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Vitamin D and the social aspects of disease

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Summary

Background: The strong association between socio-economic disadvantage and poor health in northern Europe and North America causes great public health concern but as the mechanism is not understood, government actions have been completely unsuccessful. The social gap continues to widen.
Aim: I propose that an important mechanism involved is relative deficiency of vitamin D in the socio-economically disadvantaged people.
Design: The evidence is presented by explaining apparent paradoxes, together with the analogies of geography, season and ethnicity. Vitamin D studies are also demonstrated.
Method: The picture is put together according to Hill's criteria of causation: strength of association, consistency of association, temporality, biological gradient, plausibility, coherence, experimentation and analogy.
Results: Hill's criteria of causation are met, acknowledging that they are pragmatic and not absolute. The associations between vitamin D deficiency and socio-economic deprivation are supported by analogies of geography, seasonality and ethnicity. There is also biological plausibility. The paradoxes of Albania and India show that health disadvantage and socio-economic disadvantage are not necessarily connected, if relative deficiency of vitamin D is the mediating biological factor.
Conclusion: The poor health and average early death of the socio-economically disadvantaged in the UK, together with the widening social gap of health, can be explained by relative deficiency of vitamin D. At present there is no explanation and attempts by government to close the social gap have failed. The understanding presented gives an important opportunity to improve the health disadvantages of the socio-economically disadvantaged.

The socio-economically disadvantaged people living in the cities of the UK, northern Europe and North America have relatively poor health, and I propose that an important and potentially correctable reason is a relatively low exposure to sunlight and thereby insufficiency of vitamin D.

The inequalities of health within society were obvious in the 19th and early 20th centuries. One of the objectives of the NHS, introduced in the UK in 1948, was to reduce the inequalities but by 1974 this had not been achieved and Townsend reported that the mortality gap was widening.[1] In 2010, the UK Office for National Statistics (ONS) reported that although the health of all social groups had improved, that of the socio-economically advantaged had improved at the greatest rate. In other words, the social gap had widened still further.[2]

The USA has a similar social gradient of disease and premature death, but this is compounded by an ethnic factor that is so obvious in the USA. The poor have worse health and earlier death than the affluent, especially if both poor and black.[3] However, a recent study showed that bad outcome after heart surgery is more the result of socio-economic disadvantage than ethnicity.[4]

Successive UK governments have set objectives to close the social gap, but how to achieve this has been a challenge. The simple explanation is that

the socio-economically underprivileged have poor health because they have little money, but how money converts into good health in the UK is far from clear. The possible importance of exposure to the sun and thereby vitamin D synthesis has not been officially acknowledged.

To demonstrate the potential importance of vitamin D, I will apply the causal criteria of Sir Austin Bradford Hill, namely: strength of association, consistency of association, temporality, biological gradient, plausibility, coherence, experimentation and analogy.[5] It is also necessary to examine paradoxes.

The social-health problem

Being relatively poor in the UK results in a surprisingly wide range of diseases and premature mortality, described well by Professor Sir Michael Marmot of the London School of Hygiene and Tropical Medicine. Marmot led the Whitehall study of 17 530 civil servants and noted that the 10-year mortality rate was three times higher in those with the lowest grading compared with the administrators who had the highest grading.[6] He and his co-authors concluded: ''For every cause of death except genito-urinary disease. . . . the two lower grades have higher mortality risks than the two higher grades. For nearly every cause there is a step-wise relation between grade and mortality.'' The specific diseases noted in this study included coronary heart disease (CHD), lung cancer, other cancers, stroke, bronchitis, accidents and suicide. On re-investigation 10 years later, there was found to be an overall improvement but increasing divergence.[7]

The same phenomenon was shown in Sweden, with a mortality risk in the unskilled workers twice that in the professional/executives group.[8] In Sweden and in England and Wales the prevalence of reported long-term illness was higher in the socio-economically disadvantaged, with a 3-fold gradient across social groups.[9] The plight of the long-term unemployed was not considered in these studies, probably because of very low unemployment rates at that time.

