HEALTH STATUS BY GENDER, HAIR COLOR, AND EYE COLOR: RED-HAIRED WOMEN ARE THE MOST DIVERGENT

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ABSTRACT

Red hair is associated with pain sensitivity, and more so in women than in men. Hair redness may thus interact with a female-specific factor. We tested this hypothesis on a large sample of Czech and Slovak respondents. They were asked about the natural redness and darkness of their hair, their natural eye color, their physical and mental health (24 categories), and other personal attributes (height, weight, number of children, lifelong number of sexual partners, frequency of smoking). We found that red-haired women did worse than other women in ten health categories and better in only three. In particular, they were more prone to colorectal, cervical, uterine, and ovarian cancer. Cancer risk increased steadily with increasing hair redness except for the reddest shade. Red-haired men showed a balanced pattern of health effects, doing better than other men in three categories and worse in three. Number of children was the only category where both male and female redheads did better than other respondents. Of the 'new' hair and eye colors, red hair diverges the most from the ancestral state of black hair and brown eyes. It is the most sexually dimorphic variant, not only in population frequency but also in health outcomes.

INTRODUCTION

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

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

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

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

METHODS

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

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

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

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

Data analysis Statistica v. 10 and IBM SPSS v. 21 were used for most of the statistical analysis. MANCOVAs on health effects (with gender, eye color, or hair color as predictors) were performed by "adonis" function available within Vegan package in R (18). Differences in age were tested by t-tests. Chi^2 tests were used to compare the frequencies of eye colors in men and women. Effects of gender and age on hair color, eye color, and waviness of hair were analyzed by both nonparametric (partial Kendall correlation with age or gender as a covariate) and parametric tests using general linear models with gender, age, and gender-age interaction as independent variables. Both categories of tests produced very similar results and therefore only the results of the more conservative nonparametric tests are reported. Logistic regression (Quasi-Newton estimation method) was used for the analysis of relation between cancer and hair redness and hair redness*gender interaction. Other ordinal and binary data were analyzed by a partial Kendall correlation test, which is used to measure the strength and significance of associations between binary, ordinal, or continuous data regardless of their distributions and which can be used to control for one confounding variable, here the respondent's age (19,20). To compute partial Kendall Tau and the significance of each variable, after controlling for age, we used an Excel spreadsheet available at: http://web.natur.cuni.cz/flegr/programy.php. Because many disorders tend to be more common in men than in women or vice versa, associations between the health categories and the hair/eye colors were always analyzed separately for men and women. Whenever fewer than 10 respondents reported a disorder, a Fisher exact test was used to determine the significance of the association between hair/eye color and the category of fitness. To correct for multiple tests, and the associated increase in the false discovery rate, we used the Benjamini-Hochberg procedure with the false discovery rate preset to 0.25 (21). In contrast to the Bonferroni correction, this procedure takes into account the distribution of p values of performed multiple tests. Therefore, when the studied factor has multiple effects, the number of significant results after the correction may be higher than before the correction. To measure eye color diversity, we used the Simpson index λ, which was computed as $\lambda = SUMA(p_i)^2$, where p_1–p_i denotes proportions of respondents with 1-i eye color in the population under study (22). This index reflects the probability of two randomly-selected respondents carrying the same character, here the same eye color. All raw data are available as Supporting Information S1, at https://figshare.com/s/6a02dd5cec0f90b69db9

