Day One: Discussions and polling

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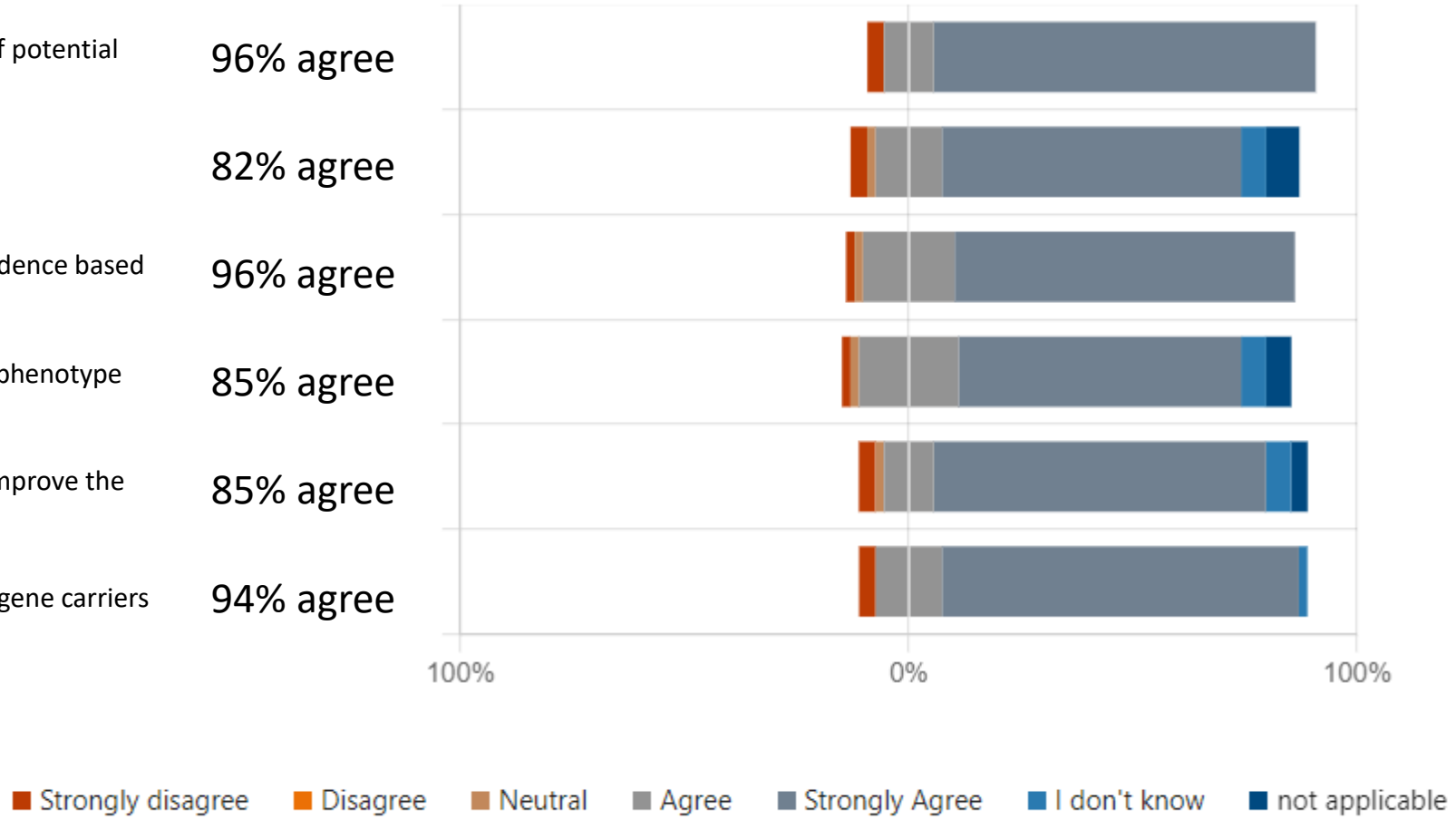
Funded by CANCER RESEARCH UK

Survey results: strong consensus on need

Clear guidelines for reporting of somatically-identified variants of potential germline origin is required	96% agree
Our centre would adopt a standardised approach to reporting	82% agree
National registry for genotype/phenotype data would enable evidence based guidelines to be developed and improve patient care	96% agree
Our centre would contribute to a national registry for genotype/phenotype data	85% agree
Our centre would support a collaborative national approach to improve the classification of germline variants of uncertain significance	85% agree
National standardised guidelines for management of unaffected gene carriers are required to ensure consistent clinical practice	94% agree



Day One consensus

Consensus reached:

- A statement on the report suggesting possible germline origin should be considered for any variant where a confirmed germline finding would have potential clinical significance, **esp if VAF >30%**
- Variants which are clearly clinically actionable in both the somatic (driver) and germline (Class 4/5 LP/P) setting can be **reported at time of somatic analysis without further discussion**
- Scientists writing somatic reports should ideally **have pre-reporting access to germline scientific/clinical expertise** when deciding if to report putative germline variants which may be VUS on germline classification
- There should be **different template phrases for actionability in different contexts –**
  - to differentiate between variants which are clearly clinically actionable in the germline (Class 4/5 LP/P) and those which may be considered a variant of uncertain significance in the germline

Consensus reached:

- Best practice to **perform an assessment of the germline class** of variant according to ACMG/CanVIG-UK/ClinGen guidelines **before the patient is offered confirmatory germline testing** for a somatically identified variant
- Best practice to **undertake diagnostic germline confirmatory testing in the proband prior to offering cascade germline testing to relatives**, although this may not be feasible all in all situations
- Best practice to **discuss incidental findings with clinical genetics prior to referring patients for confirmatory germline testing**
  - i.e. where an actionable (germline LP/P) variant is identified **NOT causally related** to the clinical phenotype but has clinical implications (e.g. *BRCA1*)

Consensus reached:

- For a variant assessed as Class 3 (VUS) in germline, confirmation is not usually indicated. If offered, it would be best practice to have and document an **MDT discussion** about the purpose and utility of confirmatory germline testing before this is offered
  - Particularly pending formal gene-specific variant interpretation guidance
- For a variant assessed as Class 3 (VUS) in germline, confirmation is not usually indicated. If offered, it would be **best practice** to have/document a MDT discussion about rationale for testing relatives esp. if impact on clinical decision making e.g. BMT

Consensus reached:

- I would support the development of an accessible forum consisting of both somatic and germline, scientific and clinical expertise for discussion of uncertain/complex/difficult somatic variants which could indicate germline predisposition
- I would support the development of an accessible forum consisting germline scientific and clinical expertise for discussion regarding the management and further work to classify germline variants of uncertain significance

Consensus reached:

- I would support providing data on somatic and germline variants to national bodies to enable further research and classification

Areas for future work: Day One

- Need for access to standardised somatic reporting templates
  - Pick up through work of S-VIG
- Need for collaborative infrastructure for variant discussion
  - Pick up through work of CanVIG-UK
- Need to develop infrastructure to enable implementation of consensus group guidelines

Huge thanks

- Patient representatives
- Delegates
- Speakers
- CanGene-CanVar team: Beth Torr
- Organising members
  - Angela Hamblin
  - Polly Talley
  - Bev Speight
  - Sarah Hamilton
  - Terri McVeigh