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PRESENTING IGNORANCE: A POSSIBILITY INTERVAL APPROACH TO DEPICT HIGH-LEVEL UNCERTAINTY DUE TO CENSORING OR NON-RESPONDENTS

Turunen JH¹, Soini EJ²

¹Equal contribution of both authors. Department of Social Pharmacy, University of Kuopio, Kuopio, Finland, ²Department of Social Pharmacy, Department of Health Policy and Management, University of Kuopio, Kuopio, Finland

Model verification/validation applies the metrics of prediction error (e.g. area under curve), information criterion (e.g. Akaike, Bayesian, deviance), model uncertainty (e.g. substitution, portioning, leave-one-out/K-fold cross-validation), and numerical convergence. However, censoring and non-respondents cause uncertainty in follow-up studies and surveys. When missing at completely random (MACR) is not true, empirical result verification is problematic. Thus, emphasis should be given on ways to illustrate ignorance related to missing values. **OBJECTIVES:** To present a possibility interval (PI) and its relation to Wald confidence intervals (CI) and Jeffreys Bayesian credibility intervals (CrI; Beta 0.5, 0.5 a priori) in 9 artificial samples of 1000 individuals (prevalence of e.g. drug utilization 10%–50%; ignorance due to censoring/non-responding 5%–25%). **METHODS:** The epistemic uncertainty is considered here as sampling ignorance. The conjunctive set of points comprised in an interval of minimum necessary level (NL) and maximum possibility level (PL) constitute a PI (i.e. where the “true” mean must be conditional to sample’s representativeness). Firstly, in possibility quantification, certainty sources (e.g. certain observations) are determined. Secondly, the dominant possibility factors causing ignorance are identified. Thirdly, NL and PL bounds are established for parameters representing the outcome/model. **RESULTS:** The NL and PL of PI depict the depth of ignorance. In the artificial samples of e.g. 1000 potential drug users, PI overlapping was related to the levels of prevalence and ignorance. If e.g. 10% difference in prevalence is observed between compared groups, 15% ignorance constitutes a threshold for inference change. In a case of 50% prevalence with ignorance between approximately 5%–10%, PIs were visually in substitutive rela-

tion to CIs and CrIs. In other cases, PIs provide complementary information. **CONCLUSIONS:** The complementary information provided by PIs is important with higher (e.g. >10%) censoring levels and, most importantly, if MACR does not hold or the prevalence of research subject is very different from 50%.

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INDIRECT COSTS OF COMMON COLD IN GERMANY

Hessel FP, Wasem J

University of Duisburg-Essen, Essen, Germany

OBJECTIVES: To estimate the indirect costs caused by productivity loss due to simple infections of the upper respiratory tract in Germany. **METHODS:** A representative sample of the working population defined by membership in the social insurance in Germany (n = 994) was interviewed concerning the annual incidence, work-off days and days at work with limited productivity. The sample was representative concerning age, sex and social status, and stratified by age, sex, region (eastern and western part of Germany) and working status e.g. employee, worker, trainee etc. Productivity losses were valued using the human capital approach (HC) and the friction cost method (FC). Data were extracted from different German administrative sources like the federal institute for statistics. **RESULTS:** The mean number of work-off days was 2.9 d. At 11.6 d per year the productivity was limited by 35% due to a cold. The total annual productivity loss per person was 7 d. The mean costs per working person were €1009 (HC) respectively €807 (FC) using stratified mean incomes of year 2004. Aggregated to the total working population of Germany the indirect costs of illness in 2004 were about 29.2 billion € (HC) respectively 23.3 billion € (FC). There was a clear trend to lower cost in men and in younger age groups. **CONCLUSIONS:** Although the direct medical costs per person for the treatment of common cold without complications are low, the high incidence of the disorder induces impressively high indirect costs caused by short-time work-off and a relevant number of days at work with a limited productivity due to a cold.

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IMPLEMENTING NATURAL HISTORY STUDIES IN EURASIA: THE NIEMANN-PICK EXPERIENCE WITH RAPIDLY CHANGING NATIONAL REGULATIONS

Madison M¹, Finegan Y¹, Sawyer R², Koval S², Cox G²

¹Abt Associates Inc, Lexington, MA, USA, ²Genzyme Corporation, Cambridge, MA, USA

OBJECTIVE: Characterizing morbidity and mortality in rare genetic diseases is challenging given the small numbers of patients, their wide geographic distribution, and the variable effects of genetic mutations. Global natural history studies aim to close the knowledge gap but require the participation of multiple countries to achieve this goal. **METHODS:** In 2006, Genzyme Corporation initiated a retrospective natural history feasibility study of acid sphingomyelinase deficiency (ASMD, also known as Niemann Pick disease Types A and B) in 8 Eurasian countries. ASMD is an inherited lysosomal storage disorder that affects approximately 2000 patients in developed countries and has no specific treatment. The goal of the study was to determine whether investigators would be able to implement a medical record abstraction study of ASMD. The objective of the post-feasibility study is to provide improved estimates of morbidity and mortality that can help facilitate drug development. **RESULTS:** Eurasian investigators were enthusiastic about participating in and improving knowledge on this rare and life-threatening disease, but they were cautious about interpreting existing/evolving regulations for each country. Some coun-

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