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RCT-traps and psychiatric epistemology

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Summary
While (Cochrane-oriented) evidence based medicine favours RCTs and RCT-based meta-analyses, psychiatry also highlights the values of individualised medicine, complexity sciences and medical epistemology. In a similar way, meta-theoretical considerations put RCTs into perspective: (i) randomisation does not necessarily generate analogous samples, (ii) differences between normal and actual distributions impact on statistical outcomes, (iii) Likert scales may not produce interval data, which are prerequisite for statistical processing, (iv) medical data may possess dynamic characteristics, and (v) standardised research designs have to be revisited from a correspondence-theoretical point of view. To overcome typical flaws, statistical correction, reliable ways of sample splitting and dynamic simulation models are in the ascendant.

Keywords: *randomised controlled trials, medical mathematics, simulation models*

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INTRODUCTION

Elucidating the question 'Psychiatria Danubina: Where we are and where we are going', Miro Jakovljević (2025) relates to the complex challenges of today's psychiatry and mental health sciences. These require inter- and transdisciplinary approaches, meta-methodological considerations, medical epistemology, and awareness of the traps of 'one-size-fits-all approach blockbuster medicine'. Jakovljević's perspective markedly coincides with Joachim P. Sturmberg's (2018) complexity-science-based redesign of health systems and the present article's aim to qualify, by means of medical mathematics and psychiatric truth-theory, the scientific value of quantitative approaches, particularly randomised controlled trials, and to make clear that these are not as robust and reliable as they usually pretend to be. Thus, the present critical analysis of RCT-standards intends to contribute to the multi-perspective paradigm of today's psychiatry and mental health sciences (Jakšić, 2024), and goes hand in hand with the call for integration of theoretical and epistemological perspectives to adequately estimate treatment effectiveness (Jakovljević, 2024).

While Cochrane-oriented evidence based medicine is partial to randomised controlled trials and RCT-based meta-analyses, meta-theoretical considerations have given rise to profound criticism (Schork, 2018) of these research designs. Moreover, psychiatric circles emphasise the value of case-series and individualised medicine alongside the advantages of dynamic systems in pathology and health care (Sturmberg & Martin, 2022). In this context, Miro Jakovljević (2023) even speaks of 'global mental health enlightenment'.

Psychiatric epistemology requires transdisciplinary syntheses and complex approaches towards the nature of mental health and pathological dynamics, both in terms of precision medicine and cultural sensitivity. Accordingly, the present article advocates (i) to regard RCTs as one approach among many others to estimate the multifaceted values of treatment, but not at all as the gold standard in medical epistemology – in this regard, Cochrane ideology seems to be biased in itself – and (ii) to realise how medical mathematics and meta-theoretical analyses unearth hidden systemic errors of standardised RCTs, hence the inevitable necessity to readjust and qualify their results.

MISCONCEPTION OF RANDOMISATION

The theory of RCTs implicitly postulates that randomisation ensures equal starting conditions of compared groups. However, both clinical analyses and mathematical simulation models falsify this assumption. To cite an instance, a recent RCT on music therapy in depressive patients at the 10th People's Hospital of Tongji University in Shanghai informally compared intervention and control groups after randomisation and

discovered considerable differences. In general, RCTs should take the probability of statistical deviations between study-samples into account and estimate related deviation bands, even if such modes of re-assessment are mathematically challenging.

A simple statistical consideration helps to get an idea of that misapprehension. Let us take a normally distributed population with mean μ and standard deviation σ – and regard all possible subsets with n elements. The standard deviation of the means of these subsets is the standard error $SE = \frac{\sigma}{\sqrt{n}}$ (Lee et al., 2015). Obviously, this fact also relates to samples generated by randomisation. Even though bigger subsets diminish deviations, the standard error is still an indicator for the central tendency of sample differences, and mathematical analyses show that randomisation does not necessarily provide two statistically similar samples (Mastnak, 2024).

In addition to estimations how the probability of sample dissimilarities impacts on statistical RCT outcomes, mathematical research is about to develop more adequate – and transparent – methods to minimise μ and σ differences between samples, and thus to optimise similarity. Regarding recent trends in medical mathematics, it is likely that randomisation will be eventually replaced by more advanced techniques.

NORMAL DISTRIBUTION

Notwithstanding the existence of non-parametric randomisation-based research, the lion's share of RCT-studies assume that samples they are dealing with fulfil criteria of Gaussian distribution. However, the high probability of dissimilarity between perfect normal distribution and raw-data-based (clinical) distributions requires 'goodness-of-fit' tests such as the classical 'Shapiro-Wilk Test for Normality'. This statistical issue also applies to psychiatry, and model-compatibility comes into play, e.g. referring to metacognition and psychopathology (Nordahl et al., 2019).

Even if RCT-studies control Gaussian goodness-of-fit, they often do not calculate how (tolerably small) differences between normal distribution and actual data distributions still influence subsequent probability estimations, e.g. type I and type II errors. However, the impact of such incongruence can be decisive, and neglect may lead to erroneous results.

In general, distribution is a key issue in medical modelling, and various distribution types – such as Fréchet-Weibull and Pareto distributions (Alshanbari et al., 2021) – have considerably improved mathematical features in medical, neuroscientific and clinical research, as well as in AI-oriented realms. New approaches go far beyond the conventional tools of evidence based medicine. This also involves dynamic simulation models that are not based on classical mathematical functions, which are – simply speaking – structures that can be described by formulae such as the Gaussian cumulative distribution function

$$\Phi = \frac{1}{\sqrt{2\pi}} \int_{-\infty}^{x} e^{-\frac{t^2}{2}}\, dt$$

or the Pareto distribution's probability density function

$$f_x(x) = \frac{a x_m^a}{x^{a+1}}$$

for $x \geq x_m$ and 0 for $x < x_m$.

