rst) and only one if the error rate on the second is too big.

Considering the time needed and the final result given (I remain that we want, if possible, more than 2 clusters), I decided to forget about this method.
The main start idea is that we do not want to reduce daily habits because we think that the one we have are meaningful enough to set many clusters.

I could be wrong, if someone want to try, it is possible with the tool given in this section and my final proof of feasibility.

K-medoids: Good but not so original, also instable (not fully build in) in libraries

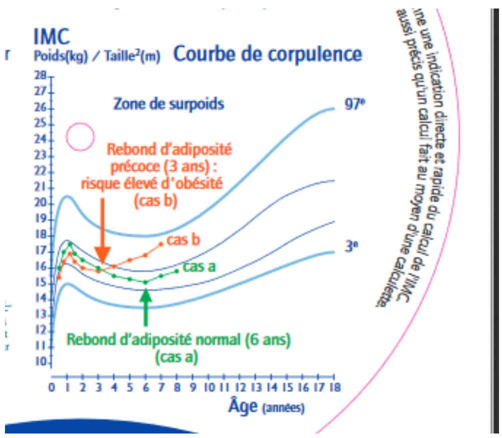
K-medoids treatment can give 5 or less acceptable interval distribution cluster like in this figure (see Annex1) : So it give following prediction :

Top : overweighted, huge Risk of obesity maintaining

Second : risk of obesity development

Third : normal course

Fourth : risk of under-weighted development

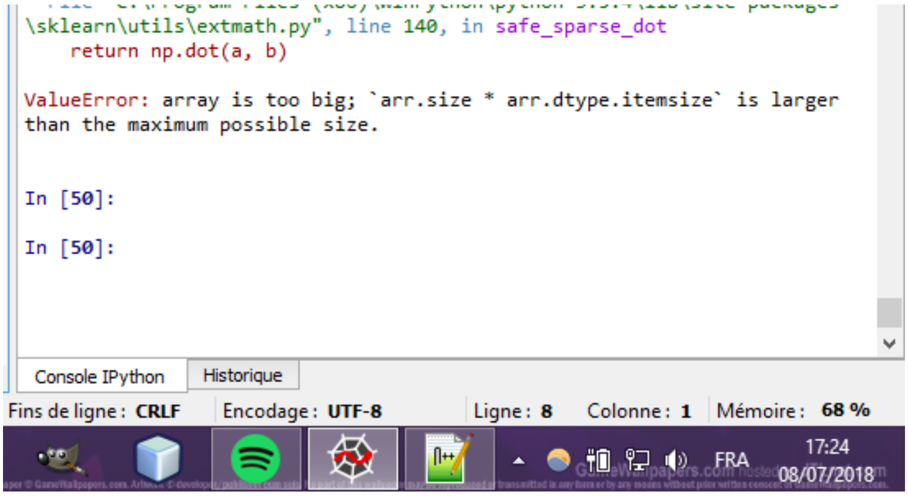


Bottom : under-weighted, risk of thinness maintaining

(This is the French reference but international references are not so different in the build in way)

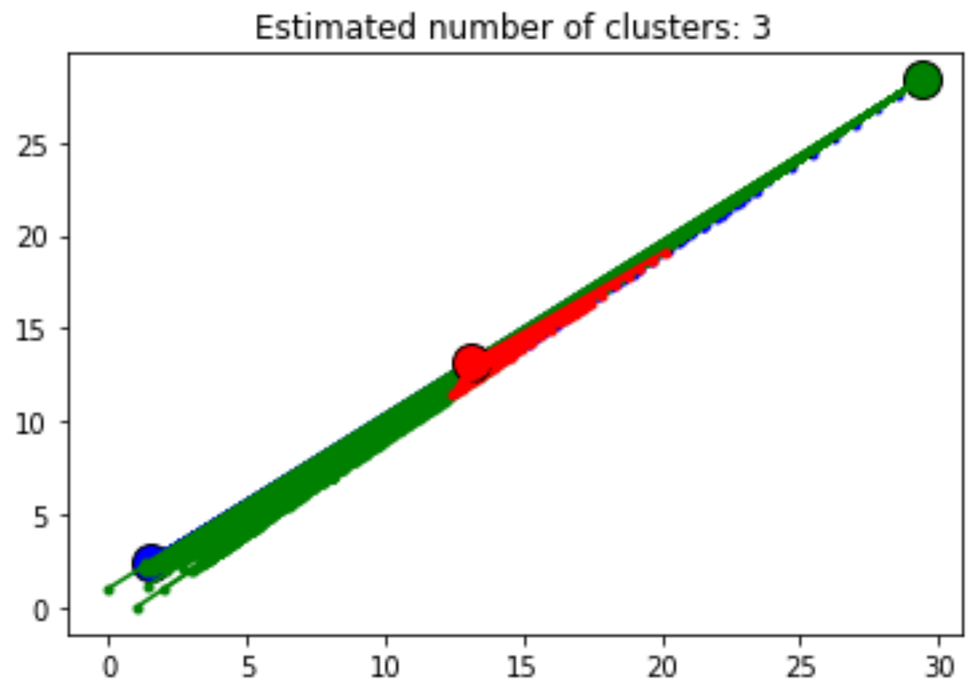
So we can process to build the 4 cluster we want, but I am not sure it make a great standard breakthrough. **But it should give different form of curves for the different groups and not be based only on the normal distribution, like in this figure.**