The UK Office of National Statistics (ONS) tells us that in 2005 a man living in a prosperous location would be expected to live to an average age of 77.4 years and would have a healthy life expectancy of 66.2 years, whereas a man in one of the least prosperous locations of the UK would be expected to live on average to 71.4 years and have a healthy life expectancy of just 49.4 years.[10]

Historically, rickets and tuberculosis were more common in the poor, and emerged in particular in the workers of the new industrial cities. Glasgow was perhaps the world's most important industrial city at the end of the 19th century. Its population developed perhaps the highest incidence of rickets and tuberculosis, and a century later the highest incidence of coronary heart disease.[11]

It was first thought that CHD was most likely to occur in the business executive, leading to the philosophy of work blaming. It became clear later that coronary events and mortality (including very early mortality) were more common in the socio-economically disadvantaged.[12,13] This has generally been interpreted as victim blaming, that the poor are responsible for their own poor health because of their behaviour, especially cigarette smoking and dietary characteristics.[14] Heart failure was also found to be more common in the socio-economically disadvantaged (7.2 vs. 6.4 per 1000 population) with a reduced survival (mean 2.8 vs. 3.5 years).[15]

Lung cancer is more common in the socio-economically disadvantaged,[6] but this is only in part the result of more cigarettes smoked. A study of 4913 men in Denmark identified that for a given number of cigarettes smoked over a long period of time, the risk of dying from lung cancer was three times higher in the most socio-economically disadvantaged group compared to those who were least disadvantaged.[16] Full adjustments were made for factors such as age and inhalation habit. Socio-economic disadvantage must be acting through a biological factor to produce such a dramatic difference in mortality rate. This factor has not yet been defined.

Death rates from several other cancers are greater in the socio-economically disadvantaged.[6] Not only are cancers more common in this group but survival is worse. This has been demonstrated in the UK for all cancers, there being a gradient of survival from the most affluent to the most deprived.[17] The 5-year survival of malignant melanoma is 10% less in the socio-economically disadvantaged,[17] with better survival known to be in those with higher blood levels of vitamin D.[18]

Diabetes also has a social distribution in favour of the affluent. A study from Liverpool investigated the variation of diabetes prevalence in the various localities within the city. It demonstrated a gradient, the prevalence of diabetes increasing with socio-economic disadvantage.[19] Peptic ulcer mortality has also been shown to be two or three times greater in the socio-economically disadvantaged, both in the USA and in England and Wales.[20]

It has been pointed out from Canada that the 'poverty is a greater predictor of heart disease than risk factors such as smoking, obesity, stress, or blood cholesterol concentrations'.[21] It appears therefore

that being socio-economically disadvantaged does not lead to a specific disease but that it makes individuals susceptible to a number of diseases, and it leads to a worse prognosis. It is as though body defence mechanisms are somehow impaired.

The poverty paradoxes

In northern countries poverty is associated with poor health whereas in sunny southern countries this does not appear to be the case.

For example, Albania has the lowest per capita income in Europe and a high infant mortality rate (greater than 40 deaths per 1000 live births compared to less than 10 in the UK). But Albania has one of the lowest mortality rates for CHD in Europe, similar to Greece, Italy and Portugal.[22] The low cardiovascular mortality in these countries has been attributed to a Mediterranean diet but when this is seen in context with other geographical data it seems likely that the Mediterranean climate itself may have benefits.

A poverty paradox was also observed in studies comparing Scotland and India in the early years of the 20th century. Dr HS Hutchison together with his assistant SJ Shah, undertook a particularly detailed and important study in the Nasik district of the Bombay Presidency.[23] A house-to-house survey identified rickets to be present in 13.7% of children in Class 1 Hindu families and 10.2% of Class 1 Moslem families. This compared with 0.3% of children in the poor Class 2 Hindu families and 2.7% of Class 2 Moslem families. They also noted tuberculosis to be rampant in the wealthy families and rare in the poor families. Their interpretation was that the better health of the poor families was the result of outdoor activity and fresh air, whereas the women in particular in wealthy families were able to practice purdah and stay indoors. Dr Hutchinson had undertaken his studies in response to detailed studies of rickets and tuberculosis in Glasgow undertaken by Dr Margaret Ferguson, who was working for the Medical Research Council.[24] Dr Ferguson had found that rickets and tuberculosis were particularly common in the poor in Glasgow and frequently co-existed. Whereas in India lack of outdoor activity in clean air was considered to be the cause of the serious health problems in the wealthy, in Glasgow this was a characteristic of the poor.

Further evidence for the poverty paradox comes from a study conducted in India almost a century later. In this case the subject was diabetes, and it was found to much more common in those who were working, educated, prosperous and living in an urban environment, but rare in the illiterate and poor.[25] This is the opposite of what is found in the UK.[19]

We can see therefore that whereas in the UK and other northern latitude countries (Sweden, Canada, USA) the socio-economically disadvantaged have the worst health, in Albania they do not have a health disadvantage and in India they have in some respects the best health. In other words, whereas poverty is clearly associated with increased ill health in northern latitudes, it does not have this association in sunny countries closer to the equator.

