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Neuroticism, a central link between somatic and psychiatric morbidity: path analysis of prospective data

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ABSTRACT

Background. Neuroticism and somatic complaints are linked, and the aim of this study is to disentangle which mechanisms may be responsible for this association.

Method. In a stratified sample of 7076 adults (18–65 years), neuroticism, 22 self-reported chronic somatic conditions and five broad CIDI-diagnosed psychiatric syndromes were assessed at baseline and, in 3625 (51%) subjects, 3 years later. Using path analysis we examined whether neuroticism has direct links with future somatic morbidity and, conversely, whether morbidity at baseline is linked with higher neuroticism later on.

Results. Neuroticism at baseline is associated with psychiatric and somatic morbidity at follow-up after 3 years (31% and 24%, respectively, are direct associations, i.e. unmediated by each other or neuroticism at follow-up and independent of morbidity at baseline). Conversely, somatic and psychiatric morbidity at baseline are associated with increased neuroticism at follow-up (27% and 15%, respectively, are direct associations).

Conclusions. Neuroticism raises risk for psychiatric and somatic morbidity but also results from them. It represents a central nexus in the process of morbidity accumulation.

INTRODUCTION

Neuroticism is defined as a lifelong tendency to experience negative emotions (Costa & McCrae, 1987). Some view it as an enduring personality trait (Costa & McCrae, 1987); others consider it as individuals' characteristic level of sub-threshold minor psychiatric symptoms (Duncan-Jones *et al.* 1990). Whichever view one takes, neuroticism is a strong risk factor for manifest psychiatric disorder (Jorm *et al.* 2000). Links also exist between neuroticism and self-reported somatic ill health, but the status of this association remains open to debate (Costa & McCrae, 1987). Various mechanisms may contribute to it. It may reflect over-reporting of physical symptoms by neurotic (Costa & McCrae, 1987) or mentally ill persons (Katon *et al.* 2001) (mechanism 1). The absence, in some studies (Neeleman *et al.* 1998), of links between neuroticism and premature natural mortality is often cited in favour of this (Costa & McCrae, 1987).

The higher levels of reported physical ill health in neurotic individuals might be attributable to the psychiatric disorders they often suffer (Neeleman *et al.* 2001) and which may negatively influence physical health (mechanism 2), for instance through lifestyle factors like smoking (Jorm *et al.* 1999), or lead to over-reporting of physical symptoms as in somatization disorder.

Neuroticism may also raise the risk of somatic illness more directly (mechanism 3), independent of biased reporting and unmediated by manifest psychiatric disorder. Physiological effects (Goebel *et al.* 1998) or lifestyle factors

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(Freeman, 1971) may account for such direct links. Studies linking premature natural death to traits such as hopelessness (Everson *et al.* 1996) and tension (Eaker *et al.* 1992) support this possibility.

Reverse causality is also possible as illness, whether psychiatric or somatic, may lead to increased neuroticism (mechanism 4). This possibility receives divided support. Some studies report 'scarring', i.e. increased neuroticism following depression (Rohde *et al.* 1994), but others do not (Costa & McCrae, 1987; Duggan *et al.* 1991).

Several studies have examined prospective links between somatic and psychiatric morbidity (Aneshensel *et al.* 1984; Hotopf *et al.* 1998; Cohen *et al.* 1999), but few have taken personality features like neuroticism levels into account. Thus, the relative contribution of the four mechanisms outlined above to the overall association between neuroticism and reported somatic ill health, remains unclear. We tested, using path analysis, the hypothesis that somatic illness and neuroticism are linked not only through reporting bias (mechanism 1) or effects of manifest psychiatric disorder on somatic health (mechanism 2), but that neuroticism raises the risk of future somatic disorder (mechanism 3), while, conversely, somatic and psychiatric disorder also lead to increased neuroticism later (mechanism 4).

METHOD

Subjects

The data come from the 1996 (t_1) and 1999 (t_2) waves of the Netherlands Mental Health Survey and Incidence Study (NEMESIS), which was designed to chart incidence and prevalence of mental illness in Dutch adults (Bijl *et al.* 1998). Sampling at t_1 was stratified according to urban density. Ninety municipalities were selected according to size and location. According to the population size of each municipality, a certain number of households were chosen. In the selected households, the person (between 18 and 65 years old) with the most recent birthday was asked to participate. After the study was described to the subjects, their written informed consent was obtained. The participation rate was 69·7%, giving 7076 subjects. Those who refused and those who participated did not differ demographically. Individuals between 18 and 24 years old were under-represented, but otherwise the sample's age–gender composition represented the Dutch population well. The sample's stratified nature is taken into account in the analyses by means of sampling weights.

Data

Data collection procedures were comparable on both occasions. Trained interviewers assessed participants at home using the computerized version of the Composite International Diagnostic Interview (CIDI) excluding the somatoform disorder section. The present analysis uses 1-year prevalences at t_1, and 2-year prevalences at t_2, for five broad categories of psychiatric disorder (schizophrenia, mood, anxiety disorder, eating disorder, and substance/alcohol abuse/dependence) according to DSM-III-R criteria (American Psychiatric Association, 1987). Diagnostic exclusion criteria were not applied so that freely overlapping hierarchy-free syndromes were obtained (Boyd *et al.* 1984). Participants also completed a checklist concerning their experience during the preceding period (1 year at t_1, 2 years at t_2) of 22 somatic conditions (Fig. 1) and whether they had taken prescribed medication for these. Of those reinterviewed at t_2 (4848), 1223 (25%) failed to complete the somatic disorder checklist, which on that occasion was sent to them after the interview, while at t_1, they completed it beforehand. Thus, complete psychiatric and somatic data were available for a subcohort of 3625 (51%) subjects. On both occasions, subjects also completed Eysenck's personality inventory (14 items) (Eysenck, 1959) which gives a neuroticism score (range 0–28).

