The interaction of psychosocial and physical risk factors in the causation of mammary cancer, and its prevention through psychological methods of treatment.

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Interaction of Psychosocial and Physical Risk Factors in the Causation of Mammary Cancer, and It’s Prevention through Psychological Method of Treatment

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Abstract

Some 8059 healthy women (mean age 58 years) were studied in 1973 with the aim of establishing the presence or absence of a variety of physical and psychological risk factors for mammary cancer. Mortality was established in 1988, 15 years later. Both physical and psychological risk-factor predictors were highly significant. Physical risk factors were more predictive than psychological ones, but both interacted synergistically to predict mortality. Alone, psychological (stress) factors had little effect, while physical factors did. However, psychological factors seemed to potentiate the effect of physical factors, particularly in the middle range. The causal relevance of psychological factors was established in a special intervention study using autonomy training as a method of prophylactic therapy and comparing outcome with the effects of no therapy (control).
"The concept that cancer might in some way be related to stress or other emotional factors is probably as old as the history of recorded medicine itself." (Eysenck, 1979, p. 187). Almost 2000 years ago, Galen noted in his book *De Tumoribus* that melancholic women were much more susceptible to cancer than other females, and similar involvement of psychological factors was noted in the medical literature of the last three centuries (Rosch, 1979, 1980). Sir William Osler (1986), often called the Father of English Medicine, stated the case well when he said, "It is very often much more important what person has the disease, than what disease the person has." Some form of diathesis-stress model is becoming more widely accepted, although such models present many difficulties of theoretical elaboration and empirical investigation (Grossarth-Maticek, Eysenck, & Boyle, 1994; Rende & Plomin, 1992).

Until the middle of this century, support for the importance of psychosocial factors in the genesis and development of malignant growths was largely anecdotal (Temoshok & Dreher, 1992). However, there were also some empirical studies, typical of which is one by Snow (1891), who reported that of 200 patients with mammary and uterine cancer at the London Cancer Hospital, 150 had experienced "immediately antecedent trouble, often in very poignant form as the loss of a near relative." A good review of this early work is given by Le Shan and Worthington (1956) and by Greer (1983) (see also Baltrusch, Austarheim, & Baltrusch, 1963, 1964a,b; Baltrusch, Stangel, & Waltz, 1988).

Later, the pioneering work of Le Shan (1959, 1961, 1977; Bahnson 1969, 1976, 1980a,b; Bahnson & Bahnson, 1966, 1969; Kissen & Le Shan, 1964; Le Shan & Le Shan, 1971; Le Shan & Reznikoff, 1960; Schmale & Iker, 1971), and many
others listed by Eysenck (1985) and Temoshok and Dreher (1992) demonstrated
the truth of the two major hypotheses advanced by the earlier writers—Cancer is
more likely (1) in people who suppress their emotions and self-regarding
instincts, appearing bland and exaggeratedly helpful and altruistic, and (2) in
people who cannot cope with stress, develop feelings of hopelessness, and finally
depression (Eysenck, 1985).

Those early studies tended to use psychoanalytic concepts, but the lack of
usefulness of and support for these notions led investigators towards a more
pragmatic approach (Le Shan, 1977); more recent work has tended to disregard
psychoanalytic theories altogether (Cooper, 1983, 1984, 1988; Cooper & Payne,
1991). Stress-coping, the personality traits related to a person's likelihood to
experience stress, and the use of proper coping strategies have become
acknowledged as important factors in cancer genesis and development, probably
through the impact of psychological factors, like depression, on the immune
system (Ader, 1981; Antoni, 1987; Evans, Bristow, Hucklebridge, Clow, &
Cohen, 1993; Schneider, Smith, Minning, Witcher, & Hermanson, 1990; Eysenck,
1987a,b, 1992, 1993 Zakowski, Hall, & Barnes, 1992). The link between
personality-stress-emotion and the immune system is probably via cortisol, ACTH,
and the endogenous opiates (Eysenck, 1991a).

There are certain obvious weaknesses in many of these studies. The number
of subjects often is rather too small to give convincing results, and the comparisons
made are usually between patients suffering from cancer and control groups. This
paradigm does not rule out the possibility that the disease process has affected the
personality of the patient, rather than the other way about. Finally, we are dealing
throughout with correlations that cannot be interpreted in causal terms. An
exception to these criticisms is the work of Grossarth-Maticek (1976, 1979, 1986,
1989), who used large numbers of subjects and organized prospective studies as his paradigm (i.e., assessed healthy probands for personality and stress, as well as for physical-risk factors and followed them up for up to 20 years to ascertain mortality and cause of death). Finally, he employed therapeutic intervention in an attempt to reverse the personality-stress factors correlated with cancer, thus providing direct evidence for a causal interpretation (Eysenck, Grossarth-Maticek, & Everitt, 1991; Grossarth-Maticek, 1980a; Grossarth-Maticek & Eysenck, 1991). A general survey of the Grossarth-Maticek studies is given by Eysenck (1991a), who emphasizes the point that results have been replicated several times and in different countries.

