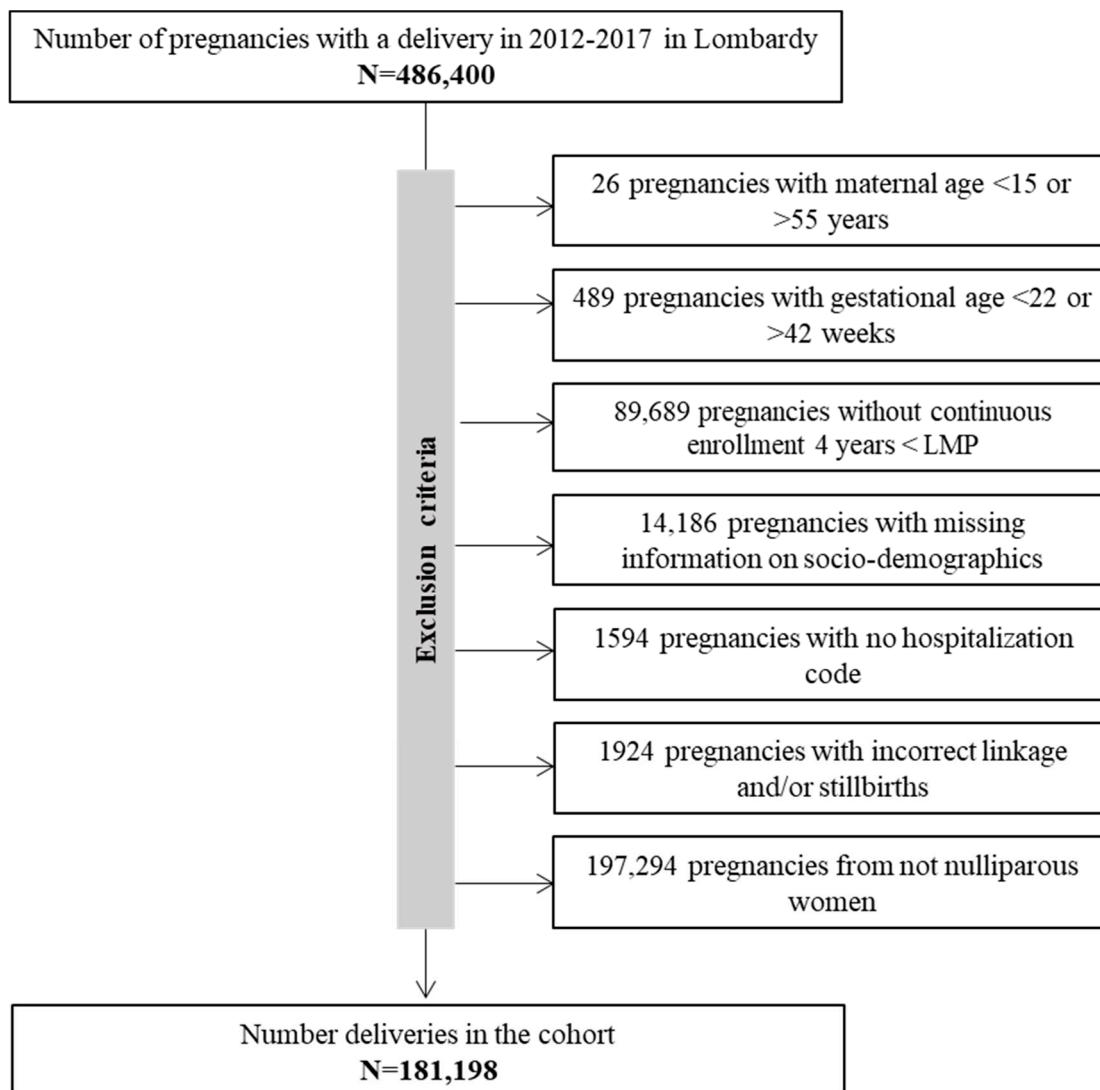


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**Figure S1.** Flow-chart of the cohort.

