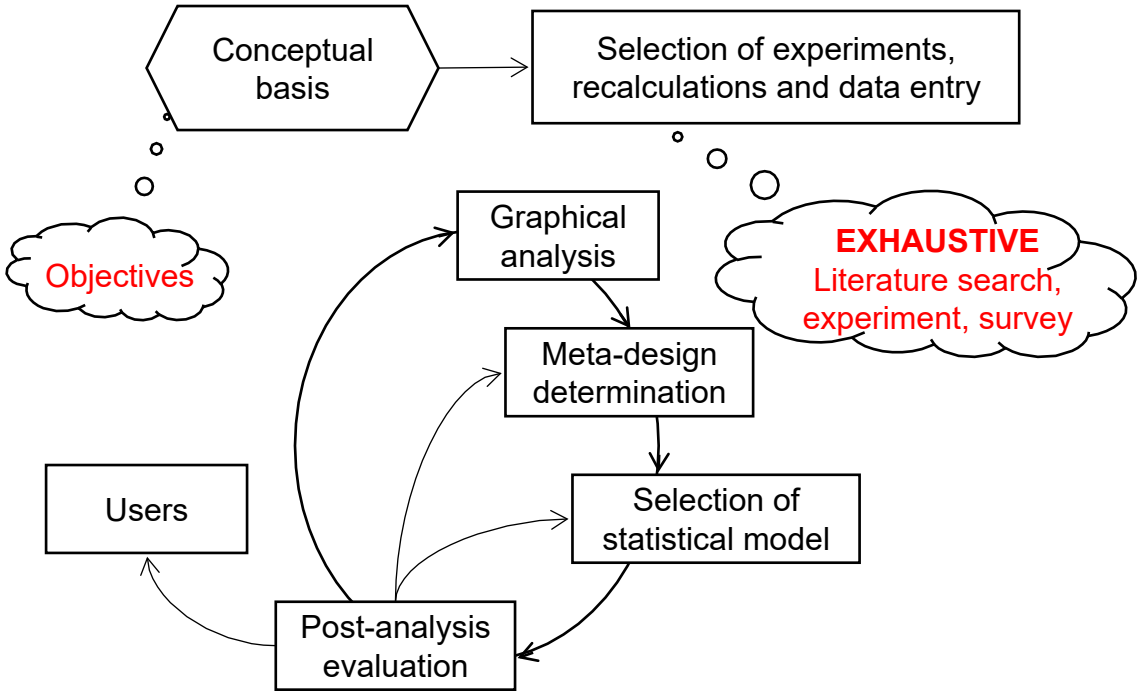
META-ANALYSIS IN ANIMAL SCIENCE: A VALUABLE TOOL TO GENERATE NEW KNOWLEDGE FROM PREVIOUS EXPERIMENTS

MP Létourneau-Montminy, C Loncke, JB Daniel, M Boval, P Schmidely, D Sauvant

Laboratoire International Associé

Nutri-Mod



To Daniel, who was much more than our PhD director…

> Context

- Analytical methods and response criteria measured are increasing phenomenally.
- Scientists facing more and more information
- Research users need the most accurate quantitative information possible to improve system efficiency and performance

Results → knowledge

Nutri-Mod

UNIVERSITÉ LAVAL INRAE AgroParisTech

> Context

- Meta-analysis has proven to be efficient to create new knowledge based on already published data through empirical models, allowing progress in
  - understanding,
  - highlighting research effort and lack of information
  - obtain improve prediction.

- It’s a useful tool to analyze sets of heterogeneous data that gain popularity in animal science since the 2000s with an increase of 15%/ year of published meta-analysis

Nutri-Mod

UNIVERSITÉ LAVAL INRAE AgroParisTech

> Context

- Throughout the years, the methodology of meta-analysis previously developed in medicine, have been perfectioned in animal science and described in 3 important papers of Sauvant and colleagues

1. **St-Pierre NR (2001)** Invited review: integrating quantitative findings from multiple studies using mixed model methodology. Journal of Dairy Science 84, 741–755.

