

Critical Appraisal of Biological Variation Data

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"Our hope is that the comparability of such data might be provided by use of a common study design and analysis of data"

Fraser & Harris 1989 Crit Rev in Clin Lab Sci. 1989;27(5)409-437

Background

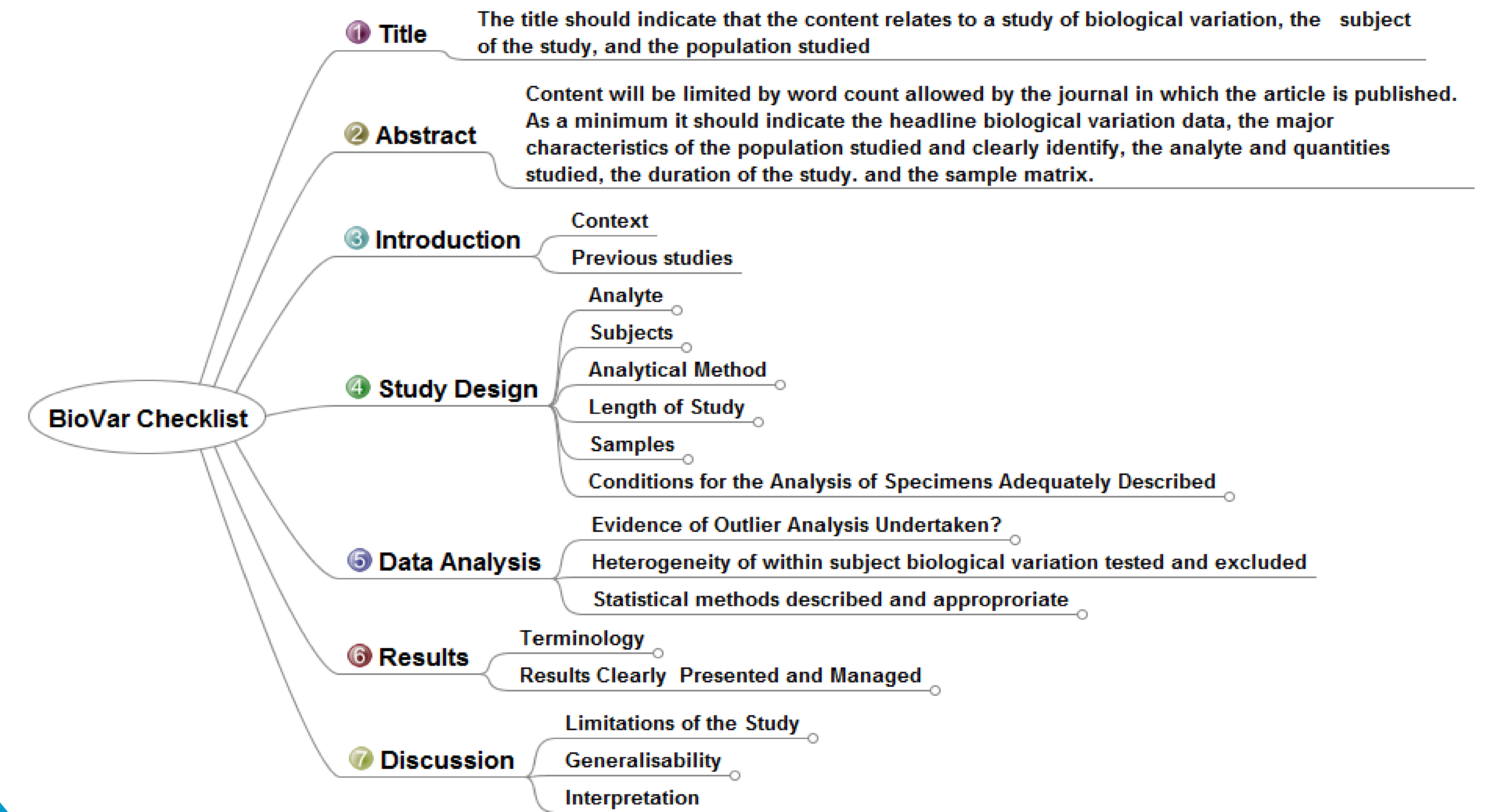
Biological variation data have many established applications ranging from the setting of analytical goals for imprecision and definition of quality specifications to, assessment of significance of change in serial results (reference change values (RCV)). Review of the literature on biological variation identifies a significant volume of work stretching back some 40 years. Much of this data has been incorporated into published reviews and web based databases that make them accessible to laboratory specialists.

