### Personality and fatal diseases: Revisiting a scientific scandal

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#### Abstract

During the 1980s and 1990s, Hans J Eysenck conducted a programme of research into the causes, prevention and treatment of fatal diseases in collaboration with one of his protégés, Ronald Grossarth-Maticek. This led to what must be the most astonishing series of findings ever published in the peer-reviewed scientific literature with effect sizes that have never otherwise been encounterered in biomedical research. This article outlines just some of these reported findings and signposts readers to extremely serious scientific and ethical criticisms that were published almost three decades ago. Confidential internal documents that have become available as a result of litigation against tobacco companies provide additional insights into this work. It is suggested that this research programme has led to one of the worst scientific scandals of all time. A call is made for a long overdue formal inquiry.

#### **Keywords**

cancer epidemiology, personality and cancer, personality and heart disease, research ethics, research misconduct

Half a dozen years ago, while on a family visit to the Science Museum in London, we found the 'Mind Your Head' exhibit. This was a celebration of advances in psychology since the establishment in 1901 of the British Psychological Society. It was dominated by a full-scale reproduction of the laboratory that was set up after retirement by the late Hans Eysenck to continue his research on intelligence, personality, fatal diseases and the causes and effects of smoking (Bunn, 2001). Serious criticisms of this work were published during the 1990s (Amelang, 1991, 1993, 1997; Amelang et al., 1996; Amelang and Schmidt-Rathjens, 1992; Cooper and Faragher, 1991; Derogatis, 1991; Fox, 1991, 1995; Kiecolt-Glaser and Chee, 1991; Lee, 1991; Levy, 1991; Pelosi and Appleby, 1992, 1993; Schuler and Fox, 1991; Spiegel, 1991; Suinn, 1991; Temoshok, 1991; Van Der Ploeg, 1991, 1992; Van Der Ploeg and Kleijn, 1993; Van Der Ploeg and Vetter, 1993; Vetter, 1993), but were never investigated by any appropriate authority. I hope to demonstrate in this review how the continued influence of this research mocks not only medicine and psychology but also science in general. Authoritative guidance now exists on how to limit the damage to science and to the public health in situations such as these (Committee on Publication Ethics, 2012; Deutsche Forschungsgemeinschaft, 2013; Universities UK, 2012). This article will hopefully prompt a long-overdue formal investigation.

# Research on aetiology and prevention

Eysenck (1965) was one of many scientists who questioned whether early investigations showing

**Corresponding author:** Anthony J Pelosi, Glasgow, UK. Email: anthony.pelosi@nhs.net a statistical association between smoking and lung cancer indicated a causal relationship. An alternative explanation is that certain personality traits that lead to smoking also increase the risk of developing cancer. In 1980, he teamed up with Ronald Grossarth-Maticek, a physician and social scientist who had conducted a decadelong cohort study of more than 1300 subjects in the Yugoslav town of Crvenka. This found strong associations between suppression of aggressive feelings - which he refers to as rationality/antiemotionality - and the subsequent development of lung and other cancers (Eysenck, 1990b, 1997; Grossarth-Maticek, 1980a; Grossarth-Maticek et al., 1985). It turns out that Grossarth-Maticek had also conducted a vast programme of research in Heidelberg, Germany.

According to Eysenck (1991b, 1997), Grossarth-Maticek was at the end of his tether when they first met. He was not coping with the amount of data he had gathered in the previous decade and was aware of rumours circulating among former collaborators and in-house scientists of the tobacco industry (Hayes, 1985). We can get some idea of these rumours from confidential internal documents that have become available as a result of litigation against cigarette manufacturers. Frank Colby of R.J. Reynolds Tobacco Company wrote in a report of June 1980:

Dr Grossarth-Maticek is well known in the media in Germany and he has apparently some solid connections with some of the fund-dispensing German Government health authorities.

On the surface, his data seem to agree, at least in part, with the constitutional hypothesis on smoking and health, with special reference to psychosomatic aspects of lung cancer and heart disease.

I have, however, always been skeptical regarding the validity or even the integrity of some of his findings; for that reason I have in the past not made the slightest effort to meet with him. Since I was, however, offered an opportunity to become acquainted with Dr Grossarth-Maticek, and especially since it was his initiative, I decided to take advantage of that opportunity. I have come back from that discussion more skeptical than ever since Dr Grossarth-Maticek is – at the very least – highly neurotic; I also felt unable to decide whether one should feel sorry for him or totally distrust him. On the other hand, there is also a minimal possibility that the negative aspects may be deceiving. However, I definitely recommend against any involvement between Dr Grossarth-Maticek and us, or the Industry in general (Colby, 1980).

A memo was attached:

Please note and discard: I discussed my apprehension regarding Dr Grossarth-Maticek with Dr Adlkofer, since he is considering supporting him financially.

Adlkofer was the Head of the Scientific Committee of the Association of Cigarette Industries of Germany - the Verband - whose members included German and Austrian manufacturers as well as the transnational firms Philip Morris, R.J. Reynolds and British American Tobacco. Much to the annoyance of R.J. Revnolds (Pelz, 1982), the Verband Board went ahead and funded Grossarth-Maticek's work to the tune of at least 300,000 Deutschmarks (about US\$210,000) (Verband der Cigarettenindustrie, n.d.). They also paid Peter N Lee, a freelance epidemiologist and statistician, to re-analyse the Yugoslav cohort study and then secretly ghost write a paper that would be suitable for submission to a major medical journal (Lee, 1984; Scientific Committee of the VdC, 1982). The eventual publication reported that about a third of 1353 subjects had scored 10 or 11 on an 11-item rationality/antiemotionality questionnaire. Over the ensuing decade every single one of the 38 lung-cancer deaths and 120 out of 128 deaths from all other cancers were in this high scoring group (Grossarth-Maticek et al., 1985).

