Italian Bayesian Day - Agenda

		Orario
Giovanna Jona Lasinio Sapienza Università di Roma	Saluto della Direttrice del Dipartimento di Scienze Statistiche	09.45 – 10.00
Stefania Gubbiotti, Fulvio De Santis, Luca Grassano, Marco Costantini	Introduzione alla giornata	10.00 – 10.20
Relatore	**Titolo presentazione**	
Stefania Gubbiotti Sapienza Università di Roma	Borrowing historical information using a dynamic power prior	10.20 – 10.50
Fabio Rigat Astra Zeneca	A Conservative Approach to Leveraging External Evidence for Effective Clinical Trial Design	10.50 – 11.20
Pausa Caffè		11.20 – 11.50
Sara Urru Università di Padova	Comparison of borrowing methods for the incorporation of historical data in a phase II clinical trial	11.50 – 12.20
Mauro Gasparini Politecnico di Torino	Bayesian Estimation of Vaccine Efficacy	12.20 – 12.50
Pranzo		12.50 – 14.00
Andrea Callegaro GSK	Vaccine clinical trials with dynamic borrowing of historical controls: Two retrospective studies	14.00 – 14.30
Stefano Vezzoli Chiesi Farmaceutici S.p.A.	Bayesian dynamic borrowing of adult efficacy data in a paediatric trial: a case study	14.30 – 15.00
Nina Deliu Sapienza Università di Roma	Enhancing Patient Outcomes and Statistical Efficiency in Rare Disease Trials: The Stratosphere Study	15.00 – 15.30
Q&A e chiusura		15.30 – 16.00

ABSTRACTS

Borrowing historical information using a dynamic power prior

Stefania Gubbiotti

In Non-inferiority trials historical information is often available on the control treatment, to be compared with a new experimental intervention. Methods for exploiting past information (if sufficiently homogeneous with current data) may be useful to increase precision and reduce costs. We propose a Bayesian method based on a dynamic power prior for the parameter of the control arm that dynamically regulates the degree of information-borrowing. An application to vaccine trials is illustrated. Pre-posterior analysis for type-I error/power assessment and for sample size determination is also discussed.

A conservative approach to leveraging external evidence for effective clinical trial design

Fabio Rigat

Prior probabilities of clinical hypotheses are not systematically quantified and used when planning clinical trials, mainly due to a concern that poor priors may lead to inadequate error rate control. To address this concern, a conservative approach to Bayesian trial design is illustrated here, requiring that the operational characteristics of the primary trial outcome are stronger than the prior. This approach is complementary to current Bayesian design methods, in that it insures against prior-data conflict by defining a sample size commensurate to a fixed design prior. This approach is also ethical, in that it requires quantification of the level of clinical equipoise at design stage and it ensures that the design is appropriate to disturb initial equipoise by pre-specified levels. Examples are discussed, illustrating design of trials with binary or time to event endpoints. Moderate increases in sample size are shown to deliver stronger levels of overall evidence, whether positive or negative, and to preserve or increase conclusiveness of the trial outcome compared to current practice. Levels of negative evidence provided by group sequential designs are found negligible, highlighting the importance of complementing efficacy boundaries with appropriate futility rules.

Comparison of borrowing methods for the incorporation of historical data in a phase II clinical trial

Sara Urru

There has been a growing interest in using historical information in clinical trials. By incorporating such data into current trials, researchers can design more efficient and smaller studies, which in turn can save time and costs. This study aims to illustrate and compare the latest borrowing methods developed for leveraging historical data in terms of power and type I error implications.

Bayesian Estimation of Vaccine Efficacy

Mauro Gasparini

Vaccine Efficacy is first defined, then few Bayesian approaches are presented to give an interval estimate of it. As an example, we reconsider the statistical methodology of the BioNTech/Pfizer protocol, which in 2020 led to the first approved anti-Covid-19 vaccine.

Vaccine clinical trials with dynamic borrowing of historical controls: Two retrospective studies

Andrea Callegaro

Traditional vaccine efficacy trials usually use fixed designs with fairly large sample sizes. Recruiting a large number of subjects requires longer time and higher costs. Furthermore, vaccine developers are more than ever facing the need to accelerate vaccine development to fulfill the public's medical needs. A possible approach to accelerate development is to use the method of dynamic borrowing of historical controls in clinical trials. In this paper, we evaluate the feasibility and the performance of this approach in vaccine development by retrospectively analyzing two real vaccine studies: a relatively small immunological trial (typical early phase study) and a large vaccine efficacy trial (typical Phase 3 study) assessing prophylactic human papillomavirus vaccine. Results are promising, particularly for early development immunological studies, where the adaptive design is feasible, and control of type I error is less relevant.

Bayesian dynamic borrowing of adult efficacy data in a paediatric trial: a case study

Stefano Vezzoli

When practical factors limit the ability to recruit large samples in a pediatric trial, information from previous adult studies may provide some useful information that is relevant to the paediatric population. A case study from Chiesi experience will be presented, where Bayesian dynamic borrowing of adult efficacy data using a robust mixture prior was considered.

Enhancing patient outcomes and statistical efficiency in rare-disease trials: the stratosphere study

Nina Deliu

Designing early- and late-phase clinical trials for rare conditions pose unique challenges, ranging from ethical considerations to generating robust inferences from limited sample sizes. In this work, guided by a rare-disease precision-medicine case study, we outline the potential of innovative designs for addressing the above challenges in small populations. We build on a response-adaptive randomization framework and incorporate Bayesian principles for utilising the continuously accrued responses to skew the allocation probabilities toward the most promising arms. Using prior patient data, extensive simulations are carried out for sample size evaluation with 20 patients per stratum. Compared to a traditional balanced design, the flexibility of the proposed framework results in substantial gains in both statistical power and a higher chance for patients to receive the superior arm.

<u>RELATORI</u>

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