Psychological factors interact, of course, with physical ones, and this interaction has been found not to be additive but synergistic; in other words, effects multiply rather than add (Eysenck, 1994; Eysenck, Grossarth-Maticek, & Everitt, 1991). This is an important finding, and we shall be testing its applicability in this study. These studies have, of course, been criticized; one is perhaps a target article on Grossarth-Maticek's contribution (Eysenck, 1991b), followed by critiques of some two dozen invited contributors, followed in turn by the original author's reply (Eysenck, 1991c). More important, for a proper evaluation of this work than these rather adversarial debates, are new contributions consisting of independent replications. It is known that the best indication of the validity of scientific findings is independent replication, and several successful such replications have been reported (e.g., Arnelang & Schmidt-Rathjens, 1992; Bleiker, 1995; Fernandez-Ballesteros, Zamarron, Ruiz, & Sebastian, 1994; Larsson et al., 1995; Quander-Blaznick, 1991; Sandin, Chorot, Jimenez, & Santed, 1993; Sandin, Chorot, Navas, & Santed, 1992; Santin, Chorot, Santed, & Jimenez, 1993; Schmitz, 1992, 1993; Shigehisa, 1991; Shigehisa, Fukui, & Motraki, 1989, 1991). Clearly, the theories taken over from antiquity and adapted by Le Shan, 1977; Bahnson & Bahnson, 1969; and Grossarth-Maticek, 1976, 1979, 1980a, b, 1986, 1989; when submitted
to experimental analysis, stand up very well to such investigation. Even the most crucial deduction from these theories, namely that childhood personality should predict longevity, has been shown to be supported by empirical research (Friedman et al., 1993).

The most relevant prospective study for our purpose is one reported by Bleiker (1995), who followed up a large sample of women for two to four years, administered personality questionnaires at the beginning of the study, and finally compared cases (women who developed breast cancer) with controls (women who did not). In her discussion of results, Bleiker gives a Table (Table 31, p.147) comparing cases and controls, reporting results for 11 scales developed by various authors to measure cancer proneness. Of these, only the Grossarth-Matichek scale of anti-emotionality statistically was significant in predicting breast cancer. For a four-item scale, as compared with much longer ones measuring anger, anxiety, depression, optimism, social support, emotional expression, and emotional control, this is a remarkable finding and one that supports the theory on which the Grossarth-Matichek scales are based.

Also, specifically concerned with breast cancer is a large-scale study by Cooper and Faragher (1992, 1993). This is a quasi-prospective study of 2163 women attending a breast-cancer screening clinic for a routine medical check up. Results showed that certain types of coping strategies and personality dispositions predispose some women to an increased risk of developing breast cancer following the occurrence of a major life event, such as bereavement or other loss-related event. Cancer of the breast was particularly likely to occur under these circumstances, "if the individual was unable to externalize her emotions and obtain appropriate help and counselling" (p.653). Anger as a coping style was found to be related to a good prognosis, while denial was found to be related to a poor prognosis (p.661). These results are in good agreement with
the Grossarth-Maticek theory and Bleiker findings.

Equally important is another method of answering criticisms. The first Grossarth-Maticek study along prospective lines (Grossarth-Maticek, Bastiaans, & Kanazir, 1985) was carried out in the former Yugoslavia and was followed by two similar studies carried out in Heidelberg (Eysenck, 1988; Grossarth-Maticek, Eysenck, & Vetter, 1988) incorporating a 10-year follow up. The high predictive accuracy of the interviewer-administered questionnaires employed gave rise to the criticism that perhaps some of the interviewers (over 100 specially trained students were employed in order to collect the data) might have used evidence of morbidity in the subjects interviewed to alter questionnaire responses to improve forecasting accuracy. To allay fears on such grounds, the two Heidelberg samples were subjected to a second follow up of 4 years, making the total follow up almost 15 years. Dr. H. Vetter, a statistician who was in possession of the relevant data and who had made the original suggestion that such irregularities might have given rise to results "too good to be true" (Vetter, 1991a), analyzed the new data and was forced to retract the "morbidity hypothesis" (Vetter, 1991b). The full set of data from this second follow up has been published (Eysenck, 1993a) and should set to rest any doubts about the genuineness of the Grossarth-Maticek findings.

One frequently made criticism remains, however. Most of Grossarth-Maticek's work has been concerned with the prediction of cancer, yet oncologists emphasize that different cancers may have very different origins, follow a different course, and respond differentially to treatment (Blaney, 1984). Hence, it may be meaningless to throw together a random collection of cancers into a general 'cancer' category. The reason for doing so will be obvious; even in a large group of healthy people followed up for between 10 and 20 years, very few will develop a particular kind of cancer; it would need tens of thousands, or even
more, to make it possible for more specific analyses to be undertaken. This, indeed, may be the reason why epidemiologists and oncologists largely have avoided prospective studies; to follow up such large numbers over long periods of time is both difficult and extremely expensive, and the return, in terms of the number of affected probands, is still quite small. It can, of course, be argued that the success of predicting cancer from psychosocial factors suggests that the criticism is probably invalid, but an actual demonstration of the possibility of predicting a particular type of cancer from stress, coping, and personality questionnaires seemed needed and is presented in this paper.