It is understandable that tobacco companies would wish to pursue such findings. However, their relationship with Grossarth-Maticek was a complex one. The Verband's Technical Research Committee (1983) minuted,

Professor Adlkofer had to admit that this project (statistical evaluation) dealing with Grossarth-Maticek's hypothesis (psychological factors can cause cardiovascular diseases), applied to his more recent prospective study in Heidelberg, had turned out to be a complete failure since some data appeared to be fudged and added that [Frank Colby] might have been correct in his criticism of Grossarth-Maticek. Prof Adlkofer stressed that he was critical vis-à-vis Dr Grossarth-Maticek [sic] from the beginning but it was worth the money to find out that Grossarth-Maticek is a charlatan. Adlkofer promised to make the data available to the member companies. (The *sic* is in the original; I think it refers to uncertainty amongst tobacco company scientists about whether Grossarth-Maticek is a medical doctor.)

At a meeting of the Verband the following year:

Professor Adlkofer summarised the experience and results from the collaboration up to now:

The prospective Heidelberg study contains serious shortcomings. Some of these are to be attributed to inadequate organisation, and some also to a lack of scientific appreciation on the part of the investigators.

Deliberate manipulation of the data to fit the aim must be excluded. This is clear from the evaluation which has been carried out and from the documentation presented by Grossarth-Maticek.

There are reasons for assuming that a more detailed evaluation will discover further 'manipulations'.

With respect to the existing part of the evaluations, the results obtained are probably correct but incomplete. The results are hardly suitable for publication.

Prof Adlkofer reported that the results of the study could be interpreted in such a way that psychosocial factors have an influence on the overall mortality and on individual causes of death. Since he – Prof Adlkofer – still regarded this line of research as very important, he requested DM 50,000 from the board and obtained approval for this. The amount was to be used for maintaining the Grossarth-Maticek working team. (Fink, 1984)

Despite widespread concerns such as these, Eysenck was able, with some difficulty, to convince R.J. Reynolds and Philip Morris International to provide what they describe as 'a gift' and grants to the Institute of Psychiatry for continuation and development of the Heidelberg programme (Eysenck, 1997; Grossarth-Maticek and Eysenck, n.d.; Lincoln, 1987; R.J. Reynolds Tobacco Company, 1986).

As has been pointed out by Temoshok (1991), there was then a complete change in descriptions of the research. Emphasis shifted from traits of rationality/antiemotionality to a fourpart typology of personalities that had never previously been mentioned by Grossarth-Maticek in his published papers. These were: a cancerprone type (characterised by 'passivity in the face of stressful stimulation from the outside'); an ischaemic heart-disease-prone personality ('inability to leave an unsatisfactory situation [which] constantly increases their anger and hostility'); a mixed type; and a healthy autonomous personality. The disease-prone personality types are not uncommon. Within those groups of subjects that were more or less representative the hypothesised cancer-prone, heart-diseaseprone and mixed types were each found in about a fifth of subjects. The rest were categorised as having the healthy autonomous personality (Grossarth-Maticek et al., 1988b; Grossarth-Maticek and Eysenck, 1991).

Grossarth-Maticek had previously referred to one Heidelberg cohort study of about 1000 fairly representative middle-aged people that started in 1972. It gradually emerged that he also had a cohort of 1443 people who were healthy but at 'high psychosomatic risk' and had gathered data from more than 30,000 Heidelberg residents in 1973 (Eysenck, 1992; Grossarth-Maticek et al., 2001; Pelosi and Appleby, 1992). All subjects had been categorised using these authors' four-part or later six-part classification of personalities.

Grossarth-Maticek had described treating 50 people who were considered at risk of cancer based on his earlier psychosomatic hypotheses. He appears to have used an integrated model of insight-oriented psychoanalytic and supportive psychotherapy (Grossarth-Maticek, 1980b; Grossarth-Maticek et al., 1982). For some reason, until he began working with Eysenck, he never mentioned that in 1972 he had started a clinical trial on 50 closely matched pairs of cancer-prone subjects and 46 pairs with the heart-disease-prone personality drawn from the 'high psychosomatic risk' observational cohort (Grossarth-Maticek and Eysenck, 1991). This was a trial of his own method of behavioural psychotherapy which they subsequently called 'creative novation therapy'. It is explicitly stated in papers coauthored by Eysenck that insight-oriented approaches are avoided in creative novation therapy. This seems less clear in earlier descriptions:

[Creative novation therapy] has been developed by Grossarth-Maticek for use with cancer patients. It is a form of cognitive behaviour therapy, uniting the principles of learning underlying conventional behavioural techniques with psychodynamic concepts. The therapy is designed to 'hysterize' the patient, i.e. it enables the patient to express needs that have previously been inhibited, and to engage in more satisfying social interactions. (Grossarth-Maticek et al., 1984: 330)

The huge 1973 cohort had yielded 245 matched pairs of people with unhealthy personalities for a trial of group creative novation therapy and 1200 subjects for a trial of 'biblio-therapy' (Eysenck and Grossarth-Maticek, 1991). Bibliotherapy consisted of 'a written pamphlet outlining the principles of behaviour therapy as applied to better, more autonomous living, and avoidance of stress' plus up to 5 hours of individualised discussion of its contents (Eysenck, 1991a).

#### Astonishing findings

This collaboration led to what must be the most astonishing series of findings ever to be published in the scientific literature. Across the decade-long Yugoslav and first two Heidelberg cohort studies involving 3235 people, 38.5 per cent of the cancer-prone subjects died of cancer compared with only 0.3 per cent of those with

the healthy personality. The resultant relative risk of 121 is perhaps the highest ever identified in non-infectious disease epidemiology (except for certain very rare occupational hazards and some of these authors' previous and subsequent results).

