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SmartCow project

Ethics in experiments on animals

Adjustment of animal numbers in experimentation

Question : Why is this important?

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Tuesday September 22, 2020

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"Classical" statistical theory for using a test :

the initial framework of this presentation …

1 - as part of a one-sided hypothesis test:

H_0 : « $\mu_1 \leq \mu_0$ » *versus* H_1 : « $\mu_1 > \mu_0$ »

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for the user, in this presentation the hypothesis « H_1 » is the hypothesis of interest

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the user therefore wants to highlight a difference in means: « delta = μ_1 - μ_0 »

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the initial framework of this presentation …

2 - for a random variable of interest « Y » which follows a Gaussian distribution with standard deviation « σ_Y »

using a statistic of test: « T »
whose law (distribution) is known under H_0

and whose value is « T_{obs} » after the measurement results of a sample size « N »

example statistic « T »: the empirical mean

$$\overline{Y_N} = \frac{1}{N} . \sum_{i=1}^{i=N} Y_i$$

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the standard deviation « σ_Y » is the precision of the studied variable « Y »

this precision « σ_Y » is important given that we want to be able to highlight a difference between two means « delta = µ1 - µ0 » with the variable « Y »

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an example is the student test statistic when « Y » follows a Gaussian distribution

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the initial framework of this presentation …

3 - after choosing:

a risk of error of the first kind: « $\alpha = 0.05$ »

⟺

a confidence coefficient for the Confidence Interval (CI): « $\Upsilon = 0.95$ »

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a particular value of the test statistic: « T_0 » under H_0

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↓

« $\alpha = 0.05$ » is the risk of error conventionally taken in practice

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4 - we are led to take a "*decision*" from the result « T_{obs} » obtained on the sample :

either: *« we cannot reject H_0 »* ***which means: « $T_{obs} \leq T_0$ » or « Pvalue ≥ α »***
either: *« we accept H_1 »* ***which means: « $T_{obs} > T_0$ » or « Pvalue < α »***

without knowing the « reality » …

	« reality » H_0	« reality » H_1
« decision » H_0	« ϒ = 0.95 »	?
« decision » H_1	« α = 0.05 »	?

α = error of the first kind "controlled *a priori*"

⟺

it is the user who chooses its value *a priori*

$\alpha = 1 - \gamma$

α is the probability of concluding that there is a difference when there is none *[“notion of false positive”]*

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« decision » H_1	« α = 0.05 »	?

$\alpha = 1 - \gamma$

α = error of the first kind "controlled *a priori*"

« α » and « γ » with the concept of confidence interval (CI) :

ϒ = « probability that the CI:] -∞, T_0] contains the observed value: T_{obs} under H_0 »

α = « probability that the CI:] -∞, T_0] no contains the observed value: T_{obs} under H_0 »

it is the notion of equivalence between doing a test or calculating a confidence interval

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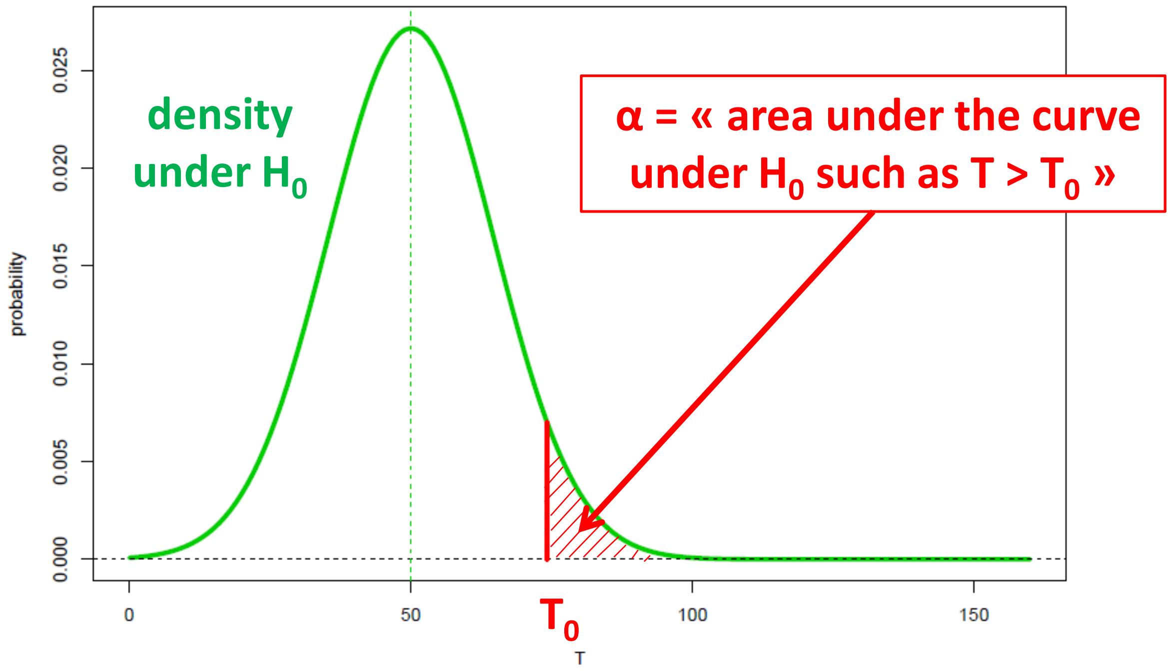
We can visualize this with the density distribution of "T" under H_0 with « N = 6 » and « σ_Y = 36 »