The wide range of diseases found to excess among the socio-economically disadvantaged in northern countries suggests that it might be futile to look for a common cause. It might be more productive if we were to search for a common susceptibility factor that would lead to the suppression of body defence mechanisms. Three analogies will help us to understand the high incidence of disease in the socio-economic disadvantaged in northern Europe and North America.

Evidence from geography

It is known that latitude of residence is associated with health risk. Within the UK there is a gradient of risk of death from CHD with minimum mortality rate in the south-east and maximum in north-west of England, in Scotland and in Northern Ireland.[26] This cannot be explained on the basis of diet or other conventional factors.[27] Within France there is a similar latitude effect for deaths from myocardial infarction (MI), with the age-adjusted mortality rate being higher in Lille (21 per 1000) compared with Toulouse (11 per 1000), while Strasbourg (18 per 1000) takes an intermediate position in both latitude and mortality rate.[28] Within Europe there is a mortality gradient from the south to the north-west, with maximum mortality in Scotland and Finland.[29] The variation cannot be explained on the basis of diet. The most detailed study compared middle-aged men in Belfast with those of Toulouse. The health differences were striking, with much higher mortality rates from all causes, CHD and cancer in Belfast.[30] Apart from a higher rate of cigarette smoking among middle-aged men in Toulouse, there were no significant dietary or social patterns.[28] Simply living in Toulouse rather than Belfast appeared to deliver a health advantage. And it is not red wine: evidence from the Albanian paradox tells us that the country with the lowest wine consumption Europe is among those with the lowest CHD mortality rate.

An obvious factor explaining the influence of latitude on health is the sunlight energy reaching

ground level, and this of course determines the synthesis of vitamin D in the skin. It is interesting to note that in the USA there is an inverse relationship between altitude of residence and cardiovascular disease.[31,32] UVB which promotes synthesis of vitamin D in the skin is absorbed by the atmosphere and so increases in strength with altitude. This evidence supports the view that sunlight, acting via vitamin D, promotes cardiovascular health.

Cancers also have an incidence related to latitude, first identified in North America in 1941. As latitude of residence increased from 10–30 to 50–60 degrees north, the mortality rate due to cancer increased by a factor of 2.5.[33] Death rates from breast and colon cancer show a gradient increase from the south of Europe to the north.[34] Lifetime risk of developing adenocarcinoma of the oesophagus is maximal in Scotland, reducing by 60% in France and the USA, with England and the Netherlands in intermediate positions.[35] Survival of men from cancer is better in the south of England than in the north,[36] also specifically from colon cancer.[17]

Within the UK there is an additive effect of social class and geography, as identified in the 2001 Report of the Chief Medical Officer of the Department of Health.[37] The age-standardized death rate in the north-west compared with the south-east for a person in social Class I was only minimally higher. But the gap widened with progression along the social scale. In social Class V the age-standardized death rate was twice as high in the north-west compared with the south-east, 1080 vs. 540. Mortality in Scotland is higher in all social classes than it is in England, and a number of diseases, notably multiple sclerosis, are more common in Scotland than in England.[38]

The analogy of geography strengthens the proposal that relative deficiency of vitamin D is responsible for a high incidence of several diseases and that it may account for much ill health of the socio-economically disadvantaged.

Evidence from seasonality

The second important physical factor is the variation of illness, disease and death throughout the year, and there are many examples of this. Excess deaths in the winter months are particularly well recorded, mainly because death is more accurately measured than illness.[39] It is recorded in many temperate countries in both hemispheres.[40]

Specific diseases identified as having a higher incidence or mortality rate in the winter include respiratory illnesses and CHD.[41] Tuberculosis has its peak incidence in the early spring, when the minimum levels of vitamin D allow its activation.[42] The spring peaks of tuberculosis notifications in India are more obvious in northern states, where there is an overall higher incidence,[43] again suggesting a vitamin D effect. In the first half of the 20th century in western Scotland there was an increased incidence of perforated peptic ulcer during the winter.[44]

There are some lesser known and perhaps surprising influences of season on health. An autumn or early winter birth following late gestation during the summer gives the offspring a significantly reduced risk of developing multiple sclerosis[45] and diabetes[46] in later life, as well as a later age of menopause.[47]

The analogy of season again suggests an association between vitamin D insufficiency and ill health supporting the proposal that relative deficiency of vitamin D is responsible for much ill health of the socio-economic disadvantaged in high latitude countries.

