**Supplementary Table 1.** Number and types of antibiotic purchases before index date[a] in the matched case-control study of 950 children as compared with antibiotic purchases in the whole Fin-HIT cohort of 11 407 children (born 2000-2005) from birth until 31 December 2018.

| **Antibiotic types** | **Number of antibiotic purchases before index date[a] in the matched case-control study**<br><br>**N= 8 604 (%)** | **Number of all antibiotic purchases in the Fin-HIT cohort**<br><br>**N=130 440 (%)** |
|---|---|---|
| **Penicillins, N(%)** | 3 453 (100) – **40.1%** | 52 633 (100) – **40.4%** |
| *Phenoxymethylpenicillin (J01CE02)* | 431 (12.5) | 8 399 (16.0) |
| *Amoxicillin (J01CA04)* | 3 009 (87.1) | 43 657 (82.9) |
| *Flucloxacillin (J01CF05)* | 0 | 42 (0.1) |
| *Pivmesillinam (J01CA08)* | 13 (0.4) | 535 (1.0) |
| **Macrolides, N(%)** | 1 949 (100) – **22.7%** | 26 318 (100) – **20.2%** |
| *Erythromycin (J01FA01)* | 2 (0.1) | 56 (0.2) |
| *Roxithromycin (J01FA06)* | 4 (0.2) | 188 (0.7) |
| *Clarithromycin (J01FA09)* | 229 (11.7) | 3 737 (14.2) |
| *Azithromycin (J01FA10)* | 1 714 (87.9) | 22 325 (84.8) |
| *Telithromycin (J01FA15)* | 0 | 12 (0.0) |
| **Amoxicillin-clavulanic acid (**J01CR02), **N(%)** | 1 295 (100) – **15.1%** | 18 262 (100) – **14.0%** |
| **Cephalosporines, N(%)** | 1 202 (100) – **14.0%** | 20 993 (100) – **16.1%** |
| *Cephalexin (J01DA01)* | 1 023 (85.1) | 18 713 (89.1) |
| *Cefuroxime (J01DA06)* | 33 (2.7) | 435 (2.1) |
| *Cefaclor (J01DA08)* | 115 (9.6) | 1 500 (7.1) |
| *Cefadroxil (J01DA09)* | 30 (2.5) | 338 (1.6) |
| *Ceftriaxone (J01DA39 and J01DA63)* | 1 (0.1) | 7 (0.0) |
| **Sulphonamides and trimethoprime, N(%)** | 168 (100) – **7.2%** | 8 958 (100) – **6.9%** |
| *Trimethoprime (J01EA01)* | 65 (10.5) | 860 (9.6) |
| *Trimethoprime sulphate (J01EE01 and J01EE02)* | 553 (89.5) | 8 098 (90.4) |
| **Tetracyclins, N(%)** | 54 (100) – **0.6%** | 2 555 (100) – **2%** |
| *Doxicyclin (J01AA02)* | 30 (55.6) | 1 097 (42.9) |
| *Lymecyclin (J01AA04)* | 20 (37.0) | 1 049 (41.1) |
| *Tetracyclin (J01AA07)* | 4 (7.4) | 409 (16.0) |
| **Clindamycin** (J01FF01), **N(%)** | 23 (100) – **0.3%** | 443 (100) – **0.3%** |
| **Fluoroquinolones** | 4 (100) – **0.0%** | 220 (100) – **0.2%** |
| *Ciprofloxacin* (J01MA01 and J01MA02) | 4 (100) | 193 (87.7) |
| *Levofloxacin* (J01MA02) | 0 | 19 (8.6) |
| *Moxifloxacin* (J01MA14) | 0 | 8 (3.6) |
| **Others** (nitrofurantoin (J01XE01) and metronidazole (J01XD01 and P01AB01), **N(%)** | 6 (100) – **0.1%** | 58 (100) – **0.0%** |

[a] Index date= date of diagnosis for children who developed autoimmune diseases and compatible date for their matching controls.