	« reality » H_0	« reality » H_1
« decision » H_0	« ϒ = 0.95 »	?
« decision » H_1	« α = 0.05 »	?



we are led to take a "*decision*" from the result « T_{obs} » obtained on the sample :

if « $T_{obs} \leq T_0$ »
or « Pvalue ≥ α »
« we cannot reject H_0 »
H_0 : « $\mu_1 \leq \mu_0$ »

if « $T_{obs} > T_0$ »
or « Pvalue < α »
« we accept H_1 »
H_1 : « $\mu_1 > \mu_0$ »

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therefore, it is classically the user who chooses a priori:

- ✓ **the hypotheses to be tested: H_0 : « $\mu_1 \leq \mu_0$ » versus H_1 : « $\mu_1 > \mu_0$ »**
- ✓ **the test and therefore the test statistic “T” under H_0**
- ✓ **a sample size « N »**
- ✓ **a risk of error of the first kind: « $\alpha = 0.05$ », therefore the confidence coefficient « $\gamma = 1 - \alpha$ » and therefore a particular value of the test statistic: « T_0 » under H_0.**

from the observation « T_{obs} » obtained on the sample the user has his result

Ok, but where is the problem ?

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Ok, but where is the problem ?

The problem is that you have to define the "sensitivity" of a test, that is, its ability to identify a difference when it exists.

Note: We have the same problem when we take a measurement with a device. We try to know its sensitivity before using it.

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5 – on the other hand, we have "no" a priori information on "reality" under H_1 , while we also have a possible error (called « β »), *either that of « deciding H_0 » while the « reality is H_1 »*.

?

	« reality » H_0	« reality » H_1
« decision » H_0	« ϒ = 0.95 »	« β » ?
« decision » H_1	« α = 0.05 »	« 1 – β » ?

β = second kind error "not known *a priori*"
because in general we do not know
the distribution of T under H_1
and because we do not know the value of « μ_1 »

1 - β = power of the test
= « ability of the test to detect
a difference when it exists »

β is the probability of concluding that there is no difference when there is one *[“notion of false negative”]*

The « power of the test » is ultimately the "sensitivity" of the statistical test to be able to "detect" a difference.

It is important that the power of the test is as great as possible

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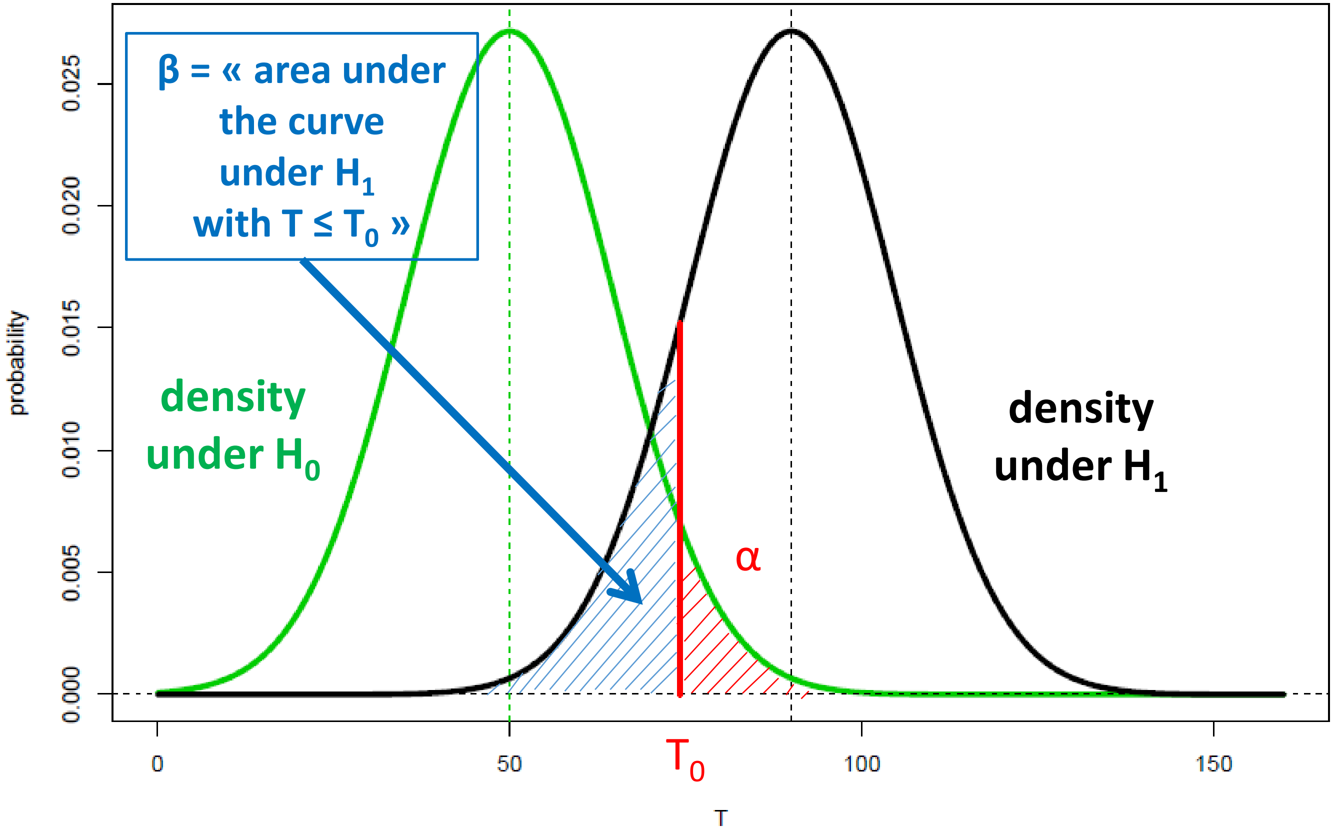
example of density distribution of statistical « T » under H_0 and under H_1

