

Figure 3. This info-graphic shows our new, proposed workflow for research-grade and clinical-grade genomic data through the entities relevant to clinical interpretation of variants. (A, G) Research participant samples are deposited separately as before, but the ILDB resource now allows clinical testing labs to deposit their patient datasets (those with appropriate consent) and be included in the process from the start. The combination of patient and participant records will provide increased statistical power to detect disease associated genomic variation – as evidenced by the chart to the top-right corner. (B, H) While incorporation of research data into analysis stays unchanged, appropriate processes to hide/transform the relevant fields in patient data need to be developed. Subsequent downstream analysis will be restricted to "variant" and "gene" level information, with curators only accessing aggregate statistics on phenotype and patient health fields. The level of statistical summarization and granularity of the patient information exposed to curators will be determined by the ILDB workgroup's analysis of privacy-vs.-utility tradeoffs in the context of variant interpretation (C, D) The ClinGen crowd curation infrastructure (phone-app, web-interface) will bring together teams of domain experts for scalable interpretation of a much larger pool of associated variants. The curation and triage process for each disease domain will adhere to common standards, and remove lab-specific biases in interpretation. (E, F) Variant interpretations will be deposited in the new ClinGenKB repository, with any additional patient records, research samples or associated variants being iterated through the entire process, as before.