2. **Sauvant et al. (2008)** Meta-analyses of experimental data in animal nutrition. Animal

3. **Sauvant et al. (2020)** Review: Use and misuse of meta-analysis in Animal Science. Animal

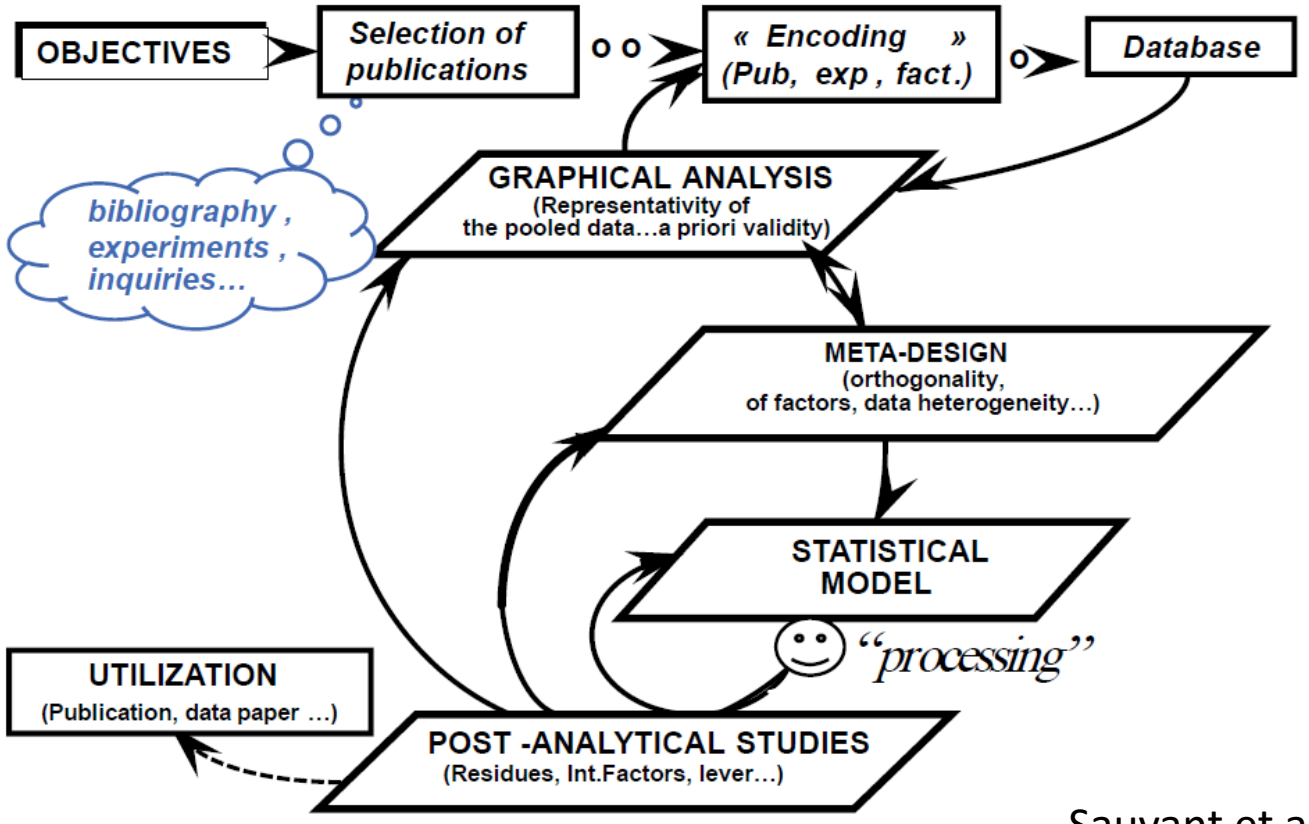
> Objectives

The later review of Sauvant et al. (2020) aims at highlighting not only the strengths, but also the potential pitfalls of meta-analyses in Animal Science which will be described briefly in this short talk by highlighting the most important elements to do quality meta-analysis.

Nutri-Mod

UNIVERSITÉ LAVAL INRAE AgroParisTech

> Methodology



(1) The **completeness** of the collection of candidate publications

Sauvant et al. (2020)

Nutri-Mod

UNIVERSITÉ LAVAL INRAE AgroParisTech

> Methodology

(2) The **coding** of selected data to reflect original experimental design and isolate specific experimental factors

Objective: Group relevant treatments to study the factors of variation defined by the studied question.