**Supplementary Table 2.** Association between types and age of first antibiotic purchase and the onset of autoimmune diseases (DM, AIT, JIA, and IBD).

| First antibiotic purchase | AD (N=242) | Matched controls (N=708) | DM (N=102) | Matched DM controls (N=280) | AIT (N=68) | Matched AIT controls (N=190) | JIA (N=54) | Matched JIA controls (N=156) | IBD (N=27) | Matched IBD controls (N=73) |
|---|---|---|---|---|---|---|---|---|---|---|
| **Median age, years (IQR)** | 1.06 (0.65-1.82) | 1.00 (0.65-1.69) | 1.09 (0.71-1.84) | 1.02 (0.68-1.85) | 1.10 (0.74-2.09) | 0.97 (0.60-1.68) | 0.84 (0.50-1.30) | 1.11 (0.65-1.70) | 1.15 (0.72-1.87) | 0.88 (0.56-1.56) |
| **Antibiotic type, N(%)** | | | | | | | | | | |
| No antibiotics | 14 (5.8) | 34 (4.8) | 9 (8.8) | 16 (5.7) | 2 (2.9) | 4 (2.1) | 4 (7.4) | 11 (7.1) | 0 | 2 (2.7) |
| Penicillin | 133 (55.0) | 386 (54.5) | 56 (54.9) | 157 (56.1) | 40 (58.8) | 93 (49.0) | 27 (50.0) | 85 (54.5) | 16 (59.3) | 45 (61.6) |
| Cephalosporine | 15 (6.2) | 58 (8.2) | 6 (5.9) | 21 (7.5) | 4 (5.9) | 20 (10.5) | 4 (7.4) | 13 (8.3) | 1 (3.7) | 4 (5.5) |
| Macrolide | 51 (21.1) | 135 (19.0) | 25 (24.5) | 57 (20.4) | 14 (20.6) | 43 (22.6) | 11 (20.4) | 21 (13.5) | 2 (7.4) | 12 (16.4) |
| Amoxicillin-clavulanic acid | 25 (10.3) | 85 (12.0) | 5 (4.9) | 23 (8.2) | 7 (10.3) | 28 (14.7) | 6 (11.1) | 25 (16.0) | 8 (29.6) | 9 (12.3) |
| Sulphonamides and trimethoprim | 4 (1.6) | 10 (1.4) | 1 (1.0) | 6 (2.1) | 1 (1.5) | 1 (0.5) | 2 (3.7) | 1 (0.6) | 0 | 1 (1.4) |
| Others | 0 | 1 (0.1) | 0 | 0 | 0 | 1 (0.5) | 0 | 0 | 0 | 0 |

[a]

AD=autoimmune diseases. Cases=children with ADs (represented with DM (type 1 diabetes mellitus), AIT (autoimmune thyroiditis), JIA (juvenile idiopathic arthritis), and IBD (inflammatory bowel diseases)). Nine children had two diagnoses. IQR=Interquartile Range. The association between types of first antibiotics and the onset of ADs were estimated using conditional logistic regression with penicillin as reference. P>0.05 in every analysis comparing cases and matched controls.

**Supplementary Table 3.** Additional information for Figure 3. Association between types of antibiotic purchases in different periods and the development of an autoimmune disease (AD), represented by type 1 diabetes (DM), autoimmune thyroiditis (AIT), juvenile idiopathic arthritis (JIA), or inflammatory bowel diseases (IBD)[a].

