

1 **HEALTH STATUS BY GENDER, HAIR COLOR, AND EYE COLOR: RED-HAIRED WOMEN**  
2 **ARE THE MOST DIVERGENT WITH THE LOWEST VIABILITY AND THE HIGHEST**  
3 **FERTILITY**

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19 **ABSTRACT**

20 **Background:** Red hair is associated with pain sensitivity, and more so in women than in men. Hair redness  
21 may thus interact with a female-specific factor. We tested this hypothesis on a large sample of Czech and  
22 Slovak respondents. They were asked about the natural redness and darkness of their hair, their natural eye  
23 color, their physical and mental health (24 categories), and other personal attributes (height, weight, number  
24 of children, lifelong number of sexual partners, frequency of smoking).

25 **Results:** We found that red-haired women did worse than other women in ten health categories and better in  
26 only three. In particular, they were more prone to colorectal, cervical, uterine, and ovarian cancer. Cancer  
27 risk increased steadily with increasing hair redness except for the reddest shade. Red-haired men showed a  
28 balanced pattern of health effects, doing better than other men in three categories and worse in three.  
29 Number of children was the only category where both male and female redheads did better than other  
30 respondents. We also confirmed earlier findings that red hair is naturally more frequent in women than in  
31 men.

32 **Conclusion:** Red-haired women had higher fecundity and sexual attractiveness, but this selective advantage  
33 seems offset by worse health outcomes and therefore lower viability. The resulting equilibrium between  
34 these two counterbalancing forces might explain why red hair has remained less common than other hair and  
35 eye colors. Of the 'new' hair and eye colors, red hair diverges the most from the ancestral state of black hair  
36 and brown eyes. It is the most sexually dimorphic variant, not only in population frequency but also in  
37 health outcomes. This sexual dimorphism seems to have resulted from a selection pressure that acted  
38 primarily on early European women and which led to a general and apparently rapid diversification of hair  
39 and eye colors.

40  
41 **Keywords:** Red hair, Hair color, Fecundity, Sexual dimorphism, Sexual selection, Balancing selection,  
42 Frequency dependent selection, Rare female advantage hypothesis, Cancer

## 13 **BACKGROUND**

14 It has long been known that redheads are at higher risk of sunburn and skin cancer. This is to be expected  
15 because red hair is associated with fair skin, which is more vulnerable to the harmful effects of UV radiation  
16 [1]. Less expectedly, red hair is also associated with increased pain sensitivity and a higher risk of  
17 endometriosis and Parkinson's disease [2,3,4,5,6,7]. These associations seem to involve a risk factor not  
18 directly related to fairness of skin and vulnerability to UV.

19 This risk factor seems to be specific to women. Pain sensitivity is greater in female redheads than in  
20 male redheads, and the association between red hair and endometriosis is obviously specific to women [2,5].  
21 Red hair alleles promote Parkinson's disease by compromising the integrity of dopaminergic neurons, but no  
22 one has determined whether this disorder affects red-haired women more often than red-haired men [8]. If a  
23 female-specific factor is interacting with red hair to facilitate these medical conditions, a plausible candidate  
24 may be higher levels of estrogen in the fetal environment, which promote not only certain health outcomes  
25 but also certain hair and eye colors. Prenatal estrogen particularly seems to favor red hair. According to a  
26 twin study, women are likelier than men to have red hair even when the genotype is the same [9]. Prenatal  
27 estrogen may also affect eye color. Face shape is more feminized in blue-eyed men than in brown-eyed men  
28 of the same ethnic background [10,11]. In addition to favoring blue eyes over brown eyes, prenatal estrogen  
29 seems to favor green eyes over blue eyes, the so-called blue-eye genotype being expressed in women more  
30 often as green eyes [12]. In sum, there seems to be a general tendency for women to exhibit less frequent  
31 hair and eye colors at the expense of more frequent ones [13,14].

32 Prenatal estrogen may therefore mediate the apparent effect of red hair on certain health outcomes,  
33 including some that remain unsuspected. It was only by chance that researchers discovered the three-way  
34 association between being a woman, having red hair, and feeling more sensitivity to pain. There has been no  
35 systematic effort to identify all female-specific associations between human health and red hair, let alone  
36 between human health and each of the different hair and eye colors.

57 For these reasons, we wished to find out how different aspects of human health vary as a function of  
58 hair/eye color. We also wished to see how well the variance is explained by the two known risk factors: 1)  
59 vulnerability to UV, as measured by relative importance of skin cancer; and 2) gender, specifically being a  
60 woman. To this end, we used an existing pool of data collected for an unrelated purpose: a survey on the  
61 effects of RhD factor on various health categories in a Czech and Slovak population. This survey  
62 encompassed a very large number of individuals and could thus capture small effects. On the other hand, the  
63 data were collected by self-report, a method prone to noise because of differences in self-evaluation among  
64 respondents.

## 65 **METHODS**

66 **Respondents and recruitment.** The present study reanalyzed data originally collected for a survey on the  
67 effects of RhD factor on human health. Respondents were recruited by a Facebook-based snowball method  
68 [15], as described by [16]. In short, potential volunteers were invited to participate in “research to  
69 investigate how blood groups and other biological factors relate to personality, performance, morphology,  
70 and health.” The invitation was posted on the Facebook wall page “Guinea Pigs” (in Czech “Pokusni  
71 kralici”) for Czech and Slovak nationals willing to take part in evolutionary psychology experiments  
72 ([www.facebook.com/pokusnikralici](http://www.facebook.com/pokusnikralici)) [17]. The first page of the electronic questionnaire described the goals  
73 of the study. The following note was also included: “The questionnaire is anonymous and obtained data will  
74 be used exclusively for scientific purposes. Your cooperation with the project is voluntary, and you can  
75 terminate it at any time by exiting this website.” The first and final pages of the questionnaire both had a  
76 Facebook share button and the following request: “We need the highest possible number of respondents.  
77 Therefore, please share the link to this questionnaire with your friends, for example on Facebook.” The  
78 share button was pressed by 575 respondents, with the result that we finally obtained data from 7,044  
79 Czechs and Slovaks between 28/4/2014 and 12/09/2016. The study, including the method of obtaining  
80 informed consent (by pressing the Next button on the first page), was approved by the IRB of the Faculty of  
81 Science, No. 2014/21.

32 **Questionnaire** The questionnaire was distributed as a Czech/English Qualtrics survey (<http://1url.cz/q05K>).  
33 In the first part of the questionnaire, respondents were asked, among other questions, to rate the natural  
34 darkness of their hair and eyes and the natural redness and waviness/curliness of their hair on a 6-point  
35 Likert scale (0- light, not curly/wavy/red at all 5- very dark, red, curly/wavy). They were also asked to  
36 choose the natural color of their eyes from a list of eight colors (blue, green, brown, black, grey, amber,  
37 hazel, yellow). Finally, they were asked about their body height and weight, number of children, lifelong  
38 number of sexual partners, and how often they smoked (0- never, 1- maximum of once per month, 2-  
39 maximum of once per week, 3- maximum of once per day, 4- several times a day, 5- more than 20 cigarettes  
40 a day, 6- more than 40 cigarettes a day).

41 The medical part of the questionnaire was prepared by two physicians: a clinician  
42 (internist/hematologist), and a researcher (molecular geneticist). Questions fell into two parts, one using  
43 subjective measures of health status and the other more objective measures. Respondents were first asked to  
44 rate the presence and intensity of their health problems on a 6-point Likert scale. These questions were on  
45 physical health and mental health in general, and on more specific health categories: allergies; cancer;  
46 digestion; fertility; genitourinary system; heart and vascular system; hematology; immune system;  
47 metabolism, including endocrine system; musculoskeletal system; nervous system; respiratory organs; sense  
48 organs; and sexual function. The second part of the questionnaire was designed to provide objective  
49 information on health status. For example, respondents were asked how many physician-prescribed drugs  
50 they were currently taking per day, how many “different herbs, food supplements, multivitamins, superfoods  
51 etc.” they were currently taking per day, and how often they had used antibiotics during the past 365 days.

52 As a benchmark for the relative importance of associations between hair/eye color and the 24 health  
53 categories, we looked for associations between these categories and two unrelated but well-known risk  
54 factors: body mass index (BMI) and smoking. Finally, as another benchmark, we looked for significant  
55 associations between hair waviness and these categories.

16 For some of these categories, we also asked the respondents to state the specific disorders they had or  
17 used to have. For the ‘Cancer’ category, respondents were asked “What kind of cancer are you suffering  
18 from or have you suffered from?” They then read a list of disorders and ticked the appropriate boxes.