Analysis

Overall links of neuroticism with separate somatic and psychiatric conditions

Overall links between neuroticism at t_1 and the separate somatic and psychiatric disorders at t_2 were quantified using logistic regression giving odds ratios (ORs) with 95% confidence intervals (CIs). Neuroticism was standardized so that the ORs refer to effects per standard deviation (S.D.) increase in neuroticism. Likelihood ratio tests for interaction (LRI) were used to examine whether ORs differed significantly between

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the conditions. This was done separately for psychiatric and somatic morbidity by evaluating the interaction terms between neuroticism and a variable indicating the 20 somatic and the five psychiatric conditions respectively. Finally, the overall link of neuroticism at t_1 with somatic and psychiatric morbidity, respectively, at t_2 was adjusted for neuroticism scores at t_2.

Path analysis: rationale

Path analysis using MPlus (Muthen & Muthen, 1999) was employed to separate prospective direct links of somatic and psychiatric morbidity with neuroticism over the observation period (3 years), from cross-sectional and indirect associations between them. Path analysis is an extension of simple regression modelling of one dependent variable on independent variables. In the path analysis framework, dependent variables are termed endogenous, and independent variables, exogenous. The extension lies in the fact that the model allows for intervening endogenous variables that are affected by exogenous variables, like age and gender, but that in turn also affect other endogenous variables. Path analysis or its extension, structural equation modelling, has been used in psychiatric research to evaluate hypotheses concerning how variables are linked (Kendler *et al*. 1993), for instance over time, in which case the term 'cross-lag correlation' has been used (Aneshensel *et al*. 1984). The strength of the association of endogenous with exogenous or intervening endogenous variables is represented by β coefficients and in path diagrams by straight directed arrows. These β coefficients are partial regression coefficients quantifying the strength of the association between two variables if all else is held constant in the model (Sobel, 1996). Directions of influence cannot be determined between endogenous variables measured simultaneously, and their association is represented by partial correlation coefficients (r) and two-headed curved arrows. Applied to the present data, such cross-sectional associations, for instance between somatic morbidity and neuroticism, represent a mixture of reporting bias and unbiased links. These cannot be separated since dates of onset of psychiatric and somatic morbidity were not recorded. Associations between an intervening endogeneous variable, say psychiatric morbidity at t_1, and another, like somatic morbidity at t_2, that remain after the cross-sectional associations between them have been discounted, should therefore be free of reporting bias and reverse causality and represent a mixture of direct and indirect prospective effects of the outcome at t_1 on the outcome at t_2. Indirect effects run via any, or more, other endogenous variables at either assessment. The overall link between a variable assessed at t_1 and one assessed at t_2 is the sum of the direct and all indirect effects. An indirect effect via a given route is quantified by multiplication of the path coefficients along it.

Model fitting was hypothesis-driven. The reference model represented the null hypothesis and contained three degrees of freedom (df), in that the coefficients on the paths from psychiatric and somatic morbidity at t_1 to neuroticism at t_2 (mechanism 4, β_{37}, β_{57}), and from neuroticism at t_1 to somatic morbidity at t_2 (mechanism 3, β_{46}) were set to zero (for r values and β values with subscripts, see Fig. 2). The coefficient representing the link between neuroticism at t_1 and psychiatric morbidity at t_2 (mechanism 2, β_{48}) was left unconstrained as the literature strongly supports the existence of this association (Neeleman *et al*. 2002). All others, whether prospective or cross-sectional including those representing age and gender effects on all variables, were left unconstrained. The effect of stratification of the reference model by gender was examined first by allowing path coefficients to vary between genders. Secondly, to obtain more degrees of freedom, non-significant ($P > 0{\cdot}050$) path coefficients were set to zero, starting with the smallest, until the model's fit deteriorated upon the reference model's or no non-significant coefficients remained – whichever came first. Subsequently, the zero constraints were released on the paths from psychiatric disorder (t_1) to neuroticism (t_2) (mechanism 4, β_{57}), somatic disorder (t_1) to neuroticism (t_2) (mechanism 4, β_{37}) and, finally, from neuroticism (t_1) to somatic disorder (t_2) (mechanism 3, β_{46}).

Outcome specification and model evaluation

All path analyses were weighed for the stratified sampling. Somatic and psychiatric morbidity at both waves were classified in two manners. First as polychotomies representing the number of conditions reported or diagnosed (multi-morbidity) (Table 1) and, secondly, as dichotomies, according to whether or not any

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conditions at all had been reported or diagnosed. Specification of dichotomous and polychotomous outcomes implies a threshold liability model which assumes that a continuously distributed latent variable (liability) underlies the observed outcome categories that are separated by one or more thresholds (Falconer, 1965). Model fit was evaluated using weighted least squares parameter estimates with robust standard errors that give χ^2 values. Large χ^2 values relative to the degrees of freedom indicate an inadequate fit of the model to the data (Scott Long, 1983). However, with large sample sizes, even trivial discrepancies between data and model can give large χ^2 values, small P values and unwarranted model rejection. Therefore, root mean square errors of approximation (RMSEA) ($\sqrt{(\chi^2-\mathrm{df})/\mathrm{df}/\mathrm{n}}$) are also given, as they provide sample-size adjusted estimates, indicating good model fit when $<0{\cdot}050$ (Arminger *et al.* 1995). Fit of simplified relative to fuller models was examined by comparing RMSEA values. Path coefficients were fully standardized and therefore comparable within and between models.

Missing data

The impact of missing data was evaluated using the missing at random (MAR) approach (Arminger *et al.* 1995). The somatic and psychiatric multi-morbidity counts were treated as continuous outcomes, this being a requirement of MAR that is robust to non-normality. MAR further assumes that values of missing data can be predicted by non-missing data and that whether a given score misses does not depend on the value it should have had. The fit of the missing data model was evaluated using maximum likelihood parameter estimates with robust standard errors.