Evidence from ethnicity

Ethnicity is an important factor determining life expectancy and the incidence of a wide range of diseases, including CHD, diabetes, chronic renal failure, tuberculosis, rickets and osteomalacia. The major ethnic groups at risk in North America and Europe are South Asians, African Blacks and Caribbean Blacks. In the UK the incidence of tuberculosis is much higher in all these ethnic groups than the national average, in recent years it has been especially high in African Blacks as a result of AIDS.[48] Rickets is still seen in both ethnic Black and South Asian children.[49,50] They share a high incidence of diabetes[51] and also chronic renal failure independent of diabetes,[52] which in both ethnic groups is linked to low blood levels of vitamin D.[53] The high incidence of death from CHD in both groups is a serious problem. In ethnic South Asians in the UK it is a greater problem in the second generation immigrants.[54] Skin pigmentation is an obvious common factor between these ethnic groups, and the reduced efficiency of vitamin D synthesis by pigmented skin[55] suggests that vitamin D deficiency might be critical.

There is also an additive effect of ethnicity and geography. Within Great Britain it is men living in Scotland who have the highest CHD risk, but among these it is the international migrants (mainly from South Asia) within Scotland who have the highest risk of all, 50% higher than the Scottish average and five times higher than those immigrants who settled in the south of England.[56]

The analogy of ethnicity strengthens the proposal that relative deficiency of vitamin D is responsible for poor health of the socio-economically disadvantaged.

Vitamin D studies

Blood levels of vitamin D are no longer just a research tool but part of clinical practice, leading to an increasing awareness of the extent and significance of vitamin D deficiency. The results of important recent studies have received little attention.

In a USA study, the all-cause standardized mortality risk of the lowest vitamin D quartile was 80% higher than the highest quartile.[57] The lowest quartile had a blood level of vitamin D as 25(OH)D <40 nmol/l (17.8 ng/ml) and the highest quartile >70 nmol/l (32.1 ng/ml). The overall range is higher than in UK studies, reflecting the fact that the vitamin D levels are lower in the UK. This may be expected because the UK is much further north, New York being on the same latitude as Madrid.

A UK study also used quartiles and provided a great deal of social information.[58] The social classification was the usual I–V but in addition identified the unemployed, known to have the worst health. Profound vitamin D deficiency was defined, as in clinical practice, as 25(OH)D <25 nmol/l (<10 ng/ml). In the winter it was found in 25% of the unemployed, twice that of social Classes I and II. It is remarkable and of great concern that one quarter of the unemployed had such profound deficiency of vitamin D during the winter months, and about 8% during the summer. It is at this level of vitamin D that osteomalacia can be expected to occur.

The amount of time spent out of doors is important in determining adequacy of vitamin D levels. The mean summer level of vitamin D in those spending <30 min per day out of doors in the UK was found to be 50 nmol/l (20 ng/ml) compared to 65 nmol/l (28 ng/ml) in those spending >4 h per day out of doors with a gradient between these two extremes.[58] The low vitamin D levels of poor people can be explained by the observation that many of them spend less time outdoors: 'The poorest spend around 11 hours per week more than the richest watching television.... A cultural underclass might be developing as those on low incomes are restricted to the cheaper entertainment of television while those on higher incomes take advantage of other leisure activities'.[56] Television viewing is also associated with low levels of vitamin D, most obvious in the summer months, and once again there is a gradient effect.[59]

A north/south gradient in vitamin D deficiency is found in the British Isles. Profound vitamin D deficiency was found in 23.5% of the population sample in Scotland in the winter, compared with 12.5% in the south of England. In the summer the corresponding results were 8.3% and 2.7%.[58]

The observation of a health gradient within France[28] and comparison between Toulouse and Belfast[30] did not include vitamin D measurements or assessments. This was an unfortunate omission but vitamin D measurements within France have been performed subsequently. The result is as expected, that vitamin D levels correspond to latitude, with the highest levels in the south of France, the lowest in the north and a gradient between the two extremes.[60] The highest morbidity and mortality rates are found where the blood levels of vitamin D are lowest.

