Cancer in twin pairs discordant for smoking: The Nordic Twin Study of Cancer

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### Supplement Table 1. Cases of first cancer diagnosis and cumulative incidence rate/1000 by smoking status

| Cancer Sites in Alphabetical Order | Never smoker N=59,093 | | | | Former smoker N=21,168 | | | | Current smoker N=47,314 | | | | Total number of cases | |
|-----------------------------------|----------------------|----------------------|----------------------|----------------------|----------------------|----------------------|----------------------|----------------------|----------------------|----------------------|----------------------|----------------------|----------------------|
|                                   | Number of cases      | Cumulative incidence rate / 1000³ | Number of cases      | Cumulative incidence rate / 1000³ | Number of cases      | Cumulative incidence rate / 1000³ |
|                                   | Men | Women | Men | Women | Men | Women | Men | Women | Men | Women | Men | Women | Men | Women |
| Bone marrow / Acute myeloid leukemia¹,² | 17 | 44 | 1.36 | 1.40 | 13 | 6 | 1.12 | 0.96 | 31 | 17 | 1.69 | 1.34 | 128 |
| Colon¹,² | 194 | 450 | 16.7 | 15.4 | 146 | 84 | 14.9 | 18.4 | 281 | 161 | 14.9 | 15.4 | 1316 |
| Esophagus¹,² | 16 | 35 | 1.21 | 0.93 | 20 | 5 | 2.42 | 0.54 | 67 | 22 | 3.74 | 2.38 | 165 |
| Kidneys¹,² | 58 | 110 | 4.41 | 3.80 | 52 | 18 | 6.50 | 4.59 | 132 | 47 | 7.04 | 4.69 | 417 |
| Larynx¹,² | 5 | 8 | 0.37 | 0.36 | 13 | 0 | 0.41 | 0 | 64 | 12 | 0.48 | 1.32 | 102 |
| Liver¹,² | 35 | 70 | 3.28 | 1.78 | 32 | 10 | 3.96 | 2.17 | 82 | 32 | 4.67 | 3.41 | 261 |
| Lung¹,² | 29 | 99 | 2.41 | 3.46 | 130 | 57 | 3.12 | 4.48 | 724 | 389 | 44.3 | 39.0 | 1428 |
| Nasal cavity / sinus¹ | 4 | 4 | 0.40 | 0.09 | 7 | 1 | 0.89 | 0.11 | 12 | 10 | 0.62 | 1.03 | 38 |
| Oral cavity¹,² | 9 | 20 | 0.37 | 0.53 | 7 | 3 | 0.81 | 0.63 | 29 | 18 | 1.67 | 1.55 | 86 |
| Pancreas¹,² | 68 | 179 | 5.71 | 6.07 | 53 | 14 | 5.91 | 2.86 | 144 | 91 | 7.75 | 8.66 | 549 |
| Cancer Sites in Alphabetical Order | Never smoker N=59,093 | Former smoker N=21,168 | Current smoker N=47,314 | Total number of cases |
|-----------------------------------|-----------------------|------------------------|-------------------------|-----------------------|
|                                   | Number of cases       | Cumulative incidence rate / 1000[^3] | Number of cases       | Cumulative incidence rate / 1000[^3] | Number of cases       | Cumulative incidence rate / 1000[^3] |                                   |
|                                   | Men | Women | Men | Women | Men | Women | Men | Women | Men | Women | Men | Women | Men | Women |
| Pharynx[^1,^2]                    | 9   | 13    | 0.71 | 0.34  | 15  | 2     | 1.73 | 0.15  | 35  | 15    | 2.13 | 1.31  | 89  |
| Rectum[^1,^2]                     | 121 | 242   | 10.1 | 8.37  | 117 | 40    | 12.5 | 7.05  | 221 | 91    | 12.3 | 8.65  | 832 |
| Stomach[^1,^2]                    | 100 | 201   | 8.54 | 6.85  | 92  | 21    | 10.0 | 3.71  | 198 | 62    | 10.5 | 5.27  | 674 |
| Urinary Bladder + other urinary organs[^1,^2] | 123 | 124 | 10.5 | 3.41  | 179 | 37    | 18.1 | 9.47  | 439 | 102   | 24.2 | 10.3  | 1004 |
| Female cancer sites               | Never smoker N=38,266 | Former smoker N=9,213 | Current smoker N=21,024 |
|                                   | Number of cases       | Cumulative incidence rate | Number of cases       | Cumulative incidence rate | Number of cases       | Cumulative incidence rate |
|                                   | Men | Women | Men | Women | Men | Women | Men | Women | Men | Women | Men | Women |
| Cervix uteri[^1,^2]               | 155 | 5.08  | 49  | 8.79  | 157 | 10.6  | 361 |
| Ovary + uterine adnexa[^3]        | 310 | 11.6  | 44  | 9.84  | 130 | 11.2  | 484 |