19

20 **Data analysis** Statistica v. 10 and IBM SPSS v. 21 were used for most of the statistical analysis.  
21 MANCOVAs on health effects (with gender, eye color, or hair color as predictors) were performed by  
22 “adonis” function available within Vegan package in R [18]. Differences in age were tested by t-tests. Chi<sup>2</sup>  
23 tests were used to compare the frequencies of eye colors in men and women. Effects of gender and age on  
24 hair color, eye color, and waviness of hair were analyzed by both nonparametric (partial Kendall correlation  
25 with age or gender as a covariate) and parametric tests using general linear models with gender, age, and  
26 gender-age interaction as independent variables. Both categories of tests produced very similar results and  
27 therefore only the results of the more conservative nonparametric tests are reported. Logistic regression  
28 (Quasi-Newton estimation method) was used for the analysis of relation between cancer and hair redness  
29 and hair redness\*gender interaction. Other ordinal and binary data were analyzed by a partial Kendall  
30 correlation test, which is used to measure the strength and significance of associations between binary,  
31 ordinal, or continuous data regardless of their distributions and which can be used to control for one  
32 confounding variable, here the respondent’s age [19,20]. To compute partial Kendall Tau and the  
33 significance of each variable, after controlling for age, we used an Excel spreadsheet available at:  
34 <http://web.natur.cuni.cz/flegr/programy.php>. Because many disorders tend to be more common in men than  
35 in women or vice versa, associations between the health categories and the hair/eye colors were always  
36 analyzed separately for men and women. Whenever fewer than 10 respondents reported a disorder, a Fisher  
37 exact test was used to determine the significance of the association between hair/eye color and the category  
38 of fitness. To correct for multiple tests, and the associated increase in the false discovery rate, we used the  
39 Benjamini-Hochberg procedure with the false discovery rate preset to 0.25 [21]. In contrast to the  
40 Bonferroni correction, this procedure takes into account the distribution of p values of performed multiple

41 tests. Therefore, when the studied factor has multiple effects, the number of significant results after the  
42 correction may be higher than before the correction. To measure eye color diversity, we used the Simpson  
43 index  $\lambda$ , which was computed as  $\lambda = \text{SUMA}(p_i)^2$ , where  $p_1-p_i$  denotes proportions of respondents with 1-i  
44 eye color in the population under study [22]. This index reflects the probability of two randomly-selected  
45 respondents carrying the same character, here the same eye color. All raw data are available as Supporting  
46 Information S1, at <https://figshare.com/s/6a02dd5cec0f90b69db9>

## 47 **RESULTS**

### 48 **Characteristics of respondents**

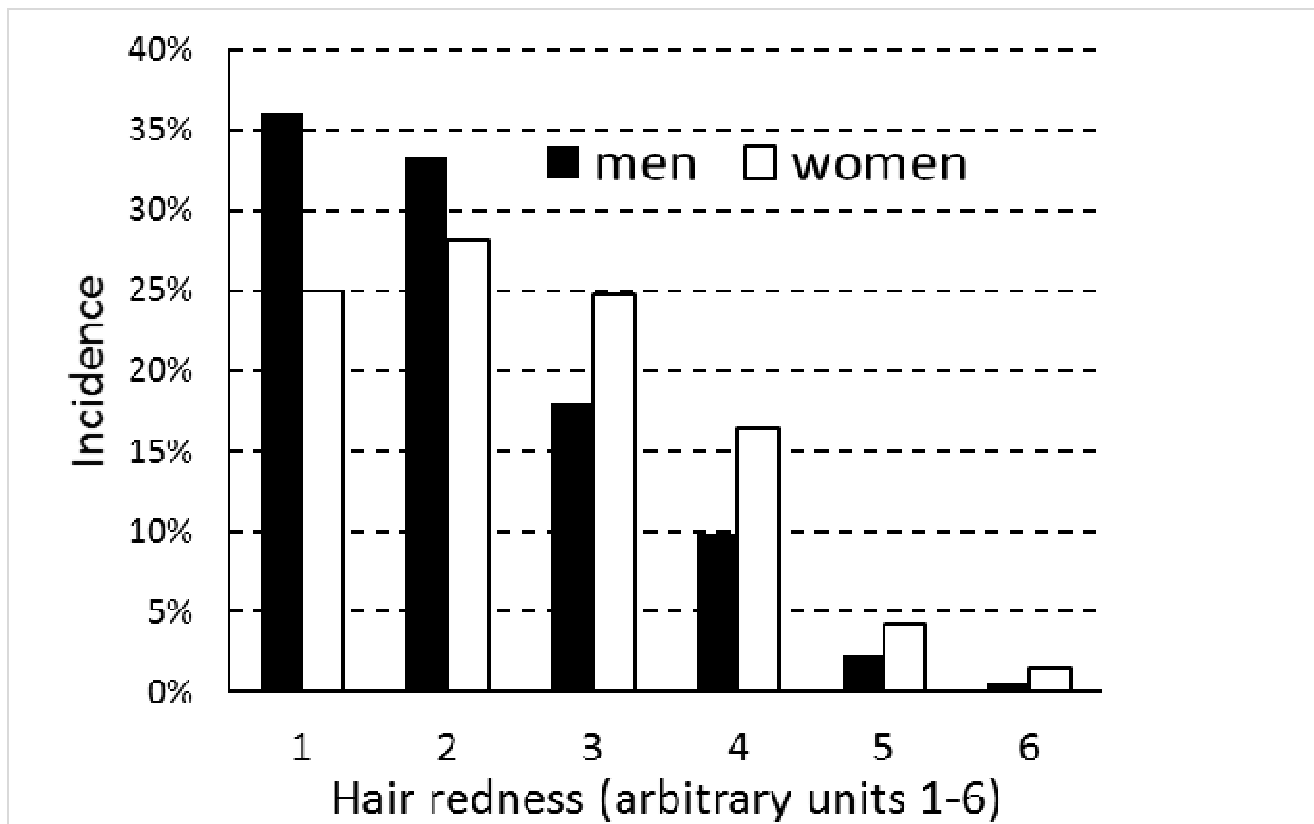
49 Information on eye color, hair color, and hair waviness was provided by 2,558 men and 4,472 women out of  
50 7,030 Czech and Slovak respondents (the others did not complete the questionnaire part of the test). Mean  
51 age of the men (36.8, std. dev. 13.5) was somewhat higher than mean age of the women (34.6, std. dev.  
52 13.0)  $t_{7028} = 6.9, p < 0.0005$ .

53 Figures 1, 2, and 3 show how different gradations of hair redness, hair darkness, and eye darkness  
54 were distributed among male and female respondents. In keeping with the findings of an earlier twin study,  
55 red hair was more frequent in women than in men [9]. Hair tended to be lighter in women than in men, but  
56 eyes were equally dark. A closer look at the data, however, showed that eye color was more diverse in  
57 women than in men, with green eyes being more frequent in women and blue and brown eyes more frequent  
58 in men (Figure 4 and Table 1). This gender difference in eye-color diversity is seen in a higher Simpson  
59 index for men (0.263) than for women (0.234). Women had higher eye-color diversity in all 5-year age  
60 groups, except for the 41-45 age group.

61 Age was associated in women with darker eyes, darker hair, redder hair, and less wavy hair (Table  
62 2), and in men with redder hair and less wavy hair. After controlling for the effect of age, we still found  
63 gender differences: male hair was significantly darker (mean 4.07 vs. 3.87,  $p < 0.0005$ ), less red (mean 2.09

54 vs. 2.51,  $p < 0.0005$ ), and less wavy (mean 2.30 vs. 2.56,  $p < 0.0005$ ). No gender difference was observed in  
55 eye darkness (mean 3.39 vs. 3.42,  $p = 0.56$ ).