Their results in regard to prevention of cancer (all cancers, not just one individual cancer) are even more amazing. The 50 pairs who were healthy but categorised as having the cancer-prone personality type were randomised to no treatment or individual psychotherapy from Grossarth-Maticek himself. Sixteen (32%) of the control subjects but none of the treated subjects died of cancer in the next 13 years. In the trial of group therapy, which was also delivered by Grossarth-Maticek, 111 of 245 (45%) controls and 18 of the 245 (7%) treated subjects are known to have died of cancer after 7 years. In the bibliotherapy randomised trial, 128 of the 600 (21%) controls died of cancer over 13 years compared with 27 of 600 (4.5%) treated subjects. Such results are otherwise unheard of in the entire history of medical science.

Not content with conquering cancer, these two scientists report the most important ever findings in regard to the other major cause of death in the developed world, namely, ischaemic heart disease. Compared with the healthy autonomous subjects, those with the hypothesised heart-disease-prone personality in the Yugoslav and main Heidelberg cohorts were 27 times more likely to die of this condition. The prevention trials showed massive reductions in deaths from heart disease similar to those for cancer.

The all-cause mortalities for treated versus untreated subjects in their individual psychotherapy and group therapy trials were 15 per cent versus 62 per cent over 13 years and 20 per cent versus 76 per cent over 7 years, respectively.

Readers should have a look at the bibliotherapy document that is reproduced on page 15 and the top of page 16 of Grossarth-Maticek's and Eysenck's *Behaviour Research and Therapy* article. There are eight sections, four of which are quoted here in full: *I. How do problems develop which are in part due to your own actions?* 

Problems arise because you continue with a certain course of action, or maintain certain views and attitudes, which result in consequences that are negative, harmful, and unpleasant. Possibly you expect positive, pleasant, agreeable consequences, such as the affection or love of somebody who is important to you, and suffer because this acceptable state of affairs is not realized.

### *V. What can you do when you have no idea what else you can do?*

You can only accept that state of affairs, but continue to observe your own behaviour in order to discover the conditions which prevent you from achieving satisfaction and happiness.

### VI. The most important aims of autonomous self-activation

(1) Your aim should always be to produce conditions which make it possible for you to lead a happy and contented life.

(2) To increase the positive consequences of your behaviour, and to reduce the negative consequences – go for what makes you happy, abandon what makes you unhappy.

## *VII. What is the role of other people in helping you solve your problems?*

The aim of autonomy training is not to be a completely independent person, but someone who is able to create the best possible conditions which lead to pleasure and contentment. You will often find that the support and help of other people can be of great assistance. Consequently it is usually important to enlist the help and assistance of other people. When you have a problem, such as giving up alcohol, or reducing weight, then try to enter into a contract with another person who will hold you to your promises. When you cannot solve the problem by yourself, it is very helpful to have an obligation to another person to stand by the rules you have agreed on, such as not to eat more than 1000 calories per day.

They claimed a lot for their wee pamphlet. Over the next 13 years, the all-cause mortality for the 600 subjects randomised to bibliotherapy was 32 per cent compared with no less than 82 per cent of the 600 controls (Eysenck, 1991a, 1991c; Eysenck and Grossarth-Maticek, 1991).

#### Scientific criticism

Various scientists have attempted to make some sort of sense of these findings (Amelang, 1991, 1997; Amelang et al., 1996, 2004; Amelang and Schmidt-Rathjens, 1992; Cooper and Faragher, 1991; Derogatis, 1991; Michael Eysenck, 2004, 2016; Fox, 1991; Kiecolt-Glaser and Chee, 1991; Lee, 1991; Levy, 1991; Pelosi and Appleby, 1992, 1993; Schuler and Fox, 1991; Spiegel, 1991; Suinn, 1991; Temoshok, 1991; Van Der Ploeg, 1991, 1992; Van Der Ploeg and Kleijn, 1993; Van Der Ploeg and Vetter, 1993; Vetter, 1993; Wills, 1991; Yousfi et al., 2004). Van Der Ploeg (1991) tried his best to do so in cooperation with the authors. He reported that he found unequivocal evidence of manipulation of data sheets and interchanging of lists of deceased subjects with alterations of names, addresses and causes of death.

Van Der Ploeg and Herman Vetter, a statistician who has worked closely with Grossarth-Maticek, reported numerous instances of identical questionnaire responses for two or three or four subjects that could not be explained by chance. This led them to,

safely conclude that the interviews were used twice deliberately or by some systematic accident. In either case, this is bad news for the trustworthiness of the data of the Heidelberg 1972 studies and of their really empirical origin from really empirical interviews. (Van Der Ploeg and Vetter, 1993: 66)

In an article entitled 'Further Dubious Configurations in Grossarth-Maticek's Psychosomatic Data', Vetter describes how he was asked to analyse data on 191 subjects in terms of whether the sum of scores for three unhealthy personality types was greater than the sum of scores for three healthier types. The hypothesised healthy and unhealthy personality types were based on

Eysenck's theories. Each was measured on a scale of 0-9; therefore, subjects' total scores could range from -27 to +27. The range of scores in this particular group of subjects was from -21 to +18. There was not a single death from lung cancer in those with a higher total for the healthier types. Lung cancer was seen only once the total for the unhealthy personalities was higher – by just one point. But then, there was no trace whatsoever of a 'dose-response relationship' in the 33 people who died of this disease. As Vetter (1993) puts it, 'the regression of lung-cancer mortality on the difference score is a pronounced step function with the step exactly at that one point ... that I had been advised to use ...'. He continued in a technical yet most regretful tone,