[^1]: Cancer type listed as tobacco related in the Cancer Atlas 2014
[^2]: Cancer type listed as tobacco related in the Surgeon General Report 2004/2014
[^3]: Men: Time0=63.7 & Time1=77.2; Women: Time0=64.7 & Time1=80
**Supplement Table 2. Associations of smoking status with site of first cancer diagnosis: Individual-based survival analyses adjusted for sex and country-specific cohort**

| Cancer Site                   | Former Smokers vs. Never Smokers | Current Smokers vs. Never Smokers |
|------------------------------|----------------------------------|----------------------------------|
|                              | HR 95%CI                         | HR 95%CI                         |
| Bone marrow/Acute myeloid leukemia<sup>1,2</sup> | 0.98 0.57, 1.70 | 1.27 0.85, 1.90 |
| Colon<sup>1,2</sup>          | 1.08 0.92, 1.27                 | 1.13 0.99, 1.28                 |
| Esophagus<sup>1,2</sup>      | 1.25 0.75, 2.07                 | 2.52 1.74, 3.67                 |
| Kidneys<sup>1,2</sup>        | 1.14 0.85, 1.53                 | 1.55 1.24, 1.94                 |
| Larynx<sup>1,2</sup>         | 1.85 0.84, 4.08                 | 6.25 3.40, 11.5                 |
| Liver<sup>1,2</sup>          | 1.25 0.85, 1.83                 | 1.88 1.40, 2.50                 |
| Lung<sup>1,2</sup>           | 4.18 3.31, 5.26                 | 14.6 12.0, 17.6                 |
| Nasal cavity/sinus<sup>1</sup> | 2.89 1.03, 8.13               | 4.24 1.80, 10.0                 |
| Oral cavity<sup>1,2</sup>    | 0.95 0.45, 2.01                 | 2.48 1.51, 4.09                 |
| Pancreas<sup>1,2</sup>       | 0.90 0.68, 1.20                 | 1.75 1.44, 2.13                 |
| Pharynx<sup>1,2</sup>        | 1.73 0.89, 3.36                 | 2.76 1.63, 4.69                 |
| Rectum<sup>1,2</sup>         | 1.14 0.93, 1.39                 | 1.23 1.04, 1.44                 |
| Stomach<sup>1,2</sup>        | 1.08 0.85, 1.35                 | 1.34 1.12, 1.60                 |
| Cancer Type                                      | HR | 95% CI       | HR | 95% CI       |
|-------------------------------------------------|----|--------------|----|--------------|
| Urinary Bladder + other urinary organs          | 1.79 | 1.47, 2.17   | 2.58 | 2.20, 3.03 |
| Female cancers                                  |     |              |     |              |
| Cervix uteri                                    | 1.37 | 0.98, 2.57   | 2.05 | 1.63, 2.57  |
| Ovary + uterine adnexa                          | 0.87 | 0.63, 1.20   | 1.14 | 0.92, 1.40  |

