**Supplemental file to**

**Long-term ultraviolet flux, other potential risk factors, and skin cancer risk: a cohort study**

Shaowei Wu, Jiali Han, Francine Laden, Abrar A. Qureshi

**Table of contents:**

Supplemental Table 1. Relative risks of basal cell carcinoma according to quintiles of

 cumulative UV flux stratified potential risk factors in the Nurses’ Health

 Study II (1989-2009)

Supplemental Table 2. Relative risks of squamous cell carcinoma according to

 quintiles of cumulative UV flux stratified by sunburn reaction as a

 child/adolescent in the Nurses’ Health Study II (1989-2009)

Supplemental Table 3. Relative risks of skin cancer according to quintiles of

 cumulative UV flux stratified by host risk score in the Nurses’ Health

 Study II (1989-2009)

Supplemental Figure 1. A directed acyclic graph showing the relationships between

 sun exposure, other potential risk factors, and risk of skin cancer

**Supplemental Table 1. Relative risks of basal cell carcinoma according to quintiles of cumulative UV flux stratified potential risk factors in the Nurses’ Health Study II (1989-2009)**

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
|  | Cases | Reference: the 1st quintile within each subgroup |  | Reference: the 1st quintile of the 1st subgroup |
| Age-adjustedRR (95% CI) | Multivariable-adjustedRRa (95% CI) | Age-adjustedRR (95% CI) | Multivariable-adjustedRRa (95% CI) |
| **Family history of melanoma** |  |  |  |
|  **1st subgroup: family history of melanoma=No (person-years: 1805 thousands)** |  |  |  |
|  Quintile 1 | 567 | 1.00 | 1.00 |  | 1.00 | 1.00 |
|  Quintile 2 | 700 | 1.43 (1.13-1.80) | 1.37 (1.09-1.73) |  | 1.39 (1.12, 1.73) | 1.33 (1.07, 1.66) |
|  Quintile 3 | 919 | 1.86 (1.42-2.43) | 1.73 (1.32-2.26) |  | 1.74 (1.35, 2.24) | 1.62 (1.26, 2.08) |
|  Quintile 4 | 1661 | 2.19 (1.64-2.92) | 2.00 (1.50-2.66) |  | 2.00 (1.53, 2.61) | 1.83 (1.40, 2.39) |
|  Quintile 5 | 1931 | 2.82 (2.10-3.78) | 2.51 (1.87-3.36) |  | 2.53 (1.92, 3.32) | 2.26 (1.72, 2.96) |
|  *P*trend |  | <0.0001 | <0.0001 |  |  |  |
|  **2nd subgroup: family history of melanoma=Yes (person-years: 247 thousands)** |  |  |  |
|  Quintile 1 | 97 | 1.00 | 1.00 |  | 1.26 (1.01, 1.56) | 1.16 (0.94, 1.44) |
|  Quintile 2 | 129 | 1.25 (0.71-2.19) | 1.22 (0.69-2.13) |  | 1.86 (1.42, 2.44) | 1.64 (1.25, 2.14) |