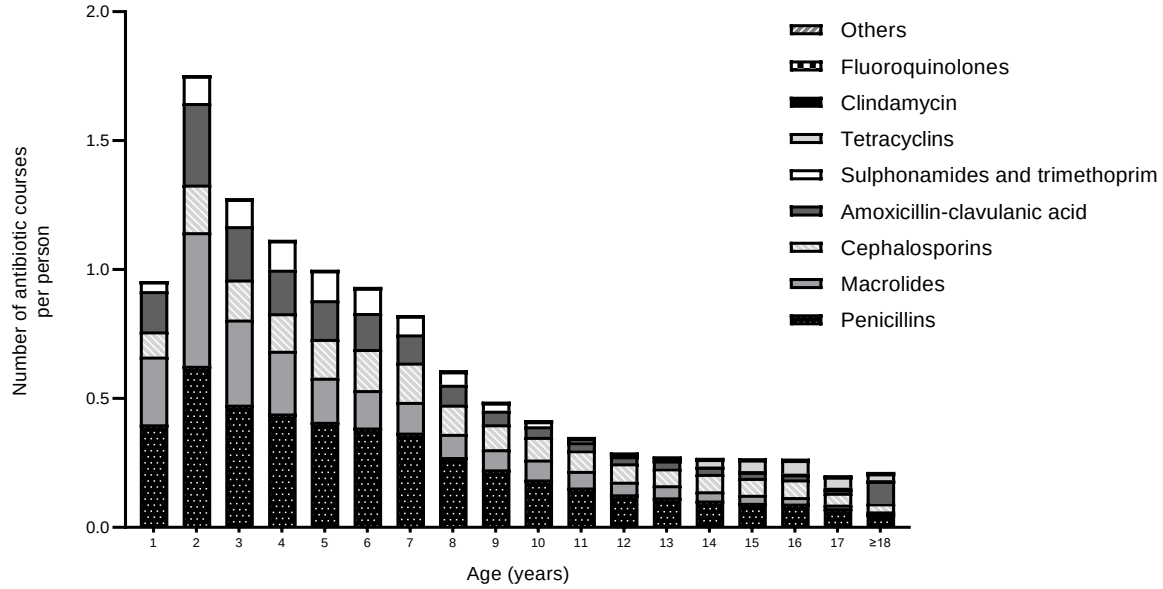
| **Antibiotic types in different periods** | **AD (N=242)** | **DM (N=102)** | **AIT (N=68)** | **JIA (N=54)** | **IBD (N=27)** |
|---|---|---|---|---|---|
| | **OR (95%CI)[b]** | **OR (95%CI)** | **OR (95%CI)** | **OR (95%CI)** | **OR (95%CI)** |
| **Throughout childhood (From birth to index date[c])** | | | | | |
| Penicillin | 1.01 (0.96-1.06) | 1.05 (0.97-1.14) | 0.96 (0.88-1.05) | 1.06 (0.94-1.19) | 1.00 (0.87-1.14) |
| Cephalosporine | 1.03 (0.95-1.12) | 1.04 (0.88-1.22) | 0.93 (0.82-1.06) | *1.25 (1.03-1.52)* | 1.16 (0.88-1.52) |
| Macrolide | 1.04 (0.90-1.09) | 1.04 (0.94-1.16) | 0.97 (0.88-1.08) | *1.21 (1.06-1.38)* | 1.03 (0.94-1.13) |
| Amoxicillin-Clavulanic acid | 1.05 (0.98-1.13) | 1.02 (0.88-1.18) | 0.97 (0.85-1.10) | *1.19 (1.02-1.39)* | 1.15 (0.98-1.34) |
| Sulphonamides and trimethoprim | 1.08 (1.00-1.16) | 1.12 (0.98-1.29) | 1.04 (0.94-1.14) | 1.31 (0.96-1.78) | 1.09 (0.82-1.45) |
| **Infancy (<age of 1 year)** | | | | | |
| Penicillin | 1.45 (0.90-2.32) | 0.90 (0.62-1.30) | 0.77 (0.49-1.23) | 1.06 (0.68-1.65) | 0.53 (0.23-1.19) |
| Cephalosporine | 0.94 (0.64-1.38) | 0.76 (0.37-1.57) | 0.68 (0.30-1.51) | *2.54 (1.01-6.38)* | 0.50 (0.08-3.00) |
| Macrolide | 1.00 (0.78-1.28) | 0.87 (0.57-1.32) | 0.83 (0.53-1.31) | *1.80 (1.08-3.01)* | 0.47 (0.14-1.61) |
| Amoxicillin-Clavulanic acid | 1.07 (0.77-1.49) | 0.65 (0.30-1.41) | 0.65 (0.30-1.38) | *1.93 (1.12-3.32)* | 1.17 (0.34-4.03) |
| Sulphonamides and trimethoprim | 1.26 (0.89-1.78) | 1.15 (0.70-1.87) | 0.65 (0.30-1.38) | 1.21 (0.19-7.58) | 0.50 (0.01-23.6) |
| **Toddler phase (From age of 1 up to third birthday)** | | | | | |
| Penicillin | 1.06 (0.95-1.19) | 1.15 (0.97-1.35) | 1.08 (0.85-1.38) | 1.02 (0.77-1.35) | 1.03 (0.76-1.40) |
| Cephalosporine | 1.11 (0.92-1.33) | 1.05 (0.78-1.41) | 0.76 (0.51-1.12) | *1.69 (1.15-2.48)* | 1.57 (0.81-3.03) |
| Macrolide | 1.09 (0.97-1.21) | 1.09 (0.91-1.31) | 1.01 (0.84-1.21) | *1.40 (1.09-1.79)* | 0.83 (0.58-1.19) |