But the method I found is not adapted for ours data because of the scale; it give this mistake :



so if you want to apply k-medoids, you must code it by yourself (I had no time for try) or use it in R, but in my mind it will not be more powerful than k-means because of the data : see under.

Affinity propagation which is kind of the same, is not working for 2Dimentional, it give a flat distance array badely clustered.



CLARENS and BIRCH algorithm

The most recent clustering methods, I was hoping a lot about it, but it is not working actually, it is processing during more than 2 hours without giving any results

Hypothesis : Our model have too many sparse values (see hierarchical clustering) and when the algorithm is searching for a center in the values, it's taking a huge time to reduce the distance between the points, which is actually not possible.

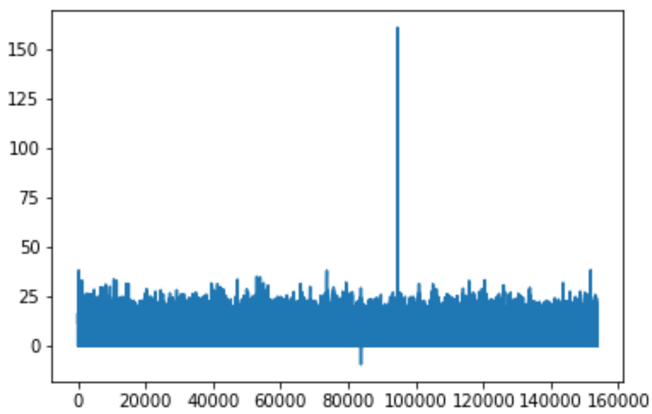
Counter measure: Should be to restart with the group given by hierarchical, but the aim is not to erase lots of values, it is very difficult to say if this is pure outliers (physiologically impossible, in which case we can erase it) or a health problem for the child.

Also, a hierarchical clustering first treatment is a first way of making clusters so it is already a clustering treatment. So it is probably useless to try to make clusters on clusters.

Retained methods:

Anomaly Detection : indispensable

By just plotting rough values in a graph : (ordinate : BMI, abscissa : dimension-less : all patient at all ages)



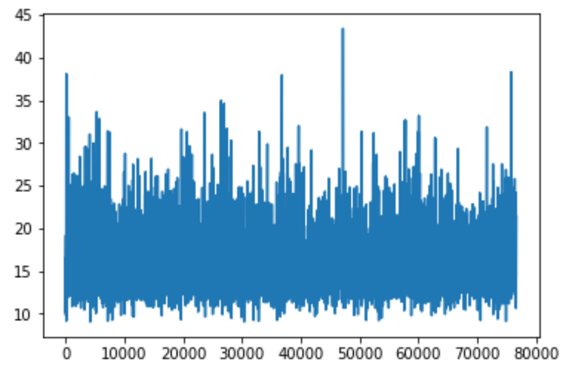
Rough value plotting

We can easily see the first issue: some BMI values are non-sense: negative values, close to 0, above 50.

On medical references according to World Health Organisation, we can see that BMI real values cannot be under 9 even at 0 years old and also not above 50 which is a +10 superior value of morbid obesity.