56 Figure 1. Gradations of hair redness: population frequencies for men and women



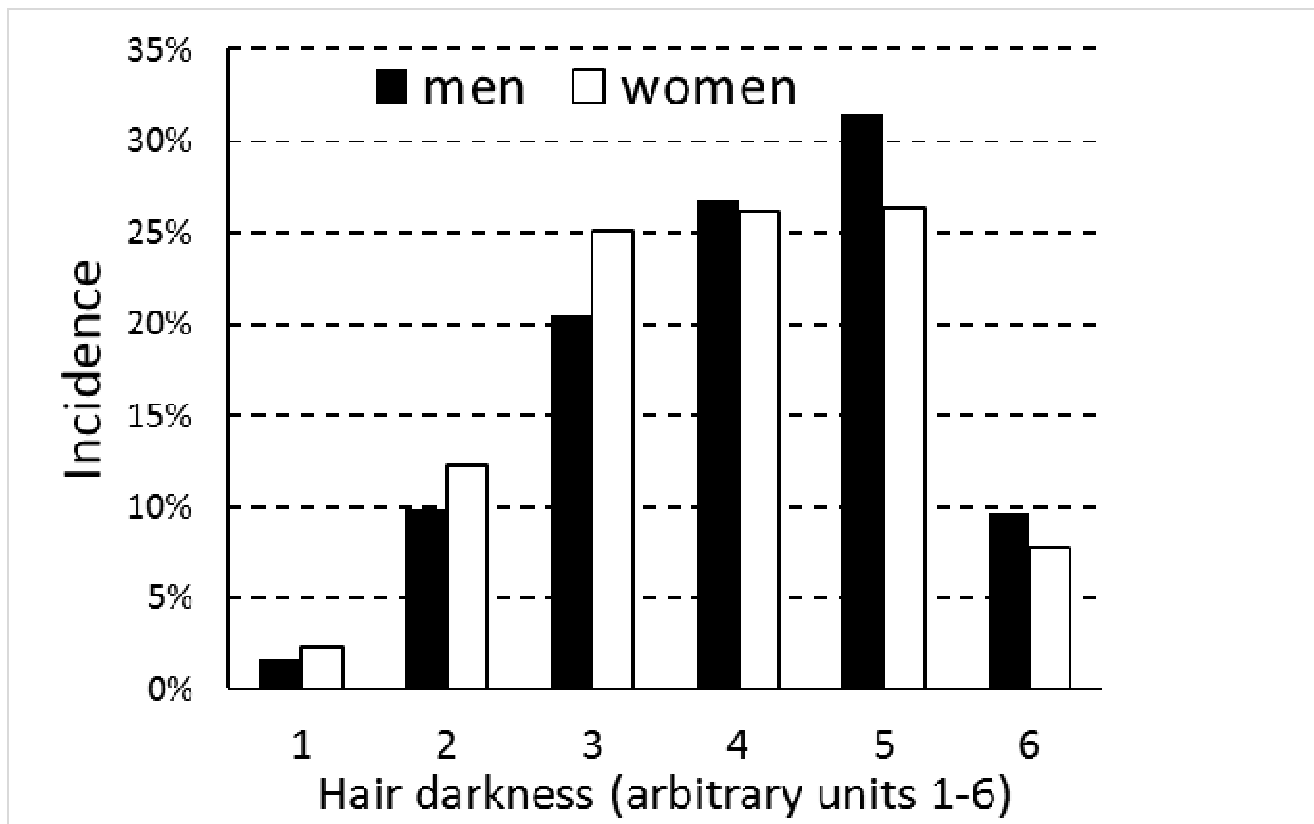
57

58 *Respondents rated hair redness on a scale of 1 to 6 where 1 = not at all red and 6 = completely red*

59



70 Figure 2. Gradations of hair darkness: population frequencies for men and women



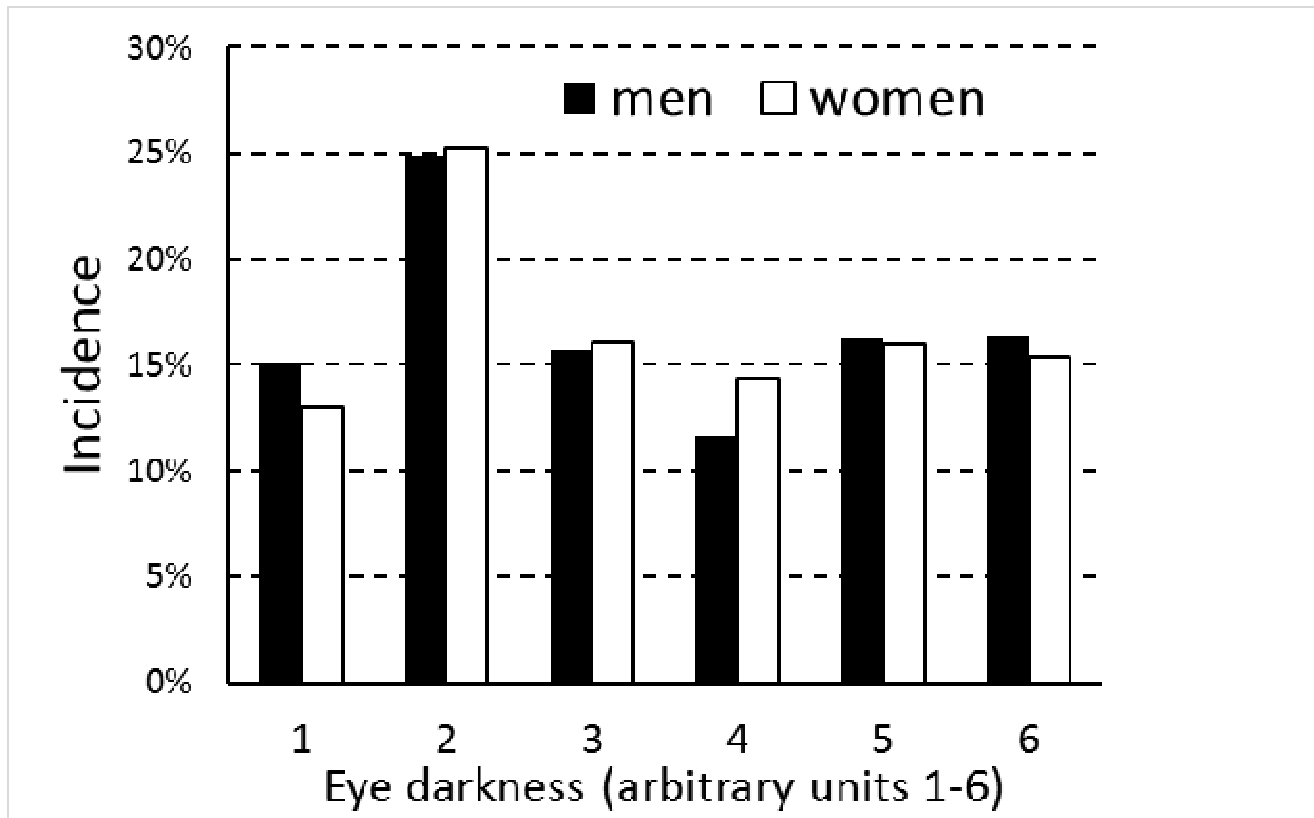
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73 Respondents rated hair darkness on a scale of 1 to 6 where 1 = not at all dark and 6 = completely dark

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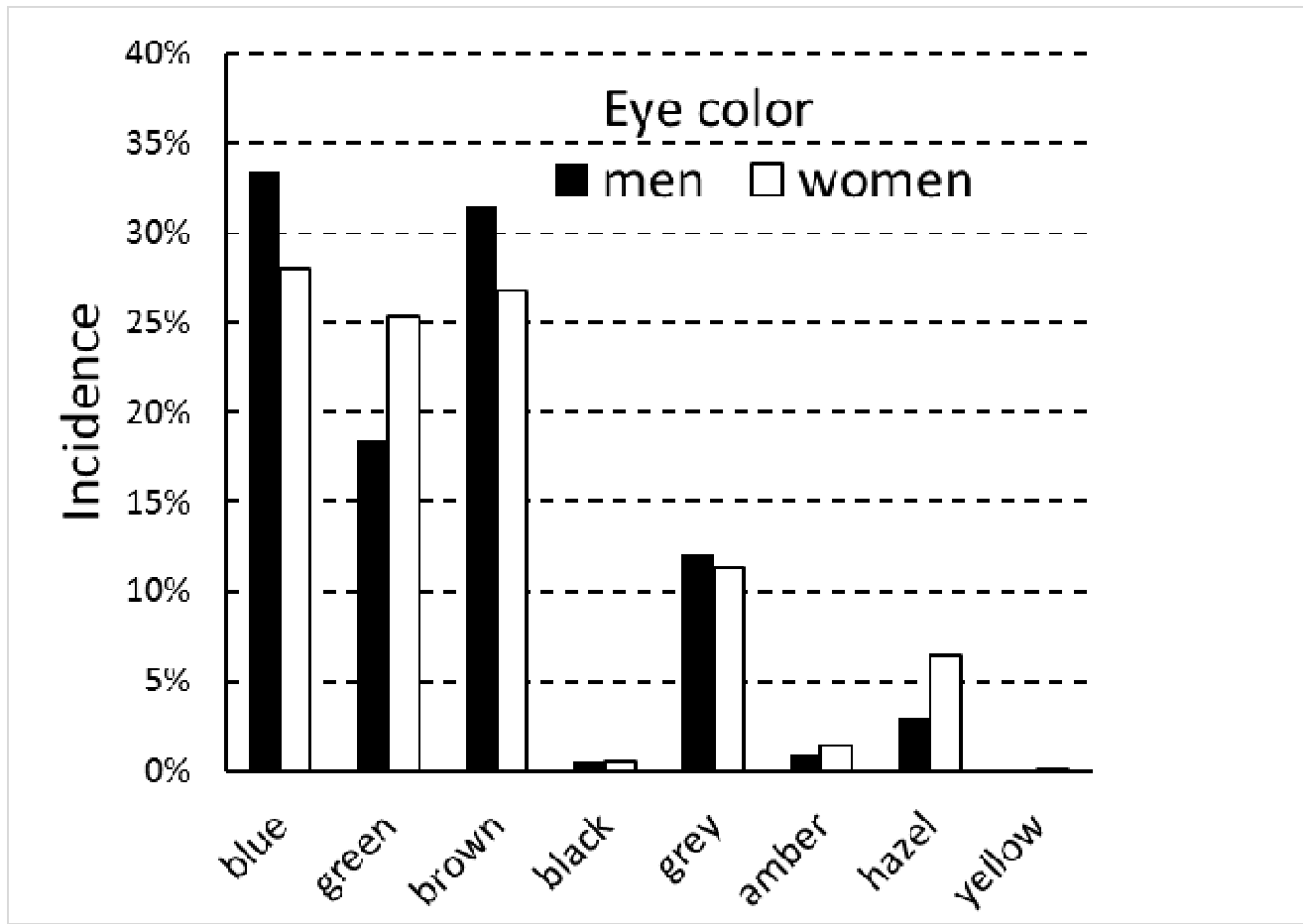
75 Figure 3. Gradations of eye darkness: population frequencies for men and women