| Amoxicillin-Clavulanic acid | *1.18 (1.01-1.37)* | 1.22 (0.98-1.54) | 0.94 (0.70-1.25) | *1.43 (1.03-2.00)* | 1.30 (0.79-2.15) |
| Sulphonamides and trimethoprim | 1.10 (0.94-1.29) | 1.10 (0.84-1.44) | 1.12 (0.89-1.41) | 1.63 (0.77-3.47) | 0.91 (0.46-1.77) |
| **Preschool to adolescence (From age 3 years to index date)** | | | | | |
| Penicillin | 1.01 (0.94-1.08) | 1.04 (0.92-1.17) | 0.94 (0.84-1.06) | 1.09 (0.94-1.28) | 1.02 (0.86-1.22) |
| Cephalosporine | 1.02 (0.92-1.13) | 1.07 (0.87-1.33) | 0.97 (0.84-1.12) | 1.12 (0.86-1.46) | 1.13 (0.84-1.53) |
| Macrolide | 1.04 (0.97-1.12) | 1.09 (0.89-1.33) | 0.94 (0.70-1.12) | 1.19 (0.98-1.45) | 1.06 (0.95-1.18) |
| Amoxicillin-Clavulanic acid | 1.03 (0.93-1.13) | 0.89 (0.69-1.16) | 1.00 (0.84-1.19) | 1.12 (0.91-1.38) | 1.18 (0.98-1.42) |
| Sulphonamides and trimethoprim | 1.10 (0.98-1.24) | *1.35 (1.03-1.77)* | 1.00 (0.84-1.16) | 1.26 (0.89-1.78) | 1.45 (0.90-2.32) |
| **Purchases within 2 years before index date** | | | | | |
| Penicillin | 0.96 (0.80-1.14) | 0.81 (0.61-1.08) | 1.03 (0.71-1.50) | 1.19 (0.84-1.71) | 0.97 (0.58-1.62) |
| Cephalosporine | 1.19 (0.98-1.45) | 1.22 (0.94-1.57) | 1.15 (0.78-1.71) | 1.01 (0.56-1.82) | 2.19 (0.90-5.32) |
| Macrolide | *1.24 (1.01-1.51)* | 1.12 (0.83-1.51) | 0.87 (0.38-2.03) | 1.35 (0.91-2.00) | 1.29 (0.81-2.04) |
| Amoxicillin-Clavulanic acid | 1.04 (0.83-1.31) | 1.01(0.70-1.48) | 0.44 (0.17-1.11) | 1.33 (0.92-1.93) | 1.23 (0.45-3.39) |
| Sulphonamides and trimethoprim | 1.15 (0.84-1.57) | 0.60 (0.22-1.64) | 1.19 (0.80-1.76) | 1.25 (0.64-2.44) | 8.08 (infinity) |

[a] Cases=children with ADs (DM, AIT, JIA or IBD). Nine children had two diagnoses

[b] OR=Odds ratio, CI= 95% Confidence Interval. Analyses was performed using conditional logistic regression.

[c] Index date= date of diagnosis for children who developed autoimmune diseases and compatible date for their matching controls.

## Supplementary Figure 1




Title: All purchased per person antibiotics in the cohort of 11,407 children born in 2000-2005. Number of tetracyclin, clindamycin, fluoroquinolone, and other antibiotics purchases were low.