Allows you to make subgroups necessary for analysis
e.g.: studies on phytase (code 1), xylanase (code 2) or the 2 (code 3)

Nutri-Mod

UNIVERSITÉ LAVAL INRAE AgroParisTech

> Methodology

(3) the study of the **meta-design**

- It refers to the database we build
- Such as its orthogonality, data heterogeneity, range of variation, etc.

It's the meta-design that dictates what we can do with the available data

Objective: study the levels of independence of factors and of the degree of data balance of the meta-design to ensure the validity of statistical processing and its limits

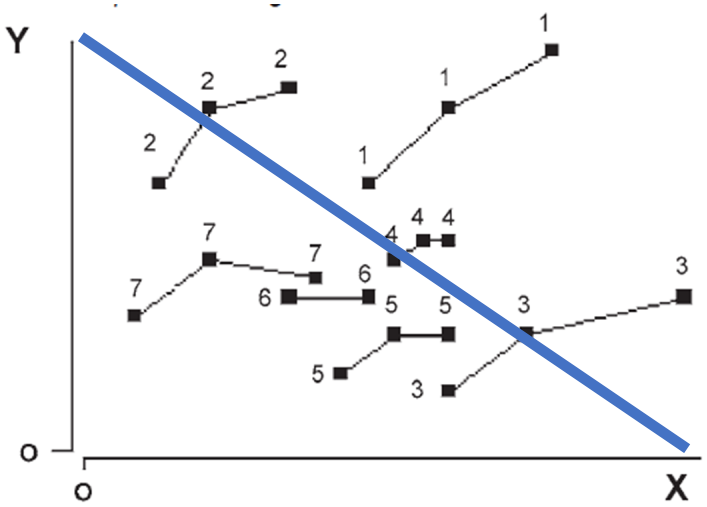
Nutri-Mod

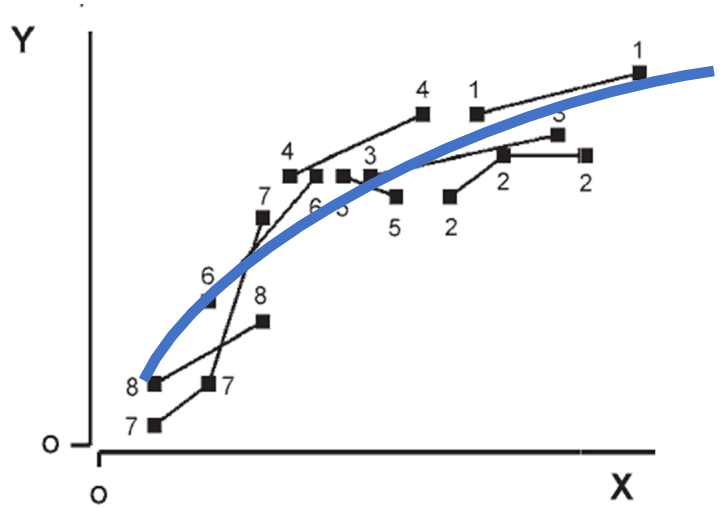
UNIVERSITÉ LAVAL INRAE AgroParisTech

> Methodology

(3) the study of the meta-design

Y as a function of X and relations INTER vs INTRA





One of the advantage of meta-analysis is to consider the INTRA experiment effect rather than just the INTER

