Schizophrenia-related deaths during the Danish malnutrition period 1999-2007

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Abstract

Background: Several studies published over the last few years have shown that malnutrition has a severe effect on schizophrenia patients.

During the period from January 1999 to January 2007 a statistically significant increase in the number of deaths related to malnutrition was found among the elderly in Denmark. Many more may have been suffering from malnutrition, but not to such a degree that it led to their deaths.

Objective: The aim of this study is to examine whether or not the effect of the malnutrition period can be seen in the number of schizophrenia-related deaths among the elderly.

Method: Regression analyses.

Results: The study found a sudden statistically significant rise in the number of schizophrenia-related deaths among the elderly to be associated with the period when the general nutritional state among the elderly in Denmark worsened (from 1999 to 2007). In addition the study found a bubble in the death rate from schizophrenia that was significantly associated with the bubble in malnutrition and was calculated to have claimed between 190 and 417 extra lives.

Conclusion: The study concludes that for the period 1999-2007 an excess death rate from malnutrition was associated with an excess death rate from schizophrenia and that women react stronger to malnutrition in relation to schizophrenia than men.

Keywords: The Danish malnutrition period, schizophrenia, death rate.

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Introduction

Studies published over the last few years have shown that malnutrition has a severe effect on schizophrenia. Studies from the Dutch famine cohort show that schizophrenia can develop as a result of prenatal malnutrition [1-3].

The Dutch famine 1944-1945

During the period from October 1944 to May 1945, a large part of the Netherlands suffered through a period of famine. The Allied offensive to liberate the Netherlands had been stopped when Operation Market Garden had failed, which left the western part of the Netherlands under German occupancy. In order to assist the Allied forces the exiled Dutch government organized a railroad strike to hinder the German transport of troops. To punish the Dutch people the German military introduced a transport embargo on food. This meant that food rations fell to between 800 and 400 kcal a day for adults.

Children conceived or born during this period have been studied closely, and the findings show that children exposed to prenatal famine have an increased risk of developing schizophrenia.

Some find that it is not the lack of calories as much as it is micronutrient deficiency that causes schizophrenia [4-5]. This gives a more narrow explanation of the relation between nutrition and schizophrenia.

Only a few studies have examined the effect of malnutrition on schizophrenia in adulthood. A study conducted in 2008 in Canada showed that being underweight was associated with increased odds of schizoid personality disorder, especially among women [6].

Being malnourished also seems to worsen negative symptoms like social isolation, reduced sense of joy and lack of energy [7].

Drugs used to treat schizophrenia are primarily fat soluble, and weight loss during treatment has in some cases been associated with serious, potentially lethal, side effects like diabetic ketoacidosis [8].

Since 1995, the literature has flourished with articles connecting nutrition with different diseases. During the period from January 1999 to January 2007 a statistically significant increase in the number of deaths related to malnutrition was found among the elderly in

Denmark [9-12]. “Malnutrition” is here the officially registered cause of death. Many more may have been suffering from malnutrition, but not to such a degree that it led to their deaths. The special interest of this article is the (broad) association between malnutrition and schizophrenia. This study is inspired by the findings from the Dutch famine studies.

Method and Data

The method applied is primarily descriptive. The cohort effects have been widely discussed in the literature [11, 13] and have been tested.

The Danish data on the *death rate* from malnutrition: The State Serum Institute [9]: Malnutrition, B-040, and Schizophrenia, B-046. In principle, the present article is based on the total dataset for deaths and death rates from malnutrition and schizophrenia in Denmark 1994-2012.

The explanatory variables are:

T	period (or year), 1960 = 1. Indicates technical progress that reduces diseases with a certain percentage every year
Age	age at death. Diseases are expected to grow almost exponentially over age
Dmalw	actual death rate (per 100 000) from malnutrition, women
Dmalm	actual death rate (per 100 000) from malnutrition, men
Dszw	actual death rate (per 100 000) from schizophrenia, women
Dszm	actual death rate (per 100 000) from schizophrenia, men

5-year age groups were applied, from the age group 55-59 to the age group 85+.