RESULTS

Subjects

The participants' mean age at t_1 ($N=7076$) was 42·2 years (S.D. = 12·2) and similar for men ($N=3299$ (46·6%)) and women ($N=3777$ (53·4%)) ($t=-0{\cdot}223$, $P=0{\cdot}824$). At t_2, 2255 men and 2593 women (68% and 69% of the original sample, respectively) completed the CIDI ($N=4848$). The somatic conditions checklist was completed by 1590 men and 2035 women (48% and 54% of the original sample), giving full data on 3625 subjects. All subsequent path analyses, except the missing data model, refer to this subsample.

The distribution of morbidity and neuroticism

At t_1, 1630 (23·0%) and at t_2, 504 (13·9%) subjects had qualified for at least one psychiatric diagnosis during the preceding period (1 and 2 years, respectively). On both occasions, multimorbidity (presence of more than one condition) accounted for a quarter of the prevalence of psychiatric morbidity. At t_1 and t_2, somatic conditions during the preceding period were reported by 3065 (43·3%) and 1574 (43·4%) of the respondents. Of these, 1967 (27·8%) and 1118 (30·8%) respectively took prescribed medication. At t_1 the proportion of persons taking medication was lowest for osteoarthritis (26·8%) and highest for stroke (90·0%). At t_2 the proportion of persons taking prescribed medication was lowest for cirrhosis (25·0%) and osteoarthritis (35·9%), and highest for stroke (100%). Unless stated otherwise, all subsequent analyses refer to conditions for which medication was prescribed. A third of the sample reported more than one such condition (Table 1). Thus, the distribution of somatic and psychiatric multi-morbidity was highly skewed on both occasions. In the main analyses these were therefore treated as ordinal outcomes. Table 2 gives the correlation matrix of the endogenous variables. The three outcomes showed high stability over time and this was most pronounced for neuroticism (correlation coefficient 0·65). Cross-sectionally, neuroticism was correlated strongly with psychiatric and less strongly with somatic morbidity.

Overall links of neuroticism at t_1 with separate somatic and psychiatric conditions at t_2

All reported somatic conditions at t_2 for which described medication was taken, except Parkinson's disease, were associated positively with neuroticism at t_1 (OR 0·69, 95% CI 0·14 to 3·50, $P=0{\cdot}651$). Overall, the 22 ORs did not differ significantly (LRI, $\chi^2=17{\cdot}8$, df = 21, $P=0{\cdot}661$); per S.D. increase in neuroticism, participants were 1·34 (95% CI 1·25 to 1·45, $P<0{\cdot}001$) times more likely to take prescribed medication for one or more somatic conditions

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Table 1. *The distribution of somatic and psychiatric multi-morbidity*

Number of conditions	Participants: At t_1 ($N=7076$) *N*	(%)	At t_2 ($N=3625$) *N*	(%)
Psychiatric morbidity				
0	5446	(77·0)	3121	(86·1)
1	1217	(17·2)	387	(10·7)
2	347	(4·9)	104	(2·9)
3	57	(0·8)	13	(0·4)
4	8	(0·1)	0	
5	1	(0·01)	0	
All conditions	1630	(23·0)	504	(13·9)
Total number of conditions measured	878		634	
Somatic morbidity*				
0	5109	(72·2)	2507	(69·2)
1	1413	(20·0)	783	(21·6)
2	365	(5·2)	220	(6·1)
3	132	(1·9)	75	(2·1)
4	37	(0·5)	24	(0·7)
5	12	(0·2)	12	(0·3)
6	6	(0·08)	2	(0·1)
7	1	(0·01)	1	(0·03)
8	1	(0·01)	0	
21†	0		1	(0·03)
All conditions	1967	(27·8)	1118	(30·8)
Total number of conditions measured	2798		1644	

* Reported conditions for which prescribed medication was taken.

† Results of subsequent analyses were unaffected by whether or not this subject was included.

Table 2. *Correlation matrix of the observed endogenous variables*

	3	4	5	6	7	8
3. Somatic morbidity t_1	(1)					
4. Neuroticism t_1 (mean = 3·8, S.D. = 3·8)	0·16	(1)				
5. Psychiatric morbidity t_1	0·14	0·47	(1)			
6. Somatic morbidity t_2	0·64	0·15	0·07	(1)		
7. Neuroticism t_2 (mean = 3·1; S.D. = 3·8)	0·17	0·65	0·36	0·19	(1)	
8. Psychiatric morbidity t_2	0·17	0·36	0·52	0·14	0·43	(1)

Numbers in bold refer to the numbering also used in Fig. 2.

at t_2 (Fig. 1). When any reported conditions were considered, irrespective of whether medication was taken, the overall OR was 1·37 (95% CI 1·28 to 1·48, $P<0·001$). After adjustment for neuroticism at t_2, the overall ORs were lower (conditions for which medication was prescribed only, adjusted OR 1·10 (95% CI 1·00 to 1·22, $P=0·059$); any reported conditions, adjusted OR 1·12 (95% CI 1·02 to 1·14, $P=0·022$)) but still indicated the existence of a prospective positive association between neuroticism and somatic morbidity. Neuroticism in t_1 predicted each of the five psychiatric syndromes in t_2. The five ORs differed significantly (LRI, $\chi^2=17·2$, df = 4, $P=0·002$), principally due to the relatively low, but still raised, estimate for alcohol/substance use/dependence. Overall, per S.D. increase in neuroticism, the likelihood 3 years later of one or more psychiatric syndromes rose 2·20-fold (95% CI 2·01 to 2·41, $P<0·001$). After adjustment for neuroticism at t_2, this OR diminished to 1·31 (95% CI 1·15 to 1·48, $P<0·001$).