76

77 Respondents rated eye darkness on a scale of 1 to 6 where 1 = not at all dark and 6 = completely dark

78 Figure 4. Eye colors: population frequencies for men and women



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32 Table 1. Frequencies of eye colors in men and women

		Blue	Green	Brown	Black	Gray	Amber	Hazel	Yellow	Totals
N	Men	846	453	813	14	312	21	72	0	2531
Percent		33.43%	17.90%	32.12%	0.55%	12.33%	0.83%	2.84%	0.00%	100%
N	Women	1243	1135	1203	19	513	66	258	5	4442

Percent		27.98%	25.55%	27.08%	0.43%	11.55%	1.49%	5.81%	0.11%	100%
N	All	2089	1588	2016	33	825	87	330	5	6973
Chi2		22.7	53.5	19.9	0.54	0.94	5.63	31.0	2.85	
p		0.000	0.000	0.000	0.463	0.333	0.018	0.000	0.091	

33

34 *Benjamini-Hochberg correction for multiple (8) Chi<sup>2</sup> tests indicated that gender differences were significant for all eye*  
 35 *colors, except for black, gray, and yellow. The p values lower than 0.0005 were coded as 0.000.*

36

37 Table 2. Correlations between eye/hair properties and age

38

	Hair darkness	Hair redness	Hair waviness	Eye darkness	Age (men)	Age (women)
Hair darkness		<b>-0.18</b>	<b>0.05</b>	<b>0.38</b>	0.00	<b>0.07</b>
Hair redness	-0.01		<b>0.08</b>	<b>-0.08</b>	<b>0.14</b>	<b>0.18</b>
Hair waviness	<b>0.09</b>	<b>0.07</b>		0.00	<b>-0.09</b>	<b>-0.06</b>
Eye darkness	<b>0.39</b>	0.00	0.00		0.02	<b>0.03</b>

39

30 *The upper-right part of the table (excluding the last two columns) shows the partial Kendall Tau correlations (age*  
 31 *controlled) for men, and the lower-left the same results for women. The last two columns show standard Kendall Tau*  
 32 *correlations between hair/eye properties and age in men and women, respectively. Significant correlations are in*  
 33 *bold.*

34

35 **Associations between health categories and hair/eye color**

36 We looked for significant associations between 24 health categories and different hair or eye colors. The  
 37 results are shown in Table 3 for men and in Table 4 for women. Yellow eye color was reported by only 5  
 38 respondents and therefore excluded from the analyses.

39

40 Table 3. Results for men: associations with eye color, hair color, hair waviness, BMI, and smoking

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	Blue	Green	Brown	Black	Gray	Amber	Hazel	Eye darkness	Hair darkness	Hair redness	Hair waviness	BMI	Smoking
Physical health problems in general	-0.015	-0.019	0.011	<b>0.033</b>	<b>0.041</b>	<b>-0.030</b>	<b>-0.025</b>	0.004	0.015	<b>-0.031</b>	<b>0.025</b>	<b>0.172</b>	<b>0.093</b>
Mental health problems in general	<b>-0.026</b>	0.009	0.014	0.014	0.015	0.003	<b>-0.024</b>	0.011	-0.024	<b>0.032</b>	0.014	<b>-0.023</b>	<b>0.083</b>
Specific health problems:													
Antibiotics/ year	0.007	-0.001	-0.004	<b>-0.032</b>	0.002	<b>-0.036</b>	<b>0.026</b>	-0.018	-0.002	0.006	<b>0.025</b>	0.014	<b>-0.050</b>
Acute care/ 5 years	0.008	<b>-0.034</b>	<b>0.048</b>	-0.006	<b>-0.034</b>	-0.004	-0.007	0.026	0.014	-0.008	<b>0.045</b>	0.011	<b>-0.034</b>
Different med. specialist seen every 2 years	0.002	-0.003	0.002	0.026	0.002	-0.015	-0.012	-0.001	-0.021	0.017	<b>0.038</b>	<b>0.083</b>	<b>-0.030</b>
Number of prescription	0.015	0.023	-0.014	<b>0.051</b>	-0.017	-0.012	<b>-0.039</b>	-0.016	-0.026	<b>0.031</b>	0.009	<b>0.133</b>	<b>-0.053</b>

drugs/day													
Number of alternative medicines/day	0.021	0.000	-0.019	-0.020	0.001	-0.015	0.007	-0.003	-0.010	<b>0.032</b>	<b>0.041</b>	0.013	<b>-0.049</b>
Allergies	-0.001	0.003	-0.004	-0.014	0.015	0.020	<b>-0.028</b>	-0.012	0.015	<b>-0.053</b>	0.016	-0.001	<b>-0.037</b>
Immunological	<b>0.024</b>	<b>-0.051</b>	0.019	-0.003	0.023	-0.023	<b>-0.037</b>	-0.005	-0.003	0.000	<b>0.029</b>	-0.015	<b>-0.034</b>
Digestive	<b>-0.033</b>	0.018	0.004	0.025	<b>0.034</b>	0.001	<b>-0.040</b>	0.020	-0.017	0.012	0.013	<b>0.023</b>	<b>0.053</b>
Heart & vascular system	-0.022	0.012	-0.007	0.003	<b>0.037</b>	<b>0.040</b>	<b>-0.044</b>	0.003	0.005	-0.008	<b>0.026</b>	<b>0.076</b>	<b>0.025</b>
Hematological	0.018	0.018	-0.015	-0.023	0.003	-0.011	<b>-0.042</b>	-0.028	-0.017	0.024	0.019	-0.002	-0.009
Metabolic	0.018	-0.013	-0.001	0.013	0.012	-0.009	<b>-0.042</b>	-0.007	-0.024	0.022	0.020	<b>0.163</b>	-0.017
Cancer	0.013	-0.030	-0.015	-0.010	<b>0.026</b>	<b>0.053</b>	-0.004	0.000	-0.020	0.018	<b>0.029</b>	<b>0.039</b>	<b>-0.019</b>
Fertility	-0.015	-0.023	0.012	<b>0.074</b>	<b>0.028</b>	0.012	<b>-0.036</b>	0.006	0.000	-0.003	-0.001	0.017	0.001
Genitourinary	0.016	-0.008	-0.004	-0.024	-0.009	0.001	0.013	-0.013	-0.025	0.018	0.004	-0.011	-0.028
Sense organs	<b>-0.034</b>	-0.002	0.025	-0.005	<b>0.027</b>	-0.004	-0.018	0.023	0.005	0.004	0.013	0.017	0.009
Neurological	<b>-0.028</b>	-0.023	0.007	0.003	<b>0.059</b>	-0.012	-0.001	0.008	0.005	0.023	0.018	-0.018	-0.012
Psychiatric	<b>-0.037</b>	0.001	0.014	<b>0.042</b>	0.007	0.002	<b>0.030</b>	0.027	0.008	0.008	<b>0.038</b>	-0.009	<b>0.095</b>
Sexual function	-0.003	0.003	-0.011	0.020	<b>0.029</b>	-0.006	<b>-0.032</b>	-0.022	-0.011	0.007	-0.003	<b>0.034</b>	<b>0.074</b>
Musculoskeletal	<b>-0.052</b>	-0.025	<b>0.063</b>	0.014	0.016	0.010	-0.017	<b>0.066</b>	0.001	0.026	<b>0.034</b>	<b>0.037</b>	<b>-0.021</b>
Respiratory	-0.011	-0.013	0.030	0.019	-0.006	0.010	<b>-0.027</b>	0.014	0.006	0.001	0.017	<b>0.045</b>	<b>0.063</b>
Tiredness (frequency)	<b>-0.034</b>	0.024	0.027	<b>0.038</b>	-0.009	-0.008	<b>-0.027</b>	0.025	0.009	-0.011	0.023	0.008	<b>0.096</b>