RESULTS

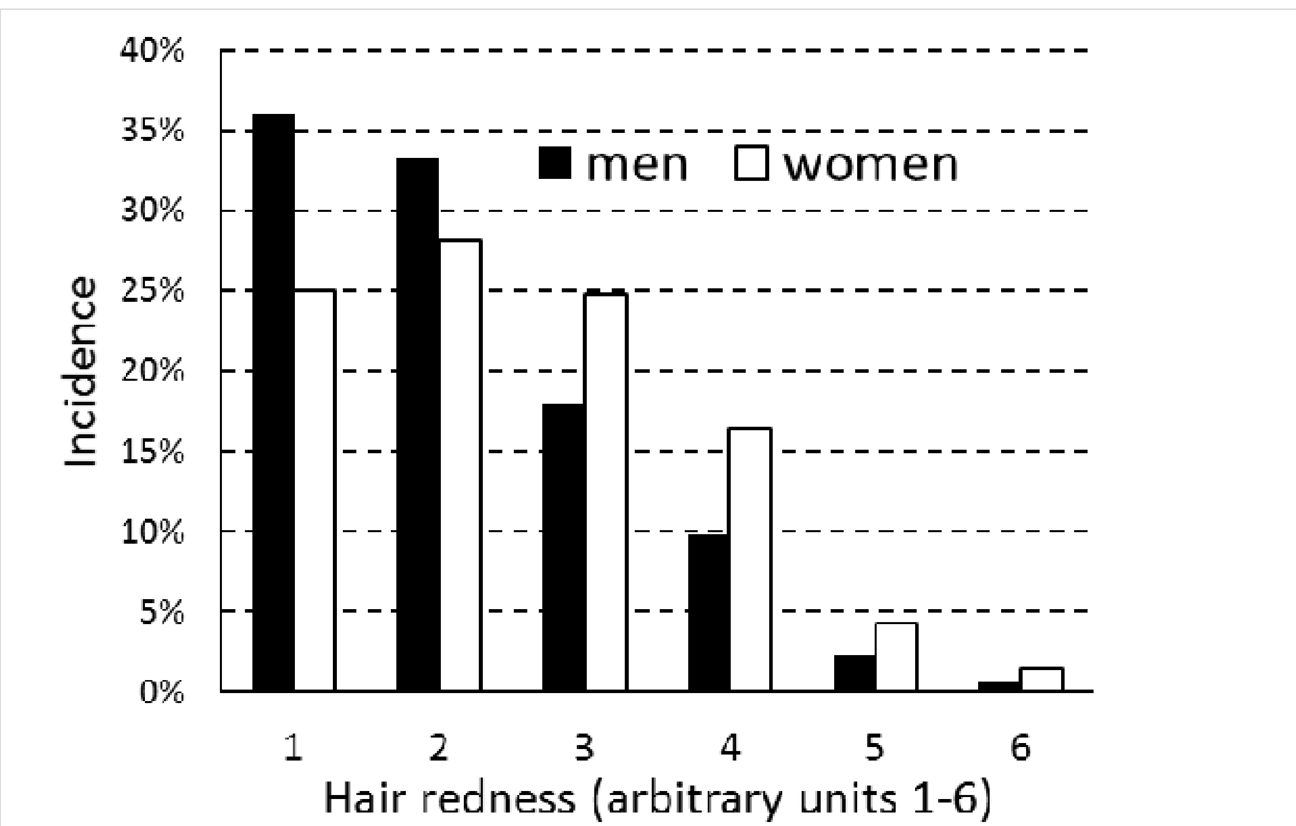
Characteristics of respondents

Information on eye color, hair color, and hair waviness was provided by 2,559 men and 4,484 women out of 7,044 Czech and Slovak respondents (the others did not complete the questionnaire part of the test). Mean age of the men (36.8, std. dev. 13.5) was somewhat higher than mean age of the women (34.6, std. dev. 13.0) $t_{7028} = 6.9$, $p < 0.0005$.

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

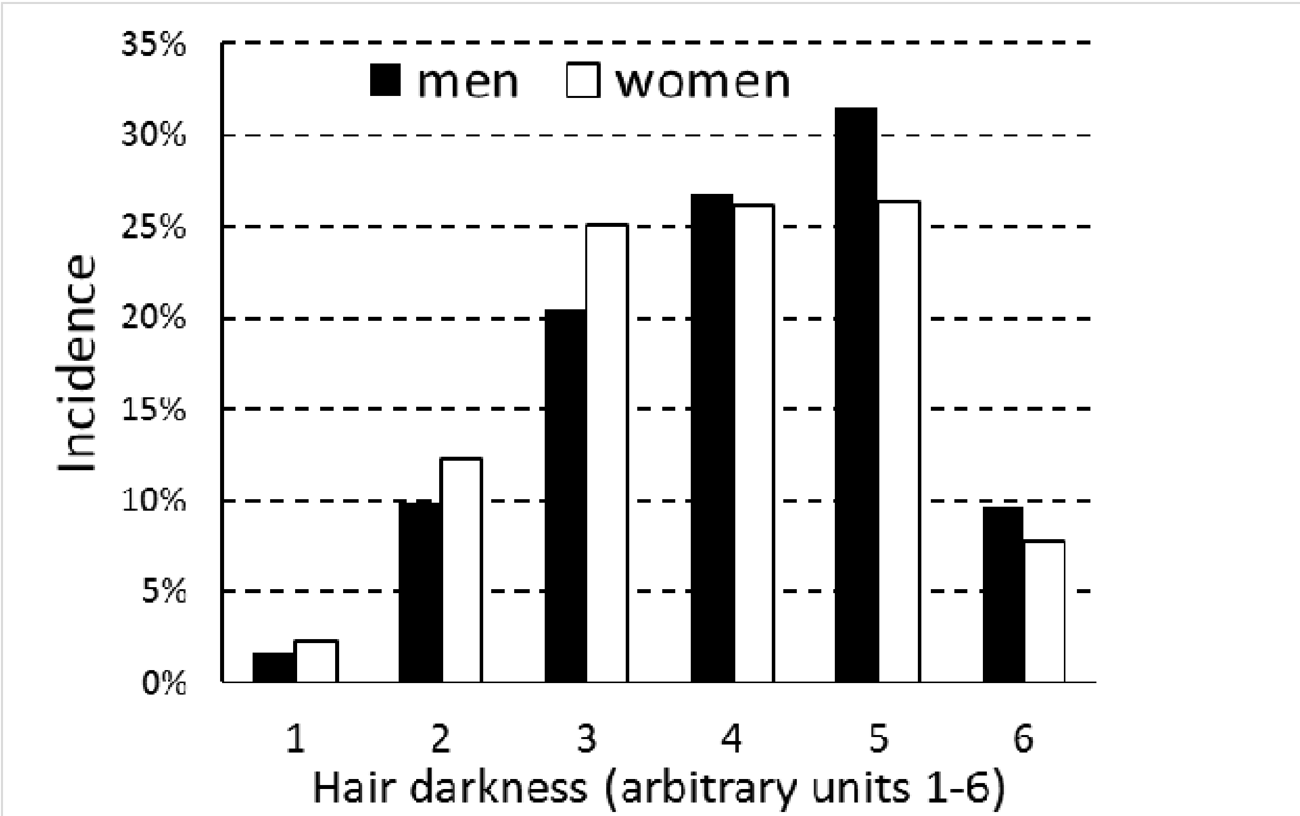
Age was associated in women with darker eyes, darker hair, redder hair, and less wavy hair (Table 2), and in men with redder hair and less wavy hair. After controlling for the effect of age, we still found gender differences: male hair was significantly darker (mean 4.07 vs. 3.87, $p < 0.0005$), less red (mean 2.09 vs. 2.51, $p < 0.0005$), and less wavy (mean 2.30 vs. 2.56, $p < 0.0005$). No gender difference was observed in eye darkness (mean 3.39 vs, 3.42, $p = 0.56$).