The death rate from malnutrition

Without the inclusion of any theory the death rate from malnutrition in Denmark from 1994 to 2012 will now be described.

Figures 1 and 2 compare the death rates from malnutrition and schizophrenia during the period 1994-2012 for men and women in the age group 85+.

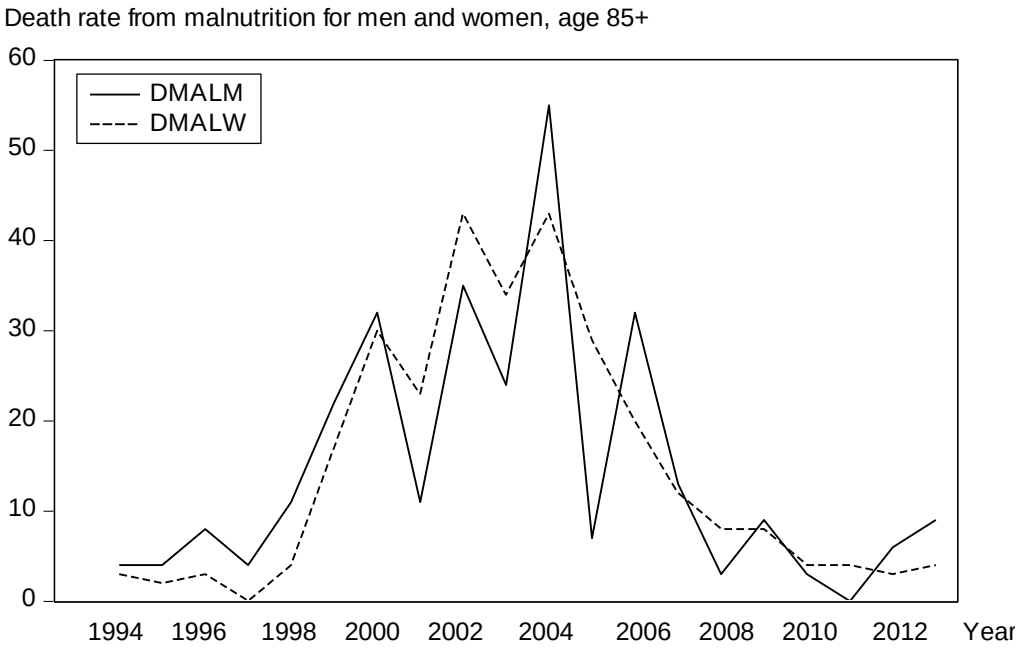

Figure 1. The death rate from malnutrition based on data for Danish men and women for age group 85+ during the period 1994-2013.