**Present Study**

**Methodology and Results**

*Population.* In this study, we have concentrated on the incidence and mortality of mammary carcinomas in healthy women first studied in 1973 and followed up in 1988.

Originally, 9229 women were approached by 84 trained student interviewers, probands being selected randomly from electoral register lists, with age limitations between 49 and 66 years, with a mean age of 57.8 years. Of these, 816 (8.8%) refused to take part or were already suffering from cancer. In 290 cases, it was impossible to discover the cause of death. For the remaining women, mortality and incidence was assessed in 1988 (i.e., after 15 years). Diagnosis was checked by reference to the physicians in charge. Of the 8123 women remaining in the study, 72 took part in an experiment on the possibility of avoiding mammary cancer by means of psychological therapy, leaving 8051 women for the major analysis of the predictive value of physical risk factors, psychosocial risk factors, and their mode of interaction. Principles of selection were the same as in previous studies (Grossarth-Maticek, 1986, 1989). It will be
noted that the percentage of women dying of cancer in our group was some 10% less than expected from the general cancer level in the Saar county. This is expected, of course, because we eliminated from our sample all women already diagnosed as suffering from cancer.

**Physical factors.** In order to assess the predictive value of psychosocial risk factors, it is important to have an accurate assessment of physical risk factors. Clearly, if smoking is an important risk factor for mammary carcinoma, and if people who are under stress smoke more, then any predictive value for a measure of stress might be due to smoking. It is well known that genetic factors are important for mammary cancer (Lichter et al., 1992), as are endocrine factors (ibid). Risk is higher in nulliparous women (older than 35 at the first delivery), women with an early first menstruation, and women with irregular and lengthy menstrual periods (Henderson & Bernstein, 1991). Risk also is increased by spontaneous or induced abortion at an early age (Howe, Senie, Bzduch, & Herzfeld, 1989). Nutritional factors (low vitamins, high fat content) are also relevant (Willett & London, 1991), as is obesity. Regular consumption of alcohol, depending on amount, is also a risk factor (Longnecker, Berlin, Orza, & Chalmers, 1988). Proliferative breast disease is a potent risk factor (Dupont & Page, 1985). There also are, of course, factors reducing risk of mammary cancer, such as having many children, an early menopause, and lengthy breast feeding (Hoskins, Perez, & Young, 1992; McTierman & Thomas, 1986).

Based on these findings, a 25-item questionnaire was constructed, giving 1 point for items like cigarette smoking, fat-rich nutrition, early menstruation, etc., and grading the number of points awarded by degree of alcohol consumption, overweight, genetic pre-disposition, or number of abortions. The listing of items and scoring is given below in Table 1. The maximum number of points gained was 19, as compared with a possible total of 25. Table 2 shows the
number of probands achieving each point score, the total mortality for each score and the percentage who died at each level; the total mammary-carcinoma mortality for each score and the percentage who died at each level as a percentage of total number of probands; and the mammary-carcinoma mortality as a percentage of total mortality (i.e., the number of probands diagnosed as suffering from mammary carcinoma, but still alive).

Certain features are obvious from this table. Total mortality increases fairly regularly as number of risk points increases. Mammary-cancer mortality increases fairly regularly as the number of risk factors increase. This raises the question of whether the questionnaire is specific enough for mammary carcinoma; it may be that the questions related quite generally to behaviors and conditions that are injurious to health in general. The column listing carcinoma mortality as a percentage of total mortality would seem to point to a rather specific impact of the risk factors in our list; the percentages increase at an increasing rate. Table 3 makes the same point. It groups together figures for point scores of 0-4, 5-9, 10-14, and 15-19 for total mortality, mammary-carcinoma mortality, and the percentage values of each. There is an increase of 68.1% from low point to high for mammary-carcinoma mortality and of 34.7% for total mortality; there is therefore a large difference. Physical risk factors appear to be quite specific for mammary cancer. All results are significant by $x^2$ at the $(p < .01)$ level.
Points Given for Various Physical Risk Factors in the Promotion of Mammary Cancer