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



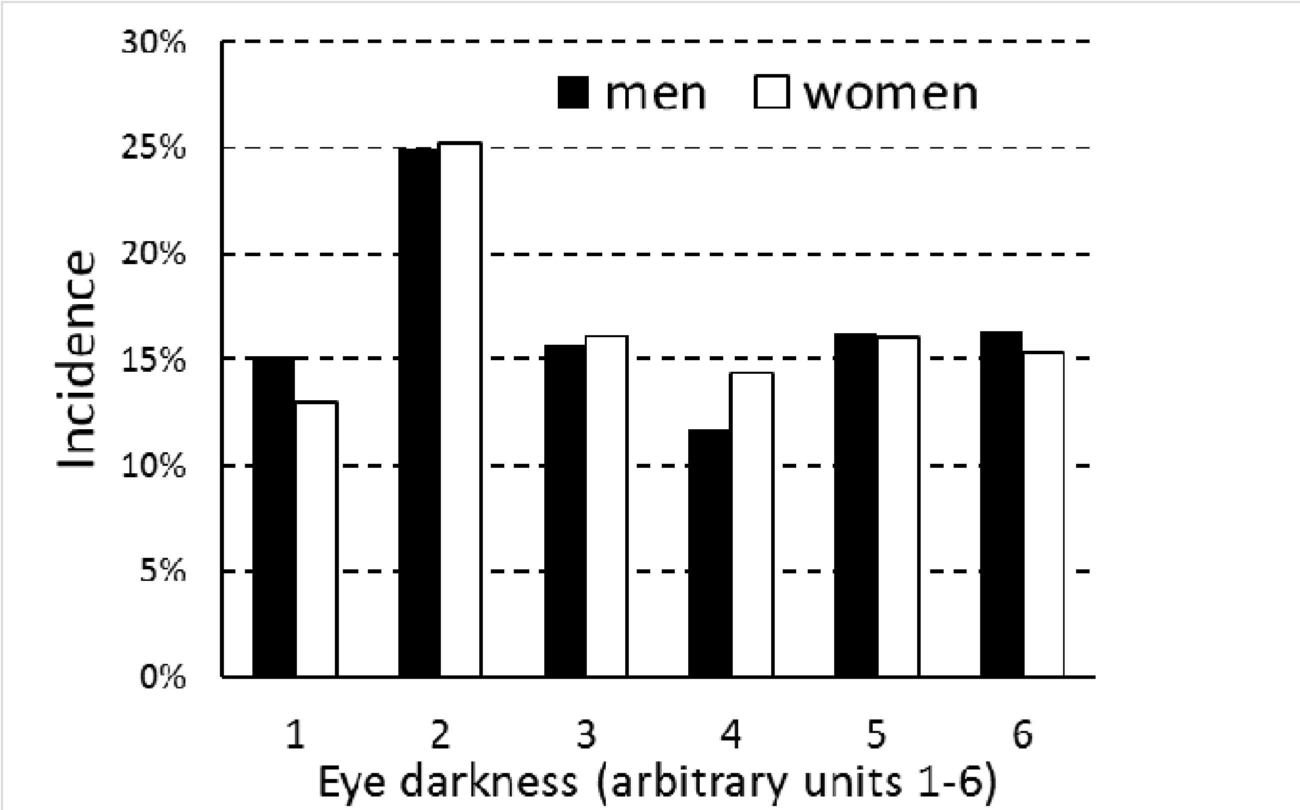
Respondents rated hair redness on a scale of 1 to 6 where 1 = not at all red and 6 = completely red