with: delta = $\mu_1 - \mu_0$

with N = 6 and σ_Y = 36

if delta = 40 → *then « β » can be estimated*



If "delta" is fixed, then we can estimate "β" and also plot the distribution under H_1.

	« reality » H_0	« reality » H_1
« decision » H_0	« ϒ = 0.95 »	*« β ≈ 0.14 »*
« decision » H_1	« α = 0.05 »	*« 1 – β ≈ 0.86 »*

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example of density distribution of statistical « T » under H_0 and under H_1

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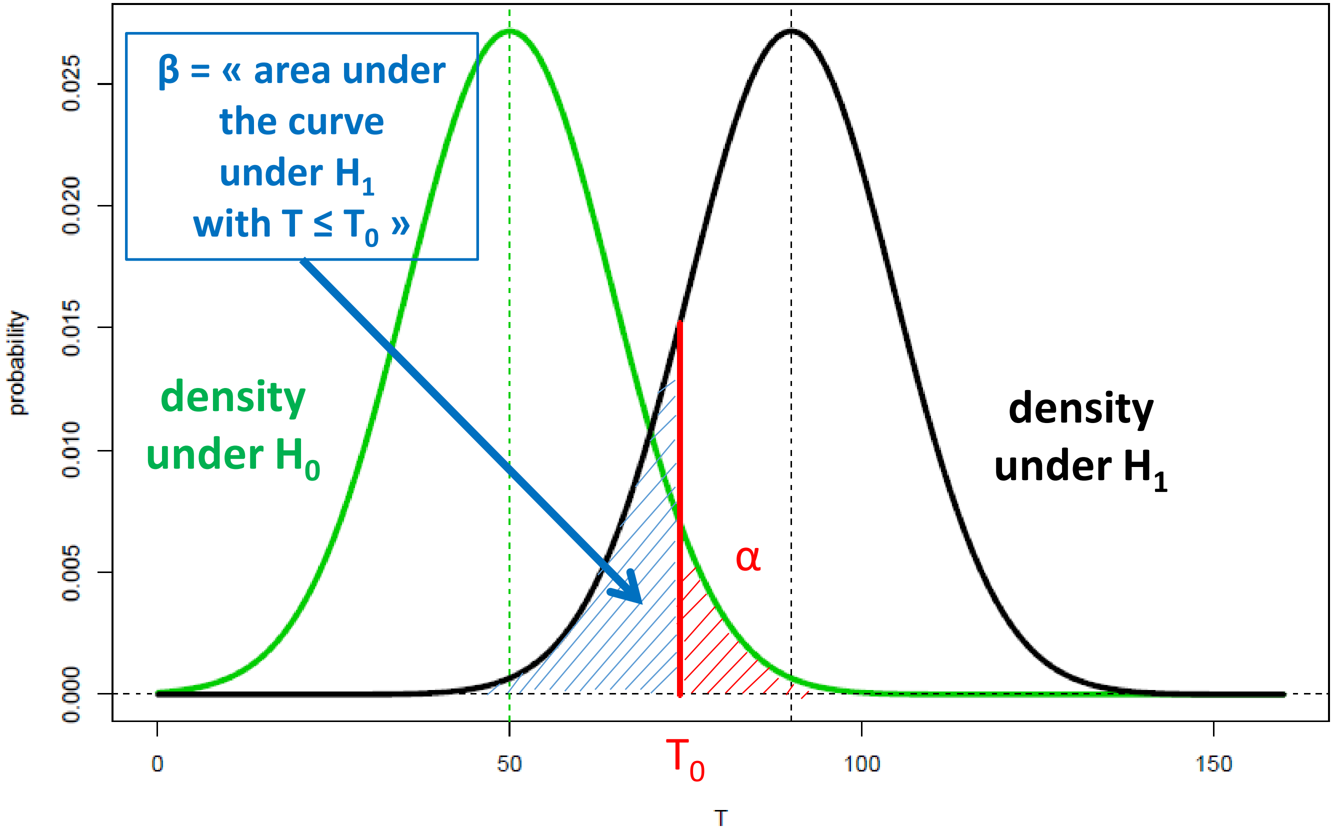

if the parameters: « α », « delta », « N » and « σ_Y » are fixed a priori, then we can estimate « β », « 1-β » and also plot the distribution under H1.