I submit that I deem a steep regression function continuing over so many values of the difference score highly unnatural and so much more improbable as the step occurs just at the point that separates 'greater' from 'not greater'. So I cannot avoid the conclusion that these data also have been produced artificially with a criterion in mind, later proposed to me, that made for an unnatural regression relation – and, alas, without pouring enough random error over it to make it appear more natural. (p. 67)

There are many more 'dubious configurations' in the methods and results that were widely disseminated by Grossarth-Maticek and, especially, by Eysenck. The precision of their research interviews in predicting death and causes of death and even the time by which deaths occurred (Fox, 1991) is uncanny. In spite of hitherto unheard of strengths of association in their initial Yugoslav and Heidelberg investigations, these scientists looked to improve the predictive accuracy of their methods in studies of subgroups from the cohort of 30,000 plus subjects. For example, they used what they call a 'dynamic' method of questionnaire administration to see if individual participants showed an improvement or no change/deterioration in scores for the healthy and unhealthy types. Around a half showed improvements in their score over a 6-month period. Based on

Eysenck's (1991a) published results, Lee (1991) has calculated massive relative risks for fatal diseases in those with no change/deterioration versus improvement in their scores. It seems impossible to understand how a one-off assessment in previous studies was able to predict causes of death with near unerring accuracy when personality measures change over time in so many subjects (Lee, 1991).

Eysenck (1991c, 1992, 1993a) considered it a scandal that replication studies of his research programme were not pursued by other scientists. In fact, Manfred Amelang and colleagues obtained financial support from *Deutsche Forschungsgemeinschaft*, the main German research funding organisation, to re-examine the putative disease-prone personality types. They did not confirm any of the reported associations in cross-sectional studies using revised versions of the measures that had been administered by Grossarth-Maticek and his research assistants (Amelang, 1997; Amelang et al., 1996; Yousfi et al., 2004).

This group went on to conduct a 10-year cohort study of more than 5000 residents of Heidelberg to examine a range of psychosocial factors as risk or protective factors for disease development (Amelang et al., 2004). They included the revised scales measuring the Grossarth-Maticek and Eysenck personality types. Five out of six of these, including the claimed heart-disease-prone and healthy autonomous types, showed no association with increased or decreased incidence of cardiovascular disease. Interestingly, an association was found between cardiovascular disease and rationality/antiemotionality with an odds ratio of 1.89 for each standard deviation increase in score. While it did not remain statistically significant after adjustment for age, gender and smoking this unadjusted odds ratio of 1.89 is, in my opinion, potentially of significance. Controversy clinical over Grossarth-Maticek's and Eysenck's cohort studies - with their odds ratios running into the hundreds (Lee, 1991) - should not be allowed to distract scientists and clinicians when considering this and other important findings from Amelang and colleagues' research (Amelang et al., 2004; Stürmer et al., 2006).

In this cohort study, none of the revised Grossarth-Maticek and Eysenck scales showed an association with the incidence of cancer. As Amelang (1997) puts it,

I know of no other area of research in which the change from an interview to a carefully constructed questionnaire measuring the same construct leads to a change from near-perfect prediction to near-zero prediction. (p. 338)

Amelang is not entirely correct in describing these scientists' predictions as near-perfect. Fox (1991) has demonstrated that the ability of some assessments to predict fatal diseases was not near-perfect and it was not perfect - it was better than perfect. He noticed that in some of Grossarth-Maticek's published results that there was a 96 per cent overall success rate in predicting what he calls internal diseases. Two of these are myocardial infarction and stroke, which were predicted with 86 per cent accuracy. Fox carried out an elegant boundary analysis and showed that predictive accuracy for development of the remaining internal diseases had to lie somewhere between an impossible 102 per cent and 113 per cent (Fox, 1991; Grossarth-Maticek et al., 1983, 1985).

Gilbert (1985), a scientist for R.J. Reynolds, also picked up the problem of better than perfect predictive accuracy. He drafted a polite and embarrassed letter to Eysenck, which contained the following:

My primary reason for writing to you at this time is my concern about the work of Grossarth-Maticek. I know you are quite familiar with his publications and have quoted him extensively in some of your recent work. I have reviewed nine different articles of his based on the Crvenka and Heidelberg prospective studies.

My reservations are based on the limitations imposed by the less-than-perfect reliability/ validity of any psychological measure. The lessthan-perfect reliability/validity of Grossarth-Maticek's rationality/antiemotionality should lead to less-than-perfect predictions. Yet he reports perfect prediction of the incidence of lung cancer from the combination of number of cigarettes smoked per day with degree of antiemotionality. I expect that the test-retest reliability of the rationality/antiemotionality scale is in the range of .64 to .81 and that the reliability of one's saying one smokes more than 20 cigarettes per day is not much higher, (.85?). Since the maximum validity of any measure is the square root of its reliability the question becomes how can  $\sqrt{0.81 * \sqrt{0.85 = 1.00?}}$ 

After making further comments on the difficulties of measuring amount of exposure to cigarette smoke, Gilbert continued,

... it seems unlikely that the reliable variance associated with the rationality/antiemotionality scale and the daily cigarette consumption measure correlate anywhere near 1.00 with the variance in physiological processes associated with the development of cancer. Such imperfect correlations should lead to further reductions in the ability of his measures to predict the development of cancer.

Chance may have sided in the direction of Grossarth-Maticek's hypotheses in the case of the above-noted smoke-exposure/personality relationships to lung cancer. However, my questioning is heightened because Grossarth-Maticek's therapeutic interventions also are more powerful that I would expect.

Based on the above concerns I wonder if some bias may have inadvertently entered into Grossarth-Maticek's data acquisition and/or analysis procedures. Do you think this may have been the case?