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



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

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



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

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

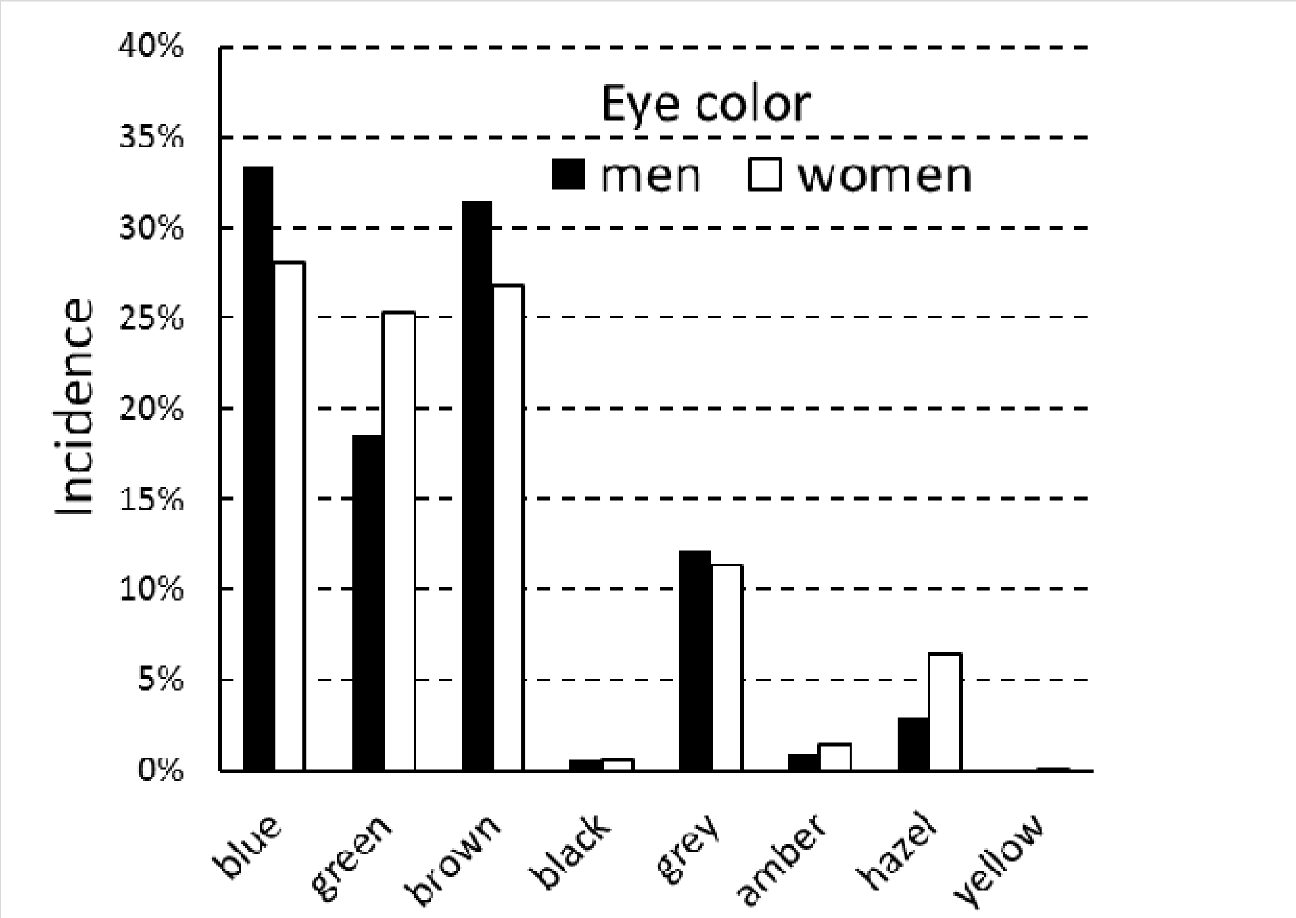


Table 1. Frequencies of eye colors in men and women

		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	

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

Table 2. Correlations between eye/hair properties and age

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

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

Associations between health categories and hair/eye color

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

Table 3. Results for men: 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	-0.015	-0.019	0.011	**0.033**	**0.041**	**-0.030**	**-0.025**	0.004	0.015	**-0.031**	**0.025**	**0.172**	**0.093**
Mental health problems in general	**-0.026**	0.009	0.014	0.014	0.015	0.003	**-0.024**	0.011	-0.024	**0.032**	0.014	**-0.023**	**0.083**
Specific health problems:													
Antibiotics/ year	0.007	-0.001	-0.004	**-0.032**	0.002	**-0.036**	**0.026**	-0.018	-0.002	0.006	**0.025**	0.014	**-0.050**
Acute care/ 5 years	0.008	**-0.034**	**0.048**	-0.006	**-0.034**	-0.004	-0.007	0.026	0.014	-0.008	**0.045**	0.011	**-0.034**
Different med.	0.002	-0.003	0.002	0.026	0.002	-0.015	-0.012	-0.001	-0.021	0.017	**0.038**	**0.083**	**-0.030**

specialist seen every 2 years													
Number of prescription drugs/day	0.015	0.023	-0.014	**0.051**	-0.017	-0.012	**-0.039**	-0.016	-0.026	**0.031**	0.009	**0.133**	**-0.053**
Number of alternative medicines/day	0.021	0.000	-0.019	-0.020	0.001	-0.015	0.007	-0.003	-0.010	**0.032**	**0.041**	0.013	**-0.049**
Allergies	-0.001	0.003	-0.004	-0.014	0.015	0.020	**-0.028**	-0.012	0.015	**-0.053**	0.016	-0.001	**-0.037**
Immunological	**0.024**	**-0.051**	0.019	-0.003	0.023	-0.023	**-0.037**	-0.005	-0.003	0.000	**0.029**	-0.015	**-0.034**
Digestive	**-0.033**	0.018	0.004	0.025	**0.034**	0.001	**-0.040**	0.020	-0.017	0.012	0.013	**0.023**	**0.053**
Heart & vascular system	-0.022	0.012	-0.007	0.003	**0.037**	**0.040**	**-0.044**	0.003	0.005	-0.008	**0.026**	**0.076**	**0.025**
Hematological	0.018	0.018	-0.015	-0.023	0.003	-0.011	**-0.042**	-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	**-0.042**	-0.007	-0.024	0.022	0.020	**0.163**	-0.017
Cancer	0.013	-0.030	-0.015	-0.010	**0.026**	**0.053**	-0.004	0.000	-0.020	0.018	**0.029**	**0.039**	**-0.019**
Fertility	-0.015	-0.023	0.012	**0.074**	**0.028**	0.012	**-0.036**	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	**-0.034**	-0.002	0.025	-0.005	**0.027**	-0.004	-0.018	0.023	0.005	0.004	0.013	0.017	0.009
Neurological	**-0.028**	-0.023	0.007	0.003	**0.059**	-0.012	-0.001	0.008	0.005	0.023	0.018	-0.018	-0.012
Psychiatric	**-0.037**	0.001	0.014	**0.042**	0.007	0.002	**0.030**	0.027	0.008	0.008	**0.038**	-0.009	**0.095**
Sexual function	-0.003	0.003	-0.011	0.020	**0.029**	-0.006	**-0.032**	-0.022	-0.011	0.007	-0.003	**0.034**	**0.074**
Musculoskeletal	**-0.052**	-0.025	**0.063**	0.014	0.016	0.010	-0.017	**0.066**	0.001	0.026	**0.034**	**0.037**	**-0.021**
Respiratory	-0.011	-0.013	0.030	0.019	-0.006	0.010	**-0.027**	0.014	0.006	0.001	0.017	**0.045**	**0.063**
Tiredness (frequency)	**-0.034**	0.024	0.027	**0.038**	-0.009	-0.008	**-0.027**	0.025	0.009	-0.011	0.023	0.008	**0.096**
Headaches (frequency)	**-0.036**	-0.009	0.023	0.020	0.017	**0.032**	-0.002	0.010	0.010	-0.011	0.015	0.008	**0.068**
Reproductive/ mating success:													
Number of children	**0.023**	-0.007	-0.026	**-0.035**	0.018	0.014	-0.006	-0.025	-0.007	**0.039**	**-0.032**	**0.099**	**-0.030**
Number of sexual partners	0.018	-0.002	0.020	0.025	**-0.046**	0.000	**-0.019**	-0.005	-0.003	0.009	0.009	**0.069**	**0.182**
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