INTERVAL SCALES

Psychiatric RCTs often use Likert-scale-based inventories to generate interval data. By contrast, mathematical simulations revealed a high probability that, e.g., 5-point Likert scales only satisfy ordinal scale criteria, while interval scales would rather require 11 points (Wu & Leung, 2017). Such issues have inspired broader research on Likert scales and similar tools (Jebb et al., 2021), not least to clarify scale characteristics which are vital for statistical processing. In case data do not satisfy interval scale characteristics, inferential statistical calculation is not possible. Such considerations also involve the even more subtle question of the inner quality of numerical representations of non-mathematical research objects, which will be more deeply discussed in the section about correspondence theory.

DYNAMIC DATA

RCTs work with 'rigid' data and a sort of black-box-model: while indicating intervention modes and end-point-data, both data-dynamics and underlying mechanisms remain disregarded. Particularly in psychiatry, stability of data is questionable, though. This also concerns reliability of self-assessment, which is a potential source of errors – notably as mental states generally depend on multiple dynamic factors. While, e.g., cardiology uses multiple-point surveys of hypertension to estimate means and deviations, psychiatric RCTs often use only one (cross-sectional) data set at the end of a

treatment-phase, which even may be considered – from a stochastic point of view – 'at random'.

Together with broader epistemological considerations, such issues have inspired the idea of dynamic models in psychiatry, which involve dynamical systems theory, network theory, instability mechanisms, chaos theory and catastrophe theory (Nelson et al., 2017). Recent approaches are intertwined with computational psychiatry, e.g. to simulate the dynamics of psychiatric symptoms (Gauld & Depannemaecker, 2023), and provide models which combine – in a sense – phenomenological evidence and underlying mechanisms, or inner-structural dynamics. Such developments cause a high probability that classical RCTs and related meta-analyses will lose their dominance and furthermore rather count as statistical trend evaluation contributing to complex representations of psychiatric entities.

CORRESPONDENCE THEORY

Taking such mathematical and truth-theoretical considerations into account, we ought to qualify numerical outcomes of RCTs – and while a study may state that results are significant at a $p \leq 0.05$ level, the real error possibilities may rank around 15%, for instance. This problem also hits meta-analyses, which usually ignore the decisive ontological difference between the mathematical sphere, i.e. the world of numbers, and the human domain, e.g. the nature of psychopathological actuality.

This issue essentially involves philosophical correspondence theory alongside conflicting coherence-theoretical arguments, two major schools of thought in early Viennese epistemology (Von Dawson & Gregory, 2009). In short, coherence theory states that only objects with similar qualities or – in other words – which belong to the same 'world', can be compared, while correspondence theory advocates the possibility of transpositions and related coding. Quantitative empirical research (tacitly) accepts correspondence theory, while meta-theoretical circles call for profound studies on adequate transformation modes, e.g. through psychopathological tests or numerical data representing neurotransmitter dynamics.

Evidence based medicine is faced with a double issue: one relates to the shift between medical realities – such as states of schizophrenia – and their numerical representation, the other concerns how inferential statistics allow generalisations, probability estimations included. RCTs and RCT-meta-analyses usually ignore these problems, which are of epistemological and truth-theoretical relevance, though. And yet, evidence based medicine is grounded in a distinct triple jump of generation, processing and interpretation of data, which calls for such philosophical scrutiny.

By way of illustration, meta-analyses typically include Forest plots, which estimate heterogeneity with parameters such as I^2, statistical optimisation such as by inverse variance, and weights, which are meant to indicate the importance of one study for the overall estimation of effects and/or effect sizes. However, all these processes relate to mathematical considerations and theories. In terms of coherence theory, such entities are exclusively housed in the mathematical world of numbers and axiomised systems, while profound correspondence-theoretical research about adequate transferability is lacking. There is even the fundamental question whether real distributions, e.g. in the sense of depressive phenomena of a given sample of patients, can be regarded as analogous or isomorphic to associated numerical distributions. These problems are not trivial, though usually neglected in RCTs and related studies.

Broadly speaking, typical evidence based medical research encompasses (i) two qualitative transitions, namely from clinical/human reality to abstract models – and back, and (ii) mathematical procedures. Although scientific trustworthiness should apply to the whole course of research, key parameters, e.g. effect sizes, exclusively adhere to statistical algorithms. These epistemological deficiencies called for two novel parameters. The 'confidence range' concerns consistent, scientifically justifiable sections, which, in various studies, only extend between the numerical raw data and the statistical results. The 'coherence size' concerns the inner methodological connection between the starting and the endpoint of a study, estimates truth-theoretical deviations and losses caused by qualitative transitions, and re-adjusts (i.e. lowers) conventionally yielded results (Mastnak, 2021).

CONCLUSION

The idea of randomisation is inextricably intertwined with the notion of 'bias', which is somehow overused in RCT-studies and meta-syntheses, and even has taken on ideological characteristics. While the avoidance of biased results has good historical reasons, today distinct mathematical and truth-theoretical approaches may replace this eventually obsolete paradigm: the goal is evidence that meets highest standards of medical epistemology and relevant theory of science.

Broadly speaking, there are three different possibilities to avoid or eliminate such systemic errors of

psychiatric RCTs: (i) statistical algorithms which estimate the possibility of deviations caused by statistically incongruent samples, specific distribution issues or other traps mentioned above, (ii) mathematical models that optimise the statistical similarity of samples and hereby allow transparent statistical estimations, and (iii) dynamic simulation models that also facilitate prospective research. In the authors opinion, particularly the last one, which also involves artificial intelligence/robotics and interrelates with computational psychiatry (Hitchcock et al., 2022), will enormously gain in importance and finally replace today's techniques of evidence based medicine.

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