1 Cancer type listed as tobacco related in the Cancer Atlas 2014

2 Cancer type listed as tobacco related in the Surgeon General Report 2004/2014
Supplement Table 3A. The numbers of pairs discordant and concordant for cancer at the end of follow-up for the smoking discordant pairs (one twin never smoker/the other former smoker) by cancer site and zygosity

| Cancer site in alphabetical order | Monozygotic | Dizygotic | Dizygotic |
|----------------------------------|-------------|-----------|-----------|
|                                  | Number of pairs discordant for cancer | Number of cancer concordant pairs | Number of pairs discordant for cancer | Number of cancer concordant pairs |
| Cancer in the former-smoker twin | Cancer in the never-smoker twin | Cancer in both twins | Cancer in the former-smoker twin | Cancer in the never-smoker twin | Cancer in both twins |
| Bone marrow/Acute myeloid leukemia<sup>1,2</sup> | 0 | 1 | 0 | 3 | 2 | 0 |
| Colon<sup>1,2</sup> | 15 | 12 | 2 | 29 | 33 | 0 |
| Esophagus<sup>1,2</sup> | 0 | 1 | 0 | 3 | 2 | 0 |
| Kidneys<sup>1,2</sup> | 3 | 3 | 0 | 16 | 5 | 0 |
| Larynx<sup>1,2</sup> | 0 | 0 | 0 | 3 | 1 | 0 |
| Liver<sup>1,2</sup> | 3 | 0 | 0 | 8 | 0 | 0 |
| Lung<sup>1,2</sup> | 3 | 1 | 0 | 20 | 8 | 0 |
| Nasal cavity/sinus<sup>1</sup> | 0 | 0 | 0 | 0 | 2 | 0 |
| Oral cavity<sup>1,2</sup> | 0 | 0 | 0 | 3 | 2 | 0 |
| Cancer site in alphabetical order | Monozygotically concordant | Monozygotically discordant | Dizygotically concordant | Dizygotically discordant |
|----------------------------------|----------------------------|----------------------------|--------------------------|--------------------------|
| Cancer in the former-smoker twin | Number of pairs discordant for cancer | Cancer in the never-smoker twin | Cancer in both twins | Cancer in the former-smoker twin | Cancer in the never-smoker twin | Cancer in both twins |
| Pancreas\(^1,2\) | 4 | 6 | 0 | 9 | 6 | 0 |
| Pharynx\(^1,2\) | 0 | 0 | 1 | 1 | 2 | 0 |
| Rectum\(^1,2\) | 5 | 11 | 0 | 20 | 22 | 1 |
| Stomach\(^1,2\) | 5 | 5 | 0 | 13 | 17 | 0 |
| Urinary Bladder + other urinary organs\(^1,2\) | 8 | 6 | 1 | 24 | 8 | 0 |
| Female cancers | | | | | | |
| Cervix uteri\(^1,2\) | 7 | 1 | 0 | 7 | 8 | 1 |
| Ovary + uterine adnexa\(^1\) | 4 | 5 | 0 | 9 | 9 | 0 |

\(^1\) Cancer type listed as tobacco related in the Cancer Atlas 2014

\(^2\) Cancer type listed as tobacco related in the Surgeon General Report 2004/2014
Supplement Table 3B. The numbers of pairs discordant and concordant for cancer at the end of follow-up for the smoking discordant pairs (one twin never smoker/the other twin current smoker) by cancer site and zygosity.