Headaches (frequency)	<b>-0.036</b>	-0.009	0.023	0.020	0.017	<b>0.032</b>	-0.002	0.010	0.010	-0.011	0.015	0.008	<b>0.068</b>
Reproductive/ mating success:													
Number of children	<b>0.023</b>	-0.007	-0.026	<b>-0.035</b>	0.018	0.014	-0.006	-0.025	-0.007	<b>0.039</b>	<b>-0.032</b>	<b>0.099</b>	<b>-0.030</b>
Number of sexual partners	0.018	-0.002	0.020	0.025	<b>-0.046</b>	0.000	<b>-0.019</b>	-0.005	-0.003	0.009	0.009	<b>0.069</b>	<b>0.182</b>
Negative health effects	1	0	2	6	9	3	3	1	0	3	11	10	10
Positive health effects	9	2	0	1	1	2	13	0	0	3	0	3	10

02

03 *The figures (age-controlled partial Kendall Tau correlations) show the strength and direction of associations between*  
 04 *variables on the top and on the left. A positive figure means a positive association between a respondent*  
 05 *characteristic (column headings) and a category of human health, including number of children and sexual partners*  
 06 *(row headings). Associations that remain significant after correction for multiple testing are in bold. The last two*  
 07 *rows show the total number of significant associations where the effect on health is either negative or positive. A*  
 08 *higher number of children and a higher number of sexual partners are classified as positive health effects.*

09

10 Table 4. Results for women: associations with eye color, hair color, hair waviness, BMI, and smoking

	Blue	Green	Brown	Black	Gray	Amber	Hazel	Eye darkness	Hair darkness	Hair redness	Hair waviness	BMI	Smoking
Physical health problems in general	-0.007	<b>-0.024</b>	<b>0.039</b>	<b>-0.027</b>	0.010	-0.020	-0.009	0.011	<b>0.020</b>	<b>0.020</b>	-0.001	<b>0.228</b>	<b>0.054</b>
Mental health problems in general	<b>-0.033</b>	0.014	0.013	<b>-0.024</b>	<b>0.019</b>	0.001	-0.007	0.003	<b>0.020</b>	<b>0.047</b>	0.008	0.013	<b>0.041</b>
Specific health problems:													
Antibiotics/ year	-0.005	<b>-0.026</b>	<b>0.020</b>	0.012	0.015	-0.005	-0.001	0.002	0.013	<b>-0.035</b>	0.010	<b>0.045</b>	<b>0.027</b>
Acute care/ 5 years	<b>-0.025</b>	-0.013	<b>0.035</b>	0.015	0.010	-0.007	-0.009	<b>0.019</b>	<b>0.025</b>	0.002	<b>0.018</b>	<b>0.047</b>	<b>0.029</b>
Different med. specialist seen every 2 years	-0.018	-0.014	<b>0.046</b>	0.006	-0.005	-0.022	-0.014	<b>0.023</b>	0.014	-0.006	0.013	<b>0.052</b>	0.013
Number of prescription drugs/day	<b>-0.055</b>	<b>-0.023</b>	<b>0.077</b>	-0.009	<b>0.021</b>	0.002	<b>-0.028</b>	<b>0.045</b>	<b>0.023</b>	0.008	-0.013	<b>0.122</b>	0.005
Number of alternative medicines/day	0.001	0.012	0.003	0.008	-0.012	-0.022	0.001	0.007	0.004	0.013	0.012	<b>-0.019</b>	-0.019
Allergies	<b>-0.039</b>	-0.001	<b>0.049</b>	0.011	-0.011	-0.001	-0.002	<b>0.034</b>	0.016	-0.012	<b>0.025</b>	<b>0.030</b>	<b>-0.025</b>
Immunological	<b>-0.020</b>	-0.015	<b>0.034</b>	<b>0.040</b>	<b>-0.020</b>	0.019	0.006	<b>0.039</b>	<b>0.039</b>	0.007	<b>0.018</b>	<b>0.020</b>	<b>0.018</b>



Digestive	-0.015	0.018	0.016	0.012	-0.002	0.010	<b>-0.037</b>	0.014	-0.001	0.008	<b>0.025</b>	<b>0.031</b>	0.009
Heart & vascular system	-0.010	0.009	0.005	-0.010	0.011	-0.006	<b>-0.019</b>	0.002	0.015	<b>0.044</b>	<b>0.021</b>	<b>0.040</b>	<b>0.017</b>
Hematological	0.004	-0.016	0.000	<b>0.036</b>	0.008	-0.014	0.009	-0.004	0.000	0.007	<b>0.039</b>	-0.006	-0.007
Metabolic	<b>-0.041</b>	<b>-0.022</b>	<b>0.039</b>	0.019	0.010	0.021	0.014	<b>0.038</b>	<b>0.023</b>	<b>0.045</b>	<b>0.020</b>	<b>0.187</b>	0.007
Cancer	0.012	<b>0.024</b>	-0.014	-0.012	<b>-0.027</b>	0.017	-0.010	0.003	-0.009	<b>0.067</b>	0.013	0.011	0.013
Fertility	<b>-0.030</b>	0.005	0.015	-0.005	0.013	0.007	0.001	0.013	0.015	<b>0.042</b>	<b>0.054</b>	0.006	-0.010
Genitourinary	-0.017	-0.007	<b>0.033</b>	-0.006	<b>0.019</b>	-0.024	<b>-0.025</b>	0.016	0.009	<b>0.028</b>	-0.011	<b>-0.026</b>	0.013
Sense organs	-0.002	-0.007	-0.016	<b>-0.034</b>	<b>0.038</b>	0.005	0.003	<b>-0.029</b>	0.000	0.011	<b>0.033</b>	<b>0.041</b>	<b>-0.024</b>
Neurological	-0.013	-0.003	0.006	<b>0.023</b>	<b>0.021</b>	-0.001	<b>-0.020</b>	-0.002	0.011	0.014	0.015	0.011	-0.005
Psychiatric	<b>-0.033</b>	<b>0.025</b>	<b>-0.020</b>	-0.012	<b>0.035</b>	0.004	0.005	-0.006	0.006	<b>0.020</b>	0.009	0.007	<b>0.098</b>
Sexual function	-0.012	0.003	0.012	-0.016	0.016	0.006	<b>-0.024</b>	-0.002	0.015	<b>0.030</b>	0.013	0.017	<b>0.016</b>
Musculoskeletal	0.000	0.010	-0.005	-0.007	0.005	-0.015	-0.005	-0.004	-0.018	<b>0.053</b>	0.007	<b>0.040</b>	0.013
Respiratory	<b>-0.026</b>	0.006	<b>0.027</b>	<b>0.026</b>	-0.006	-0.008	-0.008	<b>0.026</b>	0.013	-0.006	0.011	<b>0.084</b>	<b>0.053</b>
Tiredness (frequency)	-0.004	0.005	0.001	0.003	0.016	-0.007	<b>-0.022</b>	-0.005	0.014	0.014	0.002	<b>0.021</b>	<b>0.058</b>
Headaches (frequency)	-0.001	0.006	-0.004	0.013	0.010	-0.009	<b>-0.019</b>	-0.009	0.015	-0.002	<b>0.018</b>	0.014	<b>0.019</b>
Reproductive/ mating success:  Number of	0.006	0.004	<b>0.026</b>	-0.008	-0.016	-0.010	<b>-0.041</b>	<b>0.018</b>	<b>0.030</b>	<b>0.143</b>	<b>-0.026</b>	<b>0.096</b>	<b>-0.027</b>

children													
Number of sexual partners	0.010	0.016	-0.006	0.014	<b>-0.027</b>	0.014	-0.008	-0.001	<b>-0.021</b>	<b>0.061</b>	-0.008	0.011	<b>0.246</b>
Negative health effects	0	2	10	4	7	0	1	7	7	10	11	14	12
Positive health effects	9	4	2	3	2	0	8	2	1	3	0	3	3

11

12 *See Table 3 legend.*

13

14 The results shown in Table 3 and Table 4 suggest that women have more negative health effects associated  
 15 with hair or eye color. Red hair in particular seems associated in women with the most negative effects and  
 16 the fewest positive effects. To measure the size of health effects that disproportionately affect red-haired  
 17 women, we performed MANCOVAs (multivariate analyses of variance) on the ones found to be significant.  
 18 These effect sizes were compared with those of the three benchmarks: hair waviness, BMI, and smoking. By  
 19 order of importance, red-haired women were prone to disorders in the following health categories: (1)  
 20 Musculoskeletal; (2) Heart & vascular, Cancer, Fertility; (3) Metabolic; (4) Sexual function; (5)  
 21 Genitourinary. The sizes of these health effects seemed comparable to those of BMI and smoking, though  
 22 smaller.