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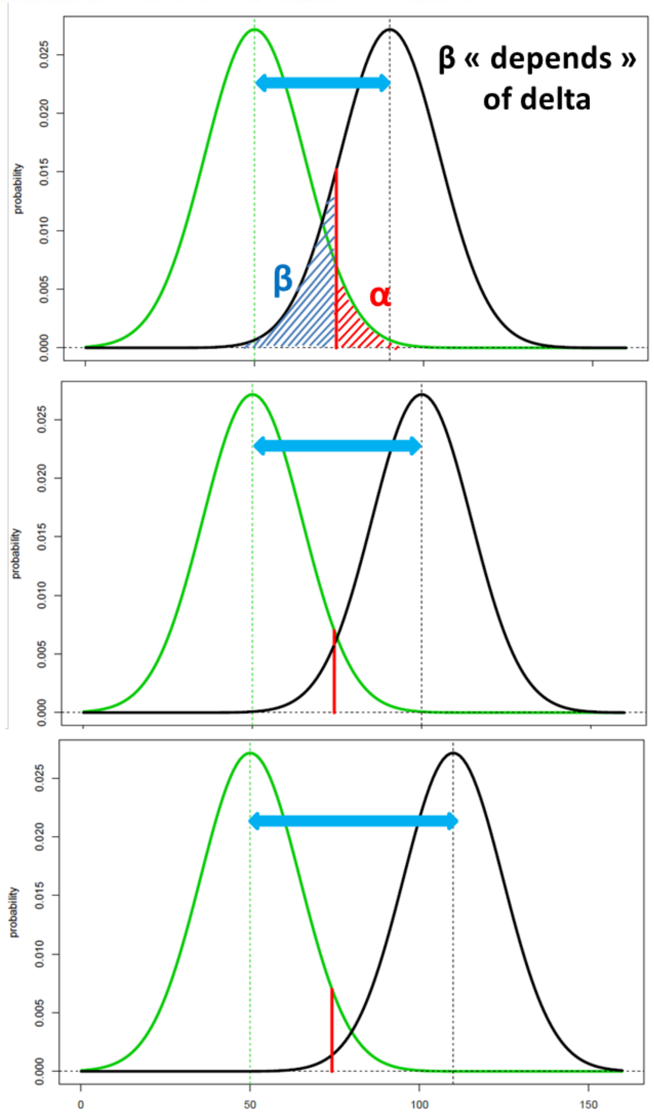
with delta = $\mu_1 - \mu_0$ and $\sigma_Y = 36$



if delta = 40 — *with N = 6*

	« reality » H_0	« reality » H_1
H_0	« ϒ = 0.95 »	*« β ≈ 0.14 »*
H_1	« α = 0.05 »	*« 1 – β ≈ 0.86 »*

if delta = 50 — *with N = 6*

	« reality » H_0	« reality » H_1
H_0	« ϒ = 0.95 »	*« β ≈ 0.04 »*
H_1	« α = 0.05 »	*« 1 – β ≈ 0.96 »*

if delta = 60 — *with N = 6*

	« reality » H_0	« reality » H_1
H_0	« ϒ = 0.95 »	*« β ≈ 0.01 »*
H_1	« α = 0.05 »	*« 1 – β ≈ 0.99 »*

For a fixed sample size “N”,
as "delta" increases,

the second kind error "β" decreases
and
the power of the test”1-β” increases

If we want a power of the test at least 0.99,
with a sample size “N = 6”,
we can only identify that
a difference in means “delta” greater than 60.

But we want to be able to identify a difference in averages of the order of 40. How do we do this?

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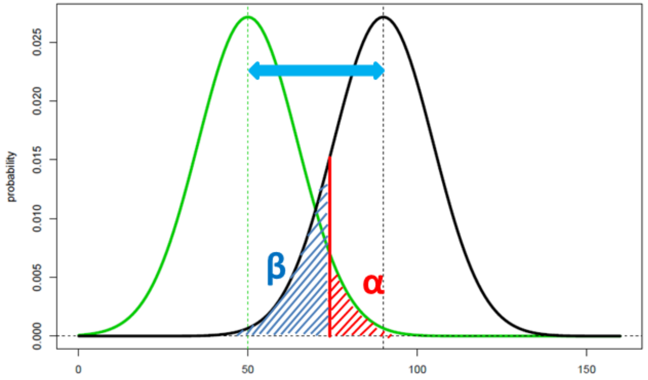
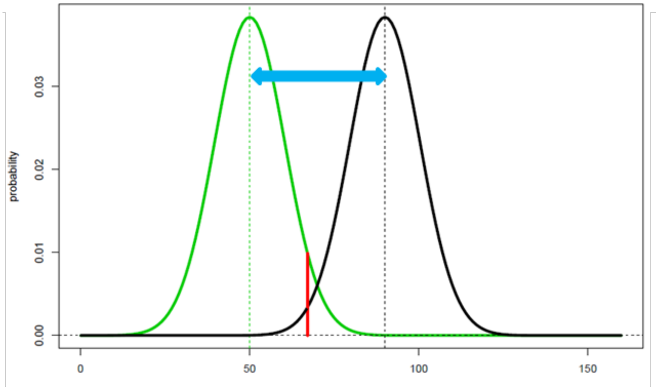
so if we want to keep a good ability to detect a « *given difference* », and so if we want to have a « *minimum sensitivity a priori* », we have two main complementary solutions:

with a « minimum delta » of 40



with N = 6

	« reality » H_0	« reality » H_1
H_0	« ϒ = 0.95 »	***« β ≈ 0.141 »***
H_1	**« α = 0.05 »**	***« 1 – β ≈ 0.859 »***



with N = 12

	« reality » H_0	« reality » H_1
H_0	« ϒ = 0.95 »	***« β ≈ 0.014 »***
H_1	**« α = 0.05 »**	***« 1 – β ≈ 0.986 »***

1st solution :
we « increase »
the size « N » of the sample

$$Var(\bar{Y}) = \frac{1}{N}.Var(Y) = \frac{1}{N}.\sigma_Y{}^2$$

For a fixed "minimum delta"
as sample size "N" increases,
the second kind error "β" decreases
and
the power of the test"1-β" increases

If we want a power of the test at least 0.986,
and
identify a difference in means "delta = 40",
We just need to take a sample size "N = 12".