I have been unable to find anything within the Tobacco Documents Library to indicate that the letter was actually sent. In any event, as someone who thought of himself as the world's leading psychometrician, Eysenck should have detected these methodological concerns.

Peter N Lee had ghost written Grossarth-Maticek's earlier paper showing massive strengths of association between rationality/ antiemotionality and lung and other cancers (Grossarth-Maticek et al., 1985; Lee, 1984; Scientific Committee of the VdC, 1982). However, in a particularly sceptical invited contribution to *Psychological Inquiry*, he pointed out that 'the strengths of the reported associations are absolutely mammoth' (Lee, 1991). He states firmly,

... there is, as far as I am aware, no previously reported case where risk of overall mortality, heart disease, or cancer varies so hugely between defined subsets of the population. Eysenck's results are so outside of my experience as an epidemiologist that I find it very difficult indeed to accept them as real. (Lee, 1991: 252)

Lee and other commentators have expressed incredulity that Grossarth-Maticek and more than 100 specially trained student interviewers could measure personality traits without any measurement error (Fox, 1991; Lee, 1991; Pelosi and Appleby, 1992). Personality assessment was a most complicated business. Commenting on methodological shortcomings in some of his father's research, Michael Eysenck (2004, 2010: 736, 2016) has pointed out,

Good questionnaire items are short and unambiguous, but here is an 84-word one from a questionnaire devised with Grossarth-Maticek:

Do you change your behaviour according to consequences of previous behaviour, i.e., do you repeat ways of acting which have in the past led to positive results, such as contentment, wellbeing, self-reliance, etc., and to stop acting in ways which lead to negative consequences, i.e., to feelings of anxiety, hopelessness, depression, excitement, annoyance, etc.? In other words, have you learned to give up ways of acting which have negative consequences, and to rely more and more on ways of acting which have positive consequences?

Grossarth-Maticek described the assessment process using such questionnaire items as follows:

We found that, as expected, prospective research results relying on the filling in of questionnaires depended very much on the kind of relation established between interviewer and subject. Interviewers with a high degree of empathy, who individual seriously differences in took behaviour, as relevant to the origin of diseases, and who managed to choose a proper moment for the beginning of questionnaire-related interview, after a friendly preliminary discussion, achieved a more reliable and valid relation between personality variables and mortality. Less empathic interviewers who denied a synergistic relation between organic and psychological factors, and only believed in physical causation of disease produced low retest-reliabilities and poor validities. (Ouoted within Eysenck (1991b: 310))

Remember these are the interviews that, it is claimed, yielded relative risks of 27 and upwards for deaths from ischaemic heart disease and over 100 for deaths from cancer during the next decade.

#### **Responses to criticisms**

Eysenck and Grossarth-Maticek simply toughed out all the scientific criticisms. They were prepared to accept that mistakes had been made, but argued that these occur in every large epidemiological investigation – without seeming to understand that unsystematic error would lower strengths of association (Eysenck, 1991b, 1992, 1993b; Grossarth-Maticek, 1991; Grossarth-Maticek quoted within Eysenck (1991b; 1993b)). Sometimes Eysenck sidestepped the most unanswerable points, stating: 'it is clearly the task of Dr Grossarth-Maticek to answer these criticisms, and accordingly I simply quote his reply ...' (Eysenck, 1991b; 312).

When responding to outright accusations of data manipulation, these scientists speculated on whether identical sets of answers from some of their subjects, 'is a statistical accident in a small number of a very large sample, or whether a lazy interviewer fabricated data'. (Eysenck, 1993b: 71). They carried out re-analyses after excluding subjects where, for example, Van Der Ploeg claimed there was evidence of data manipulation. This made no difference to the strengths of associations they had previously found. They both argued this is proof that any error in their studies was unsystematic. Eysenck and Grossarth-Maticek complained that certain of their critics showed lack of good faith in publishing concerns without first consulting them. They criticise Vetter (1993) for what they consider to be a deeply flawed analysis on the sum of scores for personality types that showed a precise step relationship with deaths from lung cancer (Eysenck, 1993b; Grossarth-Maticek quoted in Eysenck (1993b)). But, we are still left to wonder how on earth a data set that led to such a finding could possibly come to exist.

Eysenck (1991b, 1991c, 1992, 1994) has maintained that his results were not much different from some previous work in this field and that 'several explicit or implicit replications of [the Heidelberg] studies show similar relationships'. I have been unable to obtain some of the references for this assertion (Baalen and Van De Vries, 1987; Ranchor et al., 1992; Van Beek, n.d.), but I urge interested readers to chase up those that are readily available (Dixon and Dixon, 1991; Kissen and Eysenck, 1962; Kune et al., 1991; Quander-Blaznick, 1991; Schmale and Iker, 1971; Schmitz, 1992; Shigehisa et al., 1989, 1991; Van Der Ploeg et al., 1989; Wirsching et al., 1981). Some of these studies are scientifically and, in my opinion, clinically important cross-sectional comparisons of a variety of psychosocial traits in patients who do and do not have malignancies. Others examine psychometric properties and cross-sectional associations of Eysenck and Grossarth-Maticek's research measures, mainly in healthy student populations. I simply cannot fathom how anybody – scientist or non-scientist - could ever believe that investigations such as these bolster the astonishing findings of the Yugoslav and Heidelberg research programmes (Pelosi and Appleby, 1993).

In the end, Eysenck (1993b: 72) considered that the scientific controversy arose from,

a conflict between two personality types who will never learn to appreciate the virtues of the other. Grossarth-Maticek is the wide-ranging creative scientist, working on a large scale, impatient of detail, concerned with the wider issues, the broad strokes, the major breakthrough. Irritated by doubts and criticisms, conscious of the enormous social and scientific importance of his discoveries, convinced (rightly) that his work and theories are streets ahead of what his critics have to offer, he obviously does not suffer fools gladly and he may hit out at them in a rather exaggerated way.