Path analysis

Polychotomous morbidity specification

The reference model's fit ($\chi^2=36·0$, df = 3, $P<0·001$, RMSEA = 0·055) failed to improve upon gender stratification ($\chi^2=1476·4$, df = 22, $P<0·001$, RMSEA = 0·191). A simplified model was obtained by setting to zero the non-significant path coefficients between gender and psychiatric morbidity (t_1; β_{25}) ($\chi^2=25·8$, df = 4, $P<0·001$, RMSEA = 0·039), age and neuroticism (t_1; β_{14}) ($\chi^2=22·2$, df = 5, $P<0·001$, RMSEA = 0·031), somatic and psychiatric morbidity at t_2 (r_{68}) ($\chi^2=24·8$, df = 6, $P<0·029$), psychiatric morbidity at t_1 and somatic morbidity at t_2 (β_{56}) ($\chi^2=23·5$, df = 7, $P=0·001$, RMSEA = 0·026), and, finally, gender and psychiatric morbidity at t_2 (β_{28}) ($\chi^2=23·5$, df = 8, $P=0·003$, RMSEA = 0·023). Relaxation of the null constraints on the paths between: (*a*) psychiatric morbidity at t_1 and neuroticism at t_2 (β_{57}) ($\chi^2=15·6$, df = 7, $P=0·029$, RMSEA = 0·018); (*b*) somatic morbidity at t_1 and neuroticism at t_2 (β_{37}) ($\chi^2=7·8$, df = 6, $P=0·250$, RMSEA = 0·009); and (*c*), neuroticism at t_1 and somatic morbidity at t_2 (β_{46}) gave a final fit of $\chi^2=3·0$, df = 5, $P=0·697$, RMSEA < 0·001 (Fig. 2).

Cross-sectional correlations

In the fitted model, neuroticism correlated cross-sectionally with psychiatric morbidity (r_{45}, r_{78}) and with somatic morbidity (r_{34}, r_{67}) but more strongly with the former than the latter, and more strongly at t_1 than t_2. At t_1 (r_{35}), but

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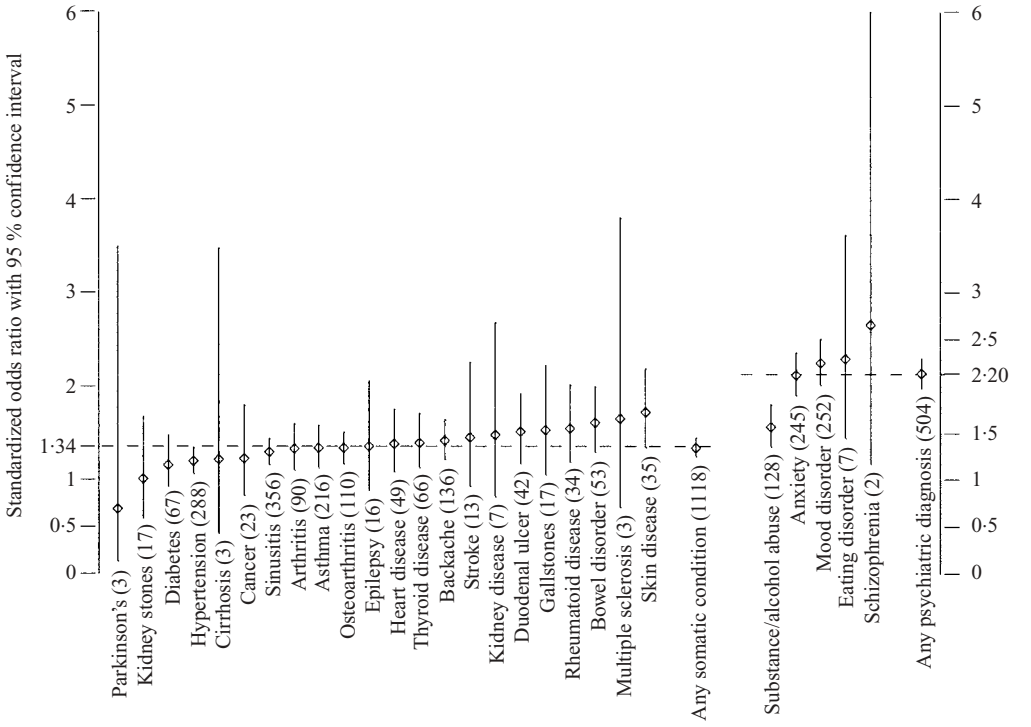

FIG. 1. Association of neuroticism with self-reported somatic conditions ($N=1644$) and psychiatric syndromes ($N=634$) 3 years later in 3625 adults.

not t_2 (r_{68}), somatic and psychiatric morbidity were correlated.

Effects of age and gender

At both waves, increasing age was associated with less psychiatric morbidity (β_{15}, β_{18}) but more somatic morbidity (β_{13}, β_{16}). There was no significant association between age and neuroticism at t_1 (β_{14}), but at t_2, older age was weakly associated with higher neuroticism scores (β_{17}). Levels of somatic morbidity were higher in women than men at both waves (β_{23}, β_{26}), but there were no gender differences with respect to psychiatric morbidity (β_{25}, β_{28}).

Prospective associations between endogenous variables

Strong associations existed over time between the three outcome variables (β_{36}, β_{47}, β_{58}), suggesting high temporal stability. This was strongest for somatic morbidity (β_{36}: 0·627) and weakest for psychiatric morbidity (β_{58}: 0·436).

Having taken account of all these associations, we found that neuroticism at t_1 remained associated directly with psychiatric morbidity (β_{48}) but also somatic morbidity (β_{46}) at t_2, accounting for 30·7% and 23·7% of its overall prospective links with these outcomes. Conversely, psychiatric and somatic morbidity at t_1 retained direct effects (β_{57} and β_{37}), responsible for 14·8% and 27·3% of the overall links, on neuroticism at t_2 (Table 3).