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

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	**-0.024**	**0.039**	**-0.027**	0.010	-0.020	-0.009	0.011	**0.020**	**0.020**	-0.001	**0.228**	**0.054**
Mental health problems in general	**-0.033**	0.014	0.013	**-0.024**	**0.019**	0.001	-0.007	0.003	**0.020**	**0.047**	0.008	0.013	**0.041**
Specific health problems:													
Antibiotics/ year	-0.005	**-0.026**	**0.020**	0.012	0.015	-0.005	-0.001	0.002	0.013	**-0.035**	0.010	**0.045**	**0.027**
Acute care/ 5 years	**-0.025**	-0.013	**0.035**	0.015	0.010	-0.007	-0.009	**0.019**	**0.025**	0.002	**0.018**	**0.047**	**0.029**
Different med. specialist seen every 2 years	-0.018	-0.014	**0.046**	0.006	-0.005	-0.022	-0.014	**0.023**	0.014	-0.006	0.013	**0.052**	0.013
Number of prescription drugs/day	**-0.055**	**-0.023**	**0.077**	-0.009	**0.021**	0.002	**-0.028**	**0.045**	**0.023**	0.008	-0.013	**0.122**	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	**-0.019**	-0.019
Allergies	**-0.039**	-0.001	**0.049**	0.011	-0.011	-0.001	-0.002	**0.034**	0.016	-0.012	**0.025**	**0.030**	**-0.025**
Immunological	**-0.020**	-0.015	**0.034**	**0.040**	**-0.020**	0.019	0.006	**0.039**	**0.039**	0.007	**0.018**	**0.020**	**0.018**
Digestive	-0.015	0.018	0.016	0.012	-0.002	0.010	**-0.037**	0.014	-0.001	0.008	**0.025**	**0.031**	0.009
Heart & vascular system	-0.010	0.009	0.005	-0.010	0.011	-0.006	**-0.019**	0.002	0.015	**0.044**	**0.021**	**0.040**	**0.017**
Hematological	0.004	-0.016	0.000	**0.036**	0.008	-0.014	0.009	-0.004	0.000	0.007	**0.039**	-0.006	-0.007
Metabolic	**-0.041**	**-0.022**	**0.039**	0.019	0.010	0.021	0.014	**0.038**	**0.023**	**0.045**	**0.020**	**0.187**	0.007
Cancer	0.012	**0.024**	-0.014	-0.012	**-0.027**	0.017	-0.010	0.003	-0.009	**0.067**	0.013	0.011	0.013
Fertility	**-0.030**	0.005	0.015	-0.005	0.013	0.007	0.001	0.013	0.015	**0.042**	**0.054**	0.006	-0.010
Genitourinary	-0.017	-0.007	**0.033**	-0.006	**0.019**	-0.024	**-0.025**	0.016	0.009	**0.028**	-0.011	**-0.026**	0.013
Sense organs	-0.002	-0.007	-0.016	**-0.034**	**0.038**	0.005	0.003	**-0.029**	0.000	0.011	**0.033**	**0.041**	**-0.024**
Neurological	-0.013	-0.003	0.006	**0.023**	**0.021**	-0.001	**-0.020**	-0.002	0.011	0.014	0.015	0.011	-0.005
Psychiatric	**-0.033**	**0.025**	**-0.020**	-0.012	**0.035**	0.004	0.005	-0.006	0.006	**0.020**	0.009	0.007	**0.098**
Sexual function	-0.012	0.003	0.012	-0.016	0.016	0.006	**-0.024**	-0.002	0.015	**0.030**	0.013	0.017	**0.010**
Musculoskeletal	0.000	0.010	-0.005	-0.007	0.005	-0.015	-0.005	-0.004	-0.018	**0.053**	0.007	**0.040**	0.013
Respiratory	**-0.026**	0.006	**0.027**	**0.026**	-0.006	-0.008	-0.008	**0.026**	0.013	-0.006	0.011	**0.084**	**0.053**
Tiredness (frequency)	-0.004	0.005	0.001	0.003	0.016	-0.007	**-0.022**	-0.005	0.014	0.014	0.002	**0.021**	**0.058**
Headaches (frequency)	-0.001	0.006	-0.004	0.013	0.010	-0.009	**-0.019**	-0.009	0.015	-0.002	**0.018**	0.014	**0.019**

Reproductive/ mating success:													
Number of children	0.006	0.004	**0.026**	-0.008	-0.016	-0.010	**-0.041**	**0.018**	**0.030**	**0.143**	**-0.026**	**0.096**	**-0.02**
Number of sexual partners	0.010	0.016	-0.006	0.014	**-0.027**	0.014	-0.008	-0.001	**-0.021**	**0.061**	-0.008	0.011	**0.24**
Negative health effects	0	2	10	4	7	0	1	7	7	10	11	14	1
Positive health effects	9	4	2	3	2	0	8	2	1	3	0	3	[illegible]

See Table 3 legend.

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

We were able to look more closely at these health effects by analyzing supplementary data on specific disorders within the health categories. For example, for the ‘Respiratory’ category, respondents had been asked “What kind of respiratory problems are you suffering from or did you suffer from in the past?” They then read a list of disorders and ticked the appropriate boxes. The list had a total of 211 disorders. The associations between these disorders and hair redness were analyzed (partial Kendall Tau correlation) with age as a covariate or by the Fisher exact test when fewer than 10 respondents reported the disorder. Of the 211 disorders, 207 were ticked by at least 1 respondent, 192 by at least 1 man, and 202 by at least one woman. In addition, 99 (48%), 28 (15%), and 47 (23%) were significantly associated with hair redness in men and women together, in men, and in women, respectively, after correction for multiple tests with the Benjamini-Hochberg procedure.

We then looked at specific disorders in six of the above seven health categories (respondents had not been given a list of specific disorders for the ‘Fertility problems’ category). The results are shown in Table 5.