Eysenck (1993b: 73) goes on to characterise the critics of this work as follows:

Pedantic to the last degree, any error, however slight, random, and unimportant from the point of view of the grand design, is a sin against the Holy Ghost, to be hunted down, exposed and eradicated. This battle is age-old, and few creative scientists escape it.

Hopefully, a properly constituted investigatory panel (Committee on Publication Ethics, 2012; Universities UK, 2012) will decide whether criticisms that have appeared in the scientific literature during the last three decades have been justified or whether they are adequately countered by Eysenck's (1993b: 73) counter-arguments and by his assertion:

Perhaps we may conclude with a syllogism that I shall leave readers to finish. If Grossarth-Maticek's data are genuine, he is a genius. His data have been shown to be genuine; ergo ...

I suspect that Eysenck was not only thinking here about his junior collaborator.

#### Ethical concerns

In my opinion, Eysenck's and Grossarth-Maticek's responses to criticisms demonstrate the 'lack of scientific appreciation' that had been noted by tobacco company employees (Fink, 1984; Pelosi and Appleby, 1993). There is also a worrying lack of clinical and ethical appreciation. For example, it is repeatedly stated that the 192 recruits to the matched-pairs randomised controlled trial of individual psychotherapy were free of severe disease. However, they describe in detail a subgroup of 41 middle-aged participants with a mean systolic blood pressure of 207 mm Hg and abnormalities of the optic retina arising from such high blood pressures. These included flame-shaped haemorrhages which are a sign of bleeding into the retina, the appearance of 'cotton wool spots' due to insufficient blood supply to layers of nerve fibres and even, in some cases, swelling of the optic disc indicating lack of blood supply to the optic nerve and possible raised pressure inside the brain.

I cannot express strongly enough for nonmedical readers just how shocking this is. These features indicate that the integrity of the small blood vessels is breaking down and that the patient is in grave and imminent danger. The blood pressure must be carefully lowered as a matter of urgency to avoid left ventricular heart failure, brain haemorrhage and kidney failure. This did not happen with the unfortunate participants in this clinical experiment. After 2 years, 51 subjects had these most alarming retinal appearances and an average systolic pressure of 211.7 mm Hg. Without a trace of insight, these scientists reported in a prestigious peer-reviewed journal (albeit one founded by Eysenck) that as many as 89 per cent of this subgroup with malignant hypertension died during the 13-year follow-up period of their randomised controlled trial (Grossarth-Maticek et al., 1991).

It is not my role to speculate on 'What Really Happened in Crvenka and Heidelberg?' (Amelang, 1993), but I can, at least, try to rescue these two scientists from their own unwitting claims of involvement in an unethical clinical experiment. This randomised trial may not have taken place as described. It is difficult to believe that a research team came across 41 people with untreated malignant hypertension in a city with a total population of 122,000 residents, especially when they claim to have found (I think the following year) another 45 men with flame-shaped haemorrhages and cotton wool spots and 15 with these sinister findings plus optic disc swelling (Grossarth-Maticek et al., 1990). The total number of recruits keeps shifting, from 90 cancerprone and 76 heart disease-prone individuals through 96 matched pairs to 192 pairs (Eysenck Grossarth-Maticek, 1991; Grossarthand Maticek et al., 1991; Grossarth-Maticek, n.d.).

Gender distributions differ across published accounts (Eysenck, 1991a, 1991c). Subjects are pair matched on age and gender according to some descriptions (Grossarth-Maticek, n.d.) and, despite the logistical challenges of individual matching across numerous factors, on no less than seven variables in others - 'age, sex, degrees of stress, intensity of cigarette smoking, blood pressure, blood sugar and cholesterol' (Evsenck and Grossarth-Maticek, 1991; Grossarth-Maticek et al., 1991). Van Der Ploeg and Kleijn (1993: 69) found that for some subjects in the reported trial, there were identical series of up to seven values for cholesterol levels and white blood cell count which, they maintain, 'did not contribute to the credibility of the reported results and the reported effects of the creative novation therapy'. Also, the interventions keep changing across the published descriptions (Eysenck, 1991b; Grossarth-Maticek and Eysenck, 1991; Grossarth-Maticek et al. (1986) as cited in Van Der Ploeg (1991)) and, as pointed out by Schuler and Fox (1991), they include components that were not considered scientifically relevant until after the stated date of commencement of the study.

More recent publications may provide clues to alternative and less troubling possible explanations. At the same time as researching psychosocial influences on fatal diseases, Grossarth-Maticek was also investigating mistletoe extract as a treatment for metastatic and non-metastatic lung, breast, cervical, ovarian, stomach, colon, rectal and skin cancers (Grossarth-Maticek et al., 2001; Grossarth-Maticek and Ziegler, 2006a, 2006b, 2007a, 2007b, 2007c). Mistletoe is a commonly used remedy for cancer within the discipline of Anthroposophical Medicine. These papers contain much more detail on his methodology for matched-pairs randomised trials and parallel observational studies using matched pairs. Subjects were drawn from a pool of 11,009 cancer patients, 5809 of whom also participated in the Heidelberg research programme on personality and fatal diseases. Another 3165 were patients who consulted the Institute for Preventive Medicine in Heidelberg which I

believe is Grossarth-Maticek's own clinic. The rest were patients of the University Surgery Clinic of Heidelberg and other clinics in the Federal Republic of Germany. Randomisation involved putting into a hat the names of two patients who were matched on age at first diagnosis, tumour stage at first diagnosis, year of first diagnosis of the tumour stage, types of conventional treatment used and, for the studies of breast and gynaecological cancers, menopausal status. One of the names was then removed by a masked research assistant. This last step does not meet scientific standards that were expected during the 1970s. More importantly (and as I have suspected from the first time I read Eysenck's and Grossarth-Maticek's publications), it is finally clearly stated: 'For the record: there was no written study protocol ...' (Grossarth-Maticek and Ziegler, 2006a: 286, 2007a, 2007b).