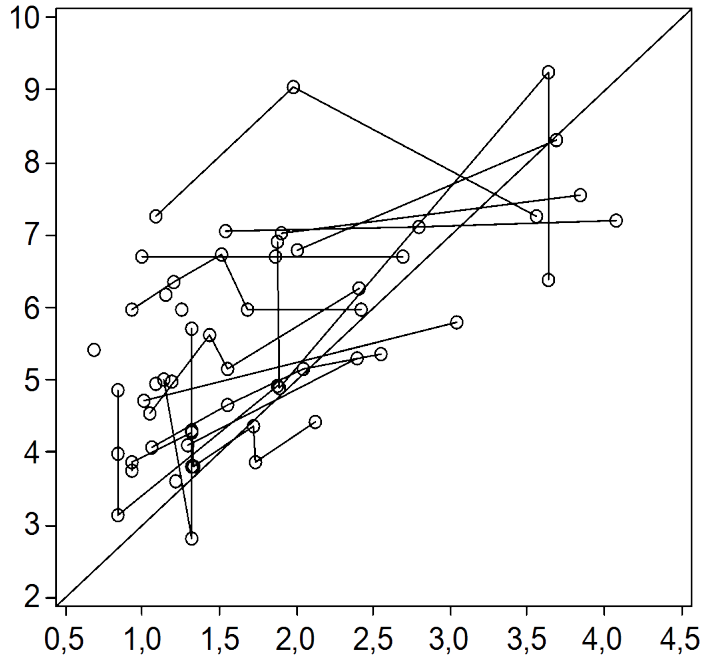
Nutri-Mod

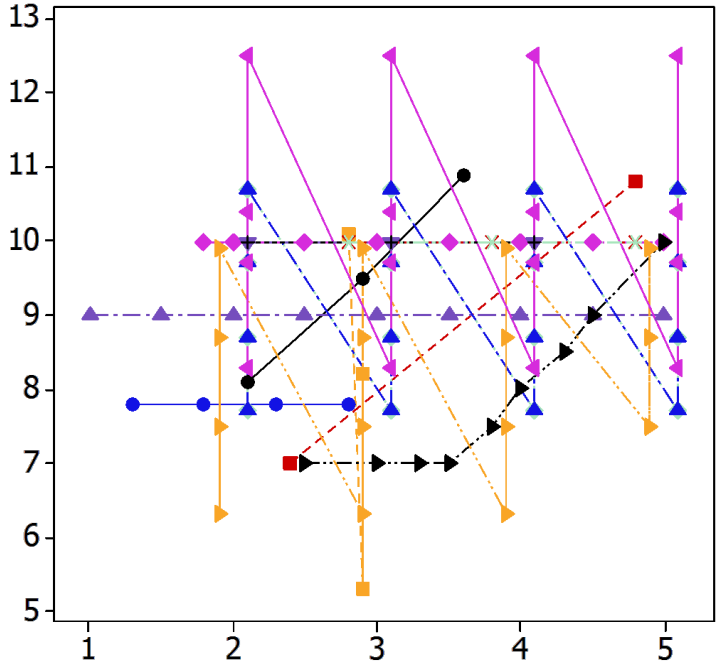
UNIVERSITÉ LAVAL INRAE AgroParisTech

> Methodology

(3) the study of the meta-design

Relation between X variables and the possibility of studying or not interactions





Nutri-Mod

UNIVERSITÉ LAVAL INRAE AgroParisTech

> Methodology

(4) **Rigor and traceability** of the analyse

- Well defined objectives, announced procedure (method)
- Anticipate approach for Statistical laws (outliers…)
- Analytic posture > global : Strategic and tactic procedure
- Exploration of alternative approach
- Justified choice at each step

<u>Traceable procedure and repeatable by others</u>

Nutri-Mod

UNIVERSITÉ LAVAL INRAE AgroParisTech

> Methodology

(4) **Rigor and traceability** : **Selection** of the studies used for an analyse

=> Importance to clearly expose the criterion of data selection

- Coherence with specification of the study (= minimal level of selection)
- Critical analyze of the selected work “by the expert” (internal coherence, errors…)

→ The reasons for withdrawing a study from the literature must be clearly **described and justified**

Objective : Other researcher must be able to obtain exactly the same results with the same data

Nutri-Mod

UNIVERSITÉ LAVAL INRAE AgroParisTech

> Methodology

(5) The **experiment effect (random or fixed)** in meta-analyses

The question : The treatment of heterogeneity between collected trials ?

Random effect ?

Each experiment is independent and considered as a sample of a wider population.
The differences between experiments are the result of random sampling variability (resulting from a lot of factors with low affect…)

➔ Need to follow a normal law (Gaussian distribution).

The aim is to control the variability of the factor
Experiment effect is more or less a "disagreement"

Nutri-Mod

UNIVERSITÉ LAVAL INRAE AgroParisTech

> Methodology

(5) The **nature of factors (random or fixed)** in meta-analyses

Fixed effect ?

