## Supplementary Table 6. Subgroup analyses of clinical manifestations in children versus adults

| Manifestation                            | Children                  | Adults                  |
|------------------------------------------|---------------------------|-------------------------|
|                                          | Pooled proportion (95% CI)| I²                      | Pooled proportion (95% CI)| I²                      |
| Clinical phenotype<sup>a</sup>            |                           |                         |                          |
| Infections only                          | 76 (57-91)                | 84                      | 38 (27-49)                | 70                      |
| Autoimmunity                             | 14 (5-27)                 | 90                      | 21 (12-30)                | 94                      |
| Polyclonal lymphocytic infiltration      | n/a                       | n/a                     | 25 (21-29)                | 0                       |
| Enteropathy                              | 10 (3-20)                 | 78                      | 14 (10-18)                | 67                      |
| Lymphoid malignancy                      | 5 (2-10)                  | 55                      | 6 (5-8)                   | 0                       |
| Malignancy                               | 5 (3-7)                   | 0                       | 16 (11-21)                | 85                      |
| Respiratory involvement                  |                           |                         |                          |
| Otitis                                   | 55 (45-64)                | 68                      | 32 (27-37)                | 42                      |
| Sinusitis                                | 62 (50-74)                | 79                      | 74 (60-86)                | 91                      |
| Upper respiratory tract infection        | 69 (45-89)                | 91                      | 79 (66-90)                | 80                      |
| Pneumonia                                | 61 (50-71)<sup>b</sup>    | 74                      | 66 (51-79)<sup>c</sup>    | 93                      |
| Bronchitis                               | 59 (11-71)                | 97                      | 72 (38-97)                | 98                      |
| Lower respiratory tract infection        | 71 (59-82)                | 0                       | n/a                       | n/a                     |
| Bronchiectasis                           | 16 (9-25)                 | 81                      | 36 (27-46)                | 93                      |
| GLILD                                    | 6 (4-9)                   | 0                       | 33 (13-57)                | 97                      |
| Lymphoid hyperplasia                     | 2 (0-6)                   | 30                      | 11 (2-24)                 | 94                      |
| Asthma                                   | 3 (5-9)                   | 93                      | 33 (21-47)                | 94                      |
| Allergic rhinitis                        | 17 (3-39)                 | 83                      | n/a                       | n/a                     |
| Allergy                                  | 49 (33-65)                | 40                      | n/a                       | n/a                     |
| Mastoiditis                              | 4 (0-15)                  | 81                      | n/a                       | n/a                     |
| Lung cancer                              | n/a                       | n/a                     | 1 (0-2)                   | 46                      |
| Interstitial lung disease                | 6 (1-14)                  | 51                      | 15 (3-35)                 | 90                      |
| Pharyngitis/tonsillitis                  | 17 (8-28)                 | 78                      | n/a                       | n/a                     |
| Conjunctivitis                           | 16 (8-25)                 | 64                      | n/a                       | n/a                     |
| Gastrointestinal involvement             |                           |                         |                          |
| Chronic diarrhea                         | 17 (11-24)                | 50                      | 34 (22-48)                | 93                      |
| Gastrointestinal tract infection         | 35 (18-55)<sup>d</sup>    | 89                      | 34 (8-65)<sup>e</sup>     | 98                      |
| Inflammatory bowel disease               | 3 (1-6)                   | 32                      | 18 (6-33)                 | 96                      |
| Celiac disease                           | 3 (1-5)                   | 10                      | 2 (1-4)                   | 32                      |
| Atrophic gastritis                       | n/a                       | n/a                     | 9 (0-26)                  | 87                      |
| Stomach cancer                           | n/a                       | n/a                     | 2 (0-6)                   | 82                      |
| Colorectal cancer                        | n/a                       | n/a                     | 1 (0-4)                   | 75                      |
| Malabsorption                            | 5 (3-8)                   | 0                       | 11 (0-32)                 | 97                      |
| Gastro-esophageal reflux disease         | 12 (1-30)                 | 90                      | n/a                       | n/a                     |
| Glandular tissue                         |                           |                         |                          |
| Sjogren’s syndrome                       | n/a                       | n/a                     | 3 (0-8)                   | 82                      |
| Breast cancer                            | n/a                       | n/a                     | 2 (1-3)                   | 49                      |
