Definition of a minimum data set to accompany indices of biological variation.

Biological Variation Working Group, European Federation of Clinical Chemistry and Laboratory Medicine, http://efcclm.eu/science/wg-biological-variation, www.biologicalvariation.com .

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Background

Biological variation data are used by laboratory professionals globally to enable interpretation of clinical laboratory test results and to set quality standards. The data are derived from varying populations with studies utilising a variety of experimental models and approaches. The data are of varying quality and sometimes poorly characterised. These data are effectively reference data and users of them need to be aware of the attributes of the data that impact upon the transferability of data across populations and time. There is a further need for users to understand the uncertainty applying to the estimates of published biological variation. The Biological Variation Working Group (BVWG), set up by the EFLM, have undertaken work to identify a minimum data set (MDS) to accompany published indices of within and between subject biological variations to enable critical appraisal of their utility to prospective users.

WWW.BIOLOGICALVARIATION.COM

Users of biological variation data (BV) need to have an understanding of the provenance and uncertainty around these data. Safe, accurate and effective application of BV data in clinical settings across the world requires that they are well characterised and accompanied by sufficient metadata to enable transferability into practice.

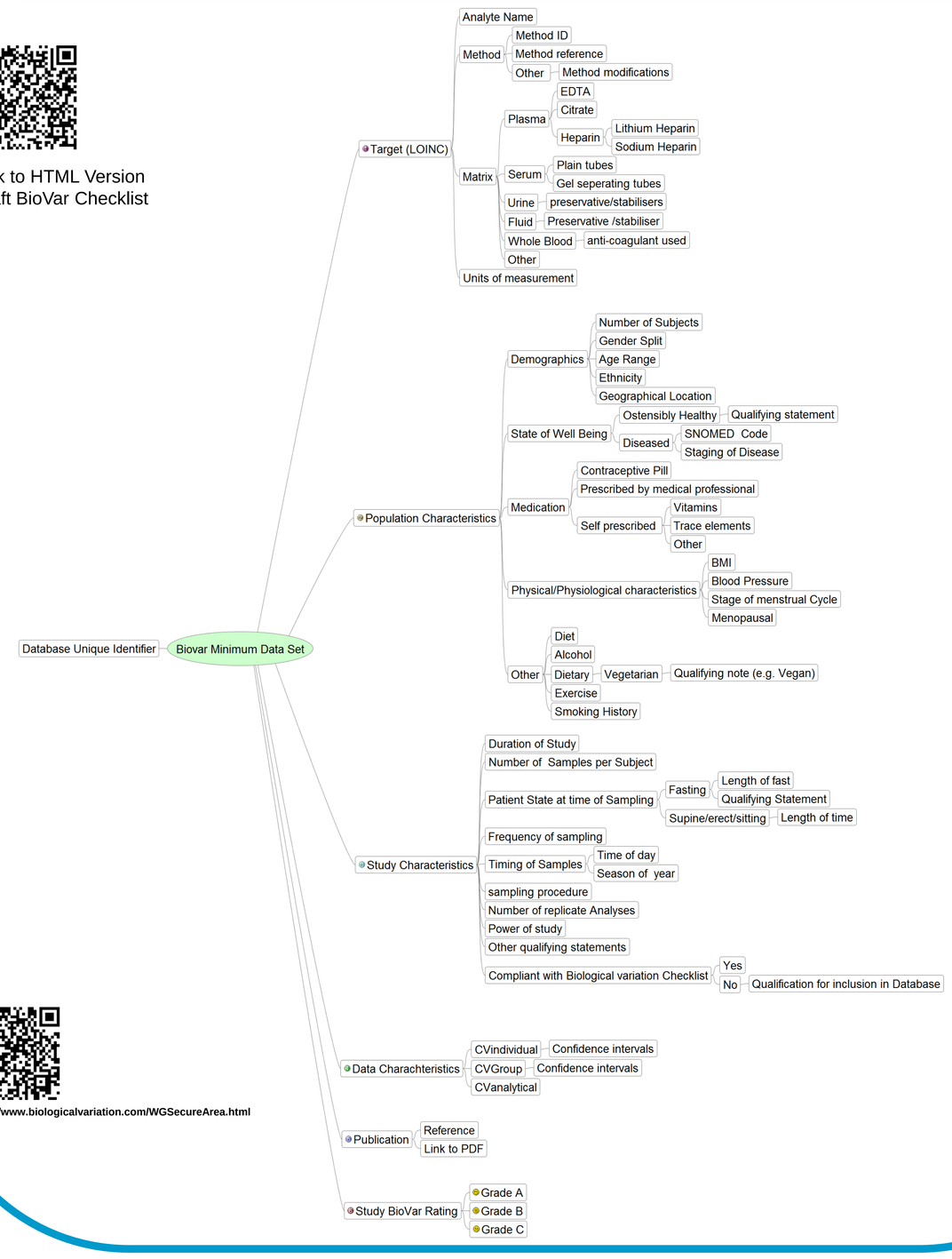
Survey of the literature indicates a high degree of heterogeneity in BV data. Publications by Braga *et al* (Clinica Chimica Acta 2010;411:1606-1610), Carobene *et al* (CCLM, 2013;51:1997-2007) and Miller et al (Clin Chem 2009;55:24-38) relating to HBA_{1c}, hepatic enzymes and urinary albumin respectively highlight the problem In Carobene's review subject variability (CV_i) of 3 liver enzymes enzymes ranged from 3% to 58% while in Miller's review of urinary albumin excretion CV_i values ranged from 4% to 103%. Those publications not only highlight significant differences in the published estimates of BV, but also identify limitations in experimental design used to derive the data, inappropriate study lengths, and poorly described of statistical methods. This clearly identifies a need for standards for production, reporting and transmission of BV data to ensure generation of fit for purpose data and to enable correct contextual application of those data in clinical practice. The EFCCLM Biological Variation Working Group on Biological Variation (BVWG) are proposing that a minimum data set (MDS) to accompany published BV data is required to enable transmission of the BV data and to enable the transferability of the data across populations. The MDS will also support the work on delivery of a critical appraisal checklist for BV publications to be considered in the design and evaluation of new experiments and assessment of the veracity of existing published studies.