**Table S1.** List of factors included in the Preterm Birth Score (PTBS), and corresponding codes.

| Variable   | Code <sup>a</sup> | Code type                                  |
|--|-------------------|--|
| <b>Drugs</b>   |                   |  |
| Pancreatic hormones                                  | H04               | ATC <sup>b</sup> code (first 3 digits)     |
| Agents acting on the renin-angiotensin system        | C09               |  |
| Sex hormones and modulators of the genital system    | G03               |  |
| Endocrine therapy                                    | L02               |  |
| Drugs used in diabetes                               | A10               |  |
| Immunosuppressants                                   | L04               |  |
| Corticosteroids for systemic use                     | H02               |  |
| Beta blocking agents                                 | C07               |  |
| Calcium channel blockers                             | C08               |  |
| <b>Hospital diagnosis</b>                            |                   |  |
| Heart failure  | 428               | ICD9-CM <sup>c</sup> code (first 3 digits) |
| Chronic renal failure                                | 585               |  |
| Diffuse diseases of connective tissue                | 710               |  |
| <b>Inpatient procedures</b>                          |                   |  |
| Other operations on rectum and perirectal tissue     | 48.9              | ICD9-CM <sup>c</sup> code (first 3 digits) |
| Diagnostic procedures on liver                       | 50.1              |  |
| Lysis of peritoneal adhesions                        | 54.5              |  |
| <b>Exemptions</b>                                    |                   |  |
| Transplant recipients <sup>d</sup>                   | 052               | National classification code               |
| Diabetes mellitus                                    | 013               |  |
| Systemic lupus erythematosus                         | 028               |  |
| Affections of the circulatory system                 | 002               |  |
| Chronic (active) hepatitis                           | 016               |  |
| <b>Outpatient services</b>                           |                   |  |
| Psychiatry   | 231               | National code of the medical branch        |
| General consultation                                 | 263               |  |
| <b>Socio-demographic conditions</b>                  |                   |  |
| Age at conception ≥ 36 years                         | -                 | -  |
| Born abroad  | -                 | -  |
| Low education  | -                 | -  |
| <b>Use of assisted medical conception techniques</b> | -                 | -  |

<sup>a</sup> No code was used to identify socio-demographic conditions and use of assisted medical conception techniques as the information was taken directly from the CedAP registry.

<sup>b</sup> Anatomical Therapeutic Chemical classification system

<sup>c</sup> International Classification of Diseases, 9th Revision, Clinical Modification

<sup>d</sup> Kidney, heart, lung, liver, pancreas, or bone marrow.

**Table S2.** Estimates of LASSO logistic regression coefficients for the 26 variables contributing to the Preterm Birth Score (PTBS)

| Variable   | Coefficient  |
|--|--------------|
| <b>Drugs</b>   |              |
| Pancreatic hormones                                  | 0.883        |
| Agents acting on the renin-angiotensin system        | 0.459        |
| Sex hormones and modulators of the genital system    | 0.332        |
| Endocrine therapy                                    | 0.251        |
| Drugs used in diabetes                               | 0.244        |
| Immunosuppressants                                   | 0.201        |
| Corticosteroids for systemic use                     | 0.052        |
| Beta blocking agents                                 | 0.128        |
| Calcium channel blockers                             | 0.108        |
| <b>Hospital diagnosis</b>                            |              |
| Heart failure  | 0.726        |
| Chronic renal failure                                | 0.385        |
| Diffuse diseases of connective tissue                | 0.221        |
| <b>Inpatient procedures</b>                          |              |
| Other operations on rectum and perirectal tissue     | 1.045        |
| Diagnostic procedures on liver                       | 0.393        |
| Lysis of peritoneal adhesions                        | 0.337        |
| <b>Exemptions</b>                                    |              |
| Transplant recipients <sup>a</sup>                   | 0.747        |
| Diabetes mellitus                                    | 0.325        |
| Systemic lupus erythematosus                         | 0.332        |
| Affections of the circulatory system                 | 0.073        |
| Chronic (active) hepatitis                           | 0.106        |
| <b>Outpatient services</b>                           |              |
| Psychiatry   | 0.046        |
| General consultation                                 | 0.048        |
| <b>Socio-demographic conditions</b>                  |              |
| Age at conception $\geq 36$ years                    | 0.226        |
| Born abroad  | 0.055        |
| Low education  | 0.049        |
| <b>Use of assisted medical conception techniques</b> | <b>0.881</b> |

<sup>a</sup> Kidney, heart, lung, liver, pancreas, or bone marrow.