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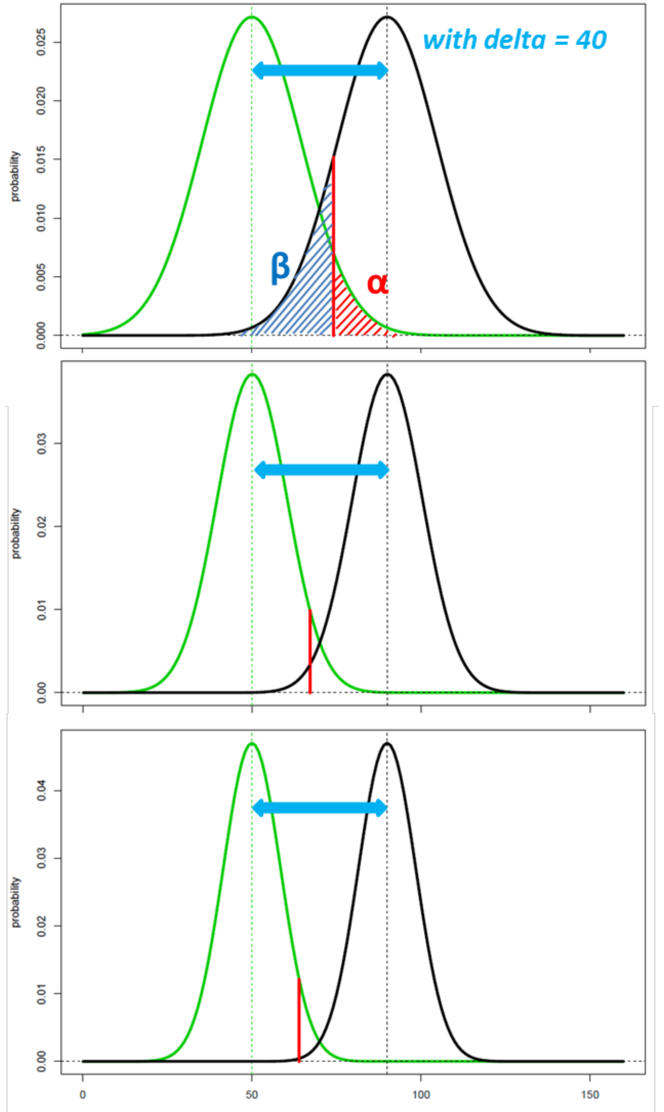

with N = 6

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with N = 18

	« reality » H_0	« reality » H_1
H_0	« ϒ = 0.95 »	« β ≈ 0.001 »
H_1	« α = 0.05 »	« 1 – β ≈ 0.999»

**For a fixed "minimum delta"
as sample size "N" increases,
the second kind error "β" decreases
and
the power of the test"1-β" increases**

$$Var(\bar{Y}) = \frac{1}{N}.Var(Y) = \frac{1}{N}.\sigma_Y{}^2$$

**In fact, the decrease in "β"
and the increase in the power of the test "1-β"
are very rapid [in (1/N)],
as the sample size "N" increases.**

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formula for N_{min}

u_p is the quantile of probability "**p**" for the Gaussian distribution *N*(0,1).

for $\alpha = 0.05$ we have **$u_{1-\alpha} = 1.644854$**

and for $\beta = 0.01$ or $(1-\beta) = 0.99$ we have **$u_\beta = -2.326348$**

The minimum « N » size allowing the desired « precision », ie « $(1-\beta) \geq 0.99$ » is such that :

$$N \geq \left[\frac{\sigma_Y \, . \left(u_{1-\alpha} - u_\beta\right)}{delta}\right]^2$$

with « delta = $\mu_1 - \mu_0$ » for the minimum detectable deviation sought
and « σ_Y » for the standard deviation of the Gaussian law of the studied and measured variable Y.

For the previous example we had « delta = 40 » and « σ_Y = 36 »
which gives « $N \geq 12.77406$ » or « $N_{min} = 13$ » for a power « $(1-\beta) \geq 0.99$ ».

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The minimum « N » size allowing the desired « precision », ie « (1-β) ≥ 0.99 » is such that :

$$N \geq \left[\frac{\sigma_Y \,.\, (u_{1-\alpha} - u_\beta)}{delta}\right]^2$$

the parameters :
« α », « β », « N », « delta » and « σ_Y »
are well linked.

with « delta = μ_1 - μ_0 » for the minimum detectable deviation sought
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$$N \geq \left[\frac{\sigma_Y \cdot (u_{1-\alpha} - u_\beta)}{delta}\right]^2$$

with « delta = $\mu_1 - \mu_0$ » for the minimum detectable deviation sought
and « σ_Y » for the standard deviation of the Gaussian law of the studied and measured variable Y.