<table>
<thead>
<tr>
<th>Points for number and intensity of physical risk factors</th>
<th>Risk Factors</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 Lack of children</td>
<td></td>
</tr>
<tr>
<td>1 One abortion</td>
<td></td>
</tr>
<tr>
<td>2 Two abortions</td>
<td></td>
</tr>
<tr>
<td>3 Three or more abortions</td>
<td></td>
</tr>
<tr>
<td>1 One close relative suffering from or died of breast cancer</td>
<td></td>
</tr>
<tr>
<td>2 Two close relatives suffering from or died of breast cancer</td>
<td></td>
</tr>
<tr>
<td>3 Three close relatives suffering from or died of breast cancer</td>
<td></td>
</tr>
<tr>
<td>1 Breast disease up to 10 years</td>
<td></td>
</tr>
<tr>
<td>2 Breast disease longer than 10 years</td>
<td></td>
</tr>
<tr>
<td>1 Never breast-fed baby</td>
<td></td>
</tr>
<tr>
<td>1 Differences greater than 60 mg (% in cholesterol)</td>
<td></td>
</tr>
<tr>
<td>1 Nutrition poor in vitamins</td>
<td></td>
</tr>
<tr>
<td>1 Nutrition rich in fat</td>
<td></td>
</tr>
<tr>
<td>1 Lack of exercise</td>
<td></td>
</tr>
<tr>
<td>1 Very sensitive to pain</td>
<td></td>
</tr>
<tr>
<td>1 Use of depressant drugs</td>
<td></td>
</tr>
<tr>
<td>1 Cigarette smoking</td>
<td></td>
</tr>
<tr>
<td>1 Menstruation before 13</td>
<td></td>
</tr>
<tr>
<td>1 No high fever (over 34 °C) in the last five years</td>
<td></td>
</tr>
</tbody>
</table>

Regular alcohol use:

- 1 30-60 grams
- 2 61-80 grams
- 3 80+ grams

Overweight:

- 1 slight
- 2 medium
- 3 large

An additional column in Table 2 lists the incidence of mammary cancer. This does not increase with number of risk factors presumably because such a high proportion of high scorers have already died. In any case, the numbers are too small to give reliable results, but the figures are given for the sake of completeness. They suggest that the dose-response relationship apparent in the table for mortality extends to time of onset; lower point scores lead to later onset so that incidence shows typically lower point scores than mortality.

**Psychosocial risk factors.** Psychosocial risk factors were evaluated by
means of two interview-administered questionnaires, one dealing with general
stress and coping behavior, the other with specific responses believed to be
characteristic of women prone to

Table 2

<table>
<thead>
<tr>
<th>Points gained Physical Risk Questionnaire</th>
<th>Total Mortality</th>
<th>Cancer Mortality</th>
<th>Mammary Carcinoma Incidence</th>
</tr>
</thead>
<tbody>
<tr>
<td>Points</td>
<td>N</td>
<td>N</td>
<td>%</td>
</tr>
<tr>
<td>0</td>
<td>1529</td>
<td>206</td>
<td>13.5</td>
</tr>
<tr>
<td>1</td>
<td>1740</td>
<td>357</td>
<td>20.5</td>
</tr>
<tr>
<td>2</td>
<td>1409</td>
<td>310</td>
<td>22.0</td>
</tr>
<tr>
<td>3</td>
<td>959</td>
<td>288</td>
<td>30.0</td>
</tr>
<tr>
<td>4</td>
<td>759</td>
<td>178</td>
<td>23.5</td>
</tr>
<tr>
<td>5</td>
<td>301</td>
<td>98</td>
<td>32.6</td>
</tr>
<tr>
<td>6</td>
<td>302</td>
<td>79</td>
<td>26.2</td>
</tr>
<tr>
<td>7</td>
<td>263</td>
<td>77</td>
<td>29.3</td>
</tr>
<tr>
<td>8</td>
<td>252</td>
<td>66</td>
<td>26.2</td>
</tr>
<tr>
<td>9</td>
<td>166</td>
<td>50</td>
<td>30.1</td>
</tr>
<tr>
<td>10</td>
<td>110</td>
<td>46</td>
<td>41.8</td>
</tr>
<tr>
<td>11</td>
<td>67</td>
<td>24</td>
<td>35.8</td>
</tr>
<tr>
<td>12</td>
<td>47</td>
<td>21</td>
<td>44.7</td>
</tr>
<tr>
<td>13</td>
<td>48</td>
<td>21</td>
<td>43.9</td>
</tr>
<tr>
<td>14</td>
<td>36</td>
<td>16</td>
<td>44.4</td>
</tr>
<tr>
<td>15</td>
<td>32</td>
<td>14</td>
<td>43.8</td>
</tr>
<tr>
<td>16</td>
<td>14</td>
<td>7</td>
<td>50.0</td>
</tr>
<tr>
<td>17</td>
<td>9</td>
<td>8</td>
<td>88.9</td>
</tr>
<tr>
<td>18</td>
<td>5</td>
<td>3</td>
<td>60.0</td>
</tr>
<tr>
<td>19</td>
<td>3</td>
<td>3</td>
<td>100.0</td>
</tr>
</tbody>
</table>

mammary carcinoma (see Appendix A). The general personality-stress inventory
has been described in detail elsewhere (Grossarth-Matick & Eysenck, 1990). It
contains six scales corresponding to six personality types prone to different
types of disease, which may be characterized as follows:

1. Marked inhibitions in the expression of emotions and the satisfaction of
   personal desires and needs.

2. Behavior characterized by inner excitement and agitation, such as anger.

4. Flexibility of self-regulation; internality.

5. Rational and anti-emotional behavior.

6. Aggressive and psychopathic behavior.

What is measured evaluation, a person is considered "stressed" when $1 + 2 + 5 > 3 + 4 + 6$.

