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| Table S5: Diagnostic rate by WES in Groups with and without the Phenotype | | | | |
| *Phenotype* | *HPO ID* | *Diagnostic Rate with the phenotype* | *Diagnostic Rate*  *without the phenotype* | *RR (95% CI)* | *FDR q*  *value* |
| Head or neck | HP:0000152 | 17/28 60,7% | 15/33 45,5% | 1,40 (0,79-2,47) | >0,99 |
| Abnormal face shape | HP:0001999 | 16/28 57,1% | 9/33 27,3% | 1,92 (1,11-3,31) | 0,260 |
| Microcephaly | HP:0000252 | 6/27 22,2% | 0/31 0% | 2,48 (1,78-3,45) | 0,176 |
| Macrocephaly | HP:0000256 | 1/27 3,7% | **2/32 6,3%** | 0,71 (0,14-3,65) | >0,99 |
| Nervous | HP:0000707 | 12/28 42,9% | **15/33 45,5%** | 0,94 (1,64-0,54) | >0,99 |
| Seizures | HP:0001250 | 3/28 10,7% | **5/33 15,2%** | 0,80 (0,31-2,03) | >0,99 |
| Cardiovascular | HP:0001626 | 13/28 46,4% | **15/33 45,5%** | 1,02 (0,59-1,76) | >0,99 |
| Limbs | HP:0040064 | 7/28 25% | **8/33 24,2 %** | 1,02 (0,55-1,91) | >0,99 |
| Abdomen | HP:0001438 | 5/28 17,9% | **9/33 27,3%** | 0,73 (0,34-1,56) | >0,99 |
| Endocrine | HP:0000818 | 7/28 25% | **3/33 9,1%** | 1,70 (1,00-2,86) | >0,99 |
| Eye | HP:0000478 | 3/28 10,7% | **3/33 9,1%** | 1,10 (0,47-2,58) | >0,99 |
| Genitourinary | HP:0000119 | 6/28 21,4% | **5/33 15,2%** | 1,24 (0,66-2,31) | >0,99 |
| Musculature | HP:0003011 | 9/28 32,1% | **11/33 33,3%** | 0,97 (0,54-1,74) | >0,99 |
| Respiratory | HP:0002086 | 8/28 28,6% | **13/33 39,4%** | 0,76 (0,40-1,43) | >0,99 |
| Skeletal | HP:0000924 | 0/28 0% | **2/33 6,1%** | - | >0,99 |
| Microcephaly AND  Abnormal face shape | HP:0000252  HP:0001999 | 5/27 18,5% | **0/31 0%** | 2,41 (1,75-3,32) | - |
| Cardiovascular AND  Abnormal face shape | HP:0001626  HP:0001999 | 7/28 25% | **5/33 15,2%** | 1,36 (0,76-2,42) | - |
| Nervous AND  Abnormal face shape | HP:0000707  HP:0001999 | 8/28 28,6% | **3/33 9,1%** | 1,82 (1,11-2,99) | - |
| Musculature AND  Abnormal face shape | HP:0003011  HP:0001999 | 4/28 14,3% | **4/33 12,1%** | 1,10 (0,52-2,35) | - |
| Cardiovascular AND limbs AND Abnormal face shape | HP:0001626  HP:0040064  HP:0001999 | 4/28 14,3% | **0/33 0%** | 2,38 (1,75-3,22) | - |
| CPR | - | 4/28 14,3% | **2/33 6,1%** | 1,53 (0,81-2,90) | >0,99 |
| Consanguinity | - | 5/28 13,3% | **3/32 9,4%** | 1,41 (0,76-2,62) | >0,99 |
| Premature Birth | - | 15/28 53,6% | **15/33 45,5%** | 1,19 (0,69-2,06) | >0,99 |
| SGA | - | 5/28 17,9% | **3/32 9,4%** | 1,41 (0,76-2,62) | >0,99 |
| VLBW and ELBW | - | 3/28 10,7% | **8/33 24,2** | 0,55 (0,20-1,49) | >0,99 |
| Organ Malformation 0-1 | - | 19/28 67,9% | **25/33 75,8%** | - | - |
| Organ Malformation ≥2 | - | 9/28 32,1% | **8/33 24,2%** | 1,23 (0,70-2,15) | >0,99 |
| First symptoms prenatal | - | 8/28 28,6% | **10/33 30,3%** | 0,96 (0,52-1,75) | >0,99 |
| First symptoms  congenital | - | 17/28 60,7% | **19/33 57,6%** | 1,07 (0,61-1,88) | >0,99 |
| First symptoms  first year | - | 5/29 17,9% | **4/33 12,1%** | 1,25 (0,65-2,43) | >0,99 |
| Organ Malformation ≥2 AND Premature Birth | - | 6/28 21,4% | **4/33 12,1%** | 1,39 (0,77-2,52) | - |
| Organ Malformation ≥2 AND SGA | - | 4/28 14,3% | **2/32 6,3%** | 1,50 (0,79-2,84) | - |
| Organ Malformation ≥2 AND Musculature | - | 2/28 7,1% | **2/33 6,1%** | 1,10 (0,40-3,04) | - |
| Organ Malformation ≥2 AND Endocrine | - | 3/28 10,7% | **0/33 0%** | 2,32 (1,72-3,12) | - |
| Abbreviations: RR, relative risk; CI, confidence interval; SGA, small gestational age; CPR, cardiopulmonary resuscitation; FDR,  false discovery rate, VLBW, very low birth weight; ELBW, extremely low birth weight.  FDR q value, corrected p-value calculated from 24 independent Fisher’s exact tests. FDR q value was not calculated for combinations of phenotypes due to interdependencies with tested single traits. | | | | | |