Six main data domains were identified by the BVWG to enable transferability of biological variation data safely, accurately and effectively (Fig. 1). The high level domains, 1 to 4, encompass a high degree of complexity and a practical difficulty arises in communication of the detail. In consequence domains 5 and 6 should form part of the MDS to enable users to link to source publications to ascertain fine detail and also enable sharing of expert opinion as to the quality of the data. The study rating (domain 6) is a concept that requires further development, but may take into account a scoring systems assessing experimental design and study power. Roraas et al (Clin Chem 2012;58:1306-13) have published and an approach to delivering confidence intervals and power calculations for within-person biological variation. They looked at the effect of analytical imprecision, number of replicates, number of samples, and number of individuals on the estimates. Such a rating might easily be included in published database. There are parallels in this approach to the rating of medical evidence.

BV data are reference data and consequently the principles under-pinning the concept and theory of reference values that requires transmission of metadata to enable the valid application of reference data to a population apply. Consistent transmission of the BV data with required meta data will however prove challenging. The use of coding systems such as SNOMED, LOINC *etc* may enable the delivery of an MDS electronically. The use of approaches that include embedded links from laboratory documentation to *bona fide* reference sites may provide a solution. An alternative might be incorporation of data into QR codes (Fig2). These can be read on mobile telephones and other electronic devices. They could be passed on *via* manufacturers kit inserts containing the full MDS or an agreed skeleton content that links to the more detailed data set.

Fig.1. Data Domains defining minimum data set to Enable transferability of biological variation data.

Link to HTML Version
Draft BioVar Checklist



http://www.biologicalvariation.com/WGSecureArea.html

Fig 2. QR Code: MDS For BV Creatinine

Conclusion

A MDS has been identified for further development to enable safe, accurate and effective transmission and transferability of biological variation data. The model includes six domains that will enable high level characterisation of the data, provision of links to the original studies and includes the concept of rating the data. All will enable users to make informed choices as to the transferability of data to their clinical practice.
The use of coding systems and electronic means of transmission will enable the adoption of this approach.