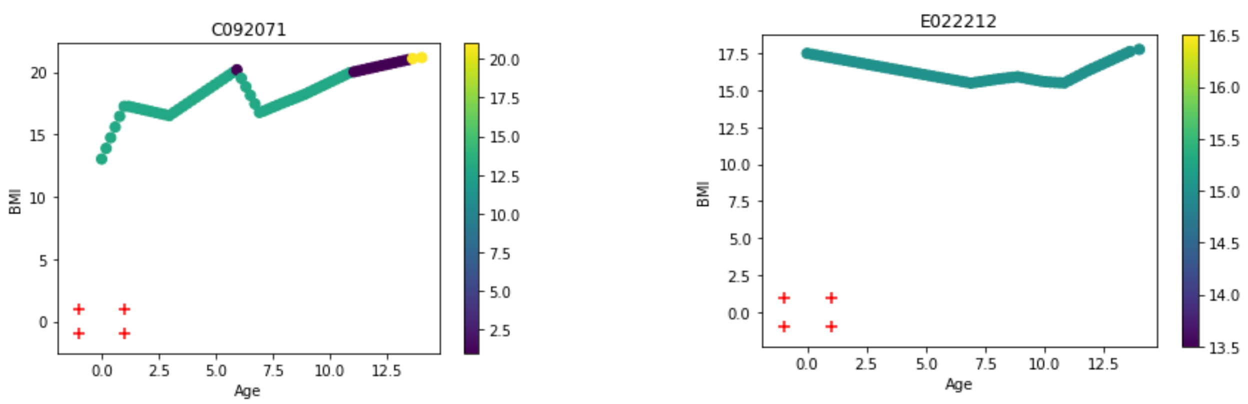
After treatment, (simple if, else if (elif) and else conditional algorithm)

17 patients values can be erased :



Treated value plotting

Data are reduced but this is just the first step, because plotting Patient by patient can show that interpolating data has also put error in certain case :



2 figures showing interpolation error : physiologically impossible curve

Patient ID on the top, colours and cross meaningless

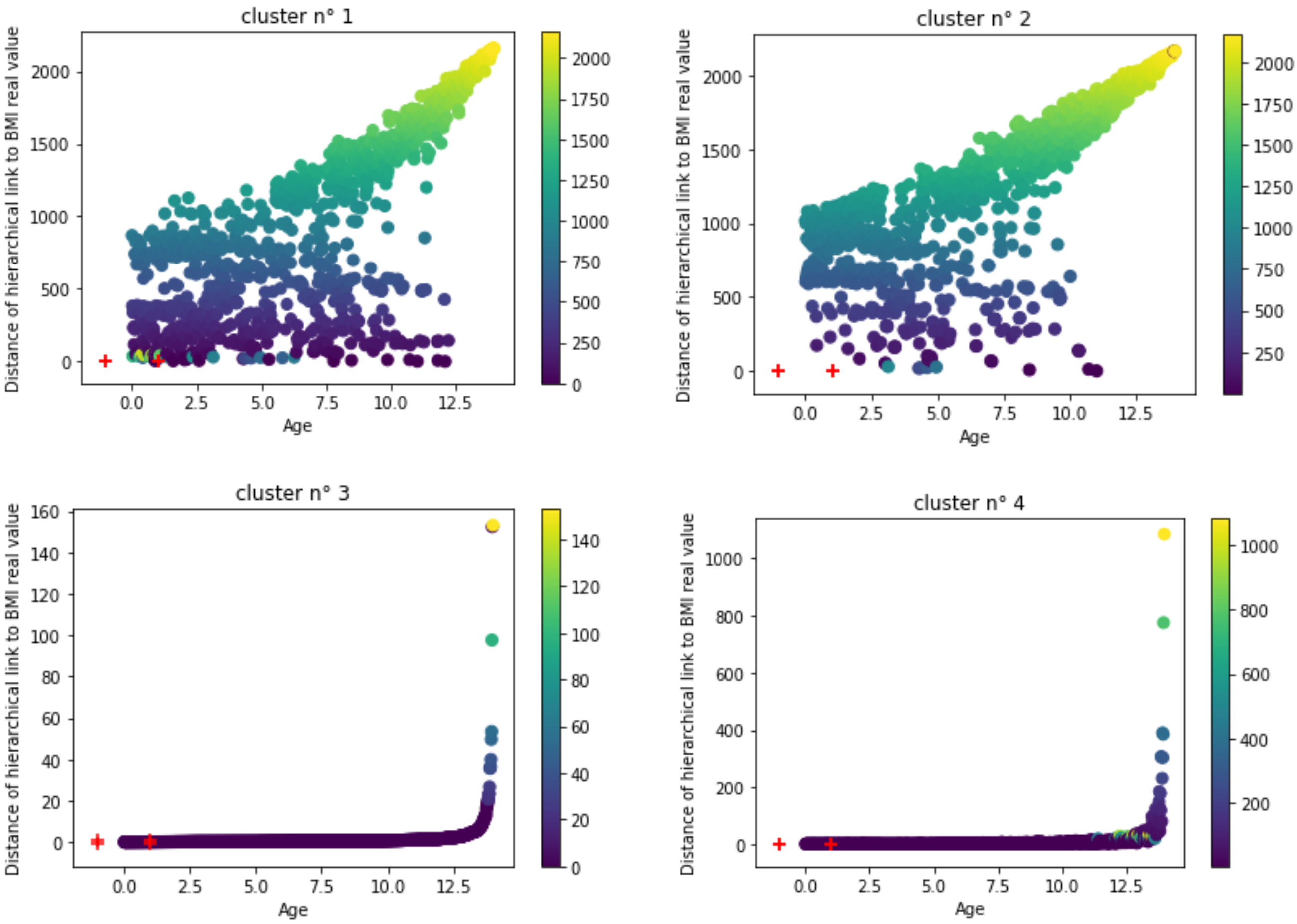
Number of values per patient : 74, 15 without interpolation