Note : as long as « delta > σ_Y » the minimum number will remain « reasonable ».
On the other hand in the opposite case, the minimum workforce may quickly « explode »
because we will be in the case where we are looking
for a « sensitivity » lower than the « measurement accuracy ».

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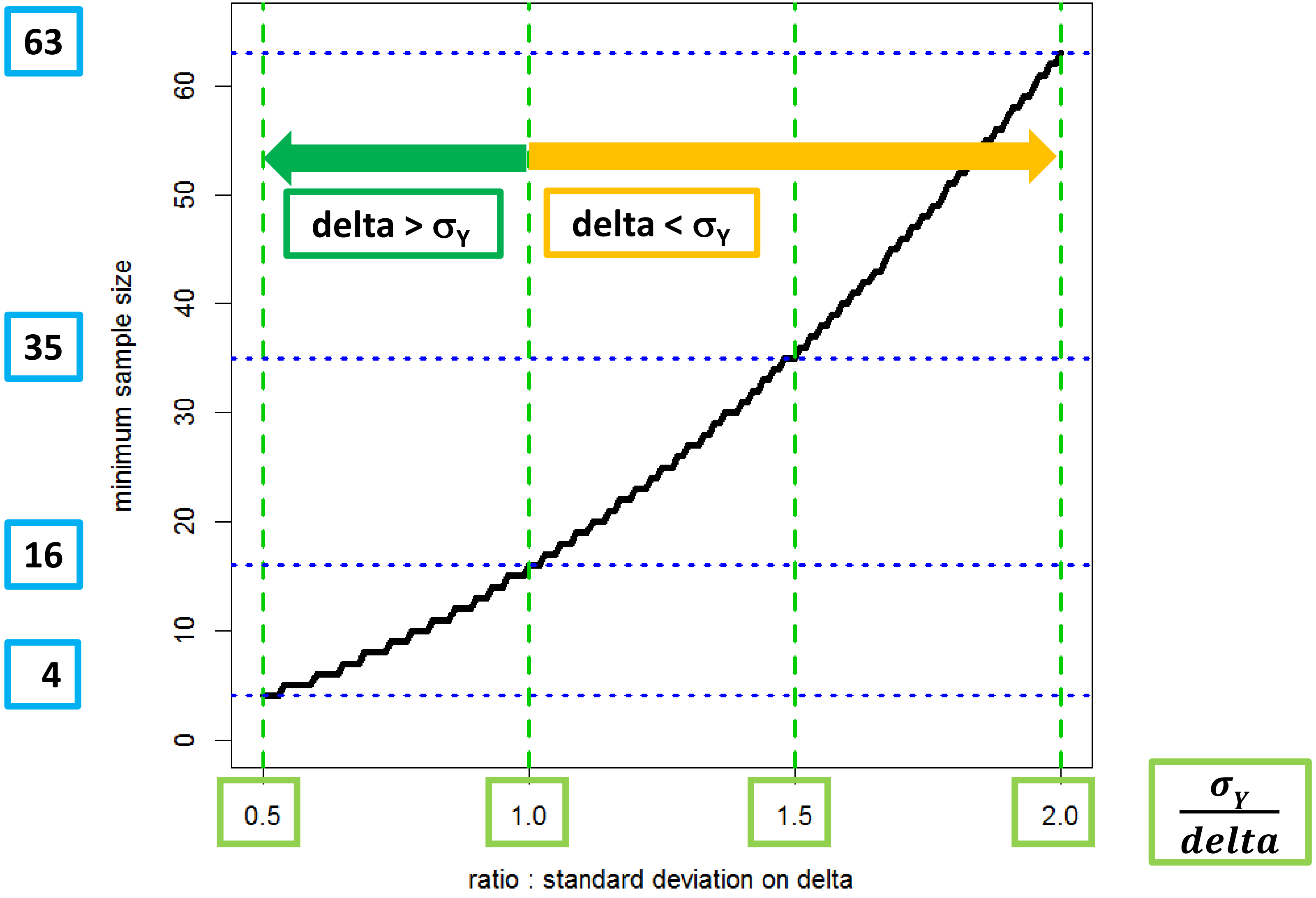
$$N \geq \left[\frac{\sigma_Y \, . \left(u_{1-\alpha} - u_{\beta}\right)}{delta}\right]^2$$

for $\alpha = 0.05$
and for $\beta = 0.01$ or $(1-\beta) = 0.99$

N_{min}



« N_{min} » depends on the ratio « σ_Y / delta »

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$$N \geq \left[\frac{\sigma_Y \,.\, (u_{1-\alpha} - u_\beta)}{delta}\right]^2$$