|  Quintile 3 | 163 | 1.26 (0.66-2.39) | 1.21 (0.64-2.29) |  | 2.27 (1.70, 3.02) | 1.93 (1.45, 2.57) |
|  Quintile 4 | 362 | 1.63 (0.82-3.21) | 1.55 (0.79-3.04) |  | 3.25 (2.45, 4.32) | 2.69 (2.03, 3.56) |
|  Quintile 5 | 426 | 1.85 (0.93-3.68) | 1.75 (0.88-3.47) |  | 4.09 (3.07, 5.44) | 3.32 (2.50, 4.42) |
|  *P*trend |  | <0.0001 | 0.0002 |  | <0.0001 | <0.0001 |
| **Number of blistering sunburns between ages 15-20**  |  |  |  |
|  **1st subgroup: none (person-years: 686 thousands)** |
|  Quintile 1 | 154 | 1.00 | 1.00 |  | 1.00 | 1.00 |
|  Quintile 2 | 203 | 1.23 (0.78-1.95) | 1.24 (0.78-1.96) |  | 1.41 (1.06, 1.88) | 1.40 (1.05, 1.85) |
|  Quintile 3 | 258 | 1.64 (0.97-2.78) | 1.66 (0.98-2.80) |  | 1.68 (1.24, 2.27) | 1.65 (1.22, 2.24) |
|  Quintile 4 | 513 | 1.99 (1.14-3.50) | 2.02 (1.15-3.54) |  | 2.00 (1.47, 2.72) | 1.97 (1.45, 2.67) |
|  Quintile 5 | 562 | 2.58 (1.45-4.57) | 2.65 (1.49-4.69) |  | 2.60 (1.91, 3.55) | 2.58 (1.89, 3.52) |
|  *P*trend |  | <0.0001 | <0.0001 |  |  |  |
|  **2nd subgroup: number of sunburns =1-4 (person-years: 1860 thousands)** |
|  Quintile 1 | 371 | 1.00 | 1.00 |  | 1.44 (1.20, 1.74) | 1.27 (1.06, 1.54) |
|  Quintile 2 | 495 | 1.33 (1.00-1.76) | 1.31 (0.99-1.73) |  | 2.08 (1.60, 2.70) | 1.82 (1.41, 2.36) |
|  Quintile 3 | 653 | 1.56 (1.13-2.15) | 1.52 (1.10-2.10) |  | 2.54 (1.91, 3.39) | 2.23 (1.67, 2.96) |
|  Quintile 4 | 1228 | 1.87 (1.33-2.64) | 1.83 (1.30-2.58) |  | 3.00 (2.22, 4.05) | 2.63 (1.95, 3.55) |
|  Quintile 5 | 1425 | 2.28 (1.61-3.24) | 2.23 (1.57-3.16) |  | 3.65 (2.69, 4.95) | 3.21 (2.37, 4.35) |
|  *P*trend |  | <0.0001 | <0.0001 |  |  |  |
|  **3rd subgroup: number of sunburns ≥5 (person-years: 198 thousands)** |
|  Quintile 1 | 137 | 1.00 | 1.00 |  | 3.09 (2.46, 3.89) | 2.36 (1.87, 2.97) |
|  Quintile 2 | 131 | 1.57 (0.98-2.54) | 1.57 (0.98-2.53) |  | 3.22 (2.39, 4.32) | 2.44 (1.81, 3.28) |
|  Quintile 3 | 170 | 1.88 (1.07-3.30) | 1.88 (1.07-3.30) |  | 3.87 (2.83, 5.29) | 2.94 (2.15, 4.02) |
|  Quintile 4 | 274 | 1.88 (1.02-3.48) | 1.92 (1.04-3.54) |  | 4.19 (3.06, 5.76) | 3.20 (2.33, 4.40) |
|  Quintile 5 | 363 | 2.18 (1.17-4.09) | 2.23 (1.19-4.18) |  | 4.92 (3.58, 6.75) | 3.79 (2.76, 5.20) |
|  *P*trend |  | 0.001 | 0.001 |  | <0.0001 | <0.0001 |