| Cancer site in alphabetical order | Monozygotic | | Dizygotic | |
|---------------------------------|---------------------------------|---------------------------------|---------------------------------|---------------------------------|
|                                 | Number of pairs discordant for cancer | Number of cancer concordant pairs | Number of pairs discordant for cancer | Number of cancer concordant pairs |
|                                 | Cancer in the current-smoker twin | Cancer in the never-smoker twin | Cancer in both twins | Cancer in the current-smoker twin | Cancer in the never-smoker twin | Cancer in both twins |
| Bone marrow/Acute myeloid leukemia\(^{1,2}\) | 6 | 8 | 0 | 8 | 8 | 0 |
| Colon\(^{1,2}\) | 33 | 30 | 1 | 71 | 68 | 0 |
| Esophagus\(^{1,2}\) | 5 | 3 | 0 | 12 | 4 | 0 |
| Kidneys\(^{1,2}\) | 7 | 6 | 0 | 19 | 14 | 0 |
| Larynx\(^{1,2}\) | 4 | 1 | 0 | 5 | 1 | 0 |
| Liver\(^{1,2}\) | 7 | 4 | 0 | 16 | 7 | 0 |
| Lung\(^{1,2}\) | 28 | 2 | 0 | 115 | 18 | 0 |
| Nasal cavity/sinus\(^{1}\) | 0 | 0 | 0 | 5 | 3 | 0 |
| Oral cavity\(^{1,2}\) | 1 | 0 | 0 | 7 | 2 | 0 |
| Cancer site in alphabetical order | Monozygotic | Dizygotic |
|----------------------------------|-------------|-----------|
|                                  | Number of pairs discordant for cancer | Number of cancer concordant pairs |
|                                  | Cancer in the current-smoker twin | Cancer in the never-smoker twin | Cancer in both twins | Cancer in the current-smoker twin | Cancer in the never-smoker twin | Cancer in both twins |
| Pancreas\(^1,2\)                  | 2           | 7         | 1         | 30          | 21         | 0             |
| Pharynx\(^1,2\)                   | 1           | 0         | 0         | 9           | 1          | 0             |
| Rectum\(^1,2\)                    | 15          | 10        | 1         | 41          | 40         | 2             |
| Stomach\(^1,2\)                   | 12          | 13        | 0         | 29          | 33         | 2             |
| Urinary Bladder + other urinary organs\(^1,2\) | 10          | 12        | 2         | 41          | 32         | 0             |
| **Female cancers**                |             |           |           |             |             |               |
| Cervix uteri\(^1,2\)              | 12          | 7         | 0         | 16          | 16         | 1             |
| Ovary + uterine adnexa\(^1\)      | 8           | 7         | 0         | 20          | 33         | 0             |

\(^1\) Cancer type listed as tobacco related in the Cancer Atlas 2014

\(^2\) Cancer type listed as tobacco related in the Surgeon General Report 2004/2014
Supplement Table 4. Associations of smoking status with site of first cancer diagnosis: Discordant pair analyses of all pairs, DZ pairs and MZ pairs.