Dichotomous morbidity specification

The reference model with somatic and psychiatric morbidity at t_1 and t_2 as dichotomous variables gave a reasonable initial fit ($\chi^2=25{\cdot}3$, df = 3, $P<0{\cdot}001$, RMSEA = 0·045). Modelling along similar lines as described above, constraining to zero non-significant path coefficients, a simplified model was obtained with an RMSEA of 0·016 ($\chi^2=15{\cdot}8$, df = 8, $P=0{\cdot}045$). Relaxation of the constraints on the paths from psychiatric and somatic morbidity at t_1 to neuroticism at t_2 (β_{57}, β_{37}) gave models with improved fit ($\chi^2=8{\cdot}0$, df = 7, $P=0{\cdot}334$, RMSEA = 0·006; and $\chi^2=4{\cdot}9$, df = 6, $P=0{\cdot}556$, RMSEA < 0·001, respectively). Relaxation of the zero constraint on the path

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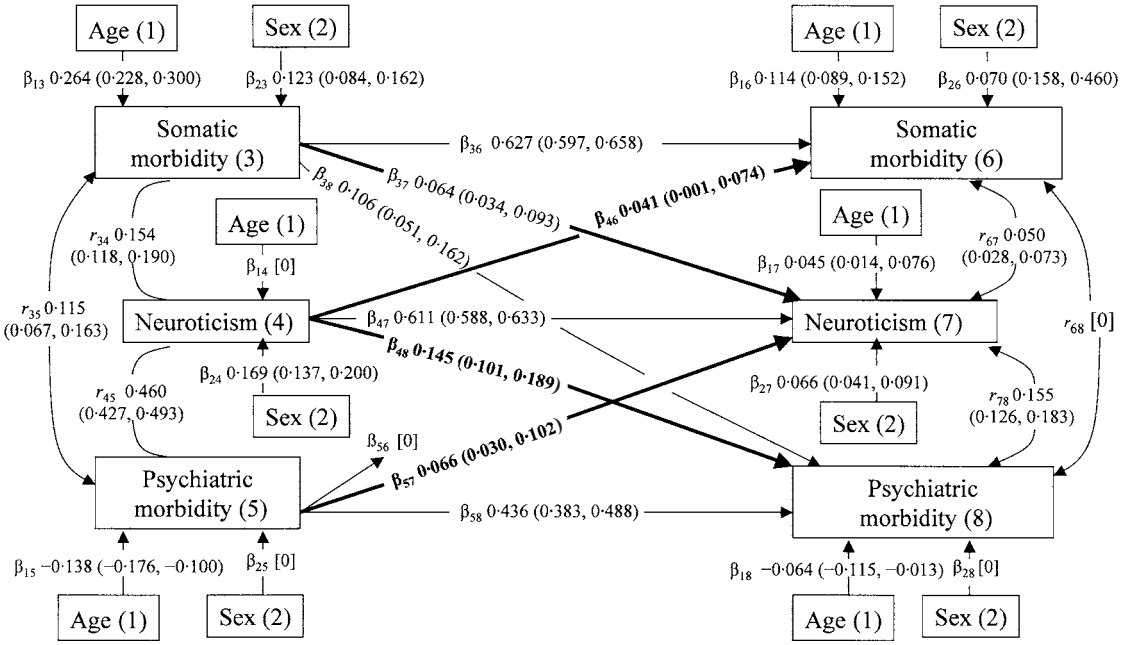

FIG. 2. Links between neuroticism and somatic and psychiatric morbidity over 3 years in 3625 adults. Weighted standardized path coefficients with 95% confidence intervals. Direct prospective paths between morbidity and neuroticism in bold. Somatic and psychiatric morbidity specified as polychotomous (multi-morbidity) variables ($\chi^2 = 3{\cdot}0$, df = 5, $P = 0{\cdot}697$, RMSEA < 0·001; [0] indicates coefficients that were constrained to zero; numbers in parentheses after characteristics indicate endogenous variables).

between neuroticism at t_1 and somatic morbidity at t_2 (β_{46}) gave the final model with an excellent fit ($\chi^2 = 2{\cdot}7$, df = 5, $P = 0{\cdot}751$, RMSEA < 0·001). It was virtually identical to the model with polychotomous outcomes, although the regression coefficient between neuroticism at t_1 and somatic morbidity at t_2 (β_{46}) just fell short of significance (Table 3).

Missing data

The baseline missing data model ($\chi^2 = 73{\cdot}5$, df = 3, $P < 0{\cdot}001$, RMSEA = 0·057) could be simplified in a similar manner, as in the previous two approaches, to a model with a fit index of $\chi^2 = 96{\cdot}2$, df = 9, $P < 0{\cdot}001$, RMSEA = 0·037. This model contained one extra degree of freedom compared with its equivalents described above as the coefficient between somatic morbidity at t_1 and psychiatric morbidity at t_2 (β_{38}), and it was also non-significant. Relaxation of the paths to neuroticism at t_2 from psychiatric morbidity (β_{57}) and somatic morbidity (β_{37}) at t_1, gave models with improved fit ($\chi^2 = 63{\cdot}7$, df = 8, $P < 0{\cdot}001$, RMSEA = 0·031 and $\chi^2 = 39{\cdot}0$, df = 7, $P < 0{\cdot}001$, RMSEA = 0·025, respectively). Relaxation of the zero constraint on the path between neuroticism at t_1 and somatic morbidity at t_2 (β_{46}) gave the final model with acceptable fit ($\chi^2 = 23{\cdot}6$, df = 6, $P < 0{\cdot}001$, RMSEA = 0·020). It was consistent with the previous two (Table 3).

Attrition

Failure to complete the somatic conditions checklist at t_2 was associated with male gender (OR 1·26, 95% CI 1·14 to 1·38, $P < 0{\cdot}001$; men *v.* women), younger age (OR 1·03; 95% CI 1·01 to 1·02, $P < 0{\cdot}001$; per year), neuroticism (t_1) (OR 1·15, 95% CI 1·10 to 1·20; per S.D.; $P < 0{\cdot}001$), psychiatric multi-morbidity (t_1) (OR 1·39, 95% CI 1·28 to 1·49; per condition; $P < 0{\cdot}001$), neuroticism (t_2) (OR 1·14, 95% CI 1·06 to 1·20; per S.D.; $P < 0{\cdot}001$) and psychiatric multi-morbidity (t_2) (OR 1·28, 95% CI 1·14 to 1·45; per condition; $P < 0{\cdot}001$). Somatic multi-morbidity (t_1) was not associated with failure to complete the checklist 3 years later (OR 1·04, 95% CI 0·98 to 1·10, per condition; $P = 0{\cdot}211$).