a MV-adjusted RR: multivariable analysis controlled for age, family history of melanoma, natural hair color, number of moles on legs, sunburn reaction as a child/adolescent, number of blistering sunburns between ages 15-20, average tanning bed use in early life, body mass index, alcohol intake, physical activity, smoking status, rotating night shifts, and menopausal status. For each stratified analysis, the stratifying variable was omitted from the model.

**Supplemental Table 2. Relative risks of squamous cell carcinoma according to quintiles of cumulative UV flux stratified by sunburn reaction as a child/adolescent in the Nurses’ Health Study II (1989-2009)**

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
|  | Cases | Reference: the 1st quintile within each subgroup |  | Reference: the 1st quintile of the 1st subgroup |
| Age-adjustedRR (95% CI) | MV-adjustedRRa (95% CI) | Age-adjustedRR (95% CI) | MV-adjustedRRa (95% CI) |
| **1st subgroup: sunburn reaction as a child/adolescent =none/some redness (person-years: 1062 thousands)** |
|  Quintile 1 | 18 | 1.00 | 1.00 |  | 1.00 | 1.00 |
|  Quintile 2 | 27 | 1.29 (0.44-3.81) | 1.27 (0.44-3.69) |  | 1.02 (0.44, 2.36) | 1.02 (0.44, 2.36) |
|  Quintile 3 | 52 | 2.74 (0.79-9.53) | 2.68 (0.78-9.19) |  | 1.43 (0.59, 3.47) | 1.42 (0.59, 3.44) |
|  Quintile 4 | 100 | 3.38 (0.90-12.7) | 3.30 (0.89-12.2) |  | 1.93 (0.78, 4.74) | 1.91 (0.78, 4.69) |
|  Quintile 5 | 137 | 4.53 (1.19-17.3) | 4.37 (1.16-16.5) |  | 2.78 (1.12, 6.88) | 2.74 (1.11, 6.77) |
|  *P*trend |  | 0.02 | 0.02 |  |  |  |
| **2nd subgroup: sunburn reaction as a child/adolescent =burn (person-years: 484 thousands)** |
|  Quintile 1 | 15 | 1.00 | 1.00 |  | 1.83 (0.92, 3.64) | 1.68 (0.84, 3.33) |
|  Quintile 2 | 27 | 0.89 (0.20-3.85) | 0.88 (0.20-3.78) |  | 2.21 (0.95, 5.11) | 2.05 (0.88, 4.74) |
|  Quintile 3 | 46 | 1.21 (0.25-5.93) | 1.19 (0.24-5.84) |  | 2.76 (1.13, 6.71) | 2.52 (1.03, 6.14) |
|  Quintile 4 | 66 | 1.44 (0.27-7.55) | 1.41 (0.27-7.38) |  | 2.82 (1.13, 7.00) | 2.58 (1.04, 6.41) |
|  Quintile 5 | 67 | 1.70 (0.32-9.15) | 1.62 (0.30-8.74) |  | 3.08 (1.23, 7.75) | 2.79 (1.11, 7.03) |
|  *P*trend |  | 0.30 | 0.38 |  |  |  |
| **3rd subgroup: sunburn reaction as a child/adolescent =painful burn/blisters (person-years: 481 thousands)** |
|  Quintile 1 | 12 | 1.00 | 1.00 |  | 1.42 (0.68, 2.94) | 1.28 (0.61, 2.66) |
|  Quintile 2 | 37 | 1.88 (0.59-5.98) | 1.91 (0.60-6.10) |  | 2.97 (1.32, 6.68) | 2.68 (1.19, 6.05) |
|  Quintile 3 | 58 | 1.35 (0.37-4.98) | 1.40 (0.38-5.18) |  | 3.39 (1.41, 8.16) | 3.08 (1.28, 7.43) |
|  Quintile 4 | 111 | 1.83 (0.48-6.98) | 1.90 (0.49-7.31) |  | 4.68 (1.91, 11.5) | 4.25 (1.73, 10.5) |
|  Quintile 5 | 107 | 1.88 (0.48-7.33) | 1.96 (0.50-7.71) |  | 4.65 (1.87, 11.5) | 4.22 (1.69, 10.5) |
|  *P*trend |  | 0.20 | 0.20 |  | <0.0001 | <0.0001 |

a MV-adjusted RR: multivariable analysis controlled for age, family history of melanoma, natural hair color, number of moles on legs, number of blistering sunburns between ages 15-20, average tanning bed use in early life, body mass index, alcohol intake, physical activity, smoking status, rotating night shifts, and menopausal status.

**Supplemental Table 3. Relative risks of skin cancer according to quintiles of cumulative UV flux stratified by host risk score in the Nurses’ Health Study II (1989-2009)**