| Cancer Site                          | All pairs | DZ pairs | MZ pairs |
|--------------------------------------|-----------|----------|----------|
|                                      | Former vs. Never | Current vs. Never | Former vs. Never | Current vs. Never | Former vs. Never | Current vs. Never |
|                                      | HR 95%CI   | HR 95%CI | HR 95%CI | HR 95%CI | HR 95%CI | HR 95%CI |
| Bone marrow/Acute myeloid leukemia\(^1,2\) | 0.79 0.24,2.59 0.57 0.23,1.43 2.27 0.52,9.92 0.77 0.27,2.21 - - - - |
| Colon\(^1,2\)                         | 1.09 0.77,1.53 1.13 0.85,1.51 1.08 0.71,1.67 0.98 0.69,1.40 1.10 0.63,1.94 1.49 0.91,2.44 |
| Rectum\(^1,2\)                        | 1.10 0.72,1.68 1.14 0.80,1.58 1.21 0.74,1.99 1.19 0.77,1.82 0.84 0.37,1.91 1.00 0.48,2.08 |
| Esophagus\(^1,2\)                    | 2.72 0.77,9.60 2.65 1.02,6.91 2.53 0.62,10.2 2.36 0.80,6.96 4.00 0.21,75.7 4.00 0.45,35.8 |
| Kidneys\(^1,2\)                       | 1.43 0.78,2.62 1.75 0.99,3.07 1.48 0.73,3.01 1.98 1.01,3.86 1.31 0.40,4.26 1.27 0.44,3.66 |
| Larynx\(^1,2\)                        | 5.24 0.56,48.8 9.31 1.12,77.1 3.68 0.37,36.2 5.98 0.65,55.0 - - - - |
| Liver\(^1,2\)                         | 2.20 0.95,5.10 3.52 1.59,7.81 1.91 0.76,4.76 4.03 1.54,10.5 5.66 0.60,53.0 3.32 0.68,16.1 |
| Lung\(^1,2\)                          | 2.82 1.67,4.75 7.60 4.72,12.2 2.34 1.32,4.13 7.06 4.23,11.8 6.80 1.49,31.0 13.8 3.22,59.1 |
| Nasal cavity/sinus\(^1\)              | 0.54 0.07,4.22 0.49 0.09,2.74 0.16 0.01,2.29 0.59 0.10,3.37 - - - - |
| Cancer Site | All pairs | DZ pairs | MZ pairs |
|-------------|-----------|----------|----------|
|             |           |          |          |
| Oral cavity\(^1,2\) | 3.60 0.64,20.3 | 5.19 1.01,26.7 | - - |
| Pancreas\(^1,2\) | 0.91 0.51,1.63 | 1.85 1.09,3.12 | 0.94 0.32,2.80 |
| Pharynx\(^1,2\) | 2.42 0.54,10.9 | 4.46 1.15,17.3 | - - |
| Stomach\(^1,2\) | 0.90 0.55,1.46 | 0.91 0.60,1.38 | 1.75 0.64,4.79 |
| Urinary Bladder + other urinary organs\(^1,2\) | 1.65 1.04,2.61 | 1.77 1.16,2.70 | 1.52 0.66,3.53 |

| Female cancers | HR 95%CI | HR 95%CI | HR 95%CI | HR 95%CI |
|----------------|----------|----------|----------|----------|
| Cervix uteri\(^1,2\) | 1.37 0.74,2.53 | 1.27 0.74,2.20 | 0.75 0.36,1.58 | 8.06 1.79,36.2 |
| Ovary + uterine adnexus\(^1\) | 0.95 0.51,1.76 | 0.83 0.51,1.33 | 0.97 0.45,2.10 | 0.96 0.33,2.79 |

\(^1\) Cancer type listed as tobacco related in the Cancer Atlas 2014

\(^2\) Cancer type listed as tobacco related in the Surgeon General Report 2004/2014
| Cancer Site                                    | Women vs. Men | Women vs. Men |
|-----------------------------------------------|---------------|---------------|
|                                               | HR 95%CI      | HR 95%CI      |
| Bone marrow/Acute myeloid leukemia            | 0.81 0.58, 1.15 | 0.85 0.59, 1.23 |
| Colon                                         | 0.77 0.69, 0.86 | 0.80 0.71, 0.90 |
| Esophagus                                      | 0.41 0.30, 0.55 | 0.52 0.37, 0.72 |
| Kidneys                                       | 0.53 0.44, 0.65 | 0.60 0.48, 0.74 |
| Larynx                                        | 0.18 0.11, 0.30 | 0.27 0.17, 0.44 |
| Liver                                         | 0.51 0.40, 0.65 | 0.60 0.46, 0.79 |
| Nasal cavity/sinus                            | 0.49 0.25, 0.94 | 0.73 0.36, 1.48 |
| Oral cavity                                   | 0.65 0.42, 0.99 | 0.78 0.50, 1.23 |
| Pancreas                                      | 0.74 0.63, 0.88 | 0.84 0.70, 1.00 |
| Pharynx                                       | 0.39 0.25, 0.62 | 0.51 0.32, 0.81 |
| Rectum                                        | 0.58 0.50, 0.67 | 0.62 0.53, 0.71 |
| Stomach                                       | 0.51 0.43, 0.59 | 0.55 0.46, 0.64 |
| Urinary bladder + other urinary organs        | 0.24 0.21, 0.28 | 0.32 0.28, 0.37 |