Justification for this formula is given elsewhere (Grossarth-Maticek & Eysenck, 1990).

The specific risk factors for mammary cancer are based on the theory of personal rejection. According to this theory, parents demand strict obedience to rules and expectations, good school achievements, and suppression of physical and emotional problems. The child accepts and incorporates these demands in the hope of being loved in return. The child develops a negative view of the self, regarding herself as unimportant and unworthy in so far as she does not live up to expectations. This tendency leads to a desire to avoid conflict by giving in to parents, idealizing parents, and inhibiting aggressive feelings. As adults, such people remain dependent on their parents and extend these feelings to their partners, on whom, in turn, they become dependent, and whom they idealize, however badly the partners may treat them. It is likely that the breast-cancer-prone woman passively expects loving devotion from the partner and experiences negation when this is not forthcoming. She may constantly feel stressed because her unreasonable expectations are constantly thwarted, and any feelings of aggression are suppressed. (Appendix A gives the brief questionnaire incorporating these theories.) It is, of course, not suggested that the behavior described is entirely caused by parental intervention; it is quite likely that genetic factors also play an important role. This question requires an empirical answer.
Table 3

Four Groups of Subjects Showing High, Medium, and Low Physical Risk Factors and Respective Total Mortality and Mammary-Cancer Mortality

<table>
<thead>
<tr>
<th>Points</th>
<th>N</th>
<th>Total Mortality</th>
<th>Percentage</th>
<th>Mammary Carcinoma</th>
<th>Total Mortality</th>
</tr>
</thead>
<tbody>
<tr>
<td>0-4</td>
<td>6396</td>
<td>1339</td>
<td>20.9</td>
<td>6</td>
<td>0.5</td>
</tr>
<tr>
<td>5-9</td>
<td>1284</td>
<td>370</td>
<td>28.8</td>
<td>41</td>
<td>11.1</td>
</tr>
<tr>
<td>10-14</td>
<td>308</td>
<td>128</td>
<td>41.6</td>
<td>37</td>
<td>28.9</td>
</tr>
<tr>
<td>15-19</td>
<td>63</td>
<td>35</td>
<td>55.6</td>
<td>24</td>
<td>68.6</td>
</tr>
<tr>
<td>TOTAL</td>
<td>8051</td>
<td>1872</td>
<td></td>
<td>108</td>
<td></td>
</tr>
</tbody>
</table>

Grossarth-Maticek and Eysenck (1990, p. 355) reported that, "Cancer-prone people ... tend to be overly cooperative, appeasing, unassertive, overly patient, avoiding conflict, seeking harmony, compliant, defensive, suppress the expression of emotion, and are unable to deal with interpersonal stress, which leads to feelings of hopelessness/helplessness and finally depression ... This in turn leads to high cortisol levels and so to immune deficiencies..."

The validity of the specific mammary-carcinoma scale is indicated by the results shown in Table 4. The total population is divided into three groups, having low (1-5 points), median (6-10 points) or high (2:11 points) scores on the scale, respectively. Of probands with a low score, 0.3% died of mammary cancer, a negligible proportion. Of those with a middling score, 2.8% died of mammary cancer, but of those with a high score, 8.5% died of mammary cancer, a very high proportion indeed. These results leave little doubt that personality as defined by the questionnaire constitutes an important risk factor for mammary cancer even though the genetic risk factors alone are extremely important. Of those who died of mammary carcinoma, 13.0% had a low score, 26.9% a middling score, and 60.2% a high score. These differences are signified by $x^2$ at $p < .01$ levels.
Combination of physical and psychosocial risk factors. The two psychosocial questionnaires described in the previous section jointly served to allocate women to either a stressed group or a nonstressed group. Those allocated to the stressed group had a total score of $1 + 2 + 5 > 3 + 4 + 6$, and also at least 8 points on the individual cancer-stress scale reproduced in Appendix 1. All other women were allocated to the nonstressed group. Table 5 shows the outcome of combining risk factors. (In what follows, we have used the term "stress" and "no stress" to refer to high and low scorers on the combined scales, respectively, or to high and low scorers on the rejection scale only; the context makes it clear which is intended.) The use of the term "stress" in this connection may be criticized; what clearly is involved is a mixture of external stress, personality predisposition to react

Table 4

<table>
<thead>
<tr>
<th>Psychosocial Risk Factors</th>
<th>Mammary Carcinoma</th>
<th>Breast-Cancer Deaths</th>
</tr>
</thead>
<tbody>
<tr>
<td>N</td>
<td>%</td>
<td>N</td>
</tr>
<tr>
<td>1-5 points</td>
<td>5050</td>
<td>73.8</td>
</tr>
<tr>
<td>6-10 points</td>
<td>1031</td>
<td>15.1</td>
</tr>
<tr>
<td>;;;11 points</td>
<td>762</td>
<td>11.1</td>
</tr>
<tr>
<td>TOTAL</td>
<td>6843</td>
<td>108</td>
</tr>
</tbody>
</table>
Table 5