Given the importance of these applications, and the many others, there is an imperative that these fundamental data are fit for purpose. If the data are flawed in any way, or inapplicable to the population to which they are being applied, then the application must be considered to be erroneous. These data, like all data, will be subject to uncertainty that will impact on their usefulness. Uncertainty arises from design of the experiments from which the data are derived, the assay characteristics and integrity of the data analysis. Furthermore, extrapolation of published data to local populations of interest requires an understanding of the factors affecting commutability of those data and a clear understanding of the characteristics of the population originally studied. The complexity of these data cannot be underestimated and valid application of them in the field requires clear understanding of their defining characteristics and limitations. Biological variation data should in fact be considered reference data and schema should exist to enable their critical appraisal and to support their publication and application.

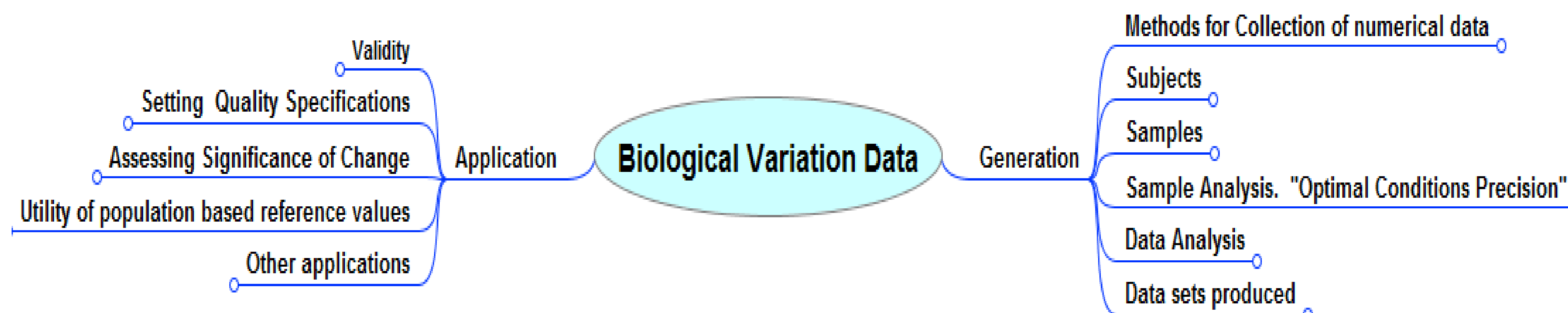
A European Federation of Clinical Chemistry (EFCCC) Working Group on Biological Variation has been established and is undertaking work to deliver a proposal for a critical appraisal checklist applicable to biological variation data. Such a checklist can be used to assess suitability of studies for publication and used to assess suitability of of data for application by users.

WWW.BIOLOGICALVARIATION.COM

Proposed Critical Appraisal Checklist: www.biologicalvariation.com/Tools.html



Biological Variation Data: Applications & factors to be considered in their Generation