- Each experiment (or group of exp) is considered as provided from a different population.
- No assumption on the statistical distribution of the experiment
- Homogeneity of objectives and designs not required (?)
- The modalities are defined by the community of researchers

The aim is to explain experiment effect …

Nutri-Mod

UNIVERSITÉ LAVAL INRAE AgroParisTech

> Methodology

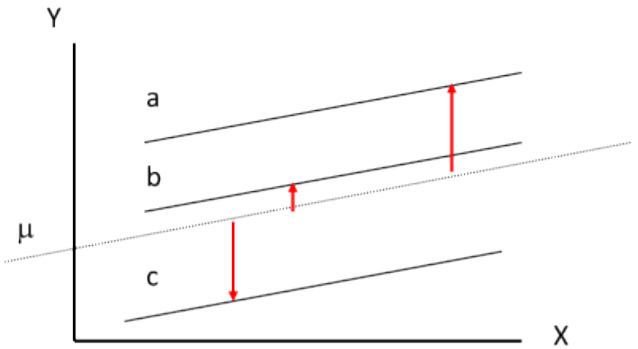
(5) The **nature of factors (random or fixed)** in meta-analyses

Implications ?

Treatments a, b et c

Fixed effect

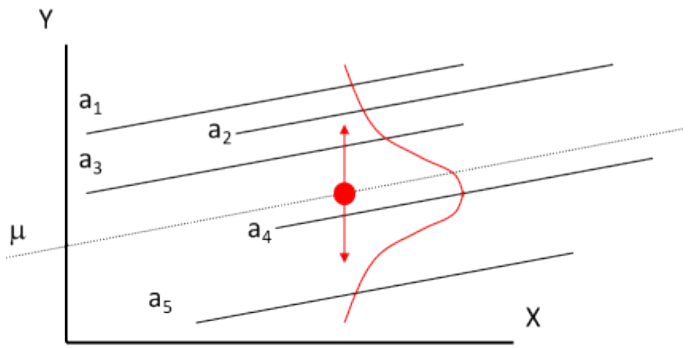
=> estimation and study **of deviation**

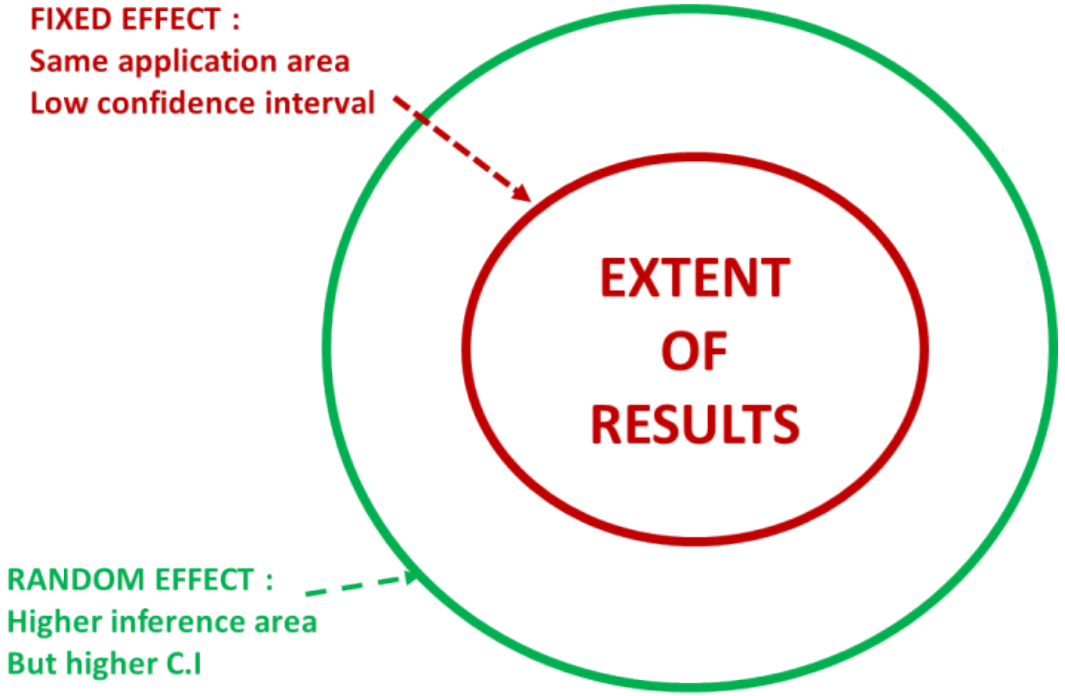


Animals a_1, a_2, …

Random effect

=> estimation of measure **of dispersion**





The choice of the model influences **inference area**

Nutri-Mod

UNIVERSITÉ LAVAL INRAE AgroParisTech

> Methodology

(6) Study of **interfering factors**

Definition: qualitative or quantitative factor, which may explain a significant part of studied variations

Why ?