Table 5. Specific disorders that disproportionately affect red-haired women (differences where p ≤ 0.05 are in bold)

	AFFECTED RED-HAIRED WOMEN	TOTAL RED-HAIRED WOMEN	% RED-HAIRED WOMEN	AFFECTED OTHER WOMEN	TOTAL OTHER WOMEN	% OTHER WOMEN	P value
CANCER	90	15,849	0.568	184	55,833	0.330	
Esophageal cancer	1	837	0.119	1	2947	0.034	0.394
Stomach cancer	1	837	0.119	1	2947	0.034	0.394
Colorectal cancer	3	837	0.358	0	2947	0.000	**0.011**
Liver cancer	1	837	0.119	0	2947	0.000	0.221
Lung cancer	0	837	0.000	0	2947	0.000	-
Melanoma, other skin cancers	4	837	0.478	10	2947	0.339	0.243
Breast cancer	7	837	0.836	15	2947	0.509	0.318
Precancerous cervical or uterine lesions	27	783	3.448	64	2787	2.296	**0.008**
Cervical or uterine cancer	20	837	2.389	45	2947	1.527	**0.003**
Corpus uteri cancer	2	837	0.239	7	2947	0.238	1.000
Ovarian cancer	5	837	0.597	5	2947	0.170	**0.015**
Prostate cancer	0	837	0.000	0	2947	0.000	-
Lymphoma, myeloma multiple	0	837	0.000	0	2947	0.000	-
Leukemia	1	837	0.119	6	2947	0.204	1.000
Bladder cancer	1	837	0.119	2	2947	0.068	0.528
Mouth, oropharyngeal cancers	1	837	0.119	0	2947	0.000	0.221
Adenocarcinoma	0	837	0.000	4	2947	0.135	0.582
Papilloma	4	837	0.478	6	2947	0.204	0.422
Other types of cancer	12	837	1.434	18	2947	0.611	**0.000**
HEART & VASCULAR	84	6688	1.256	202	23,432	0.862	
Rheumatic heart diseases	1	836	0.120	6	2929	0.205	1.000
Hypertensive diseases	42	836	5.024	62	2929	2.117	**0.012**
Ischemia	6	836	0.718	7	2929	0.239	0.932
Cerebrovascular dis., stroke	3	836	0.359	3	2929	0.102	0.128
Viral myocarditis inflammation	2	836	0.239	4	2929	0.137	0.620
Bacterial endocarditis inflammation	0	836	0.000	4	2929	0.137	0.582
Aneurysm	0	836	0.000	3	2929	0.102	1.000
Other heart	30	836	3.589	113	2929	3.858	0.831

diseases							
METABOLIC	405	14,436	2.805	1076	50,670	2.124	
Diabetes type 1	4	802	0.499	13	2815	0.462	0.795
Crohn's disease	7	802	0.873	7	2815	0.249	0.121
Immuno-deficiency	23	802	2.868	62	2815	2.202	0.751
Adrenal gland hypofunction	1	802	0.125	5	2815	0.178	1.000
Diabetes type 2	21	802	2.618	33	2815	1.172	**0.021**
Hypothyroidism	113	802	14.090	317	2815	11.261	0.390
Hyperthyroidism	13	802	1.621	50	2815	1.776	**0.046**
Goiter	3	802	0.374	10	2815	0.355	0.845
Adrenal gland hyperfunction	1	802	0.125	5	2815	0.178	1.000
Inborn metabolic diseases	2	802	0.249	9	2815	0.320	0.805
Obesity	109	802	13.591	289	2815	10.266	**0.003**
Hypoglycemia	7	802	0.873	36	2815	1.279	0.736
Osteoporosis	34	802	4.239	50	2815	1.776	**0.015**
Delayed puberty	9	802	1.122	29	2815	1.030	0.492
Precocious puberty	6	802	0.748	15	2815	0.533	0.790
Amenorrhea	12	802	1.496	44	2815	1.563	0.415
Pituitary gland diseases	2	802	0.249	3	2815	0.107	0.308
Other metabolic diseases	38	802	4.738	99	2815	3.517	0.345
MUSCULO-SKELETAL	649	8613	7.535	1950	30,701	6.352	
Spondylosis, spondylitis	12	783	1.533	31	2791	1.111	0.234
Myopathy	2	783	0.255	5	2791	0.179	0.652
Backbone pain	347	783	44.317	1034	2791	37.048	**0.002**
Osteoporosis	31	783	3.959	68	2791	2.436	0.161
Rheumatoid arthritis, inflammation	23	783	2.937	75	2791	2.687	0.553
Rheumatic fever	4	783	0.511	12	2791	0.430	0.356
Psoriatic arthritis, arthropathy	3	783	0.383	2	2791	0.072	0.073
Scoliosis	151	783	19.285	495	2791	17.736	0.222
Scheuermann's disease	7	783	0.894	31	2791	1.111	0.789
Osteoarthrosis	50	783	6.386	119	2791	4.264	0.086
Other musculoskeletal dis.	19	783	2.427	78	2791	2.795	0.268
GENITO-URINARY	660	7047	9.366	2080	25,083	8.292	
Urinary tract infections	236	783	30.140	755	2787	27.090	**0.016**
Nephrosis,	5	783	0.639	37	2787	1.328	0.677

glomerulonephritis							
Bladder infections, cystitis	100	783	12.771	312	2787	11.195	0.671
Prostate hypertrophy	0	783	0.000	0	2787	0.000	-
Gynecological infections	208	783	26.564	687	2787	24.650	0.062
Obstetric complications	48	783	6.130	119	2787	4.270	**0.021**
Recurrent abortion	25	783	3.193	54	2787	1.938	0.707
Kidney stones	21	783	2.682	52	2787	1.866	0.246
Other genitourinary dis.	17	783	2.171	64	2787	2.296	0.121
SEXUAL FUNCTION	350	6616	5.290	1273	23,474	5.423	
Erectile dysfunction	0	809	0.000	3	2867	0.105	0.135
Too low sex appetite	180	809	22.250	694	2867	24.206	0.854
Too high sex appetite	24	809	2.967	112	2867	3.907	0.065
Too low sex potency	2	809	0.247	11	2867	0.384	**0.043**
Quality of sex	104	809	12.855	353	2867	12.313	0.514
Paraphilias (severe)	1	809	0.124	4	2867	0.140	1.000
Paraphilias (mild)	9	953	0.944	21	3405	0.617	0.099
Other sex-related diseases	30	809	3.708	75	2867	2.616	**0.038**

The association between hair redness and particular disorders were tested with partial Kendall Tau. For the purposes of data description (incidences of disorders in red-hair and not red-hair women shown in the columns 2-5) the six-point scale of redness was recoded to the two-point scale 0: 0-2, 1: 3-5.