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Table 3. *Path analysis of cross-sectional and prospective links of neuroticism with somatic and psychiatric morbidity over 3 years*

Model type	Link between			
	Psychiatric morbidity (t_1) and neuroticism (t_2) (β_{57})	Somatic morbidity (t_1) and neuroticism (t_2) (β_{37})	Neuroticism (t_1) and psychiatric morbidity (t_2) (β_{48})	Neuroticism (t_1) and somatic morbidity (t_2) (β_{46})
Polychotomous outcome*				
Direct link, β (95% CI)	0·066 (0·030, 0·102)	0·064 (0·034, 0·093)	0·145 (0·101, 0·189)	0·041 (0·00, 10·074)
Overall link	0·447	0·234	0·472	0·173
Direct/overall link	14·8%	27·3%	30·7%	23·7%
Dichotomous outcome†				
Direct link, β (95% CI)	0·073 (0·035, 0·111)	0·047 (0·013, 0·081)	0·168 (0·034, 0·060)	0·031 (−0·015, 0·077)
Overall link	0·435	0·205	0·479	0·153
Direct/overall link	16·8%	23·0%	35·1%	20·2%
Continuous outcome‡				
Direct link, β (95% CI)	0·082 (0·052, 0·112)	0·058 (0·033, 0·083)	0·226 (0·192, 0·260)	0·066 (0·036, 0·096)
Overall link	0·484	0·230	0·519	0·190
Direct/overall link	16·9%	25·3%	43·6%	34·7%

* $N=3625$. Final model fit: $\chi^2=3·0$, df = 5, $P>0·050$, RMSEA = 0·000; accounting for 45·4, 30·2 and 46·9 of the variances of neuroticism, psychiatric and somatic morbidity at t_2, respectively.

† $N=3625$. Final model fit: $\chi^2=2·7$, df = 5, $P>0·050$, RMSEA = 0·000; accounting for 45·2, 29·6 and 45·3 of the variances of neuroticism, psychiatric and somatic morbidity at t_2, respectively.

‡ $N=7076$. Missing data model. Final model fit: $\chi^2=23·6$, df = 6, $P<0·050$, RMSEA = 0·020; accounting for 48·7, 19·0 and 30·4 of the variances of neuroticism, psychiatric and somatic morbidity at t_2, respectively.

DISCUSSION

Biased reporting or a general tendency to complain may account for the apparent link between neuroticism and somatic problems (Costa & McCrae, 1987). These effects may be especially pronounced when psychiatric disorder is also present (Katon *et al.* 2001), or where, as in the present study, self-report measures are used to assess both aspects. The association may also arise when morbidity results in increased neuroticism (Rohde *et al.* 1994). Finally, neuroticism may raise the risk not only of psychiatric but also genuine somatic morbidity with an organic basis. This study suggests that each of these processes may apply. Somatic morbidity is positively associated with prior neuroticism, although the link weakens after adjustment, in the logistic regression model, for simultaneous neuroticism scores. However, this is an over-adjustment since the cross-sectional association reflects not only effects of reporting bias and reverse causality but also unbiased effects (mechanism 3). Path analysis allows for the simultaneous associations of neuroticism with neuroticism later and with other endogenous variables like somatic morbidity. The results suggest that, irrespective of reporting bias, 27% of the overall association between somatic morbidity and neuroticism is attributable to direct effects of the former on the latter, and 24% to reverse effects. The strength of the direct associations, expressed by the standardized path coefficients, is moderate, but the evidence for their existence represents a new finding emphasizing the importance of personality traits in connection with morbidity accumulation. This is especially so because direct links applied irrespective of whether morbidity was somatic or psychiatric.

Neuroticism has been defined as an enduring personality trait characterized by a lifelong tendency to experience negative emotions; according to some it is distinct from mental illness (Costa & McCrae, 1987) although it is a strong risk factor for it (Jorm *et al.* 2000). Alternatively, neuroticism has been viewed as persons' stable levels of subthreshold psychiatric morbidity or their characteristic levels of minor psychiatric symptoms (Duncan-Jones *et al.* 1990). Whichever view one takes of neuroticism, in the present data its stability over time is higher than that of CIDI-diagnosed manifest psychiatric morbidity.

The analytical strategy minimizes the likelihood that inaccurate reporting of somatic conditions or temporary fluctuations in neuroticism

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due to illness can explain the main findings, but the possibility must be considered. Self-report of somatic conditions may be randomly inaccurate but also systematically biased. When inaccuracies are random, over-reporting of some conditions like arthritis (Neeleman *et al.* 2001) and under-reporting of others, like hypertension or conditions that have not yet declared themselves, may cancel out in multi-morbidity counts (Batstra *et al.* 2002). Adjustment of the prospective links of neuroticism and psychiatric morbidity with somatic morbidity for the equivalent cross-sectional associations should have removed most effects of reporting bias, increased tendencies to complain and morbidity-dependent fluctuations in neuroticism. The association of somatic morbidity with neuroticism was unaffected by whether or not unmedicated conditions were excluded, suggesting that reporting bias is unlikely to account for the link of neuroticism and manifest psychiatric morbidity, with somatic morbidity. Somatization disorder was not diagnosed but overlaps so strongly with other conditions like anxiety disorder (Battaglia *et al.* 1998) that this is unlikely to have led to underestimating the effects of reporting bias.