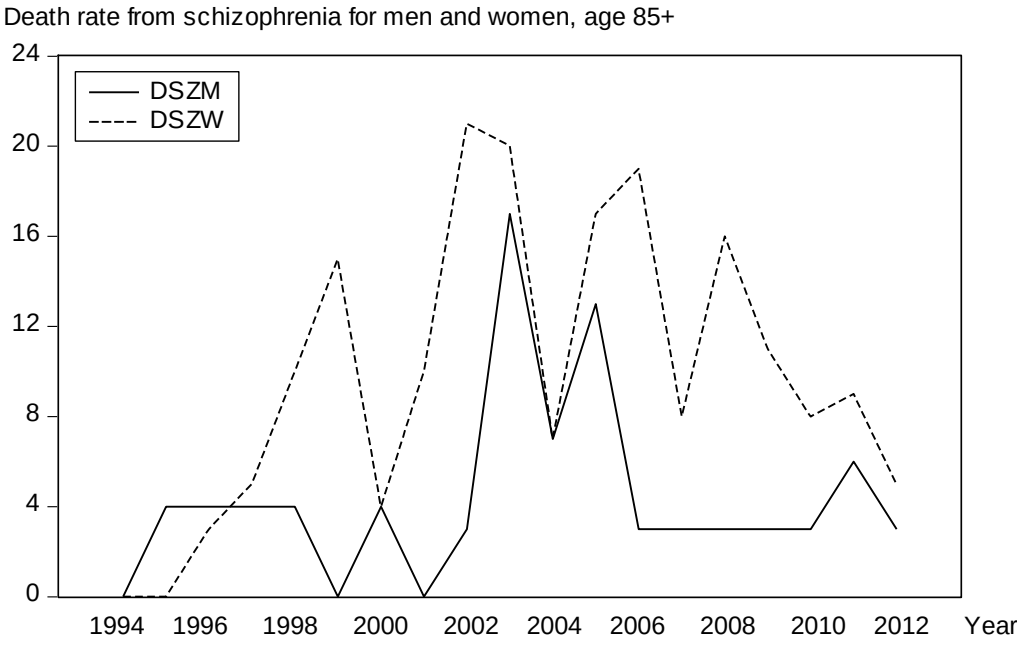

Figure 2. The death rate from schizophrenia based on data for Danish men and women for age group 85+ during the period 1994-2012.

The distributions (the bubbles) of death rates from malnutrition and schizophrenia shown in Figures 1 and 2 appear *truncated*. Both are truncated by the limit years 1994 and 2012. The distribution over time of the excess deaths from malnutrition is *bell-shaped,* while the distribution of excess deaths from schizophrenia is *skewed to the right,* indicating a prolonged effect of malnutrition on schizophrenia, especially for women.
The malnutrition period is primarily limited to the malnutrition period 1999 to 2007; however, the (truncated) effect on the death rate from schizophrenia makes it difficult to calculate how many people died from schizophrenia provoked by the malnutrition period.

The association between malnutrition and schizophrenia

An "association" is much less ambitious than a "cause-effect relationship", although they are often treated in a similar way. To the knowledge of the authors there is no solid biological evidence for a link between malnutrition and schizophrenia, only a strong indication of a common cause.

Empirical analysis

A more informative picture was established by simple econometric methods with separate models for men and women. A simple OLS-regression analysis gave the following result for women:

$$\begin{array}{lllll} Dszw = -1.83 + .000823Age^2 + .5323Dmalw - 1.22e\text{-}06Age^2 Dmalw^2 + .1338*Dmalw(-3) \\ t \quad (-1.65) \quad (3.34) \quad (4.14) \quad (-2.91) \quad (3.16) \end{array}$$

$$R^2 = .699 \qquad DW = 1.96 \qquad Obs = 112$$

and for men:

$$\begin{array}{llll} Dszm = .0300Age + .2493\ Dmalm^2 - .002936Age*Dmalm^2 + .1638Dmalm(-1) \\ t \quad (8.18) \quad (1.76) \quad (-1.76) \quad (5.12) \end{array}$$

$$R^2 = .282 \qquad DW = 1.88 \qquad Obs = 126$$

The coefficients to Dmal are highly significant for women indicating a significant association or co-variation between malnutrition and schizophrenia as well as malnutrition as the leading cause *if* there is a cause-effect relationship due to the timelag. The equation for men explains fewer of the movements in the death rate from schizophrenia than does

the equation for women. The DW values (although not quite reliable in tests like this) indicate that there is no autocorrelation problem. The equations are based on seven age groups and 19 years, in principle 133 observations. The lag structure implies that we lose 7*3 = 21 observations in the equation for women and 7*1 = 7 observations in the equation for men. The significant lagged right-hand side variables Dmalw(-3) and Dmalm(-1) are a weak indication that malnutrition causes death from schizophrenia.

The models are applied for forecasts named Dszwf and Dszmf. The observations in a scatter diagram can be divided between women and men and adjacent points connected to show the movements over the period 1994 to 2012 as shown below in Figures 2 and 3.

Figures 3 and 4 indicate that the return to a normal nutritional state is a more dangerous period for schizophrenic patients than increasing malnutrition. Shifting a person's metabolism from a catabolic to anabolic state is known to involve the risk of developing Wernicke encephalopathies and refeeding syndrome in alcoholic and malnourished patients [14]. Our data suggest that patients suffering from schizophrenia also appear to be especially vulnerable to changes in metabolism.
For women 2002-2005, and for men 2000-2007 the "malnutrition period" was at its highest and subsided, and the patients entered an unstable period.