**Table S3.** Frequency of the 26 variables contributing to the Preterm Birth Score (PTBS) in the internal validation set (Lombardy).

| Variable   | Frequency (%)          |                          |                     |
|--|------------------------|--------------------------|---------------------|
|  | Term birth<br>N=50,443 | Preterm birth<br>N=3,916 | Total<br>N=54,359   |
| <b>Drugs</b>   |                        |                          |                     |
| Pancreatic hormones                                  | 38 (0.08)              | 10 (0.26)                | 48 (0.09)           |
| Agents acting on the renin-angiotensin system        | 339 (0.67)             | 75 (1.92)                | 414 (0.76)          |
| Sex hormones and modulators of the genital system    | 9,725 (19.28)          | 1,279 (32.66)            | 11,004 (20.24)      |
| Endocrine therapy                                    | 243 (0.48)             | 69 (1.76)                | 312 (0.57)          |
| Drugs used in diabetes                               | 218 (0.43)             | 54 (1.38)                | 272 (0.50)          |
| Immunosuppressants                                   | 101 (0.20)             | 22 (0.56)                | 123 (0.23)          |
| Corticosteroids for systemic use                     | 5,607 (11.12)          | 551 (14.07)              | 6,158 (11.33)       |
| Beta blocking agents                                 | 445 (0.88)             | 55 (1.40)                | 500 (0.92)          |
| Calcium channel blockers                             | 196 (0.39)             | 33 (0.84)                | 229 (0.42)          |
| <b>Hospital diagnosis</b>                            |                        |                          |                     |
| Heart failure  | 1 (0.00)               | 0 (0.00)                 | 1 (0.00)            |
| Chronic renal failure                                | 1 (0.00)               | 1 (0.03)                 | 2 (0.00)            |
| Diffuse diseases of connective tissue                | 11 (0.02)              | 7 (0.18)                 | 18 (0.03)           |
| <b>Inpatient procedures</b>                          |                        |                          |                     |
| Other operations on rectum and perirectal tissue     | 4 (0.01)               | 0 (0.00)                 | 4 (0.01)            |
| Diagnostic procedures on liver                       | 14 (0.03)              | 0 (0.00)                 | 14 (0.03)           |
| Lysis of peritoneal adhesions                        | 276 (0.55)             | 41 (1.05)                | 317 (0.58)          |
| <b>Exemptions</b>                                    |                        |                          |                     |
| Transplant recipients <sup>a</sup>                   | 4 (0.01)               | 2 (0.05)                 | 6 (0.01)            |
| Diabetes mellitus                                    | 138 (0.27)             | 43 (1.10)                | 181 (0.33)          |
| Systemic lupus erythematosus                         | 32 (0.06)              | 13 (0.33)                | 45 (0.08)           |
| Affections of the circulatory system                 | 138 (0.27)             | 13 (0.33)                | 151 (0.28)          |
| Chronic (active) hepatitis                           | 106 (0.21)             | 8 (0.20)                 | 144 (0.21)          |
| <b>Outpatient services</b>                           |                        |                          |                     |
| Psychiatry   | 1,957 (3.88)           | 194 (4.95)               | 2,151 (3.96)        |
| General consultation                                 | 217 (0.43)             | 17 (0.43)                | 234 (0.43)          |
| <b>Socio-demographic conditions</b>                  |                        |                          |                     |
| Age at conception $\geq 36$ years                    | 9,486 (18.81)          | 1,110 (28.35)            | 10,596 (19.49)      |
| Born abroad  | 5,925 (11.75)          | 599 (15.30)              | 6,524 (12.00)       |
| Low education  | 8,780 (17.41)          | 753 (19.23)              | 9,533 (17.54)       |
| <b>Use of assisted medical conception techniques</b> | <b>2,557 (5.07)</b>    | <b>652 (16.65)</b>       | <b>3,209 (5.90)</b> |

<sup>a</sup> Kidney, heart, lung, liver, pancreas, or bone marrow.