Links between somatic and psychiatric morbidity, and neuroticism were treated, analytically, as single phenomena but can of course come in different forms which the present analysis cannot disentangle. Psychological, physical or behavioural sequelae of physical disorders may increase risk of mental illness, as may side effects of medication. Psychiatric disorder and neuroticism may, by affecting health behaviours, increase risk of somatic illness. Even more direct morbidity-dependent effects may exist if somatic lesions cause psychiatric symptoms. Reciprocal effects may be present from the onset, but may also involve a chronic disorder, for instance if treatment of psychiatric symptoms is less than vigorous in frail patients (Perez-Stable *et al.* 2001).

The analyses were robust to different outcome specifications. Use of multi-morbidity scores as polychotomous outcomes allows for the fact that high degrees of multi-morbidity refer to more serious ill health (Batstra *et al.* 2002). They may do more justice to the data than simple case/no case dichotomies. In the model based on dichotomous data, the coefficient for the association between neuroticism in t_1 and somatic morbidity in t_2 failed to reach significance, although allowing it to vary from zero did improve the overall model's fit. Given that the equivalent coefficients in the polychotomous and missing data models were significant, this inconclusive evidence in the dichotomous model is likely to reflect information loss resulting from dichotomization. The results are compatible with neuroticism being a predictor of increasing severity of psychiatric and somatic ill health whether this implies worsening of ill health or a transition from health to illness. The overall prospective links between neuroticism and separate somatic complaints were comparable in strength. This lack of symptom specificity has been reported before (Luborsky *et al.* 1973) and supports the use of multi-morbidity as an index of severity of ill health.

The assessments were separated by 3 years but effects between somatic and psychiatric morbidity may take less time (Aneshensel *et al.* 1984). More frequent assessments might have yielded stronger indirect and weaker direct links between neuroticism and morbidity. However, we focused on syndromes with a protracted course. Path analysis with repeated assessments of the same outcome adjusts for this so that direct associations are unlikely to be overestimated. Somatic and psychiatric morbidity at t_2 covered an unusual period of 2 years. However, this cannot have affected the results as similar time-frames applied to both morbidity types.

Male and younger participants had a lower risk of somatic morbidity but also higher drop-out rates. Psychiatric morbidity and neuroticism were associated with somatic morbidity at follow-up, but also with attrition. This explains why rates of psychiatric morbidity in t_2 were lower than in t_1. Thus, the results refer to a relatively healthy sample which may limit their applicability to sicker groups. Unbalanced attrition associated with neuroticism will have affected direct links more strongly than indirect links so that the strength of the former are, if anything, underestimated. The missing-data analysis supports this.

Path analysis can indicate whether data are consistent with given hypotheses but not prove it. Models may change by inclusion of other variables. We analysed only one personality trait of likely importance (Neeleman *et al.* 2002),

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since the objective was not to predict comprehensively somatic and psychiatric ill health but to examine how these outcomes interrelate. Future research needs to cover more variables of likely relevance like those related to lifestyle and also to focus on more narrowly defined morbidity types.

The final model is consistent with the literature as regards gender and age effects. Older age is associated with more somatic but less psychiatric morbidity (Neeleman *et al.* 2001). Neuroticism and somatic symptoms are known to be higher among women than men (Lynn & Martin, 1997). Having adjusted for all else, only a weak age effect remained on neuroticism. While, in line with previous findings (Costa & McCrae, 1987), our analysis qualifies this by adding that a history of previous illness, which is more common among the elderly, is associated with increased neuroticism. Evidence for such vulnerability accumulation has not been reported before.

The temporal relationship between depressive symptoms (an admixture of neurotic traits with manifest psychopathological states) and physical disorder has been described as 'self-perpetuating and mutually reinforcing' (Aneshensel *et al.* 1984). A similar picture emerges from the present analysis with the advantage that neuroticism, an enduring personality attribute (Costa & McCrae, 1987), is analysed separately from manifest pathology. The notion of neuroticism as a central nexus in the development of ill health fits well with recent physiological ideas concerning mechanisms leading to disease, such as, in particular, the allostatic load model (McEwen & Stellar, 1993). This proposes that severe stress, in the form of disease or otherwise, may, when protracted, increase the risk of many conditions but also lead to reduced stress tolerance (McEwen & Stellar, 1993). This added vulnerability, of which neuroticism may be a psychological manifestation, has physiological counterparts such as exaggerated cortisol-mediated stress reactions (Kirschbaum *et al.* 1999), explaining how it can be linked with not only psychiatric but also a whole array of somatic conditions (Boscarino, 1997). Persons threatened by psychiatric disorder because of temperamental attributes like neuroticism, may remain at risk of somatic problems even if mental illness is averted. Clinicians and researchers should focus not only on the psychiatric sequelae of adverse personality styles like neuroticism but also on their direct medical consequences.

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REFERENCES

American Psychiatric Association (1987). *Diagnostic and Statistical Manual of Mental Disorders: DSM-III-R*. APA: Washington, DC.

Aneshensel, C. S., Frerichs, R. R. & Huba, G. J. (1984). Depression and physical illness – a multiwave, nonrecursive causal model. *Journal of Health and Social Behavior* **25**, 350–371.

Arminger, G., Clogg, C. C. & Sobel, M. E. (1995). *Handbook of Statistical Modeling in the Social and Behavioral Sciences*. Plenum: New York.

Batstra, L., Bos, E. H. & Neeleman, J. (2002). Quantifying psychiatric comorbidity: lessons from chronic disease epidemiology. *Social Psychiatry and Psychiatric Epidemiology* **37**, 105–111.

Battaglia, M., Bertella, S., Bajo, S., Politi, E. & Bellodi, L. (1998). An investigation of the co-occurrence of panic and somatization disorders through temperamental variables. *Psychosomatic Medicine* **60**, 726–729.

Bijl, R. V., Zessen, G. v., Ravelli, A., Rijk, C. d. & Langendoen, Y. (1998). The Netherlands Mental Health Survey and Incidence Study (NEMESIS): objectives and design. *Social Psychiatry and Psychiatric Epidemiology* **33**, 581–586.