I was first thinking that it was created by the missing values, but this kind of curves stay after erasing curves having missing data (SQL query), so it is more a measurement problem at very little age : 0 to 6 years old

So the conclusion is that we cannot have few variances before 6 years old. We need to deal with it. This conclusion has also been find after hierarchical clustering.

Uncertain methods :

<u>Hierarchical clustering: tested, working, but not so robust.</u>



As we can see on the four figures, there is two non-satisfying cluster in our dataset: we have a huge error rate which grow up to 2 000 for cluster 1 and 2, against few error and maximum 1000 for only Two link for cluster 4 and 3.

It stay the same even after filtering, so It confirm that variance is not due to missing values but to the difficulty of measurement before 6 years old.

If we still have huge error rate, then we will conclude that agglomerative give just 2 acceptable cluster: risk of obesity and normal development.

Latent Dirichlet (Gaussian) Mixture and Esperance maximisation

As explained before, the variances is to huge before 6 years old for finding a likelihood, This method cannot be apply in consequences because it is all about separating 2 melting normal distribution.

Feed back after meeting with the Departement which launch the project (Dismiss):

My meeting and oral presentation have been dismiss due to natural diseases in the country.

Professor had finally no schedule for this study, I think this is better to speak to statistician in Shikata campus. To see what they think about the actual conclusion, and what they want to apply Next.

Many correcting measure can be proposed :

*Not beginning to enter values when it miss more than 3.
*Watch BMI curves individually to see if this is an outlier case or not.
*Compare to the World health organisation set of values to see if the standard is evolving at the country scale.
*Propose a web-site at the parent to involve them more in the study. (Python 3 is compatible to web-services) or a smartphone application.

Conclusion:

What need to be improve? What seems a good way? What should we forget about?

The first issue for clustering analysis here is, for me, the quality of the database: Data integrity and error existence. The next step is to decide a lower threshold and an upper threshold with the medical staff.

The original file ("H28sample_original.xlsx") is full of outliers: impossible values according to physiological existing values in Japan country (according to World Health Organisation base pattern, build with large scale data median).
It could be due to human or measurement machine error.

If decreasing and waving curves (see page 13) disappear, it will maybe more robust data we can use for clustering.

If we set up an SQL database, it become possible to restrict data entrance and to select particular information with Query. So it is better in my mind.

But I actually don't know if doctors want to change their way of filling in the data-base, they maybe don't have time for data formatting in Access tables.
Otherwise we can continue as I make, filtering with python and delete with Access when there is many missing values.
But we need to pay attention of the number of deleted values.

When the variance will be fully erase, maybe clustering methods will perfectly match for more than two cluster. Supervised or not.

Weight of daily habits can be measure after setting groups, by SQL query for separate by group: obese, normal, over/under-weighted and compare the BMI = f(Age) median and mean curves.
I unfortunately don't had time to do it after having the idea, because I had only two group with hierarchical and it was not so satisfying, It's better to have more cluster before.

Discussion :

An other main issue in my mind is that, even if we manage to reduce variance and meaningless data entrance, we will still have a last problem: Japanese population 70 % normal weighted.

Obesity just take +0.1% approximately in 50 years in this country, it's now 3%.
So, the obesity population is not enough a large scale one. Not enough robust in a 1083 patient data-base.

Maybe we also need others country data-base to set comparison for using this kind of clustering methods. It could also show the variability between observations and give a world alert epidemiology standard method.

Source : World health organisation website database :

Hi, here is the database about BMI : Map visualisation :
http://apps.who.int/bmi/index.jsp (you can change between obesity, normal, under etc.... and compare)

Unfortunately there is no values for child, just indicator :

http://www.who.int/growthref/who2007_bmi_for_age/en/

But it can be interesting to make comparison between countries :

http://apps.who.int/bmi/index.jsp: Japan : 70% population in the normal interval

http://apps.who.int/bmi/index.jsp : United states : 30 % normal, 30% obese but 10 % in the 19th century

http://apps.who.int/bmi/index.jsp : France : 50 % normal, 50 % overweighted

http://apps.who.int/bmi/index.jsp : India : 15% severe thiness, 30 % underweighted, 60 % normal

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