23 To determine the relative importance of skin cancer in the Cancer category, we looked at the  
 24 incidence of specific disorders within that category. The results are shown in Table 5.

25

26 **Table 5. Differences in cancer rate between redheads and non-redheads by sex and by specific type of cancer**

27

Type of cancer	Men				Women							
	Red- Can-	Red- Can+	Red+ Can-	Red+ Can+	OR	p	Red- Can-	Red- Can+	Red+ Can-	Red+ Can+	OR	p
Esophageal cancer	1762	0	268	0			2946	1	836	1	3.52	0.394
Stomach cancer	1762	0	268	0			2946	1	836	1	3.52	0.394
Colorectal cancer	1762	0	264	4	273.56	<b>0.000</b>	2947	0	834	3	109.53	<b>0.011</b>
Liver cancer	1762	0	267	1	72.57	0.132	2947	0	836	1	38.77	0.221
Lung cancer	1761	1	267	1	6.59	0.247	2947	0	837	0		
Melanoma, other skin cancers	1753	9	266	2	1.52	0.271	2937	10	833	4	1.43	0.243
Breast cancer	1762	0	268	0			2932	15	830	7	1.66	0.318
Cervical uterine precancerosis	1677	0	259	0			2723	64	756	27	1.52	<b>0.008</b>
Cervical uterine cancer	1762	0	268	0			2902	45	817	20	1.58	<b>0.003</b>
Corpus uteri cancer	1762	0	268	0			2940	7	835	2	1.04	1.000
Ovarian cancer	1762	0	268	0			2942	5	832	5	3.54	<b>0.015</b>
Prostate cancer	1753	9	266	2	1.52	0.184	2947	0	837	0		
Lymphoma, myeloma multiple	1760	2	268	0	0.31	1.000	2947	0	837	0		
Leukemia	1758	4	268	0	0.16	1.000	2941	6	836	1	0.63	1.000
Bladder cancer	1761	1	268	0	0.60	1.000	2945	2	836	1	1.85	0.528
Mouth, oropharynx cancers	1761	1	268	0	0.60	1.000	2947	0	836	1	38.77	0.221
Adeno-carcinoma	1762	0	268	0			2943	4	837	0	0.09	0.582
Papilloma cancer	1762	0	268	0			2941	6	833	4	2.37	0.422
Other types of cancer	1747	15	265	3	1.35	0.642	2929	18	825	12	2.37	<b>0.000</b>

28

29 *Red- Can- = Number of non-redheads (i.e., respondents whose intensity of redness is 1-3 on a 6-point Likert*  
 30 *scale) without the specific type of cancer*

31 *Red- Can+ = Number of non-redheads with the specific type of cancer*

32 *Red+ Can- = Number of redheads (i.e., respondents whose intensity of redness is 4-6) without the specific*  
 33 *type of cancer*

34 *Red+ Can+ = Number of redheads with the specific type of cancer*

35 *Odds Ratios (OR) and statistical significance (p) respectively are shown for men and women and for each*  
36 *specific type of cancer. The effect of age on health status was controlled by performing partial Kendall's*  
37 *correlation whenever the incidence of a specific type of cancer exceeded 9. Otherwise, Fisher's exact test*  
38 *was performed to determine statistical significance. ORs higher than 1 indicate that redness is positively*  
39 *associated with the incidence of the specific type of cancer. Results are in bold if significant in two-sided*  
40 *tests after Benjamini-Hochberg correction for multiple tests, and p-values < 0.0005 are coded as 0.000.*

41 Red-haired men were thus more prone to colorectal cancer, while red-haired women were more prone to  
42 colorectal cancer, precancerous cervical or uterine lesions, cervical or uterine cancer, ovarian cancer, and  
43 other types of cancer. This higher cancer risk was not due to a higher rate of skin cancer, which was only  
44 non-significantly more frequent in red-haired men (OR=1.52) and women (OR=1.43).

45

#### 46 **Gender effects and interactions**

47 Because health effects differed between men and women, particularly among red-haired respondents, we  
48 investigated whether gender interacted significantly with the apparent effects of hair/eye color on their  
49 health. To this end, we first performed four MANCOVAs to see whether variance in respondent health  
50 correlated significantly with gender, eye darkness, hair darkness, and hair redness. We then performed three  
51 MANCOVAs to see whether variance in respondent health correlated significantly with an interaction  
52 between gender and any of the other variables: eye darkness, hair darkness, or hair redness. Finally, we  
53 constructed a new binary variable—presence or absence of green eyes—and performed two MANCOVAs to  
54 see whether variance in respondent health correlated significantly with this new variable or with an  
55 interaction between it and gender. The results are shown in Table 6.

56

57 Table 6. Correlations of all health effects with gender, hair color, or eye color

Independent variable	R	p-value
gender	0.12	0.001***
hair redness	0.04	0.001***
hair darkness	0.02	0.35
eye darkness	0.03	0.002**
gender*hair redness	0.02	0.182
gender*hair darkness	0.01	0.583
gender*eye darkness	0.02	0.405
green eyes vs. all other eye colors	0.02	0.049*
gender*green eyes vs. all other eye colors	0.12	0.001***

