FRIDAY, 14 JUNE 2019

15:30:00 – 17:00:00

Missing data in clinical research: to impute or not to impute, that is the question

SP0156 MISSING DATA: IS IT ALL THE SAME?

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Introduction: In most studies, there are “holes” in the data set, such that data are missing partly or completely for some of the subjects. This results in reduced statistical power. More seriously, missing data may cause biased results, since data are usually not missing completely at random.

Missing data mechanisms: In which way, and to what extent, does the probability that data are missing, depend on observed and/or unobserved data values? This is called the missing data mechanism, and is important for an appropriate choice of analysis method. Three types of missing data mechanisms have been defined, see for example (Sterne et al. 2009).

MCAR: *Missing completely at random.* There are no systematic differences between the missing values and the observed values. The probability that values are missing does not depend on any of the data, observed or unobserved.

MAR: *Missing at random.* The probability that values are missing may depend on observed data values, but not on unobserved data values. For example, some variables are missing more frequently for patients with higher age. Data are missing at random *conditionally* on observed data.

MNAR: *Missing not at random.*

Even after the observed data are taken into account, systematic differences remain between the missing values and the observed values: The probability that values are missing depends on unobserved data values as well.

It is possible to distinguish between MCAR and MAR by inspecting the data at hand. But it is never possible to determine whether data are MNAR from your data.

Methods for handling missing data

Some commonly used methods, from the less to the more complex ones, are listed below, with an indication of when they give unbiased estimates:

- Complete case analysis (disregarding cases with partially missing data) (MCAR)
- Single imputation methods (sometimes under MAR but underestimates uncertainty)
- Multiple imputation (MAR)
- Full information maximum likelihood (MAR)
- Linear mixed models in longitudinal studies (MAR)

In longitudinal studies, Last observation carried forward (LOCF) is a simple method for imputing missing values. But it is not unbiased under any sensible assumptions, and should not be used (Lydersen 2019).

Reporting: In general, report the amount of missing data in the different variables, and how this was handled in the analysis. This is recommended in the Consort Guidelines (Moher et al. 2010) as well as the STROBE Statement (STROBE 2014), see also (Lydersen 2015)

REFERENCES:

- [1] Lydersen, S. 2015. Statistical review: frequently given comments. Ann. Rheum. Dis., 74, (2) 323-325. Lydersen, S. 2019. Last observation carried forward - simple but not recommended. In press, Tidsskrift for Den norske legeforening
- [2] Moher, D., Hopewell, S., Schulz, K.F., Montori, V., Gotzsche, P.C., Devereaux, P.J., Elbourne, D., Egger, M., & Altman, D.G. 2010. CONSORT 2010 explanation and elaboration: updated guidelines for reporting parallel group randomised trials. BMJ, 340, c869
- [3] Sterne, J.A., White, I.R., Carlin, J.B., Spratt, M., Royston, P., Kenward, M. G., Wood, A.M., & Carpenter, J.R. 2009. Multiple imputation for missing data in epidemiological and clinical research: potential and pitfalls. BMJ, 338, b2393
- [4] STROBE Statement 2014. Strengthening the reporting of observational studies in epidemiology.

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SP0157

PRO SESSION: IMPUTATION IS A POWERFUL ANALYTICAL TOOL, WHEN APPROPRIATELY USED

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Analysing a study with missing data very likely will yield biased results. Of course, the first principle is to avoid missing data by designing the study and the data collection very thoughtfully. If the study is already done and data collected, then one needs to study how important, and what type of missingness is affecting our data. Simple *ad hoc* methods, such as LOCF, or imputing the mean or other value are generally invalid. Multiple imputations need additional work and expertise, but generally yield better results, closer to reality.

Many statistical programmes have macros available for imputing missing values and analysing imputed data. We will review how these work. Understanding what multiple imputations do will make the decision clearer.

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SP0158

CON SESSION: PREPARE YOUR DATA COLLECTION WELL: IMPUTATION DOES NOT REPLACE ‘REAL DATA’

Maxime Dougados.

The recently proposed sophisticated statistical methods to impute missing data are very attractive.

For the clinical researchers in charge of data collection, it might be tempting to “neglect” the quality of data collection in favor of the time spent by one database manager/statistician to impute missing data.

This presentation will be a plea in favor to make all the possible efforts to collect appropriately the data in clinical research studies/trials. In particular, emphasis will be placed on the importance of writing a specific section in any research protocol describing the techniques used to avoid these missing data and also the *a priori* decided technic that will be used to manage the missing data. One point of importance in this section: to specify in advance the maximum percentage of missing data over which no imputation can be made.