Together Figures 1-4 and Tables 1 and 2 indicate that:

At increasing age:	Men become malnourished more frequently than women
	Women more often get schizophrenia than men
At increasing starvation:	Women more often get schizophrenia than men
At refeeding (the turning point):	Men have bigger problems (are more unstable) than women

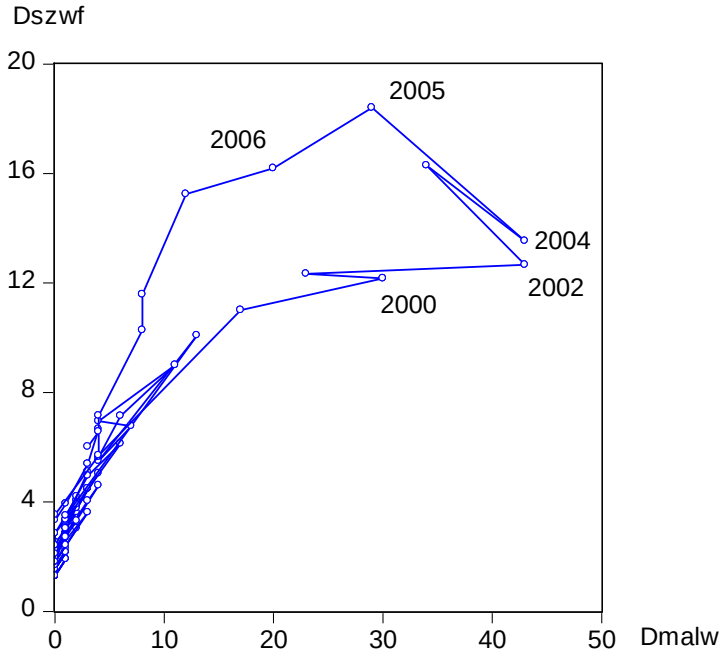

Figure 3. Scatter diagram of the association between malnutrition and the forecast of schizophrenia for women. All age groups.

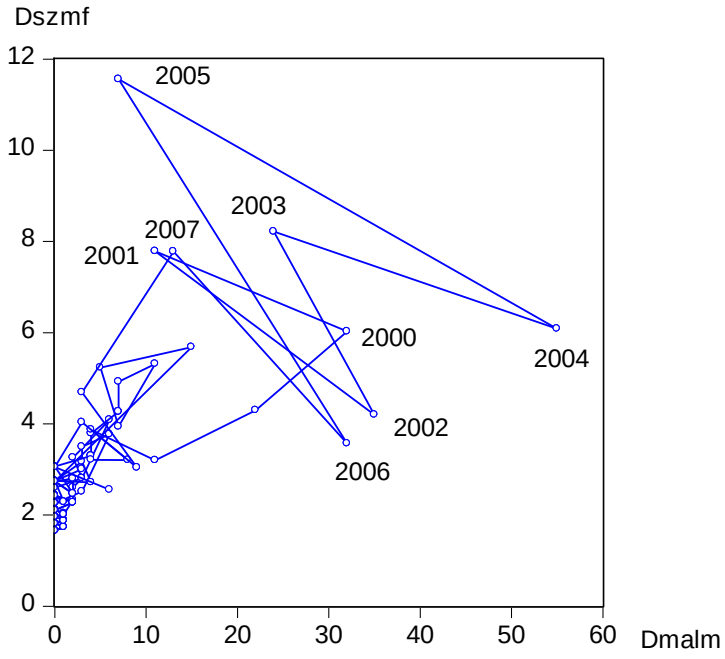

Figure 4. Scatter diagram of the association between malnutrition and the forecast for schizophrenia for men. All age groups.