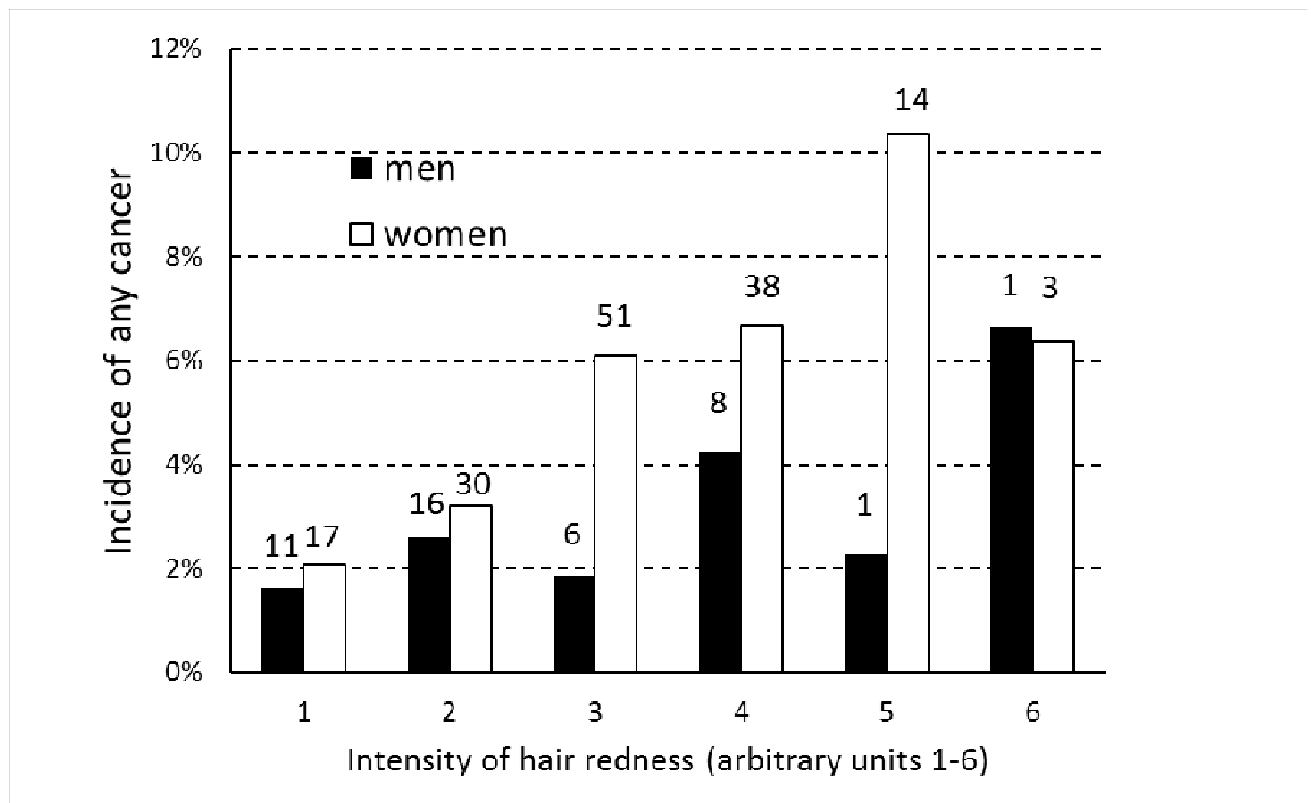
58

59 Although respondent health correlated significantly with gender, hair redness, and eye darkness taken  
60 separately, and although female respondents differed significantly from male respondents in hair redness and  
61 hair darkness (but not eye darkness), there were no significant three-way interactions between gender,  
62 respondent health, and any of the above variables for hair or eye color (Table 6). In the case of eye color, a  
63 linear regression on eye darkness may not be the best way to capture a combined effect by gender and eye  
64 color on respondent health. Indeed, the relationship between gender and eye color cannot be described  
65 simply in terms of eye darkness. As we have seen, women are less likely than men to be blue-eyed or  
66 brown-eyed, while conversely being more often green-eyed (Table 1). This was why we constructed the  
67 binary variable of green eyes versus all other eye colors, and we found that this variable significantly  
68 interacted with gender to produce effects on respondent health. In general, green-eyed women were healthier  
69 than the other respondents, except for a greater propensity to have cancer and psychiatric problems.

70 This finding made us take a second look at the relationship between female respondent health and  
71 hair redness. That relationship, too, might not be fully understood through a linear regression. We  
72 specifically looked at the data on cancer because the relationship between health outcomes and hair redness  
73 was strongest in that category, even though the well-known association between red hair and skin cancer  
74 seemed to contribute very little to this relationship. We performed a logistic regression with the incidence of  
75 any cancer as the dependent variable (0 = no cancer reported, 1 = cancer or precancerous lesion reported)  
76 and with three independent variables: gender, age, hair redness, and gender\*hair redness interaction. A  
77 separate analysis for women showed that hair redness (OR range = 3.99,  $p < 0.0001$ ) and age (OR range =  
78 12.1,  $p < 0.0001$ ) significantly affected the incidence of any cancer. In contrast, a separate analysis for men  
79 showed a significant age effect (OR range = 50.7,  $p < 0.0001$ ) but no hair redness effect (OR range = 1.63,  
30  $p = 0.457$ ). For men and women together, cancer was significantly affected by age (OR range = 17.7,  
31  $p < 0.0001$ ) and by hair redness (OR range = 3.74,  $p < 0.0001$ ) but not by gender (OR range = 0.67,  $p = 0.331$ )  
32 or by gender\*hair redness (OR range = 0.47,  $p = 0.381$ ). The results are shown in Figure 5.

33

34 Figure 5. Incidence of any cancer by gradation of hair redness, for men and women

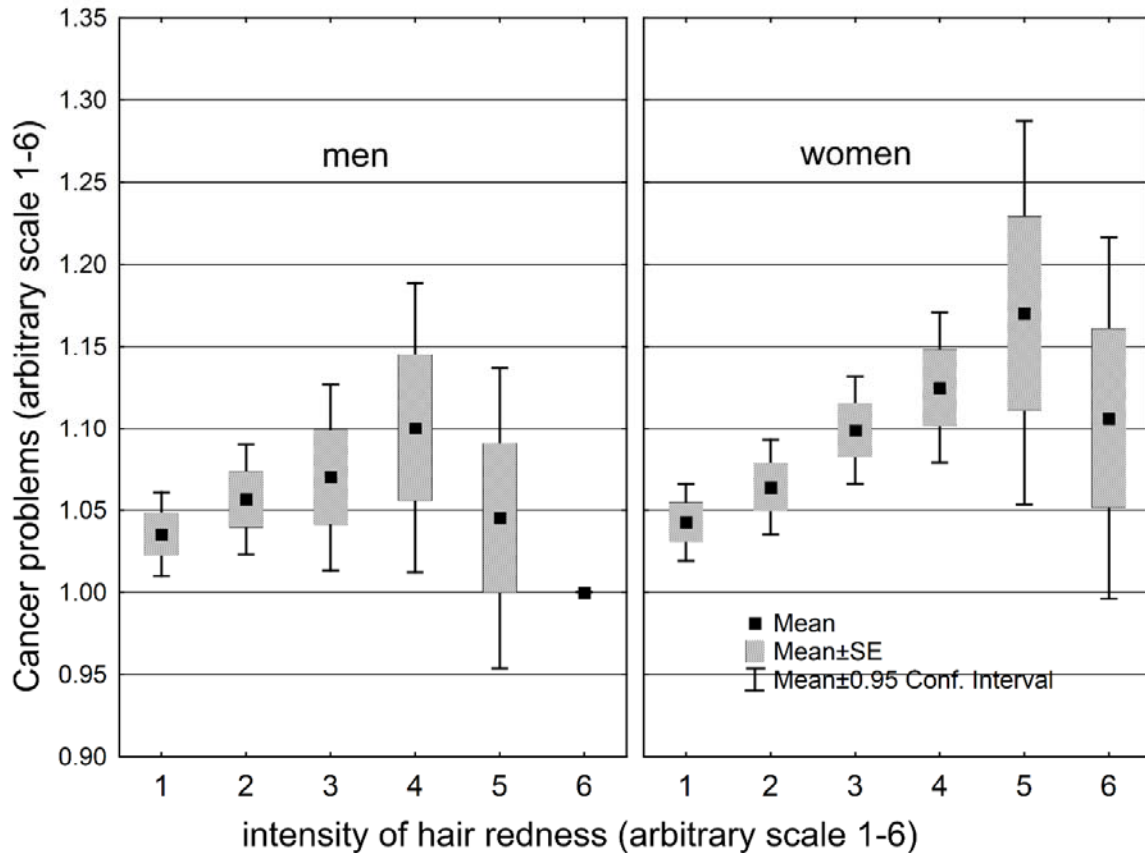


35  
36 *The numbers above the columns show numbers of subjects in particular categories.*

37  
38 The gender difference was greatest at the next-to-last gradation of hair redness. To learn more about  
39 this interaction between gender and gradation of hair redness, we plotted the reported mean seriousness of  
40 cancer (where 1 = no cancer reported and 6 = very serious problem with cancer) as a function of hair  
41 redness. This new variable may provide a clearer picture because it contains more information than simply  
42 the presence or absence of cancer. The results are shown in Figure 6. Mean seriousness of cancer increased  
43 steadily with increasing hair redness up to a certain gradation of redness and then decreased. This  
44 relationship was stronger in women than in men and peaked at a higher gradation of redness in women than  
45 in men. For women, both age ( $p < 0.0005$ ) and hair redness ( $p = 0.014$ ) significantly affected mean seriousness  
46 of cancer. Men showed significant effects for age ( $p < 0.0005$ ) but not for hair redness ( $p = 0.719$ ). For men

37 and women together, mean seriousness of cancer was significantly affected by age ( $p < 0.005$ ) and by hair  
38 redness ( $p = 0.0005$ ) but not by gender ( $p = 0.438$ ) or by gender\*hair redness ( $p = 0.292$ ).

39 Figure 6. Mean seriousness of cancer by gradation of hair redness, for men and women



30

31

## 32 DISCUSSION

33 Red hair seems to be costly for women's health. In this study, red-haired women did worse than other  
34 women in ten health categories and better in only three. In general, women incurred more costs and gained  
35 fewer benefits from red hair than from any other hair or eye color. Brown eyes held second place, but the  
36 health effects associated with brown eyes, both negative and positive, were smaller on average than those  
37 associated with red hair. Red-haired men showed a balanced pattern of health effects, doing better than other  
38 men in three categories and worse in three. Number of children was the only category where both male and



39 female redheads did better than non-redheads. In terms of reproductive and, ultimately, evolutionary  
10 success, red hair seems to be a plus rather than a minus.