Two different situations:

- Cross-sectional studies. Any item (for example HLA B27, MRI SIJ inflammation positivity) should be considered as mandatory or not before running the study.

- Longitudinal studies: any longitudinal protocol should include a section detailing the technic to appropriately follow the patients in order to avoid the “lost of follow-up patients”. This is particularly important in longitudinal follow-up of patients suffering from a recent onset disease (e.g. early synovitis cohorts, early inflammatory back pain cohorts) since it is well known that the “lost of follow-up” have specific baseline characteristics suggesting a less severe disease. It is also important to decrease at a minimum level the “lost of follow-up” patients participating at a therapeutic trial/registry since the reason of “lost of follow-up” might be related to a specific drug effect.

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Don't panic – round table discussion on risk perception

SP0159

WHAT DO WE KNOW – WHAT SHALL WE DO – WHAT DO WE TELL

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There is an increasing need for patients to be involved in research as well as matters that can influence their own clinical journey. One aspect of science that links optimal clinical care is the increased use of biomarkers for so-called personalized medicine approaches.

In my presentation I will showcase the State of the Art technologies of biomarker research and how the information that comes from this can be implemented for improving clinical care. I will discuss the revolution of molecular profiling and how the large amount of data coming from these approaches is used to molecularly classify patients into molecular fingerprints. How this technology leads to a disruptive change in medicine for the coming 5-10 years. I will close off with the role of biomarkers in the treatment of diseases, trial design and drug development for the coming 5 years.

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SP0160 DISEASE REMISSION: DO WE AIM FOR THE SAME THING?

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It is consensually accepted that the most important therapeutic goals for treating rheumatoid arthritis (as well as other inflammatory arthritis) are eliminating signs and symptoms (such as joint pain, swelling, and stiffness); preventing joint damage or its progression; and maximizing physical function and quality of life (Aletaha & Smolen, 2019). According to current medical knowledge, these aims are believed to be best accomplished by achieving disease remission, a state in which no or only minimal residual inflammation is discernible (Aletaha & Smolen, 2019). However, different studies have been providing evidence that achieving inflammatory remission is not enough as a considerable proportion of patients with no or minimal inflammation remain with high levels of pain, fatigue, functional impairment, mental health problems, among other symptoms (Boone et al., 2019; Ferreira et al., 2019; Ferreira et al., 2017). The perfect path to achieve good results is still to be defined, namely, regarding the T2T strategy (van Vollenhoven, 2019). Recent studies still show that despite a high level of patient agreement with RA T2T, patient engagement in this process needs to be improved in order to individualize therapy adjustments, make shared decisions and decide on targets that accurately reflect disease control according to patients (Benham et al., 2019). In this session I would address the following questions:

- Is aiming for one target enough nowadays?
- Do health professionals and patients aim for the same thing when defining treatment strategies?
- Do the current treatment targets pose a risk of overtreatment with immunosuppressive therapy?

This presentation is informed by current research in this area including research from our own group (Ferreira et al., 2018; Santos et al., 2018).

REFERENCES:

- [1] Aletaha, D., & Smolen, J. S. (2019). Achieving Clinical Remission for Patients With Rheumatoid Arthritis. *JAMA*, 321(5), 457-458. doi:10.1001/jama.2018.21249
- [2] Benham, H., Rutherford, M., Kirby, S., Stebbings, S., White, D., Sim, D., & Harrison, A. (2019). Treat-to-target in rheumatoid arthritis: Evaluating the patient perspective using the Patient Opinion Real-Time Anonymous Liaison system: The RA T2T PORTAL study. *International Journal of Rheumatic Diseases*. doi:10.1111/1756-185x.13514
- [3] Boone, N. W., Sepriano, A., van der Kuy, P. H., Janknegt, R., Peeters, R., & Landewe, R. B. M. (2019). Cotreatment with methotrexate in routine care patients with rheumatoid arthritis receiving biological treatment yields better outcomes over time. *RMD Open*, 5(1), e000836. doi:10.1136/rmdopen-2018-000836
- [4] Ferreira, R. J. O., Carvalho, P. D., Ndosi, M., Duarte, C., Chopra, A., Murphy, E., . . . da Silva, J. A. P. (2019). Impact of patient global assessment on achieving remission in patients with rheumatoid arthritis: a multinational study using the METEOR database. *Arthritis Care Res (Hoboken)*. doi:10.1002/acr.23866
- [5] Ferreira, R. J. O., Dougados, M., Kirwan, J., Duarte, C., de Wit, M., Soubrier, M., . . . Gossec, L. (2017). Drivers of patient global assessment in patients with rheumatoid arthritis who are close to remission: an analysis of 1588 patients. *Rheumatology*. doi:10.1093/rheumatology/kex211
- [6] Ferreira, R. J. O., Ndosi, M., de Wit, M., Santos, E. J. F., Duarte, C., Jacobs, J. W. G., . . . da Silva, J. A. P. (2018). Dual target strategy: a proposal to mitigate the risk of overtreatment and enhance patient satisfaction in rheumatoid arthritis. *Annals of the Rheumatic Diseases*. doi:10.1136/annrheumdis-2018-214199
- [7] Santos, E. J. F., Duarte, C., Ferreira, R. J. O., Pinto, A. M., Geenen, R., & da Silva, J. A. P. (2018). Determinants of happiness and quality of life in