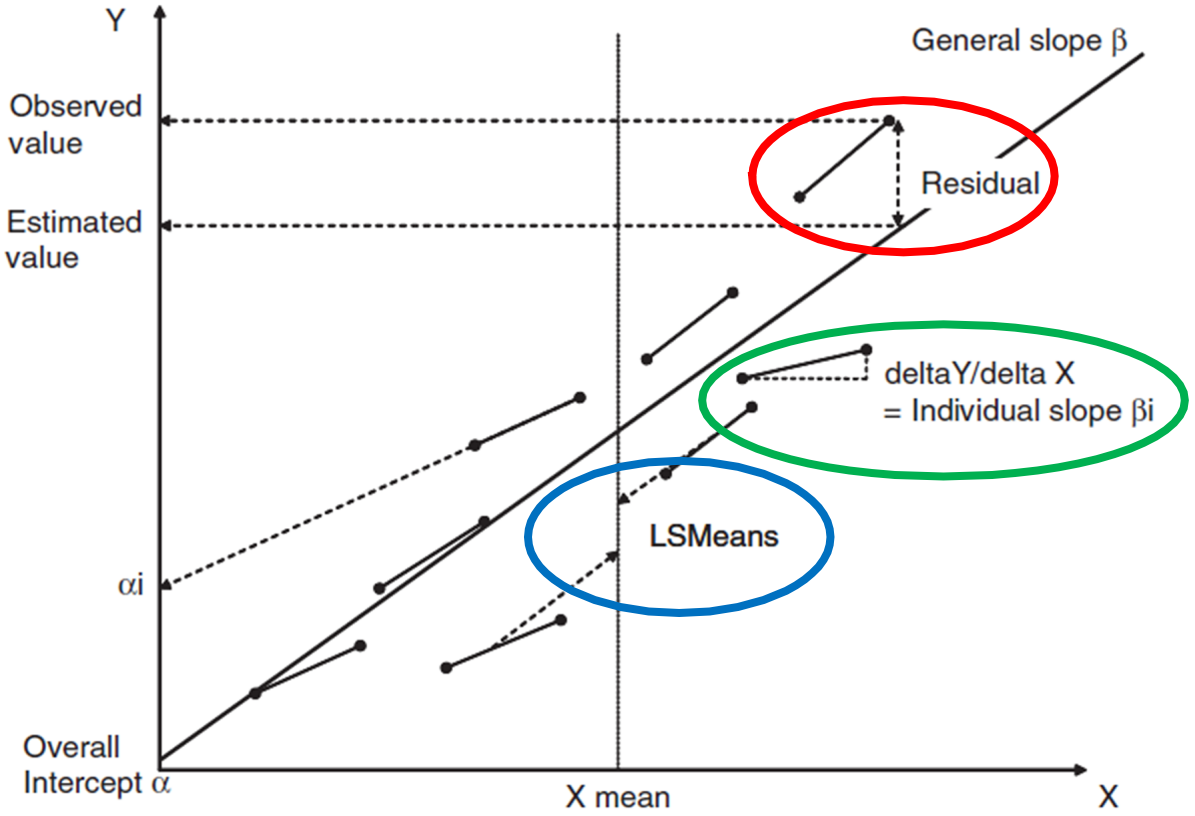
- Factor non necessary measured on all the data
- Factor with inter effect on a within-study effect

Nutri-Mod

UNIVERSITÉ LAVAL INRAE AgroParisTech

> Methodology

(6) Study of **interfering factors**



Loncke et al., 2015

Interfering factors : Three types

- On the residuals of the model
- On the within-study (individual) slopes
- On the LSMeans of the model