| Hepatic involvement                      |                           |                         |                          |
| Autoimmune hepatitis                     | 2 (0-6)                   | 42                      | 4 (0-12)                  | 92                      |
| Viral hepatitis                          | n/a                       | n/a                     | 2 (1-5)                   | 69                      |
| Liver cancer                             | n/a                       | n/a                     | 1 (0-1)                   | 44                      |
| Unexplained hepatomegaly                 | 21 (2-50)                 | 96                      | n/a                       | n/a                     |
| Urinary tract involvement                |                           |                         |                          |
| Urinary tract infection                  | 11 (8-15)                 | 0                       | 15 (12-19)                | 0                       |
| Pyelonephritis                           | 8 (0-22)                  | 70                      | n/a                       | n/a                     |
| Hematologic involvement                      | n/a     | n/a     | n/a     | n/a     |
|---------------------------------------------|---------|---------|---------|---------|
| Idiopathic thrombocytopenia                 | 9 (2-21)| 87      | 6 (2-12)| 86      |
| Autoimmune cytopenia                        | 15 (4-30)| 76      | 16 (7-27)| 67      |
| Autoimmune hemolytic anemia                 | 6 (4-9) | 0       | 5 (2-8) | 68      |
| Autoimmune neutropenia                      | 4 (0-11)| 83      | 2 (0-6) | 86      |
| Evans syndrome                              | 9 (0-26)| 86      | n/a     | n/a     |
| Pernicious anemia                           | 1 (0-3) | 61      | 1 (1-3) | 29      |
| Bloodstream infection                       | 8 (5-12)| 29      | 12 (9-16)| 47      |
| Neuromuscular involvement                   |         |         |         |         |
| Infectious meningitis                       | 7 (2-13)| 69      | 7 (4-9) | 29      |
| Bell’s palsy                                | 2 (0-17)| 78      | n/a     | n/a     |
| Multiple sclerosis                          | n/a     | n/a     | 1 (0-1) | 6       |
| Bone and joint involvement                  |         |         |         |         |
| Septic arthritis                           | 8 (1-22)| 67      | n/a     | n/a     |
| Rheumatoid arthritis                        | n/a     | n/a     | 4 (1-7) | 64      |
| Seronegative arthritis                      | 2 (0-6) | 55      | n/a     | n/a     |
| Psoriatic arthritis                         | n/a     | n/a     | 1 (0-2) | 57      |
| Osteomyelitis                               | 2 (0-6) | 68      | n/a     | n/a     |
| Kaposi’s sarcoma                            | n/a     | n/a     | 0 (0-1) | 0       |
| Lymph node and spleen involvement           |         |         |         |         |
| Lymphadenopathy                             | 22 (44-48)| 96     | n/a     | n/a     |
| Non-malignant lymphoproliferation           | n/a     | n/a     | 27 (12-46)| 89      |
| Splenomegaly                                | 20 (6-39)| 94     | 30 (16-46)| 95      |
| Non-hodgkin’s lymphoma                      | 1 (0-3) | 14      | 5 (4-6) | 40      |
| Hodgkin’s lymphoma                          | 5 (2-11)| 0       | 1 (0-2) | 0       |
| Splenectomy                                 | n/a     | n/a     | 7 (5-10)| 17      |
| Leukemia                                    | n/a     | n/a     | 1 (0-1) | 16      |
| Endocrinological involvement                |         |         |         |         |
| Thyroid disease                             | 8 (0-24)| 66      | 29 (12-50)| 96      |
| Autoimmune thyroiditis                      | 3 (1-6) | 0       | 6 (2-12) | 83      |
| Diabetes mellitus                           | 2 (0-4) | 0       | 4 (0-14) | 82      |
| Thyroid cancer                              | n/a     | n/a     | 1 (0-2) | 74      |
| Muco/cutaneous involvement                  |         |         |         |         |
| Psoriasis                                   | 1 (0-6) | 72      | 4 (2-7) | 49      |
| Atopic dermatitis                           | 16 (12-20)| 0    | n/a     | n/a     |
| Alopecia                                    | 1 (0-3) | 0       | n/a     | n/a     |
| Vitiligo                                    | 2 (1-4) | 0       | 2 (1-4) | 48      |
| Warts                                       | 6 (3-9) | 0       | 5 (3-7) | 0       |
| Skin cancer                                 | 1 (0-3) | 28      | 5 (2-8) | 64      |
| Skin infections                             | 16 (9-25)| 64     | 13 (6-23)| 73      |
| Recurrent herpes zoster infections           | 19 (12-27)| 0    | 7 (2-15) | 91      |
| Recurrent herpes simplex infections          | n/a     | n/a     | 17 (0-47)| 96      |
| Oral candidias                              | 12 (8-16)| 2     | 6 (0-20)| 96      |
| Urticaria                                   | 3 (1-6) | 28      | n/a     | n/a     |
| Clubbing                                    | 5 (1-12)| 49      | n/a     | n/a     |
| Other clinical manifestations                |         |         |         |         |
| Growth retardation                          | 19 (15-23)| 0    | n/a     | n/a     |
| Unexplained granuloma                       | 6 (2-12)| 53      | 15 (7-25)| 90      |
| Vasculitis                                  | 1 (0-5) | 47      | 2 (2-4) | 0       |
| Systemic lupus erythematosus                 | 1 (0-9) | 75      | 2 (1-3) | 0       |
According to Chapel et al.

Streptococcus pneumoniae 10% (0-29).

Streptococcus pneumoniae 10% (0-28), Haemophilus influenzae 8% (4-14), Mycobacterial infection 1% (0-2), Pneumocystis Jiruveci 1% (0-2), Pseudomonas 2% (1-5).

Giardia intestinalis 13% (7-20), Salmonella species 8% (2-18), Campylobacter species 5% (0-14).

Giardia intestinalis 12% (0-32), Salmonella species 3% (0-12), Campylobacter species 3% (0-10), Clostridium difficile 2% (0-3), Cryptosporidium species 1% (0-2), Helicobacter pylori 6% (1-12).