Table 1. Number of deaths from malnutrition related to age, 1994-2012.								
		Men				**Women**		
		1994-1998	1999-2007	2008-2012		1994-1998	1999-2007	2008-2012
55-59		**1**	**6**	**1**		0	3	0
60-64		1	3	0		0	**4**	**2**
65-69		1	5	1		1	**7**	0
70-74		1	**19**	**2**		1	16	1
75-79		0	16	1		**5**	**20**	**6**
80-84		4	27	5		**6**	**40**	**9**
85+		8	67	7		8	**178**	**20**
Total		16	143	17		**21**	**268**	**38**

Table 2. Number of deaths from schizophrenia related to age, 1994-2012.								
		Men				**Women**		
		1994-1998	1999-2007	2008-2012		1994-1998	1999-2007	2008-2012
55-59		**2**	**30**	**15**		1	22	4
60-64		**5**	**26**	**25**		2	13	16
65-69		2	**20**	**18**		2	17	12
70-74		1	25	11		**3**	**27**	**12**
75-79		4	24	10		4	**41**	**27**
80-84		5	20	12		**12**	**48**	10
85+		4	15	6		**12**	**86**	**37**
Total		23	160	97		**36**	**254**	**118**

The number of deaths from malnutrition provoked deaths from schizophrenia.

Table 1 and 2 below can be used for calculations of the number of extra deaths from schizophrenia provoked by malnutrition. Numbers in bold type in Tables 1 and 2 indicate "higher than" compared to the other gender.
:

Defining the aftermath of schizophrenia as "normal" (not provoked by malnutrition) we have:

Men	Extra deaths	160 – .9*(23+97) =	52
Women	Extra deaths	254 - .9*(36+118) =	138.6
Total			**190.6**

Assuming that malnutrition provoked the aftermath of schizophrenia (defining only the "before" situation as normal), we have:

Men	Extra deaths	160 – 9/5*23 + 97 - 9/5*23	
Men	Extra deaths	160 – 41.4 + 97 - 41,4 =	174.2
Women	Extra deaths	254 - 9/5*36 +118 – 9/5*36	
Women	Extra deaths	254 – 64.8 + 118 – 64.8 =	242.4
Total, including the aftermath			**416.6**

The number of deaths from schizophrenia provoked by the malnutrition period is thus found to be somewhere between 190 and 417.

Discussion

The high death rate from malnutrition during the period 1999-2007 is surprising. Based on the Dutch experience a possible explanation is malnutrition and a feeling of insecurity for mothers during the First World War and during the worldwide economic crisis in 1929-1933.

Year of birth	**Age in 2003**
1914-1918	**85-89**
1929-1933	**70-74**

The cohort effect makes it possible to extrapolate health conditions over almost a century. The dataset was tested for cohort effects in order to find evidence for connecting schizophrenia in old age to events at birth. Surprisingly, this was not supported by a cohort model. The cohorts born in 1914-1918 and 1929-1933 showed no extra casualties in the (between) period from birth until 2003. However, this may partly be explained by the low number of observations.

It appears that the high death rate from malnutrition in 1999-2007 has its origin in the same period.
An alternative explanation for the appearance of the malnutrition period, namely that the registration method has changed over time, was contradicted by the fact that malnutrition and schizophrenia move parallel (in death rates) over the period.

Conclusion

The death rate from malnutrition was exceptionally high in Denmark during the period 1999 to 2007. The death rate from malnutrition was to a large extend associated with the death rate from schizophrenia, which likewise was unexpectedly frequent in the same period. This is a parallel to the Dutch famine experience, however, we find the association to exist for elderly people.
Based on regression analysis we conclude (supported by the time lag) that the malnutrition period provoked an excess of between 190 and 417 deaths from schizophrenia.
The study likewise shows the different consequences of malnutrition for men and women. Women react much stronger to malnutrition than men in relation to schizophrenia.
Cohort analysis was *not* able to link this outcome (death rates) to the period of birth or the period of death. This study finds that malnutrition has a severe effect on schizophrenic patients, not only prenatally but also in old age.

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Appendix

Figure 1A shows the distribution of deaths from malnutrition, and Figure 2A shows the distribution of deaths from schizophrenia, both for the years 1994-2012.