Red-haired women were thus more prone to the following disorders:

Cancer: colorectal cancer, precancerous cervical or uterine lesions, cervical or uterine cancer, ovarian cancer, other types of cancer

Heart & vascular: hypertensive diseases

Metabolic: type 2 diabetes, hyperthyroidism, obesity, osteoporosis

Musculoskeletal: backbone pain

Genitourinary: urinary tract infections, obstetric complications

Sexual function: too low sex potency, other sex-related diseases.

Although red-haired women were more prone than other women to cancer, this difference was not due to a higher rate of skin cancer, which was only slightly (and non-significantly) more frequent in red-haired women (0.48%) than in other women (0.34%).

Gender effects and interactions

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

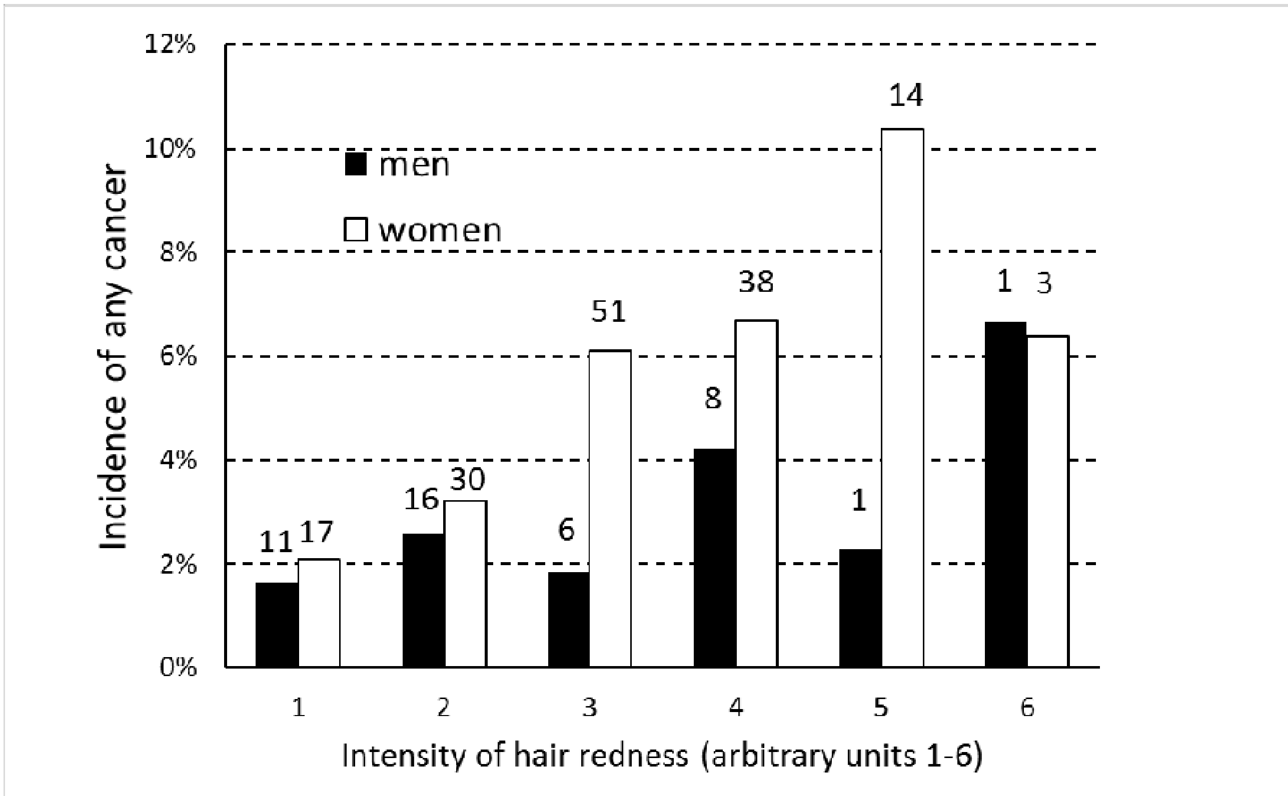
Table 6. Correlations of all health effects with gender, hair color, or eye color

Independent variable	R	p-value
gender hair redness	0.12 0.04	0.001*** 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***

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

This finding made us take a second look at the relationship between female respondent health and hair redness. That relationship, too, might not be fully understood through a linear regression. We specifically looked at the data on cancer because the relationship between health outcomes and hair redness was strongest in that category. We performed a logistic regression with the incidence of any cancer as the dependent variable (0 = no cancer reported, 1 = cancer or precancerous lesion reported) and with three independent variables: gender, age, hair redness, and gender*hair redness interaction. A separate analysis for women showed that hair redness (OR range = 3.99, $p<0.0001$) and age (OR range = 12.1, $p<0.0001$) significantly affected the incidence of any cancer. In contrast, a separate analysis for men showed a significant age effect (OR range = 50.7, $p<0.0001$) but no hair redness effect (OR range = 1.63, $p=0.457$). For men and women together, cancer was significantly affected by age (OR range = 17.7, $p<0.0001$) and by hair redness (OR range = 3.74, $p<0.0001$) but not by gender (OR range = 0.67, $p=0.331$) or by gender*hair redness (OR range = 0.47, $p=0.381$). The results are shown in Figure 5.

