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# Correction to: ACMG SF v3.0 list for reporting of secondary findings in clinical exome and genome sequencing: a policy statement of the American College of Medical Genetics and Genomics (ACMG)

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Unfortunately an error occurred in Table 2 and 3. The correct Table 2 and 3 are given below.

In addition, on page 2 of the article (right column, fifth paragraph, third sentence), the phrase "deletions of" has been added. The correct sentence is given below. Other technical difficulties were noted for genes such as *EPCAM* associated with Lynch syndrome and *GREM1*-associated polyposis, where routine detection of common deletions or duplications could be difficult at this time by ES/GS in many laboratories. On page 7 of the article (right column, third paragraph, fifth sentence), the word “high” should be replaced by “low”. The



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correct sentence is given below. MODY3 does not require insulin treatment and responds well to low dose oral sulfonylureas, typically lower doses than are customary for most type 2 diabetics. On page 8 of the article (left column, third paragraph, second sentence), the word *"SERPINC1"* should be replaced by *"SERPINA1"*. The correct sentence is given below. The SFWG decided that including gene phenotypes such as *HMBS*-associated acute intermittent porphyria and *SERPINA1*/alpha-1-antitrypsin deficiency with interventions involving environmental exposures or behavior modification was beyond the scope of this list.

The original article has been corrected.

**Table 2.**

New gene-phenotype pairs for secondary findings (SF) list.

| Gene–phenotype | Key considerations |
|---|---|
| **Genes related to cancer phenotypes** | |
| *MAX*/hereditary paraganglioma/pheochromocytoma | Penetrance met threshold to include with other PGL/PCC genes |
| *PALB2*/hereditary breast cancer | Risk of breast cancer risk meets penetrance threshold |
| *TMEM127*/hereditary paraganglioma/pheochromocytoma | Penetrance met threshold to include with other PGL/PCC genes |
| **Genes related to cardiovascular phenotypes** | |
| *CASQ2*/catecholaminergic polymorphic ventricular tachycardia (CPVT) | Risk of sudden death with preventive interventions available |
| *FLNC*/cardiomyopathy | Risk of sudden death with preventive interventions available |
| *TRDN*/catecholaminergic polymorphic ventricular tachycardia (CPVT) & long QT syndrome | Risk of sudden death with preventive interventions available |
| *TTN*/cardiomyopathy | Risk of sudden death with preventive interventions available |
| **Genes related to inborn errors of metabolism phenotypes** | |
| *BTD*/biotinidase deficiency | Features can be nonspecific; highly effective treatment in children and adults |
| *GAA*/Pompe disease | Availability of effective enzyme replacement therapy in infantile and later-onset cases |
| **Genes related to miscellaneous phenotypes** | |
| *ACVRL1*/hereditary hemorrhagic telangiectasia | Potential morbidity meets penetrance threshold and has efficacious intervention |
| *ENG*/hereditary hemorrhagic telangiectasia | Potential morbidity meets penetrance threshold and has efficacious intervention |
| *HFE*/hereditary hemochromatosis (*HFE* p.C282Y homozygotes only) | Potential morbidity meets penetrance threshold and has efficacious intervention |
| *HNF1A*/maturity-onset diabetes of the young (MODY3) | Accounts for 30–50% of known MODY cases likely to respond to low dose sulfonylureas; early treatment may prevent complications |
| *RPE65*/*RPE65*-related retinopathy | Availability of gene therapy treatment that may be more efficacious earlier in disease progression |

*PGL*/*PCC* paraganglioma/pheochromocytoma.

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**Table 3.**

Genes not selected for secondary findings (SF) list v3.0 and reasoning.

| Gene–phenotype | Category | Additional comments |
|---|---|---|
| **Technical concerns** | | |
| *EPCAM*-associated Lynch syndrome | Cancer | Concern that deletions or duplications would be difficult to detect by NGS |
| *GREM1*-related polyposis | Cancer | Concern that duplication would be difficult to detect with NGS and overall limited information about this gene |
| *HNF1B*-related maturity-onset diabetes of the young (MODY5) | Miscellaneous | Accounts for ~5% of known MODY with ~50% of cases associated with deletions difficult to detect on exome sequencing |
| *SDHA*/hereditary paraganglioma/pheochromocytoma | Cancer | Concerns about presence of many pseudogenes that could lead to false positive results that would require labs to perform extensive validation work |
| **Penetrance concerns** | | |
| *BRIP1*/*RAD51C*/*RAD51D*-related ovarian cancer | Cancer | Lack of effective surveillance modalities for ovarian cancer also a consideration |
| *DICER1*-associated tumors | Cancer | Challenges in *DICER1* missense variant interpretation |
| *HFE*-related hemochromatosis (except for *HFE* p. C282Y homozygotes) | Miscellaneous | Penetrance is driven by the p.Cys282Tyr variant, and not other variants in HFE |
| *TTR*-amyloidosis | Miscellaneous | Also considered that sudden death was rare, thus allowing time for clinical diagnosis |
| **Clinical management concerns** | | |
| *ABCD1* X-linked adrenoleukodystrophy | IEM | Severe cases have early onset and would be diagnosed by newborn screening; no specific treatment in adulthood |
| *BAP1*-related tumors | Cancer | Small number of families reported to date and no established consensus management recommendations as of time reviewed |
| *COL5A1*-associated Ehlers–Danlos syndrome | Miscellaneous | Not considered highly actionable |
| *GCH1*-related dopa-responsive dystonia | Miscellaneous | Concern that diagnosis of the classic phenotype is relatively straightforward and that the treatment efficacy was not dependent on the timing of initiation |
| *HMBS*-associated acute intermittent porphyria | Miscellaneous | Concern that avoidance of exposures and delays in diagnosis could be out of scope for the ACMG SF list |
| *MEFV*-associated familial Mediterranean fever | Miscellaneous | Concern about clinical management of acute episodes being primarily supportive, and diagnosis could then be made through diagnostic testing |
| *NOTCH3*/CADASIL | Miscellaneous | Not considered highly actionable |
| *POLD1*/*POLE*-related polyposis | Cancer | Rarity of known pathogenic variants that could be reported and uncertain risks of extracolonic cancers |
| *PRKAR1A*/Carney complex | Miscellaneous | Concerns about penetrance and questions about actionability |
| *SERPINA1*-related alpha-1-antitrypsin deficiency | Miscellaneous | Concern that avoidance of exposures could be out of scope for the ACMG SF list |

*ACMG* American College of Medical Genetics and Genomics, *IEM* inborn errors of metabolism, *NGS* next-generation sequencing.