The published descriptions of an unethical experiment on people with malignant hypertension may not be accurate. It is tempting to speculate that Grossarth-Maticek has treated a number of patients in his clinical practice and, working over so many years without a written protocol, he and his student research assistants retrospectively pair matched these patients to subjects within the large observational cohorts who had fallen ill and died. This could allow Grossarth-Maticek to convince himself that he had carried out a randomised trial of sorts thereby providing confirmation of Eysenckian theories for his famous collaborator. If, however, this research really did take place as described in print, then this raises questions well beyond the scope of my article. These would have to be considered by the appropriate legal authorities in Heidelberg.

# The need for an authoritative investigation

The findings from this research programme will probably never be fully explained, especially since all of Eysenck's papers were destroyed several months after his death (Buchanan, 2010b). However, it remains important that a formal inquiry should be conducted. Concerns about the research did not remain as gossip within tobacco industry committees, the Heidelberg research community (Hayes, 1985) and the Institute of Psychiatry cafeteria (Buchanan, 2010b). They have been published in great detail in widely read journals and have never been adequately answered.

This work truly does 'poison the well' of science (Smith, 2006). It has made its way into undergraduate and postgraduate textbooks and educational review articles (Kissane and Al-Asady, 2015). Google Scholar reveals that obviously flawed articles are still being cited frequently and uncritically in the peer-reviewed literature. Some Eysenck and Grossarth-Maticek publications have citation counts ranging from dozens to a couple of hundred. The Heidelberg research programme forms the basis of self-help books (Grossarth-Maticek, 2016; Stierlin and Grossarth-Maticek, 2006) and it is, inevitably, the Internet (KREBSon CHANCEN, 2018; Wikipedia, 2016). It has been taken at face value when expensive and otherwise important epidemiological studies have incorporated hypotheses on the role of psychosocial factors in disease development (Nabi et al., 2008). Also, these personality assessments have been used in clinical research on desperately ill patients with lung cancer (Nagano et al., 2006).

Evsenck's and Grossarth-Maticek's research distracts and undermines the many serious scientists who are grappling with this complex, difficult and important field (Coyne et al., 2010, 2011; Michael et al., 2009; Ranchor et al., 2010; Steptoe et al., 2010). A meticulous meta-analysis by Chida et al. (2008) included 50 relative risks of association between various stress-related psychosocial factors and mortality from cancers as found in 22 community-based epidemiological studies. About half of these relative risks were around one, indicating no association. Other studies showed statistically, theoretically and, in my opinion, clinically significant associations; subjects with various hypothesised psychosocial risk factors had about  $1\frac{1}{2}$  to as much as  $2\frac{1}{2}$  times the likelihood of death from a cancer. There were five extreme outlying results with relative risks of 24, 28, 60, 68 and 74, and these were sufficient to have an impact on the summary relative risk (Coyne et al., 2010; Steptoe et al., 2010). All were from the research of Grossarth-Maticek or Grossarth-Maticek and Eysenck.

If an investigatory panel is established and agrees with even some of the published concerns, it must have the authority to insist on the appropriate action. This would simply and solely be retraction of the data-reporting papers. Who should now take responsibility for such an investigation? Grossarth-Maticek and his research workers told study subjects that they were from the University of Heidelberg (Spielberger and Van Der Ploeg, 1986), but Buchanan (2010b) has found out that the University has no record of ever having employed them. In 1995, I made a formal complaint to the British Psychological Society about Eysenck because of the 'simply unbelievable' (Fox, 1988) findings and his claims of involvement in an unethical clinical experiment. The Society replied as follows in a letter of 14 September 1995:

After full consideration of all the material before it, The Investigatory Committee decided that it would <u>not</u> be appropriate to appoint an Investigatory Panel to conduct further enquiries into the matter. Its decision has been confirmed by the independent non-psychologist representative of the Disciplinary Board.

The Investigatory Committee sought comment from all relevant parties on the matters of complaint raised by you and, having considered the matter carefully, and with the benefit of all the documentation before it, concluded that Professor Eysenck's conduct was not such as to amount to misconduct, and an Investigatory Panel was not therefore appointed.

The Committee has asked me to assure you that it is confident that its purposes have been properly and satisfactorily served in bringing this matter to the attention of the subject of the allegations and trusts that you accept its position. The matter is now closed as regards the Society.

In no way did I accept the position of the British Psychological Society, but I did not know what more to do (Pelosi, 1998) – and this research programme went on to dominate the Science Museum's celebration of the Society's centenary (Bunn, 2001).

The Institute of Psychiatry employed Eysenck for four decades and then kept him on as an Emeritus Professor until his death. Grossarth-Maticek sometimes gave the Institute as his address, but its Dean wrote to the British Medical Journal to point out that he had no right to do so as he had never been awarded an academic title there (Checkley, 1993; Corrigendum, 1993). Despite this, in his publications on mistletoe, Grossarth-Maticek lists the Institute of Psychiatry as a source of funding (along with Deutsche Forschungsgemeinschaft, the University of Heidelberg and a variety of other agencies) (Grossarth-Maticek et al., 2001; Grossarth-Maticek and Ziegler, 2006b, 2007b). Eysenck and Grossarth-Maticek definitely had no right to refer to their psychotherapy trials as the 'Maudsley Intervention Project' (Checkley, 1993). They were never considered by the Maudsley's ethics committee and were not part of the joint research strategy of the Maudsley Hospital and Institute of Psychiatry (Checkley, 1993). Nevertheless, my reading of the current guidance from Universities UK (2012) and the Committee on Publication Ethics (2012) leads me to conclude that the Institute has the sorry task of conducting a long-overdue independent investigation.