11         The cancer rate was higher among red-haired women than among other women, and we initially  
12 suspected a higher rate of skin cancer as the cause. A closer look at the data, however, showed that the  
13 higher cancer rate was due not to a higher incidence of skin cancer, but rather to a higher incidence of  
14 cancers in the colorectal region, the cervix, the uterus, and the ovaries (Table 5). Because estrogen  
15 influences the development of the last three organs from the fetal stage onward, the higher cancer rate may  
16 be better explained by a higher level of prenatal exposure to estrogen, rather than by greater vulnerability to  
17 UV. This explanation is supported by the higher incidence among red-haired women of osteoporosis and  
18 obstetric complications (results not shown), both of which are either more frequent in women or specific to  
19 women. It may seem surprising that the skin cancer rate was only slightly higher for redheads than for non-  
20 redheads, given the many studies that point to red hair as a risk factor. Such studies, however, generally  
21 concern countries like the United States and Australia, whose citizens are exposed to a higher intensity of  
22 UV because they live at lower latitudes than do Czech citizens and also because a higher proportion of them  
23 have been regularly traveling to tropical or subtropical resorts for the past half-century or longer.

24         If we consider the other negative health effects associated with red hair, these too are not easily  
25 attributable to fairness of skin, and hence to UV vulnerability, again because of the greater propensity of  
26 women to exhibit these health effects. Although women are fairer-skinned than men, this gender difference  
27 is smaller in fair-skinned humans and in redheads in particular, among whom both sexes are pushed up  
28 against the physiological “ceiling” of skin reflectance [23, 24]. Moreover, if vulnerability to UV explains  
29 this pattern of health effects, we would expect to see a similar pattern with blue eyes, which are likewise  
30 associated with fair skin [1]. Yet, relative to other hair and eye colors in our sample, blue eyes imposed  
31 fewer costs on male or female health, while providing women with the highest total of benefits and men the  
32 second-highest.

33           Some of these other negative health effects are consistent with previous findings in the literature.  
34   Despite having more children on average, the red-haired women of this study had a higher incidence of  
35   fertility problems, which would be consistent with the higher incidence of endometriosis reported in  
36   previous studies. They also had more neurological problems, although none of these involved Parkinson's  
37   disease. Actually, few cases of Parkinson's would be expected, given the relatively young age of the  
38   respondents. Red-haired women showed no obvious indications of increased pain sensitivity in this study,  
39   although in some cases they might have reported more medical problems because sensitivity to pain made  
40   them seek medical assistance more readily.

41           These health effects thus seem to be due to a female-specific factor that is most strongly expressed in  
42   red-haired women. The relationship between this factor and hair redness seems curvilinear, i.e., average  
43   female health progressively worsens with redder gradations of hair, but only up to a certain point. If we take  
44   the data on seriousness of cancer, the worst health was reported by women with the next-to-last gradation of  
45   hair redness. Those with the reddest hair were actually somewhat better off (Figure 5); however, this  
46   category had only three women and one man. With respect to eye color, the female-specific factor seemed to  
47   act most strongly on women with green eyes and not on those with lighter shades. In both cases, these  
48   effects mirror the effects of estrogen on development of hair and eye color. Red hair is more frequent in  
49   women than in men (Figure 1); similarly, green eyes are more frequent in women than in men, with brown  
50   eyes and blue eyes showing the reverse pattern (Table 1).

51           In addition to the problem of modeling the curvilinear relationships between female respondent  
52   health and eye darkness/hair redness, the data suffered from a high level of noise. Inter-respondent variance  
53   was inflated by self-report and the subjective nature of the questions. As a result, even when significant  
54   correlations were found between respondent health and different variables (gender, age, hair redness, hair  
55   darkness, eye darkness, etc.), they cannot explain more than a tiny proportion of total variance in health  
56   status among the respondents. We should emphasize that this tininess may be only apparent. To provide a  
57   benchmark for the relative importance of these health effects, we also examined respondent data on BMI

58 and smoking, both of which strongly affect human health. Using the data in Table 4 (significant negative  
59 effects on women's health), we found that, on average, BMI explains twice as much variance in these  
60 negative health effects as does red hair (Tau=0.071, vs. 0.040), while smoking explains approximately the  
61 same amount (Tau=0.039). Thus, BMI and smoking overlap with hair and eye color in the magnitude of  
62 their negative effects on women's health.

63 It seems, then, that different hair and eye colors are associated with significantly different health  
64 outcomes and that these apparent effects are stronger in women than in men. Red-haired women exhibit the  
65 most divergent health effects, including a previously unreported vulnerability to colorectal, ovarian, and  
66 cervical cancer. Not all effects are for the worse. Red-haired women seem to enjoy greater reproductive and  
67 mating success, as measured by number of children and number of sexual partners. It may be that red-haired  
68 women have more children because they begin having them at an earlier age, although a recent study has  
69 reported that red-haired men and women lose their virginity at a later age on average [25]. An alternative  
70 explanation is that red-haired women attract not only more sexual partners but also better sexual partners  
71 who can support a larger family size. More research on the life history of red-haired women is needed. Red  
72 hair might be more attractive than other hair colors because it is less common. It has been argued that the  
73 different hair and eye colors of Europeans, including red hair, have coexisted in a dynamic equilibrium [13,  
74 14]. According to this argument, a hair or eye color is sexually attractive in proportion to its scarcity. It  
75 therefore loses this novelty value if it becomes too common, and the pressure of selection shifts to less  
76 common variants. In the case of red hair, there may also be an equilibrium between sexual attractiveness and  
77 negative health effects. These negative effects would depress the population frequency of red hair below the  
78 frequency it would have if sexual attractiveness were the only selection pressure. The gap between this  
79 second equilibrium and the first may explain the relative popularity of red-haired women: they have never  
80 been sufficiently numerous to lose their novelty value.

31

32           What causes these negative health effects in red-haired women? The cause can be framed in either  
33 biochemical or evolutionary terms. First, these effects might be inherent to biosynthesis of red hair pigments  
34 (pheomelanins). But why, then, are they expressed much more often in red-haired women than in red-haired  
35 men? There seems to be a female-specific factor. As argued in the Introduction, this factor may be prenatal  
36 estrogen. The same prenatal estrogen that causes red hair to be more frequent in women than in men may  
37 also explain why these negative health effects are expressed in red-haired women but not in red-haired men.  
38 In the fetal stage, such women were more likely to experience estrogen levels near the top end of the normal  
39 range for fetal development. The risk of later health problems would therefore be proportionately greater.

30           Second, in terms of evolutionary causation, red hair may have been the last hair color to emerge in  
31 modern humans; therefore, not enough time has passed for corrective evolution, either through new alleles  
32 that produce red hair with fewer side effects or through modifier genes that neutralize the side effects of  
33 existing red hair alleles. This situation is typical of rapid evolution over relatively short spans of time [26].  
34 Another possible scenario is that red hair alleles emerged among Neanderthals and then introgressed into  
35 early modern Europeans when the two groups coexisted in Europe. Such introgression could cause genetic  
36 incompatibility and thus explain the negative health effects we observed. Red hair is produced mainly by  
37 five loss-of-function alleles at the *MC1R* gene, and a recent study has identified one of them, Val92Met, as a  
38 likely Neanderthal introgression. The same study, however, found that the four other alleles are not of  
39 Neanderthal origin [27]. Given that modern humans entered Europe c. 45,000 BP and reached northern  
40 Europe c. 30,000 BP, and that the Neanderthals went extinct c. 40,000 BP, the scenario of Neanderthal  
41 introgression makes sense for Val92Met, which is found throughout Eurasia. However, the other loss-of-  
42 function alleles, which are more specific to northern Europe, probably originated in modern humans.

33           To conclude, our findings may shed light not only on the health risks associated with red hair but  
34 also on the evolution of this highly visible color trait and, more generally, on how the diverse European  
35 palette of hair and eye colors came into being. This evolution seems to have occurred for the most part in  
36 relatively recent times, probably no earlier than the entry of modern humans into northern Europe some

37 30,000 years ago and no later than the oldest DNA evidence of these alternate colors, dating to some 8,000  
38 years ago from Motala, Sweden. The short time span (< 1000 generations) suggests that some form of  
39 selection, possibly sexual selection, was driving this diversification of hair and eye colors in early  
40 Europeans. Of these 'new' color variants, red hair seems to diverge the most from the ancestral state of  
41 black hair and brown eyes. It is the most sexually dimorphic variant, not only in population frequency but  
42 also in health outcomes.

13

## 14 **DECLARATIONS**

### 15 *Acknowledgements and Funding*

16 The work was supported by Charles University (UNCE 204004) and the Czech Science Foundation (Grant  
17 No. P407/16/20958).

### 18 *Competing interests*

19 The authors declare that they have no competing interests.

20

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