Interaction of Physical Risk Factors and Stress versus No Stress in Mammary Carcinoma

<table>
<thead>
<tr>
<th>Risk Factors</th>
<th>With Stress Mammary Carcinoma</th>
<th>Without Stress Mammary Carcinoma</th>
</tr>
</thead>
<tbody>
<tr>
<td>N</td>
<td>Year.Month</td>
<td>%</td>
</tr>
<tr>
<td>0</td>
<td>774</td>
<td>55.7</td>
</tr>
<tr>
<td>1</td>
<td>639</td>
<td>56.1</td>
</tr>
<tr>
<td>2</td>
<td>613</td>
<td>57.4</td>
</tr>
<tr>
<td>3</td>
<td>425</td>
<td>55.8</td>
</tr>
<tr>
<td>4</td>
<td>289</td>
<td>54.9</td>
</tr>
<tr>
<td>5</td>
<td>177</td>
<td>55.4</td>
</tr>
<tr>
<td>6</td>
<td>182</td>
<td>55.3</td>
</tr>
<tr>
<td>7</td>
<td>145</td>
<td>57.2</td>
</tr>
<tr>
<td>8</td>
<td>115</td>
<td>56.7</td>
</tr>
<tr>
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<td>86</td>
<td>56.1</td>
</tr>
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<td>10</td>
<td>54</td>
<td>55.4</td>
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<td>58.1</td>
</tr>
<tr>
<td>12</td>
<td>23</td>
<td>56.7</td>
</tr>
<tr>
<td>13</td>
<td>25</td>
<td>55.8</td>
</tr>
<tr>
<td>14</td>
<td>20</td>
<td>56.2</td>
</tr>
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<td>15</td>
<td>17</td>
<td>55.3</td>
</tr>
<tr>
<td>16</td>
<td>8</td>
<td>55.6</td>
</tr>
<tr>
<td>17</td>
<td>5</td>
<td>54.5</td>
</tr>
<tr>
<td>18</td>
<td>2</td>
<td>53.3</td>
</tr>
<tr>
<td>19</td>
<td>54.5</td>
<td>100%</td>
</tr>
<tr>
<td>TOTAL</td>
<td>3635</td>
<td>88</td>
</tr>
</tbody>
</table>
in certain ways to stress, and experiential correlates, such as feelings of rejection. How-ever, a short term was needed to encompass this amalgam of meanings, and we chose the term "stress"; the definition clearly is operationalized, and the use of this term should not be construed to carry any meaning over and above that intended.

The following findings clearly can be seen in the table: (1) The proportion of women with mammary carcinoma significantly is larger in the stress group (2.4%) than in the no-stress group (0.5%) (i.e., almost five times as large). This demonstrates the importance of stress as a risk factor in mammary carcinoma with increasing risk factors for both the stress and no-stress group. (2) This increase starts at a much lower level of physical risk factors in the stress than in the no-stress group, suggesting a synergistic form of interaction. To put this another way, mortality is higher in the stressed group for equal levels of physical risk factors, particularly in the middle region of physical risk. When physical risk is low, psychological stress is unimportant and plays no part. The same is true when physical risks are very high; physical factors by themselves are sufficient. The greatest contribution of psychological factors is at the 8-10 point level of physical risk. In the stress group, the average point score of cancer deaths on the physical risk factor scale is 10.3, as compared with 12.6 for the no-stress group; in other words, when stress is present, fewer physical risk factors are needed to produce cancer than when it is not present. The synergistic relationship between physical and psychosocial risk factors is seen more clearly in Table 6, which divides the physical-risk-factor group into high (score of 7 and above) and low (score of 6 and below).

The table shows clearly the synergistic nature of the interaction, as have several other studies using lung cancer, general cancer, and coronary heart-disease groups.
(Eysenck, 1988; Eysenck et al., 1991; Grossarth-Maticek, 1980b). The psychosocial risk factor (stress) adds 0.4%, and physical risk factors 3.5% to the background level (0.0%), suggesting that physical risk factors are several times more important than psychosocial ones. Adding the two gives us the figure of 3.9% as the additive contribution of psycho-social and physical risk factors. However, the true figure, as the table shows, is 14.0%, suggesting the strong influence of synergistic determinants (10.1%). Thus psychosocial stress is important, in its own right, because it multiplies the effects of physical risk factors which, by themselves, would be much less lethal (although even then, still much more important than psychosocial factors by themselves). Univariate studies of risk factors, which are the usual methods of epidemiological study, are clearly unsatisfactory; multivariate studies alone are in a position to indicate the relative importance of risk factors. The interaction was tested for significance using the Vetter (1988) formula and was found to be significant at the \( p < .01 \) level.