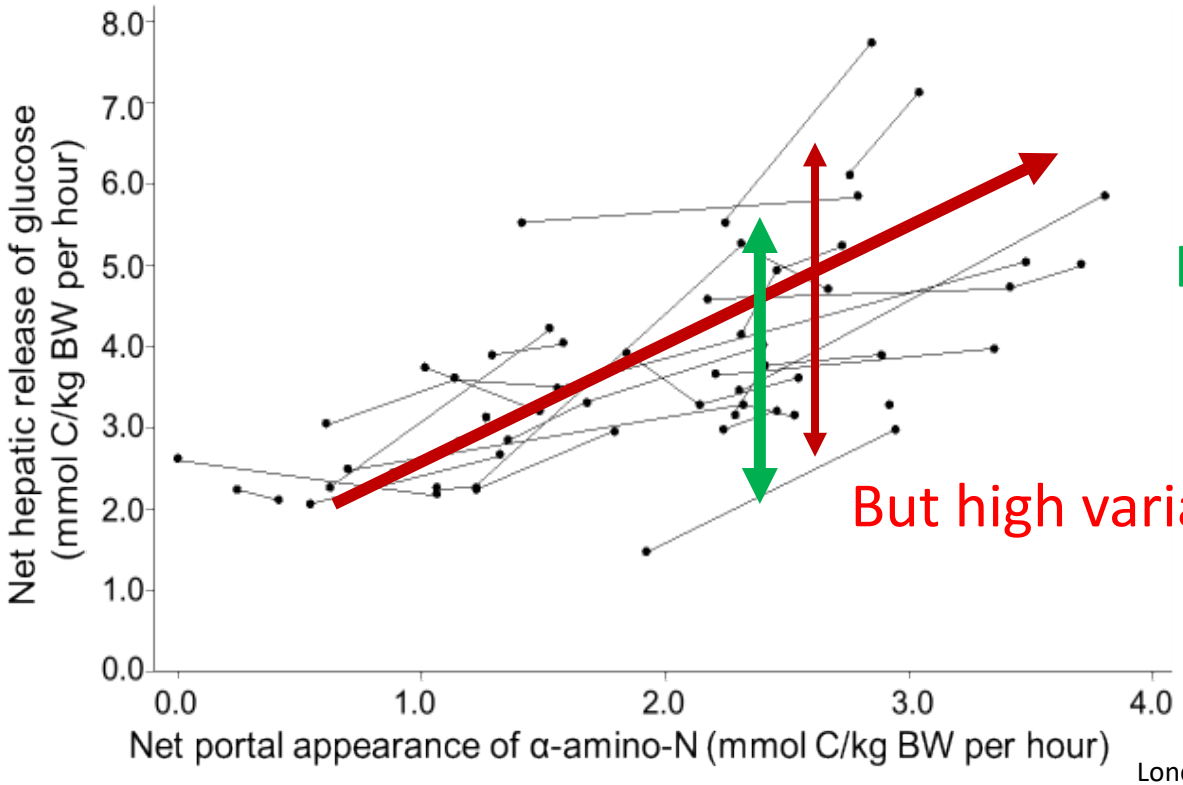
Nutri-Mod

UNIVERSITÉ LAVAL INRAE AgroParisTech

> Methodology

(6) Study of **interfering factors**

<u>Example</u>: The hepatic release of glucose can be predicted by the hepatic supply of AA



Loncke et al., 2020

Interfering Factor on LSMeans ?