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
|  | Cases | Age-adjustedRR (95% CI) | MV-adjustedRRa (95% CI) | MV-adjustedRRb (95% CI) |
| **BCC** |  |  |  |  |
|  **Low host risk score groupc** |
|  Quintile 1 | 224 | 1.00 | 1.00 | 1.00 |
|  Quintile 2 | 281 | 1.37 (1.06, 1.78) | 1.36 (1.05, 1.77) | 1.34 (1.04, 1.74) |
|  Quintile 3 | 413 | 1.89 (1.43, 2.50) | 1.89 (1.43, 2.50) | 1.84 (1.39, 2.43) |
|  Quintile 4 | 697 | 1.96 (1.46, 2.62) | 1.97 (1.47, 2.64) | 1.89 (1.41, 2.53) |
|  Quintile 5 | 817 | 2.56 (1.91, 3.44) | 2.60 (1.93, 3.49) | 2.46 (1.83, 3.30) |
|  **High host risk score groupc** |
|  Quintile 1 | 440 | 1.98 (1.68, 2.32) | 2.02 (1.72, 2.37) | 1.12 (0.94, 1.33) |
|  Quintile 2 | 548 | 2.70 (2.12, 3.44) | 2.75 (2.15, 3.50) | 1.50 (1.16, 1.93) |
|  Quintile 3 | 669 | 3.09 (2.36, 4.06) | 3.16 (2.41, 4.15) | 1.70 (1.28, 2.25) |
|  Quintile 4 | 1326 | 3.91 (2.94, 5.21) | 4.02 (3.02, 5.35) | 2.14 (1.59, 2.88) |
|  Quintile 5 | 1540 | 4.72 (3.53, 6.31) | 4.89 (3.65, 6.54) | 2.56 (1.89, 3.45) |
|  *P*trend |  | <0.0001 | <0.0001 | <0.0001 |
| **SCC** |  |  |  |  |
|  **Low host risk score groupc** |
|  Quintile 1 | 15 | 1.00 | 1.00 | 1.00 |
|  Quintile 2 | 30 | 1.36 (0.58, 3.20) | 1.38 (0.59, 3.26) | 1.37 (0.58, 3.22) |
|  Quintile 3 | 50 | 1.64 (0.66, 4.07) | 1.68 (0.68, 4.18) | 1.64 (0.66, 4.07) |
|  Quintile 4 | 97 | 2.20 (0.88, 5.54) | 2.29 (0.91, 5.77) | 2.21 (0.88, 5.56) |
|  Quintile 5 | 118 | 2.88 (1.13, 7.30) | 3.03 (1.19, 7.71) | 2.91 (1.15, 7.39) |
|  **High host risk score groupc** |
|  Quintile 1 | 30 | 2.03 (1.09, 3.77) | 2.09 (1.13, 3.89) | 0.88 (0.45, 1.71) |
|  Quintile 2 | 61 | 2.76 (1.22, 6.23) | 2.91 (1.29, 6.57) | 1.21 (0.52, 2.82) |
|  Quintile 3 | 106 | 3.47 (1.43, 8.42) | 3.72 (1.53, 9.01) | 1.52 (0.61, 3.82) |
|  Quintile 4 | 180 | 4.21 (1.69, 10.5) | 4.56 (1.83, 11.4) | 1.86 (0.72, 4.79) |
|  Quintile 5 | 193 | 4.63 (1.84, 11.7) | 5.09 (2.02, 12.8) | 2.05 (0.79, 5.34) |
|  *P*trend |  | <0.0001 | <0.0001 | 0.90 |
| **Melanoma** |  |  |  |  |
|  **Low host risk score groupc** |
|  Quintile 1 | 29 | 1.00 | 1.00 | 1.00 |
|  Quintile 2 | 31 | 0.47 (0.24, 0.93) | 0.47 (0.24, 0.94) | 0.47 (0.24, 0.93) |
|  Quintile 3 | 47 | 0.63 (0.31, 1.29) | 0.64 (0.31, 1.31) | 0.62 (0.30, 1.27) |
|  Quintile 4 | 67 | 0.75 (0.35, 1.59) | 0.77 (0.36, 1.63) | 0.73 (0.34, 1.53) |
|  Quintile 5 | 40 | 0.63 (0.28, 1.39) | 0.65 (0.29, 1.44) | 0.61 (0.27, 1.34) |
|  **High host risk score groupc** |
|  Quintile 1 | 68 | 2.46 (1.60, 3.81) | 2.39 (1.55, 3.69) | 0.82 (0.51, 1.32) |
|  Quintile 2 | 128 | 2.11 (1.15, 3.89) | 2.05 (1.11, 3.78) | 0.70 (0.37, 1.33) |
|  Quintile 3 | 102 | 1.46 (0.73, 2.89) | 1.42 (0.72, 2.82) | 0.48 (0.23, 0.97) |
|  Quintile 4 | 151 | 1.81 (0.88, 3.75) | 1.79 (0.86, 3.70) | 0.59 (0.28, 1.24) |
|  Quintile 5 | 116 | 1.82 (0.86, 3.85) | 1.81 (0.85, 3.84) | 0.58 (0.27, 1.26) |
|  *P*trend |  | <0.0001 | <0.0001 | 0.46 |

a MV-adjusted RR: multivariable analysis controlled for age, average tanning bed use in early life, body mass index, alcohol intake, physical activity, smoking status, rotating night shifts, and menopausal status.

b MV-adjusted RR: multivariable analysis were additionally adjusted for host risk factors including family history of melanoma, natural hair color, number of moles on legs, sunburn reaction as a child/adolescent, and number of blistering sunburns between ages 15-20.

c We used the lowest (1st) quintile of the low host risk score group as the reference.

**Supplemental Figure 1. A directed acyclic graph showing the relationships between sun exposure, other potential risk factors, and risk of skin cancer.**

Life-style

 Sun exposure

 Host factors

 Skin cancer

Menopause

Alcohol

intake

Smoking

Tanning

bed use

Rotating night shift

Physical

activity

Weight change

(BMI)

Number of

blistering sunburns

Sunburn reaction

as a child

Moles

/nevi

Hair color

Family history