Table 6

<table>
<thead>
<tr>
<th>Mammary Carcinoma</th>
<th>Stress</th>
<th></th>
<th>No Stress</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>N</td>
<td>%</td>
<td>N</td>
<td>%</td>
</tr>
<tr>
<td>Low Physical Risk Factors (0-6)</td>
<td>(3099)</td>
<td>13</td>
<td>0.4</td>
<td>(3900)</td>
</tr>
<tr>
<td>High Physical Risk Factors (≥7)</td>
<td>(536)</td>
<td>75</td>
<td>14.0</td>
<td>(516)</td>
</tr>
<tr>
<td>TOTAL</td>
<td>(3635)</td>
<td>88</td>
<td>(4416)</td>
<td>20</td>
</tr>
</tbody>
</table>
Synergistic interaction of risk factors: Extreme groups. In order to study further the mode of interaction between physical and psychosocial risk factors, four groups were formed that showed extreme high- and low-risk factors. Group 1 consisted of 179 women with unusual numbers of risk factors of both kinds, while Group 2 consisted of 179 women with no risk factors of either kind. Group 3 consisted of 179 women with many physical but no psychosocial risk factors, while Group 4 consisted of 179 women with a maximal number of psychosocial but no physical risk factors. (High number of physical risk factors here mean a score of between 10 and 19 points.)

Table 7 shows the figures for a direct comparison of the four groups for mammary carcinoma. Again, there is a clear-cut synergistic effect, this time with the stress effect (1.7%) being stronger than the physical effect (1.1%), and the true joint effect (14.0%) being much greater than the additive effect (1.1% + 1.7% = 2.8%).

Effects of stress and heredity. It seemed worthwhile to look separately at
the interaction of stress and heredity, as previous data on their interaction in the case of lung cancer had already been published (Eysenck, 1991a). Genetic predisposition was measured in terms of number of first-degree relatives who had died of mammary cancer before reaching the age of 70. Table 8 shows the results; clearly genetic factors are important, as is stress—figures in the stress column are much higher at each point than those in the no-stress column.

However, as the table shows, the effects of heredity and stress are not additive but synergistic. Stress effects are negligible by themselves but assume importance only because of the multiplicative interaction with heredity. The effects of heredity are stronger (2.9%), giving an additive effect of 3.0%, for stress plus genetic predisposition, as compared with the true combined (synergistic) effect (9.7%). Clearly, stress has an important effect for people with a genetic predisposition to mammary carcinoma (see Table 9).

**Prophylactic effects of psychotherapy.** The data so far discussed establish psycho-social factors as significant risk factors for mammary carcinoma but cannot be used to establish a causal nexus. As in previous studies, we have attempted to do this by means of an intervention study. If we can alter psychosocial factors by psychological therapy at the beginning of the study and demonstrate a significant prophylactic effect, then the assumption of a causal nexus becomes more plausible (Eysenck & Grossarth-Matic, 1991; Grossarth-Matic, 1980b; Grossarth-Matic & Eysenck, 1991).
Table 8

Genetic Predisposition and Stress as Risk Factors for Mammary Cancer

<table>
<thead>
<tr>
<th>Group</th>
<th>N</th>
<th>Mammary Carcinoma</th>
<th>%</th>
<th>Age</th>
<th>N</th>
<th>Mammary Carcinoma</th>
<th>%</th>
<th>Age</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>306</td>
<td>1</td>
<td>0.3</td>
<td>57.0</td>
<td>238</td>
<td>1</td>
<td>0.4</td>
<td>56.9</td>
</tr>
<tr>
<td>1</td>
<td>208</td>
<td>3</td>
<td>1.4</td>
<td>55.6</td>
<td>141</td>
<td>6</td>
<td>4.3</td>
<td>55.7</td>
</tr>
<tr>
<td>2</td>
<td>70</td>
<td>3</td>
<td>4.3</td>
<td>54.1</td>
<td>68</td>
<td>6</td>
<td>8.8</td>
<td>54.1</td>
</tr>
<tr>
<td>3</td>
<td>28</td>
<td>3</td>
<td>10.7</td>
<td>53.8</td>
<td>29</td>
<td>11</td>
<td>37.9</td>
<td>53.6</td>
</tr>
</tbody>
</table>

The sample consisted of 72 women showing high stress and scoring 18 or 19 points on the physical risk scale. Women were matched in pairs of equal age and assigned to a therapy and a control group on a randomized basis. The method of therapy used was that of autonomy training (Grossarth-Maticek & Eysenck, 1991), continued over a period of 10 weeks, alternating individual and group sessions once per week. Twelve women at a time took part in the group sessions, and the therapy was begun in 1974.