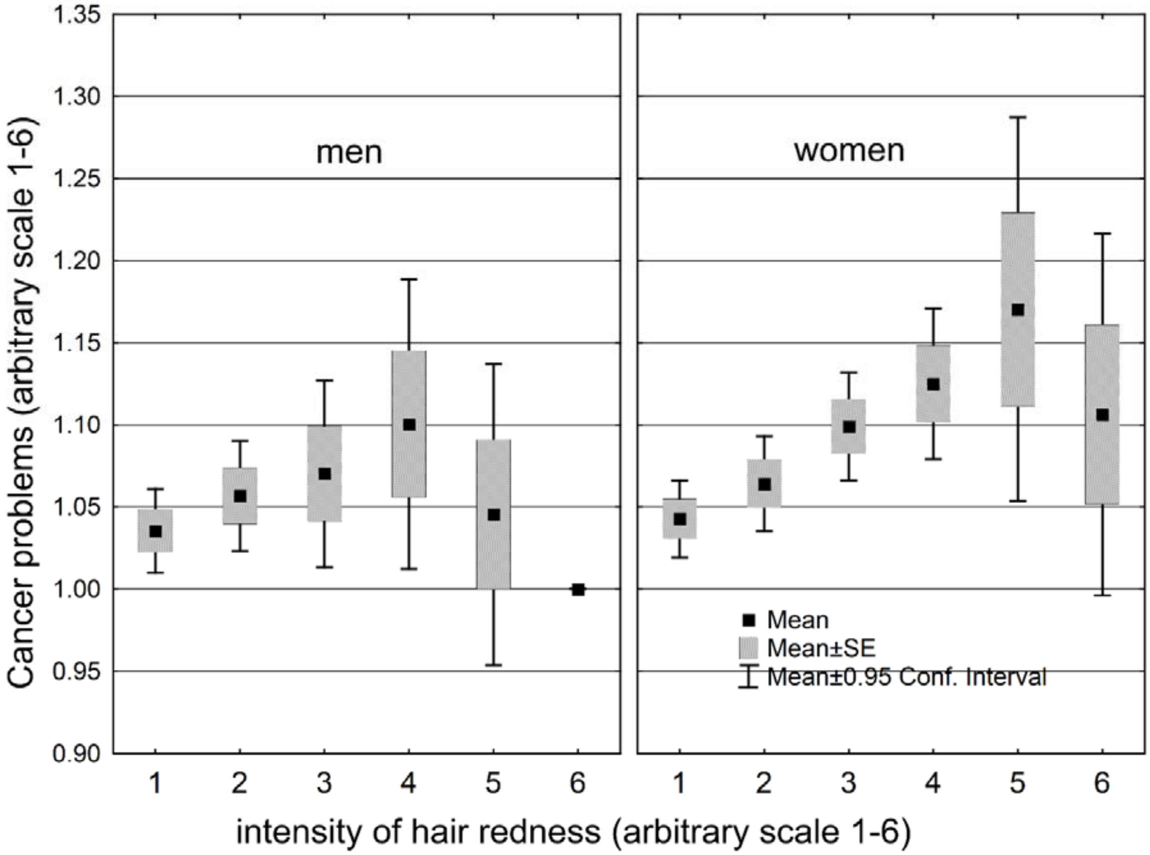
Figure 5. Incidence of any cancer by gradation of hair redness, for men and women



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

The gender difference was greatest at the next-to-last gradation of hair redness. To learn more about this interaction between gender and gradation of hair redness, we plotted the reported mean seriousness of cancer (where 1 = no cancer reported and 6 = very serious problem with cancer) as a function of hair redness. This new variable may provide a clearer picture because it contains more information than simply the presence or absence of cancer. The results are shown in Figure 6. Mean seriousness of cancer increased steadily with increasing hair redness up to a certain gradation of redness and then decreased. This relationship was stronger in women than in men and peaked at a higher gradation of redness in women than in men. For women, both age ($p<0.0005$) and hair redness ($p=0.014$) significantly affected mean seriousness of cancer. Men showed significant effects for age ($p<0.0005$) but not for hair redness ($p=0.719$). For men and women together, mean seriousness of cancer was significantly affected by age ($p<0.005$) and by hair redness ($p=0.0005$) but not by gender ($p=0.438$) or by gender*hair redness ($p=0.292$).

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



DISCUSSION

Red hair seems to be costly for women. In this study, red-haired women did worse than other women in ten health categories and better in only three. In general, women incurred more costs and gained fewer benefits from red hair than from any other hair or eye color. Brown eyes held second place, but the health effects associated with brown eyes, both negative and positive, were smaller on average than those associated with red hair.

Red-haired men showed a much more balanced pattern, doing better than other men in three categories and worse in three. Number of children was the only category where both male and female redheads did better than everyone else. In terms of reproductive and, ultimately, evolutionary success, red hair seems to be a plus rather than a minus.

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

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

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

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

In addition to the problem of modeling the curvilinear relationships between female respondent health and eye darkness/hair redness, the data suffered from a high level of noise. Inter-respondent variance was inflated by self-report and the subjective nature of the questions. As a result, even when significant correlations were found between respondent health and different variables (gender, age, hair redness, hair darkness, eye darkness, etc.), they cannot explain more than a tiny proportion of total variance in health status among the respondents. We should emphasize that this tininess may be only apparent. To provide a benchmark for the relative importance of these health effects, we also examined respondent data on BMI and smoking, both of which strongly affect human health. In comparison to hair and eye color, BMI explains 1 to 17 times more of the variance among respondents, and smoking 1 to 3 times more. Thus, BMI and smoking overlap with hair and eye color in the magnitude of their effects on human health.

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

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

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

To conclude, our findings may shed light not only on the health risks associated with red hair but also on the evolution of this highly visible color trait and, more generally, on how the diverse European palette of hair and eye colors came into being. This evolution seems to have occurred for the most part in relatively recent times, probably no earlier than the entry of modern humans into northern Europe some 30,000 years ago and no later than the oldest DNA evidence of these alternate colors, dating to some 8,000 years ago from Motala, Sweden. The short time span ($<$ 1000 generations) suggests that some form of selection, possibly sexual selection, was driving this diversification of hair and eye colors in early Europeans. Of these 'new' color variants, red hair seems to diverge the most from the ancestral state of black hair and brown eyes. It is the most sexually dimorphic variant, not only in population frequency but also in health outcomes.

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