**Table S4.** Frequency of the 26 variables contributing to the Preterm Birth Score (PTBS) in Marche region.

| Variable   | Frequency (%)          |                        |                   |
|--|------------------------|------------------------|-------------------|
|  | Term birth<br>N=13,785 | Preterm birth<br>N=918 | Total<br>N=14,703 |
| <b>Drugs</b>   |                        |                        |                   |
| Pancreatic hormones                                  | 12 (0.09)              | 6 (0.65)               | 18 (0.12)         |
| Agents acting on the renin-angiotensin system        | 137 (0.99)             | 14 (1.53)              | 151 (1.03)        |
| Sex hormones and modulators of the genital system    | 2,332 (16.92)          | 280 (30.50)            | 2,612 (17.77)     |
| Endocrine therapy                                    | 142 (1.03)             | 20 (2.18)              | 162 (1.10)        |
| Drugs used in diabetes                               | 144 (1.04)             | 22 (2.40)              | 166 (1.13)        |
| Immunosuppressants                                   | 73 (0.53)              | 10 (1.09)              | 83 (0.56)         |
| Corticosteroids for systemic use                     | 4,595 (33.33)          | 344 (37.47)            | 4,939 (33.59)     |
| Beta blocking agents                                 | 184 (1.33)             | 19 (2.07)              | 203 (1.38)        |
| Calcium channel blockers                             | 63 (0.46)              | 10 (1.09)              | 73 (0.50)         |
| <b>Hospital diagnosis</b>                            |                        |                        |                   |
| Heart failure  | 2 (0.01)               | 0 (0.00)               | 2 (0.01)          |
| Chronic renal failure                                | 2 (0.01)               | 0 (0.00)               | 2 (0.01)          |
| Diffuse diseases of connective tissue                | 4 (0.03)               | 2 (0.22)               | 6 (0.04)          |
| <b>Inpatient procedures</b>                          |                        |                        |                   |
| Other operations on rectum and perirectal tissue     | 0 (0.00)               | 0 (0.00)               | 0 (0.00)          |
| Diagnostic procedures on liver                       | 4 (0.03)               | 0 (0.00)               | 4 (0.03)          |
| Lysis of peritoneal adhesions                        | 70 (0.51)              | 10 (1.09)              | 80 (0.54)         |
| <b>Exemptions</b>                                    |                        |                        |                   |
| Transplant recipients <sup>a</sup>                   | 2 (0.01)               | 0 (0.00)               | 2 (0.01)          |
| Diabetes mellitus                                    | 32 (0.23)              | 8 (0.87)               | 40 (0.27)         |
| Systemic lupus erythematosus                         | 6 (0.04)               | 2 (0.22)               | 8 (0.05)          |
| Affections of the circulatory system                 | 43 (0.31)              | 1 (0.11)               | 44 (0.30)         |
| Chronic (active) hepatitis                           | 16 (0.12)              | 2 (0.22)               | 18 (0.12)         |
| <b>Outpatient services</b>                           |                        |                        |                   |
| Psychiatry   | 237 (1.72)             | 15 (1.63)              | 252 (1.71)        |
| General consultation                                 | 34 (0.25)              | 4 (0.44)               | 38 (0.26)         |
| <b>Socio-demographic conditions</b>                  |                        |                        |                   |
| Age at conception $\geq 36$ years                    | 2,629 (19.07)          | 274 (29.85)            | 2903 (19.74)      |
| Born abroad  | 1,301 (9.44)           | 114 (12.42)            | 1415 (9.62)       |
| Low education  | 1,638 (11.88)          | 133 (14.49)            | 1,771 (11.94)     |
| <b>Use of assisted medical conception techniques</b> | <b>560 (4.06)</b>      | <b>137 (14.92)</b>     | <b>697 (4.74)</b> |

<sup>a</sup> Kidney, heart, lung, liver, pancreas, or bone marrow.