The social and physical geography of vitamin D levels generally match observations of health data. The seasonal effect on vitamin D levels also matches the seasonal variation in illness and mortality. The UK peak mean vitamin D in September was found to be 68 nmol/l (29 ng/ml), falling to 32 nmol/l (13 ng/ml) minimum in February.[58]

Finally the ethnic dimension. There are many reports of the re-emergence of rickets in the UK[49] and the USA,[50] usually in South Asian or Black ethnic children. Vitamin D deficiency is well established in these groups, a significant proportion of whom are socio-economically disadvantaged. Studies of vitamin D status have shown their blood levels to be particularly low. For example in a US study, 86% of white-skinned people had a blood level >70 nmol/l (>30 ng/ml) compared to only 4% in Black and 3% in Mexican Americans.[57]

Behavioural factors

The analogies between the geographic, social and ethnic patterns of illness cannot be ignored, and are suggestive of a common factor—vitamin D deficiency. There are obviously overlaps between ethnicity and socio-economic disadvantage, both in Europe and North America. Poor survival following cardiac surgery in the USA suggests that social factors are much more important than skin colour.[4] If vitamin D is the key factor then this observation is entirely plausible. There is however some controversy as to the efficiency of vitamin D synthesis in pigmented and non-pigmented skin. Recent carefully controlled research suggests that pigmented skin might have an equal ability to synthesize vitamin D as white skin.[61] In other words it is possible that vitamin D deficiency in South Asians and Blacks

in the UK and North America is due not just to skin pigmentation but also to behavioural factors of deliberate or cultural sun avoidance, as appears to be the case with the white socio-economically disadvantaged.

Perhaps maximizing sun exposure to the skin is genetically determined behaviour in white-skinned people. It is obvious however that dark-skinned people have no incentive to sit or lie in the sun to develop a tan. They are culturally adapted to cover the skin so as to protect themselves from the equatorial sun, and Moslem women have religious/cultural pressures to cover their skin almost completely. Hindus are usually vegetarian and obtain little or no dietary vitamin D, and this has been considered to be the reason for the excess risk of tuberculosis in Hindus compared to Moslems in London.[62]

It is the enforced behaviour of the socio-economically disadvantaged in the UK and other northern latitude countries that leads to little sun exposure and therefore vitamin D deficiency. Residence is likely to be in inner city areas with more atmospheric pollution. Housing is likely to be without a garden (having a garden is associated with higher vitamin D levels[63]) and there is unlikely to be the opportunity for outdoor leisure or a usable local park. The families particularly of the long-term unemployed will be unlikely to have access to the countryside or appropriate clothing to blend into this social environment. Leisure is likely to be indoors, focussed on the television. There is unlikely to be sufficient money for holidays in the sun, even in the present era of unprecedented opportunities for travel. Relative deficiency of vitamin D is thus inevitable.

Hill's criteria

So far Hill's criteria have been met. I have demonstrated the strength of associations between socio-economic deprivation, poor health with premature death and vitamin D deficiency. I have demonstrated the consistency of association and a biological gradient of effect. I have provided analogies of the geography and seasonality of vitamin D deficiency and a variety of illness linked to it. I have also demonstrated the important ethnic dimension of interactions between poor health and vitamin D deficiency, which are similar to those of socio-economic disadvantage.

Temporality is incomplete at the present time as widespread blood testing for vitamin D is only just becoming available. We have seen that blood levels of vitamin D are associated with life expectancy.[57] We know that the lowest blood levels of vitamin D are associated with the highest risk of subsequent multiple sclerosis,[64] and similarly associated with the subsequent development of colorectal cancer.[65]

There are other measures of temporality. We know from previous observational studies that a low dietary intake of vitamin D is associated with a subsequent increased incidence of disease, for example multiple sclerosis.[66] We also know that vitamin D supplement in only minimal dose provides future protection against low birth weight,[67] diabetes,[68,69] multiple sclerosis,[66] prostate cancer (ultraviolet radiation exposure),[70] colorectal cancer,[71] and it improves outcome from lung cancer following surgery, with an additional beneficial effect from diagnosis and treatment during the summer.[72] What is not yet known is whether vitamin D supplements given to the socio-economically disadvantaged, in a dose adequate to optimize blood levels, will close the social gap. This is the potential for future research.