for α = 0.05
and for β = 0.01 or (1-β) = 0.99

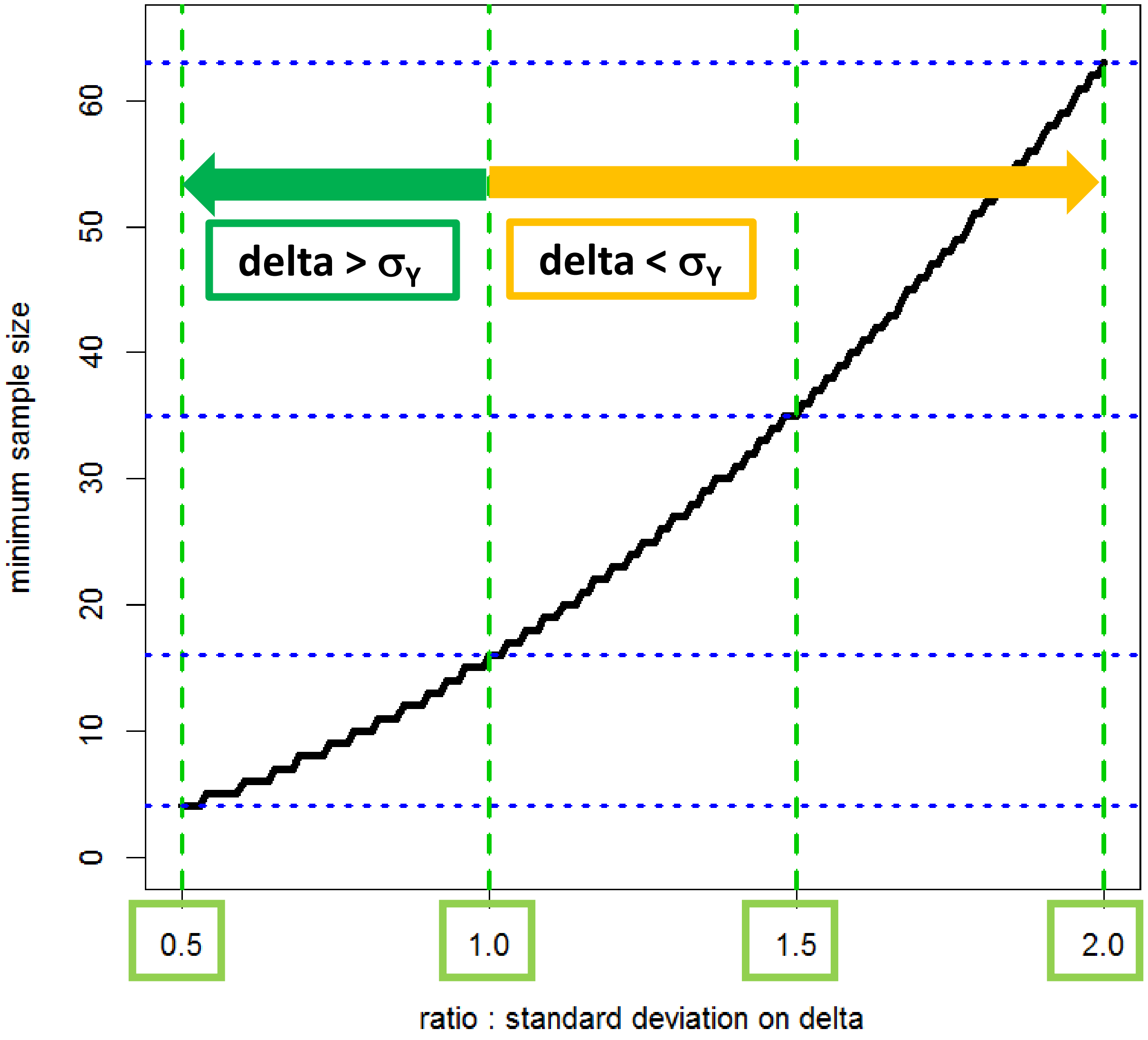
for a given sample size N a priori we can "correctly" identify a difference of at least

$$delta \geq \frac{\sigma_Y . (u_{1-\alpha} - u_\beta)}{\sqrt{N}}$$

for example, with N = 6 we have delta ≥ 1.6 σ_Y or (σ_Y / delta) ≤ 0.62

N_{min}

63
35
16
4



$$\frac{\sigma_Y}{delta}$$

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so with the 1st solution:

when we "increase" the size "N" of the sample
the variance of the estimator "decreases"
the risk of error β "decreases"
and the power of the test "increases".

$$Var(\bar{Y}) = \frac{1}{N}.Var(Y) = \frac{1}{N}.\sigma_Y{}^2$$

therefore by choosing "N" according to the "minimum difference" (or "delta")
that we want to be able to highlight *a priori*,
we "select" *a priori* the "power of the test" that we want,
and therefore the "expected sensitivity" of the test is thus determined.