**Table S5.** Frequency of the 26 variables contributing to the Preterm Birth Score (PTBS) in Sicily region.

| Variable   | Frequency (%)          |                          |                     |
|--|------------------------|--------------------------|---------------------|
|  | Term birth<br>N=58,604 | Preterm birth<br>N=3,527 | Total<br>N=62,131   |
| <b>Drugs</b>   |                        |                          |                     |
| Pancreatic hormones                                  | 41 (0.07)              | 17 (0.48)                | 58 (0.09)           |
| Agents acting on the renin-angiotensin system        | 398 (0.68)             | 63 (1.79)                | 461 (0.74)          |
| Sex hormones and modulators of the genital system    | 7,434 (12.69)          | 671 (19.02)              | 8,105 (13.05)       |
| Endocrine therapy                                    | 163 (0.28)             | 18 (0.51)                | 181 (0.29)          |
| Drugs used in diabetes                               | 625 (1.07)             | 102 (2.89)               | 727 (1.17)          |
| Immunosuppressants                                   | 142 (0.24)             | 14 (0.40)                | 156 (0.25)          |
| Corticosteroids for systemic use                     | 10,578 (18.05)         | 747 (21.18)              | 11,325 (18.23)      |
| Beta blocking agents                                 | 567 (0.97)             | 57 (1.62)                | 624 (1.00)          |
| Calcium channel blockers                             | 136 (0.23)             | 21 (0.60)                | 157 (0.25)          |
| <b>Hospital diagnosis</b>                            |                        |                          |                     |
| Heart failure  | 0 (0.00)               | 0 (0.00)                 | 0 (0.00)            |
| Chronic renal failure                                | 9 (0.02)               | 2 (0.06)                 | 11 (0.02)           |
| Diffuse diseases of connective tissue                | 20 (0.03)              | 5 (0.14)                 | 25 (0.04)           |
| <b>Inpatient procedures</b>                          |                        |                          |                     |
| Other operations on rectum and perirectal tissue     | 1 (0.00)               | 0 (0.00)                 | 1 (0.00)            |
| Diagnostic procedures on liver                       | 12 (0.02)              | 2 (0.06)                 | 14 (0.02)           |
| Lysis of peritoneal adhesions                        | 332 (0.57)             | 30 (0.85)                | 362 (0.58)          |
| <b>Exemptions</b>                                    |                        |                          |                     |
| Transplant recipients <sup>a</sup>                   | 14 (0.02)              | 3 (0.09)                 | 17 (0.03)           |
| Diabetes mellitus                                    | 210 (0.36)             | 49 (1.39)                | 259 (0.42)          |
| Systemic lupus erythematosus                         | 0 (0.00)               | 0 (0.00)                 | 0 (0.00)            |
| Affections of the circulatory system                 | 1 (0.00)               | 0 (0.00)                 | 1 (0.00)            |
| Chronic (active) hepatitis                           | 24 (0.04)              | 3 (0.09)                 | 27 (0.04)           |
| <b>Outpatient services</b>                           |                        |                          |                     |
| Psychiatry   | 382 (0.65)             | 38 (1.08)                | 420 (0.68)          |
| General consultation                                 | 142 (0.24)             | 15 (0.43)                | 157 (0.25)          |
| <b>Socio-demographic conditions</b>                  |                        |                          |                     |
| Age at conception $\geq 36$ years                    | 7,226 (12.33)          | 2,853 (19.11)            | 7,900 (12.72)       |
| Born abroad  | 2,390 (4.08)           | 176 (4.99)               | 2,566 (4.13)        |
| Low education  | 16,661 (28.43)         | 1,100 (31.19)            | 17,761 (28.59)      |
| <b>Use of assisted medical conception techniques</b> | <b>1,330 (2.27)</b>    | <b>138 (3.91)</b>        | <b>1,468 (2.36)</b> |

<sup>a</sup> Kidney, heart, lung, liver, pancreas, or bone marrow.