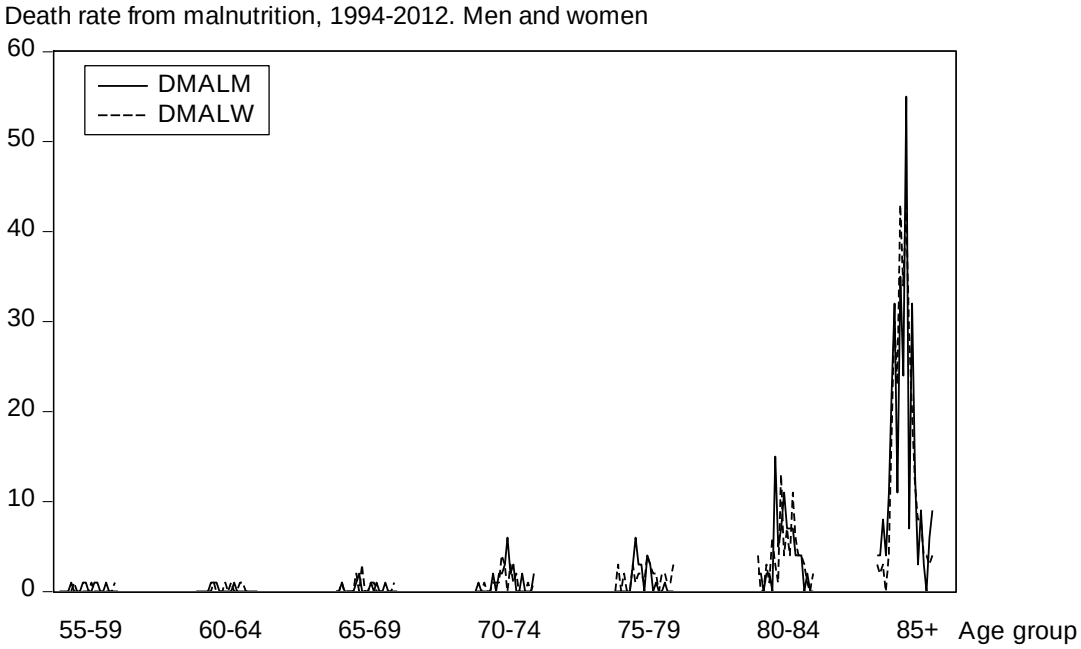

Figure 1A. The death rate from malnutrition based on data for Danish men and women for each age group from 55-59 to 85+ during the period 1994-2012.

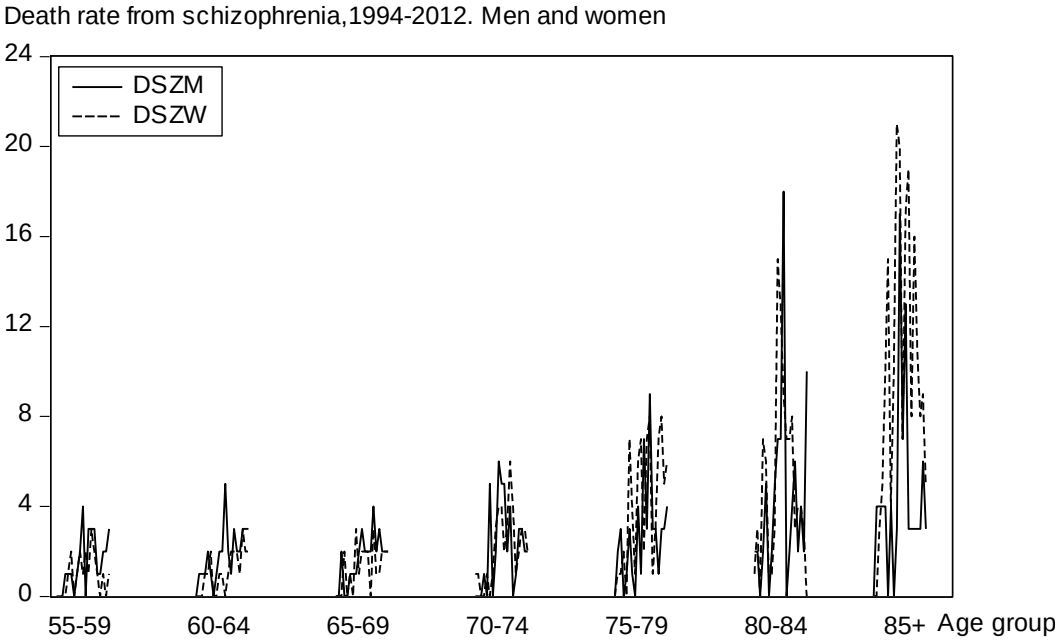

Figure 2A. The death rate from schizophrenia based on data for Danish men and women for each age group from 55-59 to 85+ during the period 1994-2012.