R.J. Reynolds and Philip Morris International should carry out their own investigations. No doubt they thought they were fortunate to have close links with such a senior scientist and shareholders certainly stood to benefit from the Heidelberg results and their use by Eysenck and others when testifying in anti-tobacco litigation (Eysenck, 1990b, 1990c; Marks, 2001). The minutes of a meeting between R.J. Reynolds' scientific adviser and a Heidelberg University research group illustrate the potential dangers of these academia-tobacco industry relationships:

[The lead researcher] presented data which attempted to correlate the questionnaire with certain types of cancers in smokers and nonsmokers. She was unable to give a correlation better than 61 to 62% which is approximately the same as rolling the dice. She was also unable to show that the Eysenck questionnaire was any better than the earlier questionnaires used. Overall, her program has little to be gained by continuing it although there may be some significance to keeping [her] around as one who might prepare certain types of review articles. Her young colleague ... felt they could develop better questionnaires.

[The two younger researchers] will be meeting with Professor Eysenck to review the data sometime in the next month or so in London. Maybe they will be able to massage the data and interpret different results but I doubt it. (Hayes, 1985)

I cannot make up my mind whether this senior industry scientist is expressing admiration or contempt for Professor Eysenck.

The funding of Eysenck's research programme and the ways in which his data were used were among the numerous activities that led the US Courts to find certain cigarette manufacturers guilty of having maintained an illegal racketeering enterprise under the Racketeer Influenced and Corrupt Organisations Act (United States District Court, District of Columbia, 2006; United States Court of Appeals for the District of Columbia Circuit, 2009). These companies' websites indicate that they are trying to improve their reputation. This can only suffer from the horrid, mutually exploitative relationship with Eysenck that is so clearly documented in his autobiographies and in letters, memos, minutes, reports, research proposals, court testimony, documentary film (Illustra Films, 1976), news footage (British Broadcasting Corporation, 1980) and US Senate testimony (Eysenck, 1983; Senate Hearing, 1982) within the tobacco companies' files. Their current in-house scientists should now make a clear statement about the Heidelberg research

programme and thereby play their part in 'unpoisoning' this particular scientific well.

#### A further concern

I hope one last concern will be considered. Some of the most damning criticisms of this research were made by Bernard Fox and Georges Schuler – based solely on a close reading and careful re-analysis of the reported results (Fox, 1991; Schuler and Fox, 1991). I agree with them that,

one gets a compelling impression that Grossarth-Maticek believes unreservedly in his own ideas and cannot entertain rational objections ... The problem of cancer and the psyche is now in vogue, and there is a strong emotional need in the public with which he identifies. (Schuler and Fox, 1991: 261)

Grossarth-Maticek's motivation seems to have arisen from a quasi-religious belief that he can prevent cancer and delay death from terminal metastatic disease (Eysenck and Grossarth-1991; Maticek, Grossarth-Maticek and Eysenck, 1991, KREBS-CHANCEN, 2018). Many fringe medical practitioners hold the same conviction. Unlike them, Grossarth-Maticek tried to prove his beliefs, but with no epidemiological training (Frentzel-Beyme, 1991) and, in my opinion, serious shortcomings in his scientific and clinical understanding.

Grossarth-Maticek had the misfortune to become a protégé of the most influential psychologist of his generation, who needed data to support his theories on the psychogenic causes of cancer. Eysenck also had strong views on the health risks of coffee and other stimulant drinks (Grossarth-Maticek and Eysenck, 1990a), the benefits of sport participation (Grossarth-Maticek et al., 1990), the causes of political and religious prejudice (Grossarth-Maticek et al., 1989), the 'cures' for these prejudices (Grossarth-Maticek et al., 1989), the risks to health of being opposed to smoking (Grossarth-Maticek et al., 1988a), the risks to health of antismoking campaigns (Grossarth-Maticek and Eysenck, 1989) and the lethal dangers of psychoanalytic psychotherapy (Grossarth-Maticek and Eysenck, 1990b). Lo and behold, Grossarth-Maticek was able to provide data to back up his senior colleague's theories in each of these areas. Any inquiry should not only investigate the alleged manipulation of data but also my concern that Eysenck appears to have mercilessly manipulated over many years an untrained (Buchanan, 2010b; Frentzel-Beyme, 1991), isolated (Eysenck, 1991b, 1997) and vulnerable (Colby, 1980) collaborator.

Those interested in trying to understand how Eysenck ended up publishing work such as this should read Rod Buchanan's (2010b) biography, *Playing with Fire: The Controversial Career of Hans J. Eysenck.* This was toned down by the publishers' lawyers (Buchanan, 2010a, 2011), but it still raises troubling questions about how this self-confessed maverick (Corr, 2016a, 2016b; Eysenck, 1990a) could persist in and get away with his seemingly reckless approach to scientific endeavour for so much of his career.

#### Conclusion

There is a complicated and multi-layered scandal surrounding Hans Eysenck's work on fatal diseases. In my opinion, it is one of the worst scandals in the history of science, not least because the Heidelberg results have sat in the peer-reviewed literature for nearly three decades while dreadful and detailed allegations have remained uninvestigated. In the meantime, these widely cited studies have had direct and indirect influences on some people's smoking and lifestyle choices. This means that for an unknown and unknowable number of individual men and women, this programme of research has been a contributory factor in premature illness and death. How can members of the public and their policymakers turn to science for help with difficult decisions when even this most extreme of scientific disputes cannot be resolved?

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