But high variability for a same supply

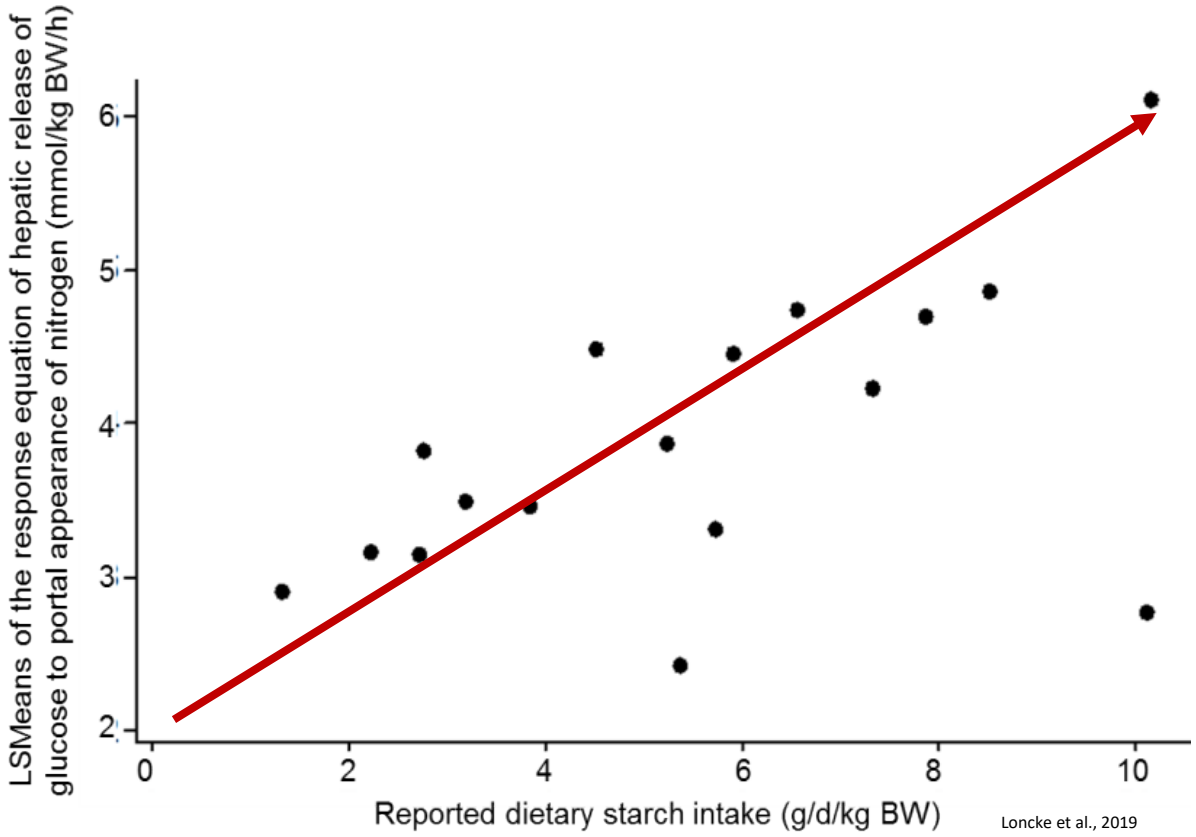
Nutri-Mod

UNIVERSITÉ LAVAL INRAE AgroParisTech

> Methodology

(6) Study of **interfering factors**

Example:



Loncke et al., 2019

When dietary starch increases => LSMeans increase

➡ Starch is an interfering factor on the LSMeans *(for a same supply of AA to the liver, net hepatic release of glucose increases when starch intake increases)*

Nutri-Mod

UNIVERSITÉ LAVAL INRAE AgroParisTech

> Methodology

(7) **Post analyses**

- Residual variability *(normality, structure…)*
- Studentized residues
- Leverage effects of observations
- “Contributions” of observations on the model
- Cook distances
- Try to explain experiment effect

Nutri-Mod

UNIVERSITÉ LAVAL INRAE AgroParisTech

> Conclusions

- The increasing number of publications using meta-analysis shows that it’s a widely accepted and applied method in Animal Science, especially in nutrition.

- The required levels of reporting and traceability evolve and are a concern for many journals for greater transparency and a better repeatability.

Nutri-Mod

UNIVERSITÉ LAVAL INRAE AgroParisTech

> Conclusions

Good practices in meta-analysis include:

- representativeness of the work with respect to the applications
- construction and the coding of the database
- study of the meta-design
- systematic analysis of interfering factors in situations where many candidate independent variables are available

Nutri-Mod

UNIVERSITÉ LAVAL INRAE AgroParisTech

> Futur trends

- More implications in other modern approaches such as systemic and mechanistic modeling.
- Usefulness in the development of precision livestock farming as well as in the processing of large and heterogeneous data sets?
- Interpret databases of individual laboratory?; Advantages and limits should be study.
- With the current moving towards a reduction/abolition of animal experimentation the meta-analysis will be useful to potentiate the data and identify the lack of information.

Nutri-Mod

UNIVERSITÉ LAVAL INRAE AgroParisTech

THANK YOU FOR YOUR ATTENTION

QUESTIONS ???

Laboratoire International Associé

Nutri-Mod

UNIVERSITÉ LAVAL INRAE AgroParisTech
Talents d'une planète soutenable