patients with rheumatoid arthritis: a structural equation modelling approach. *Annals of the Rheumatic Diseases*, 77(8), 1118-1124. doi:10.1136/annrheumdis-2017-212934

- [8] van Vollenhoven, R. (2019). Treat-to-target in rheumatoid arthritis - are we there yet? *Nature Reviews. Rheumatology*, 15(3), 180-186. doi:10.1038/s41584-019-0170-5

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SP0161 LOOKING FOR A NEEDLE IN A HAYSTACK: HELPING YOUNG PEOPLE TO MAKE SENSE OF EVIDENCE BASED HEALTH CARE

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While it has been suggested that there are no differences in the occurrence of risk-taking behaviours in young people with chronic conditions compared with healthy peers, young people with chronic conditions often face the dilemma of balancing twice the amount of risk to that of other young people, owing to their condition and treatment. For example, young people with juvenile idiopathic arthritis taking methotrexate face the risks of alcohol consumption plus the increased risk of toxicity from consuming alcohol while taking methotrexate. However, such issues are often ignored or overlooked (1). Research has suggested that a lack of experience with, and not worrying about serious health consequences may desensitise young people with chronic conditions to potential health risks (2). It is also recognised that young people's perceived focus of health and wellbeing can often be on short-term goals; which is often paradoxical to the focus of families and healthcare professionals thinking about longer-term outcomes and prognosis.

It has been demonstrated that young people with chronic conditions value interventions that enable them to live a "normal" life – extending beyond the clinical management of their condition (3). The emotional, social, and vocational consequences of condition management can be profound (4). When this is coupled with the challenges of accessing accurate, trusted and individualised information and support, it can often leave young people and their families feeling as though they are looking for a 'needle in a haystack'. Finding the best evidence requires knowledge of the best quality and most appropriate sources, as well as the ability to use and navigate such resources appropriately (5). In an era where health information is easier and faster to find than ever before, it is often a challenge for young people to be able to filter the 'good' from the 'not so good'. There are significant amounts of unreliable and irrelevant content on the internet, which ultimately places the responsibility for interpretation of information and advice onto young people and their families.

Therefore, age- and developmentally- appropriate opportunities to discuss health, wellbeing and the effects of treatment need to be provided early and regularly, across the lifecourse, in multiple formats to suit individual needs and circumstances. Attempts have already been made to make health information more accessible, for example, with the introduction of the Accessible Information Standard within the National Health Service (6). However, this is not necessarily enough to engage and support young people with chronic conditions in making sense of evidence-based healthcare. Information needs to be taken, in the right formats, to where young people are interacting, such as on certain social media platforms. This needs to be multifaceted, using peer- and community-driven approaches to enhance engagement. Furthermore, periodic consideration of the long-term risks and benefits of health and wellbeing interventions needs to happen across the lifecourse, both as a prompt for young people to air their concerns, but to also check their understanding. Only through understanding young people's values, preferences, and concerns can a sustainable balance between condition control, treatment burden and quality of life be achieved.

REFERENCES:

- [1] McDonagh JE. Getting It Right For Young People: Developing Adolescent Rheumatology Services. *Future Rheumatol* 2008; 3(2):133-41.
- [2] Greening L, et al. Predictors of children's and adolescents' risk perception. *J Ped Psych* 2005; 30(5):425-35.
- [3] van Houtum L, et al. Do everyday problems of people with chronic illness interfere with their disease management? *BMC Public Health* 2015;15:1000.
- [4] Hart RI, et al. Being as normal as possible: how young people ages 16–25 years evaluate the risks and benefits of treatment for inflammatory arthritis. *Arthritis Care Res* 2016; 68(9):1288-94.
- [5] NHS England. Accessible information: Specification v1.1. 2017.