Boscarino, J. A. (1997). Diseases among men 20 years after exposure to severe stress: implications for clinical research and medical care. *Psychosomatic Medicine* **59**, 605–614.

Boyd, J. H., Burke, J. D., Gruenberg, E., Holzer, C. E., Rae, D. S., Geroge, L. K., Karno, M., Stoltzman, M. & McEvoy, L. (1984). Exclusion criteria of DSM-3: a study of co-occurrence of hierarchy free syndromes. *Archives of General Psychiatry* **41**, 983–989.

Cohen, P., Pine, D. S., Must, A., Kasen, S. & Brook, J. (1999). Prospective associations between somatic illness and mental illness from childhood into adulthood. *American Journal of Epidemiology* **147**, 232–239.

Costa, P. T. & McCrae, R. R. (1987). Neuroticism, somatic complaints and illness: is the bark worse than the bite? *Journal of Personality* **55**, 299–316.

Duggan, C. F., Sham, P., Lee, A. S. & Murray, R. M. (1991). Does recurrent depression lead to a change in neuroticism? *Psychological Medicine* **21**, 985–990.

Duncan-Jones, P., Fergusson, D. M., Ormel, J. & Horwood, L. J. (1990). *A Model of Stability and Change in Minor Psychiatric Symptoms: Results from Three Longitudinal Studies*. *Psychological Medicine Monograph-Supplement 18*. Cambridge University Press: Cambridge.

Eaker, E. D., Pinsky, J. & Castelli, W. P. (1992). Myocardial infarction and coronary death among women: psychosocial predictors from a 20-year follow-up of women in the Framingham Study. *American Journal of Epidemiology* **135**, 854–864.

Everson, S. A., Goldberg, D. E., Kaplan, G. A., Cohen, R. D., Pukkala, E., Tuomilehto, J. & Salonen, J. T. (1996). Hopelessness and risk of mortality and incidence of myocardial infarction and cancer. *Psychosomatic Medicine* **58**, 113–121.

Eysenck, H. J. (1959). *Manual of the Maudsley Personality Inventory*. University of London Press: London.

Falconer, D. S. (1965). The inheritance of liability to certain diseases, estimated from the incidence among relatives. *Annals of Human Genetics* **29**, 51–76.

Freeman, J. (1971). Smoking and neuroticism. *Lancet* ii, 1260.

Goebel, P. N., Peter, H., Mueller, S. K. & Hand, I. (1998). Neuroticism, other personality variables, and serum lipid levels in patients with anxiety disorders and normal controls. *International Journal of Psychiatry in Medicine* **28**, 449–462.

Hotopf, M., Mayou, R., Wadsworth, M. & Wessely, S. (1998). Temporal relationships between physical symptoms and psychiatric disorder. *British Journal of Psychiatry* **173**, 255–261.

Jorm, A. F., Rodgers, B., Jacomb, P. A., Christensen, H., Henderson, S. & Korten, A. E. (1999). Smoking and mental health: results from a community survey. *Medical Journal of Australia* **170**, 74–77.

Jorm, A. F., Christensen, H., Henderson, A. S., Korten, A. E. & Rodgers, B. (2000). Predicting anxiety and depression from personality: is there a synergistic effect of neuroticism and extraversion? *Journal of Abnormal Psychology* **109**, 145–149.

Katon, W., Sullivan, M. & Walker, E. (2001). Medical symptoms without identified pathology: relationship to psychiatric disorders, childhood and adult trauma, and personality traits. *Annals of Internal Medicine* **134**, 917–925.

Kendler, K. S., Kessler, R. C., Neale, M. C., Heath, A. C. & Eaves, L. J. (1993). The prediction of major depression in women: toward an integrated etiologic model. *American Journal of Psychiatry* **150**, 1139–1148.

Kirschbaum, C., Prussner, A., Stone, A., Federinko, I., Gaab, J., Lintz, D., Schommer, N. & Heilhammer, D. H. (1999). Persistent high cortisol responses to repeated psychological stress in a subpopulation of healthy men. *Psychosomatic Medicine* **57**, 468–474.

Luborsky, L., Docherty, J. P. & Penick, S. (1973). Onset conditions for psychosomatic symptoms: a comparative review of immediate observation with retrospective research. *Psychosomatic Medicine* **35**, 187–204.

Lynn, R. & Martin, T. (1997). Gender differences in extraversion, neuroticism, and psychoticism in 37 nations. *Journal of Social Psychology* **137**, 369–373.

McEwen, B. S. & Stellar, E. (1993). Stress and the individual: mechanisms leading to disease. *Archives of Internal Medicine* **153**, 2093–2101.

Muthen, L. K. & Muthen, B. (1999). *MPlus*. Muthen & Muthen: Los Angeles.

Neeleman, J., Wessely, S. & Wadsworth, M. (1998). Predictors of suicide, accidental death and premature natural death in a general-population birth-cohort. *Lancet* **351**, 93–97.

Neeleman, J., Ormel, J. & Bijl, R. (2001). The distribution of psychiatric and somatic ill-health; associations with personality and socio-economic status. *Psychosomatic Medicine* **63**, 231–247.

Neeleman, J., Systema, S. & Wadsworth, J. (2002). Propensity to psychiatric and somatic ill-health; evidence from a birth cohort. *Psychological Medicine* **32**, 793–803.

Perez-Stable, J., Miranda, J., Munoz, R. F. & Ying, Y. (2001). Depression in medical outpatients; underrecognition and misdiagnosis. *Archives of Internal Medicine* **150**, 1083–1088.

Rohde, P., Lewinsohn, P. M. & Seeley, J. R. (1994). Are adolescents changed by an episode of major depression? *Journal of the American Academy of Child and Adolescent Psychiatry* **33**, 1289–1298.

Scott Long, J. (1983). *Covariance Structure Models: An Introduction to LISREL*. Sage Publication: Newbury Park.

Sobel, M. E. (1996). An introduction to causal inference. *Sociological Methods and Research* **24**, 353–379.