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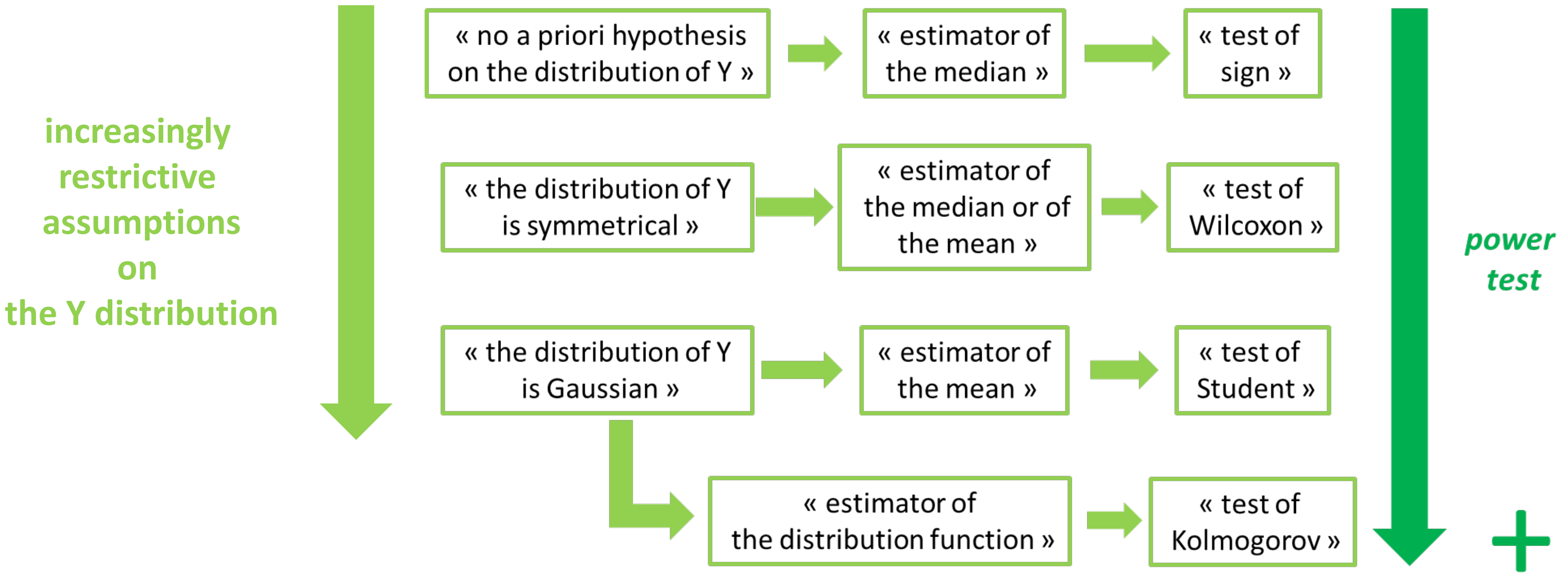
2nd complementary solution: choose the most suitable test to the assumptions that can be made a priori on the distribution of the measured variable "Y".

for the same value of "delta" a priori, and the same sample size "N" a priori



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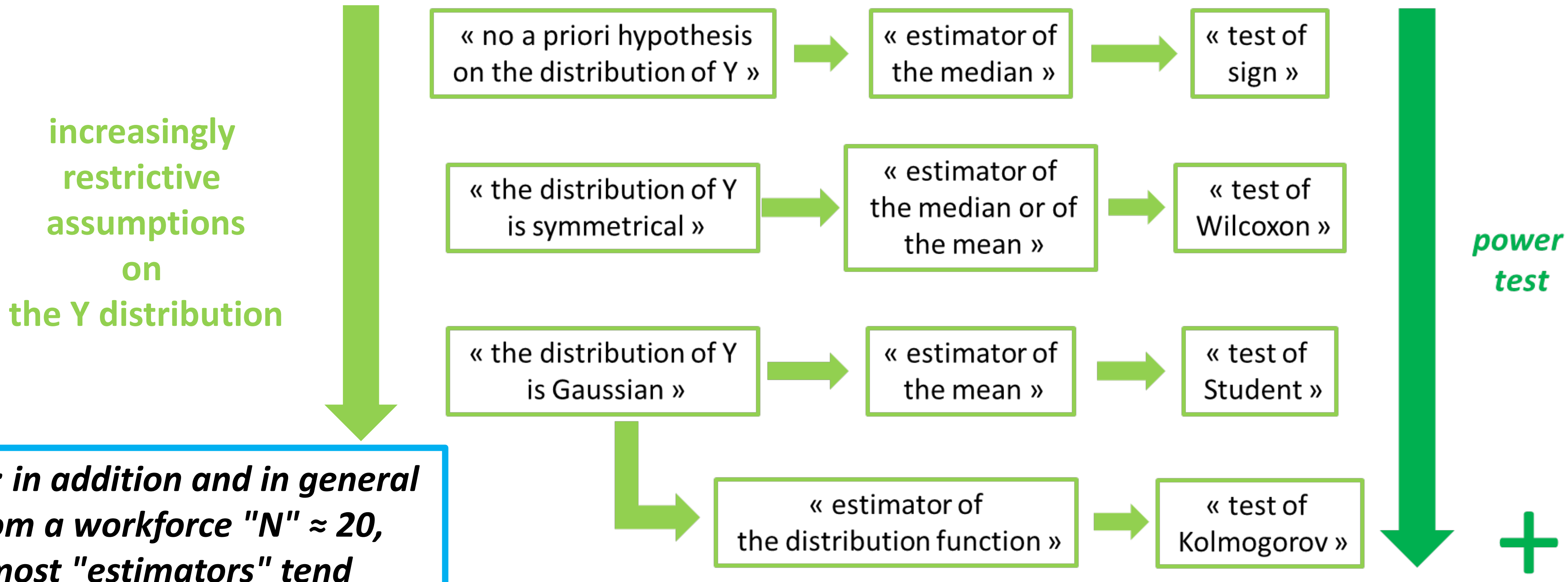
for the same value of “delta” a priori, and the same sample size “N” a priori



Note: in addition and in general from a workforce "N" ≈ 20, most "estimators" tend to a Gaussian distribution.

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in conclusion

Question: Why is this important?

Answer: choose the size of the sample N a priori
allows to "calibrate" a priori
the "desired sensitivity" of the statistical test to be used
taking into account a priori knowledge such as a minimum standard deviation σ_Y.

the smaller σ_Y
the smaller the sample size N required

“a statistician is not a magician”

Thank you for your attention.