The results of the study after a 14-year follow-up period are shown in Table 10. Clearly, the therapy group has fewer members who died of mammary cancer (1 as against 7 in the control group) and has fewer members who died of other cancers (5 vs. 12) or of other causes (7 vs. 9); however, only the results for deaths due to mammary cancer are statistically significant. In the therapy group, there are 23 survivors; in the control group only 8-this difference is statistically significant at the \( p < .001 \) level. It seems very clear that those individuals who underwent autonomy training were at much less risk for developing breast cancer and of dying from it than were those assigned to the no-treatment control condition. Previously, Grossarth-Maticke and Eysenck (1991, p. 13) had reported that cancer patients who exhibited spontaneous remission "showed a marked change in their personality and behaviour, as
compared with a comparison group ... suggesting a transformation from Type 1 to Type 4." Consequently, it is almost certain that the psychosocial variables targeted by this very brief psychotherapy did, in fact, change as a result of therapy. These results suggest the prophylactic value of the psychological treatment used (cf. Boyle, Eysenck, & Grossarth-Maticek, 1996), and suggest that the link between stress and mortality is not only a statistical one, but may be causal.

Table 9

<table>
<thead>
<tr>
<th>Mammary Carcinoma</th>
<th>No Stress</th>
<th>Stress</th>
</tr>
</thead>
<tbody>
<tr>
<td>No Predisposition</td>
<td>0.3</td>
<td>0.4</td>
</tr>
<tr>
<td>Predisposition</td>
<td>2.9</td>
<td>9.</td>
</tr>
</tbody>
</table>
### Table 10

**Effects of Autonomy Training as Prophylactic Therapy for the Prevention of Mammary Cancer Deaths**

<table>
<thead>
<tr>
<th></th>
<th>Mammary Carcinomas</th>
<th>Other Carcinomas</th>
<th>Other Causes of Death</th>
<th>Living in 1988</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Intervention</strong></td>
<td>N 1973</td>
<td>N %</td>
<td>N %</td>
<td>N %</td>
</tr>
<tr>
<td>Autonomy training</td>
<td>36 55.6</td>
<td>2.8</td>
<td>5 13.8</td>
<td>7 19.4</td>
</tr>
<tr>
<td>Controls</td>
<td>36 55.9</td>
<td>7 19.4</td>
<td>12 33.3</td>
<td>9 25.0</td>
</tr>
</tbody>
</table>

---

**Summary and Conclusions**

The results of this long-term follow-up study seem to justify certain conclusions that replicate those of earlier studies concerned with cancer in general and with lung cancer in particular (Eysenck, 1991a). This investigation of over 8000 healthy women aged, on average, 58 years established that (1) physical risk factors predict future death from mammary carcinoma with considerable accuracy; (2) psychosocial risk factors (stress, personality) predict future death from mammary carcinoma at a lower level of accuracy; (3) physical and psychosocial risk factors interact synergistically (i.e., their effects multiply); (4) prophylactic effects of psychotherapy (autonomy training) suggest that the psychosocial risk factors are causal and not merely statistical agents in producing mammary cancer; (5) the results suggest that the psychological theories underlying the measuring devices used to establish stress and personality differences
may be along the right lines; and (6) the present findings add to those of other studies (e.g., Fawzy, 1995; Fawzy, Fawzy, Arndt, & Pasnau, 1995; Fawzy, Pasnau, Wolcott, & Ellsworth, 1983; Spiegel, Bloom, Kraemer, & Gottheil, 1989; Teich & Teich, 1986) that collectively suggest a string of highly significant advances in psychosocial oncology.

References


Psychiatry, 24, 318-326.


International Foundation for Biosocial Development and Human Health.


Appendix A

Questionnaire for Psychosocial Stress Factors in Mammary Carcinoma

1. I often feel that work or interpersonal conflicts make excessive physical and psychological demands on me.
   Agree/Disagree

2. I have memories of my father and/or my mother as being rejecting rather than loving.
   Agree/Disagree

3. I often feel rejected emotionally by other people (e.g., by my parents) or by important people in my education or my profession.
   Agree/Disagree

4. Over the years, I have constantly experienced repeated rejection by people who were important to me, such as parents, partner, superiors, colleagues, or friends.
   Agree/Disagree

5. I tend to take a negative view of myself, as unimportant and unworthy.
   Agree/Disagree

6. I tend to value people who are important for me excessively highly, to idealize them, and to overlook their faults.
   Agree/Disagree

7. I tend to put my own interests last when dealing with other people.
   Agree/Disagree

8. I find it difficult to behave aggressively, even when I am being frustrated.
   Agree/Disagree

9. I am usually very inhibited when it comes to expressing my own needs and expectations.
   Agree/Disagree
10. I am always inhibited in expressing my own annoyance and excitation.  
   Agree/Disagree

11. I tend to adapt too readily to people and situations when I am emotionally involved, following their lead and not bothering them with my own problems and difficulties.  
   Agree/Disagree

12. I am emotionally very dependent on people who are emotionally important to me.  
   Agree/Disagree

13. I am only content when someone I love pays attention only to me, and is happy.  
   Agree/Disagree

14. Loss or death of someone whom is important to me leaves me for a long time quite shattered, and makes it impossible for me to feel contented and happy.  
   Agree/Disagree

15. Separation from or loss of an emotionally important person (partner, child, parent) leaves me hurt and depressed, and incapable of settling down properly.  
   Agree/Disagree