With increasing *age* the death rates for both men and women are clearly increasing. During the *period* 1994-2012, it looks as if the death rates peak around 2002-2004.

Figure 1A shows the association between the death rate from malnutrition and schizophrenia (sum for men and women).

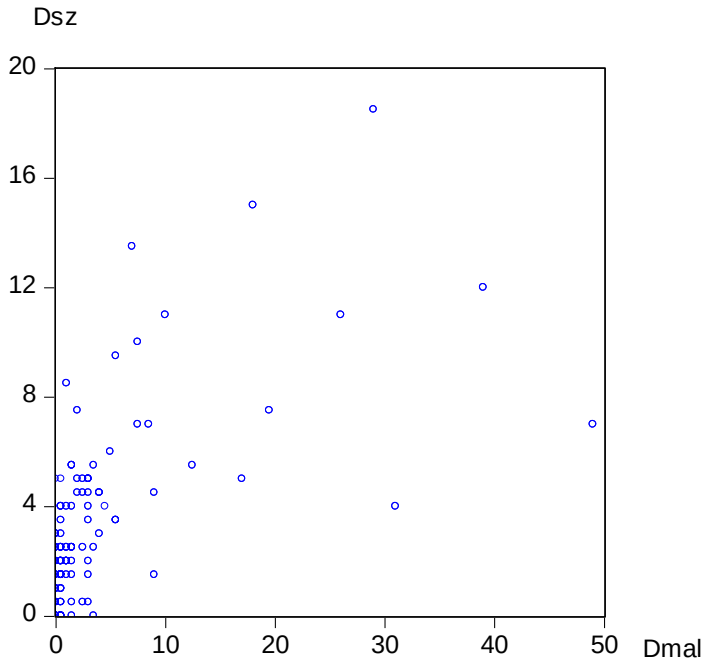

Figure 1A. Scatter diagram of association between malnutrition and schizophrenia.

As shown in Tables 1A and 2A the death rate from malnutrition as well as for schizophrenia is related to age. In fact, colloquially we can say that the two diseases are *caused* by age. Besides it is our theory that both diseases are *caused* by an unknown factor called X.

Table 1A. Death rates from malnutrition related to age, 1994-2012.

		Men				Women		
		1994-1998	1999-2007	2008-2012		1994-1998	1999-2007	2008-2012
55-59		**1**	**4**	**1**		0	2	0
60-64		**1**	3	0		0	3	2
65-69		1	5	**1**		1	7	0
70-74		1	**20**	**2**		1	16	1
75-79		0	**23**	1		5	20	6
80-84		8	**63**	10		8	55	**12**
85+		**20**	242	21		8	**255**	**27**

Table 2A. Death rates from schizophrenia related to age, 1994-2012.

		Men				Women		
		1994-1998	1999-2007	2008-2012		1994-1998	1999-2007	2008-2012
55-59		**2**	**17**	**9**		1	14	3
60-64		**5**	**17**	**13**		2	9	10
65-69		2	**18**	**11**		2	14	8
70-74		1	29	11		**3**	29	11
75-79		**6**	31	14		4	**43**	**29**
80-84		11	45	24		**17**	**69**	14
85+		12	54	18		8	**141**	**49**

The *association* between malnutrition and schizophrenia is modeled in the following way:

The supposed true *cause-relationship* models are:

$$Dsz = f_1(Age, X) \qquad (1A)$$

$$Dmal = f_2(Age, X) \qquad (2A)$$

X can be eliminated by transforming the equations to the *associations*:

$$Dsz = f_{1.1}(Age, Dmal) \qquad (3A)$$

$$Dmal = f_{2.1}(Age, Dsz) \qquad (4A)$$

Empirical calculations, however, show that Dmal leads Dsz.