

Table 3) Top 11 combinations of clinical phenotypes and their association with PID (Cohorts 1 and 2).

The table presents combinations which had at least one phenotype in addition to PID. Phenotypes were selected hierarchically (based on ORs; see Figures 3 and 4), introducing at least one new phenotype combination in each table row (per cohort) and by including the highest number of possible combinations with significant ORs>3.00 (all P values< 1.00 × 10⁻³ indicated with †). The X/ Y/ Z numbering indicates the total number of phenotypes in each combination and how many of these had a median of first diagnosis greater than 3 (indicated with *) and 6 months (**) before PID diagnosis, respectively. PD: Physiological development; UNS: Unspecified; ENC: Encounter; LT: Long-term; MED: Medications; BCC: Blood cell count; IM: Immune mechanism; NEC: Not elsewhere classified.

Phenotype Combination	Odds Ratio (95% CI)	Number of phenotypes
Cohort 1		
Genetic carrier/ susceptibility to disease;** Asthma;** Lack of normal PD UNS.**	4.84 (1.72-7.96) †	3 / 3 / 3
Asthma;** Pneumonia;** Genetic carrier/ susceptibility to disease**.	5.85 (3.43-8.27) †	3 / 3 / 3
Pneumococcal pneumonia; Disorders involving the IM;** Asthma.**	5.98 (4.67-7.29) †	3 / 2 / 2
Other alveolar and parietoalveolar pneumonopathy; Bacterial pneumonia; Asthma.**	6.13 (4.39-7.87) †	3 / 1 / 1
Valvular heart disease/ heart chambers;** ENC for LT use of MED;* Asthma.**	6.46 (5.68-7.24) †	3 / 3 / 2
Lack of normal PD UNS;** Valvular heart disease/ heart chambers;** Pneumonia.**	5.78 (4.02-7.54) †	3 / 3 / 3
Decreased white BCC;** Asthma.**	5.41 (3.72-7.10) †	2 / 2 / 2
Decreased white BCC;** Bacterial pneumonia; ENC for long term use of MED;* Asthma.**	6.97 (4.89-9.05) †	4 / 3 / 2
Bronchiectasis;** Decreased white BCC;** ENC for long term use of MED.*	5.75 (3.45-8.05) †	3 / 3 / 2
Disorders involving the IM;** Decreased white BCC;** Asthma.**	6.53 (2.22-8.75) †	3 / 3 / 3
Decreased white BCC;** Disorders involving the IM;** Bacterial pneumonia; ENC for LT use of MED;* Asthma.**	4.98 (3.23-6.73) †	5 / 4 / 3
Cohort 2		
Autoimmune disease NEC;** Pneumonia;** Fever of unknown origin.**	5.79 (3.34-8.24) †	3 / 3 / 3
Valvular heart disease/ heart chambers;** Asthma;** Fever of unknown origin.**	5.30 (2.94-7.66) †	3 / 3 / 3
Chromosomal anomalies;** Pneumonia;** Valvular heart disease/ heart chambers.**	5.22 (3.88-6.56) †	3 / 3 / 3
Myopathy;** Pneumonia;** Asthma.**	5.32 (3.26-7.38) †	3 / 3 / 3
Non hodgkins lymphoma;** Pneumonia;** Fever of unknown origin.**	6.96 (3.76-10.20) †	3 / 3 / 3
Thrombocytopenia;* Non hodgkins lymphoma;** Pneumonia.**	6.75 (3.49-10.01) †	3 / 3 / 2
Pneumococcal pneumonia; Non hodgkins lymphoma;** Fever of unknown origin.**	5.88 (3.74-8.01) †	3 / 2 / 2
Disorders involving the immune mechanism;** Chromosomal anomalies;** Fever of unknown origin.**	5.25 (3.73-6.77) †	3 / 3 / 3
Asthma;** ENC for long term use of antibiotics; Fever of unknown origin.**	6.33 (3.27-9.39) †	3 / 2 / 2
Bone marrow /stem cell transplant;** Decreased white BCC;** Pneumonia.**	5.65 (3.47-7.83) †	3 / 3 / 3
Myeloproliferative disease;** Asthma;** Fever of unknown origin.**	5.89 (3.23-8.54) †	3 / 3 / 3

Table 3) (Continued)

Phenotype Combination	Odds Ratio (95% CI)	Number of phenotypes
Cohort 3		
Other deficiencies of circulating enzymes; Disorders involving the IM.**	4.86 (2.73-6.93) †	2 / 1 / 1
Autoimmune disease NEC;** Asthma.**	4.76 (2.33-7.14) †	2 / 2 / 2
Bone marrow /stem cell transplant;** Disorders involving the IM;** Asthma.**	6.38 (4.67-8.29) †	3 / 3 / 3
Pneumonia;** Bone marrow /stem cell transplant;** Disorders involving the IM.**	6.35 (3.87-8.84) †	3 / 3 / 3
Bone marrow /stem cell transplant;** Chromosomal anomalies.	5.46 (3.68-7.24) †	2 / 1 / 1
Genetic carrier /susceptibility to disease;* Asthma.**	6.78 (5.02-8.54) †	2 / 2 / 1
Genetic carrier /susceptibility to disease;* Other disorders of purine and pyrimidine metabolism.	5.81 (4.72-6.89) †	2 / 1 / 0
Celiac disease;** Asthma.**	5.37 (2.89-7.85) †	2 / 2 / 2
Decreased white BCC;* Pneumonia;** Asthma.**	5.75 (4.45-7.04) †	3 / 3 / 2
Decreased white BCC;* Cardiac congenital anomalies.*	6.83 (4.22-9.44) †	2 / 2 / 0
Perforation of tympanic membrane;** Asthma.**	5.58 (4.23-6.92) †	2 / 2 / 2
Cohort 4		
Chromosomal anomalies;* Cardiac congenital anomalies; Lack of normal PD UNS.	6.09 (5.75-6.43) †	3 / 1 / 0
Disorders involving the IM;* Non hodgkins lymphoma;** Asthma.**	6.07 (5.71-6.44) †	3 / 3 / 2
Bone marrow /stem cell transplant;** Disorders involving the IM.*	5.86 (5.31-6.41) †	2 / 2 / 1
Autoimmune disease NEC;** Celiac disease.**	5.75 (4.03-6.52) †	2 / 2 / 2
Bone marrow /stem cell transplant;** Bronchiectasis;* Non hodgkins lymphoma.**	5.98 (3.75-8.21) †	3 / 3 / 2
Autoimmune disease NEC;** Asthma.**	5.35 (3.51-7.19) †	2 / 2 / 2
Autoimmune disease NEC;** Celiac disease;** Disorders involving the IM.*	4.56 (2.85-6.27) †	3 / 3 / 2
Psoriatic arthropathy;** Autoimmune disease NEC;** Asthma.**	6.25 (4.73-7.77) †	3 / 3 / 3
Psoriatic arthropathy;** Disorders involving the IM;* Asthma.**	5.33 (3.27-7.39) †	3 / 3 / 2
Non hodgkins lymphoma;** Psoriatic arthropathy;** Disorders involving the IM.*	5.65 (4.47-6.83) †	3 / 3 / 2
Disorders involving the IM;* Non hodgkins lymphoma.**	5.29 (4.23-6.34) †	2 / 2 / 1