The synthesis of 7-dehydrocholesterol (7-DHC) by primitive organisms such as plankton became a fundamental step in evolution. By a physical process a single bond of this molecule is split by the action of ultraviolet radiation from the sun to form vitamin D. Its wide-ranging effects are only just being appreciated but they include not just bone development but immune competence,[73] control of malignant process[74] and modulation of gene expression.[73,75]

The model presented is coherent and plausible. I do not suggest that vitamin D deficiency causes directly any disease other than rickets and osteomalacia, but it does lead to a form of immunodeficiency syndrome, by no means as severe as that caused by the human immunodeficiency virus (HIV), but much more common. This leads to susceptibility to a number of disease processes—acute infections, chronic infections, inflammatory diseases and several cancers. If we wish to improve resistance so as to minimize disease then attention to vitamin D deficiency should be a priority. This would be particularly important if we wish to close the social health gap, something that has failed spectacularly in the past 60 years.

Hill's final criterion is experimentation. This is generally considered to be the randomized controlled trial, but this will only take place if there is a plausible basis for it, effectively meaning that the other criteria have been met. It is only this that will ultimately determine if the social gap can be closed by giving attention to vitamin D, starting during gestation. The difficulty would be placebo control with informed consent, knowing that vitamin D is a natural vitamin component of food and not a drug, and that low blood levels are associated with significant health disadvantage. Clinical trials of drug treatment

are well established, usually after the introduction and use of the pharmaceutical agent, but disease prevention by a natural food component presents a much greater organizational challenge.[76] A safe and effective dose of vitamin D would be 2 000iu per day,[77] but a trial should ideally involve adjusting the vitamin D supplement given to an individual so as to achieve a target blood level of 100–150 nmol/l (40–60 ng/ml).

Nature has provided us with an experimental model—vitamin D receptor (VDR) polymorphisms. Vitamin D in its fully activated form calcitriol $1,25(OH)_2D$ is a hormone that combines with VDRs, complex intracellular proteins that are genetically encoded, creating a heterodimer that activates vitamin D-responsive elements (VDREs) concerned with gene expression. This is particularly important within T-lymphocytes leading to a rapid defence process in response to infection.[73] If defective VDR polymorphisms are inherited, then although the blood level of vitamin D might be ideal the effects of vitamin D deficiency will be seen. The most obvious and well recognized are vitamin D resistant rickets and osteomalacia. However several other conditions are associated with VDR polymorphisms and these include tuberculosis,[78,79] advanced prostate cancer,[80] occult hepatitis B virus infection,[81] Crohn's disease,[82] colon cancer in ulcerative colitis.[83] Such experiments of nature, by virtue of determination at the moment of conception, provide temporality to complete Hill's criteria.

Conclusion

Conventional thinking provides no answer to the poor health of the socio-economically disadvantaged. Marmot, who has done so much to identify the problem, suggests that the reason is lack of perceived status within peer group and within society.[84,85] Although this sounds superficially attractive, it is based on psychological models which themselves are very doubtful. The link between 'lack of status', disturbed physiology and pathology lacks plausibility—there is no obvious mechanism based on existing scientific principles, and Hill's criteria are far from fulfilled. It is an untestable hypothesis, pseudoscience.[86]

There have been in the past attempts to identify a common cause for the so-called diseases of western civilization, including CHD, stroke, diabetes and cancers. The principle was 'association is a clue to causation',[87] and the suggested culprit was diet, in particular the industrial refining of carbohydrate. This idea was superficially attractive and had an effect on eating patterns. However it lacked the power to explain so much and it had to compete with the diet-cholesterol-heart hypothesis, despite the many paradoxes and shortcomings of the latter. Associations can be more than coincidence. For example the increased risks of various cancers with pre-existing diabetes, and their worse outcome, are not easily understood, but in a recent review the social dimension and the possible role of vitamin D were not considered.[88]

It must be remembered that in science there is no such thing as absolute truth and Hill's criteria are not absolute. Science works by paradigms, models of understanding that are the most coherent and plausible at the time, models that explain most observed phenomena, and which have the fewest paradoxes. The social divergence of health and premature death is at present in the pre-paradigm era: there is no understanding and there has been a total failure of helpful intervention. I propose on the evidence presented that relative vitamin D deficiency is the major reason for the widening social gap of health in the UK. There are of course other behavioural factors such as drug-related deaths and accidents that have other explanations, but these are not so readily recognized or reversible.[89] This is the challenge for the future, but today it is possible to identify and correct vitamin D deficiency. This could be met by population-based vitamin D supplement, but ideally it should be targeted and corrected on an individualized basis, as with diabetes and hypertension.

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