BV data are Reference Data Requiring Standardisation

Standards for Production

- Experimental Design
- Data Analysis

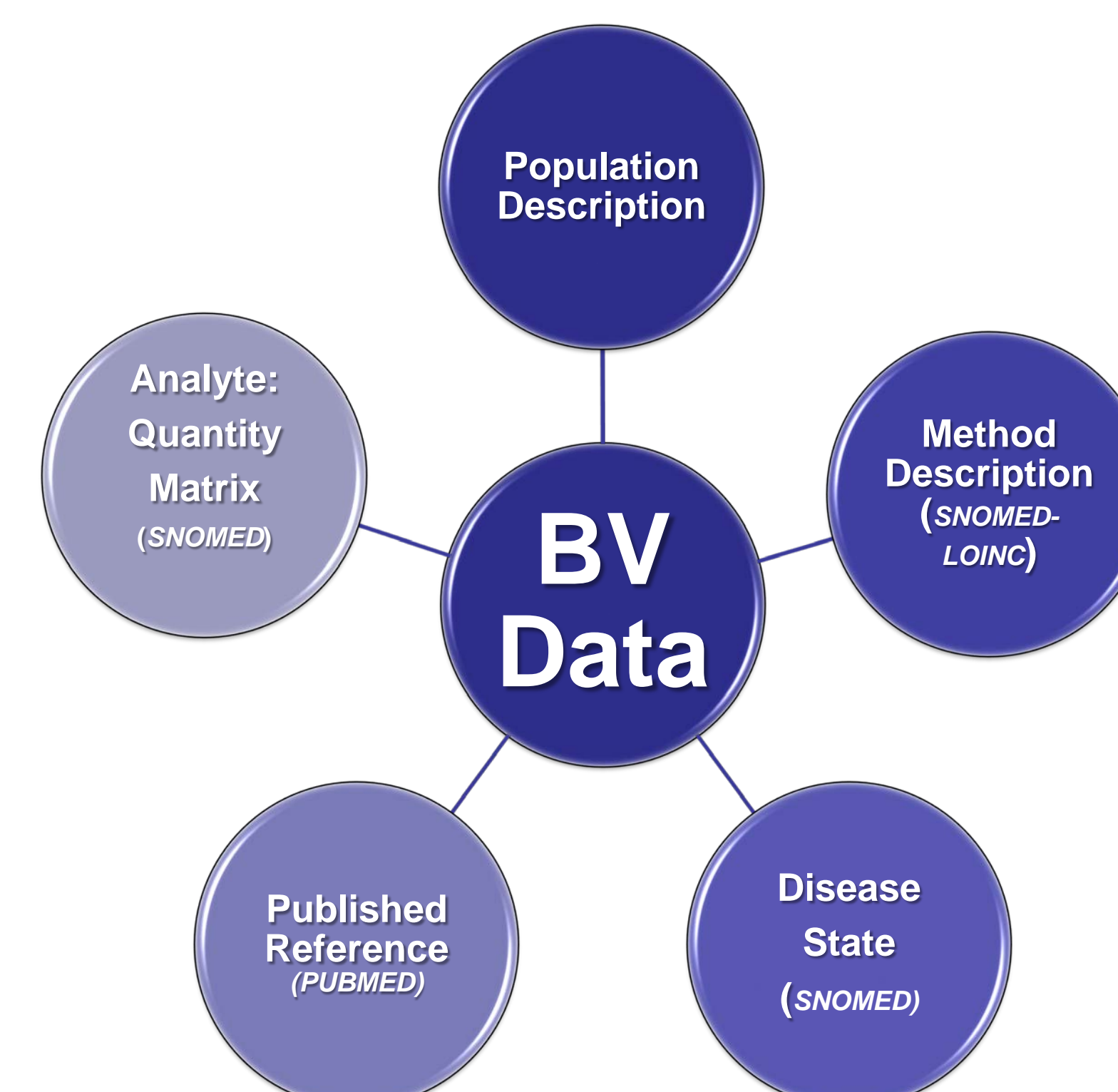
Standards for Reporting

- Enables Critical Appraisal
- Enables Commutability

Standards for Transmission

- Data Archetype required ?
- Commutability & Valid Application

Data Archetype: Transmission



Need for Standardisation and Checklist

Publications by Braga *et al* (Clinica Chimica Acta 2010;411:1606-1610) and Miller *et al* (Clin Chem 2009;55:24-38), reviewing published biological variation data pertaining to haemoglobin A_{1c} and urinary albumin excretion respectively, highlight the need for critical appraisal of such data. They identified limitations in experimental design used to derive the data, inappropriate study lengths, and poorly description of statistical methods. Differing methodologies with differing analytical characteristics impacted on the biological variation data as do disease states. All of these confounding factors will impact on the commutability of these important data which have an important role in not only derivation of analytical goals and quality standards, but also in assessment of significance of change through definition of reference change values.

In Miller's study 40 publications were cited the within subject coefficients of variation (CV) ranged from 4 to 103%. Thus highlighting an issue. Users of biological variation data need to have an understanding of the uncertainty around these data and standards need to be set for their production, reporting and transmission. The development and validation of a critical appraisal checklist to enable assessment of suitability of data for publication and application is presented here and in more detail at www.biologicalvariation.com. The development of a data archetype that describes the attributes of biological variation will enable commutability of the data and will constitute a basic data set that should be stored against it in biological variation databases.

The EFCC Biological Variation Working Group is beginning work to assess the veracity of this checklist and the approach. Further commentary about this work can be directed to through the web site (www.biologicalvariation.com) or to b.bartlett@dundee.ac.uk.