A Multicountry Ecologic Study of Risk and Risk Reduction Factors for Prostate Cancer Mortality

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Abstract

Objective: The objective of this research is to identify and determine the relative importance of dietary and environmental risk and risk reduction factors for prostate cancer mortality.

Materials and Methods: A multicountry ecologic approach was used in multivariate regression analyses with prostate cancer mortality rates and dietary factors and solar ultraviolet-B (UV-B) radiation. Prostate cancer mortality rates for 32 predominantly Caucasian countries for the late 1990s were obtained from the World Health Organization. Dietary supply data were obtained from the Food and Agriculture Organization. Annual solar UV-B dose data were obtained from European ground stations and used to estimate values elsewhere. Linear and multiple linear regression analyses were conducted for all 32 countries as well as the 20 European countries.

Results: The strongest risk factor for prostate cancer mortality was animal products, with the nonfat portion of milk and alcohol being somewhat weaker; the strongest risk reduction factors were onions, other protective vegetable products (excluding alcohol, oils, and sweeteners), and solar UV-B radiation. Dietary data for 1979–81 yielded the highest correlations.

Conclusions: These results are consistent with insulin-like growth factor-I (IGF-I), being an important risk factor for prostate cancer, with alcohol and calcium being less important risk factors, and with allium family vegetables, and, to a lesser extent, vitamin D being important risk reduction factors. These results should provide guidance for additional studies on dietary and environmental links to prostate cancer.

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Keywords: Alcohol; Allium; Calcium; Insulin-like growth factor-I (IGF-I); Lycopene; Milk; Prostate cancer; UV-B radiation; Vitamin D

1. Introduction

Environmental factors such as diet and smoking are generally thought to account for 60–70% of cancer incidence and mortality [1,2]. Since smoking is not a risk factor for prostate cancer [3], the role of diet is likely to be quite high. Indeed, prostate cancer mortality (PrCM) rates in northern Europe are approximately 5 times higher than in Hong Kong, Iran, Japan, and Turkey [4]. Thus, a better understanding of dietary links to prostate cancer may help to prevent this disease.

Studies on dietary links to prostate cancer generally find that animal products [5–11] are risk factors, while vegetable products other than alcohol, oils and sweeteners are risk reduction factors [9,11,12–15]. In addition, solar UV-B radiation (280–320 nm) and vitamin D are often identified as risk reduction factors [16–21]. Some micronutrients such as S-cysteinyl compounds in allium family vegetables [22,23], lycopene, abundant in tomatoes [24–28], vitamin E [29–33] and selenium [21,32] are also risk reduction factors, while
calcium is a risk factor [33,34]. Recent reviews are useful in this regard [11,35,36], including one review of the proposed mechanisms of action of various dietary substances [37]. Although there is consensus agreement on the roles of some dietary factors with respect to prostate cancer, there are inconsistent findings regarding other factors and little apparent consensus on the relative importance of the various factors as judged by comparing recent reviews [35–37].

The large range of values for many dietary components in international diets is a potential advantage for the ecologic approach compared with the case-control and cohort approaches, an advantage that can help determine the relative importance of many of the dietary and environmental risk and risk reduction factors for prostate cancer.

### 2. Materials and methods

Prostate cancer mortality data for the late 1990s were obtained from the World Health Organization [4]. Data are given by country and age-adjusted to the world population age distribution. The values are based on the best and latest data available at the time for each country along with models for the country and region. While incidence data are also available, they were judged not to be of sufficient quality to use in this study: incidence data for many countries are modeled rather than obtained directly, and several countries have artificially high incidence values due to recent introduction of the prostate specific antigen (PSA) screening test [38]. However, PSA screening may [39] or may not [40] have much effect on mortality rates; it is assumed that the mortality data used are independent of PSA testing rates.

Data for 32 countries with predominantly Caucasian populations were included (see Table 1). The reason for restricting the study to Caucasian countries is that genetic and lifestyle factors that vary by ethnic origin are difficult to model. Additional criteria for inclusion were: population greater than 3.5 million, average life expectancy >60 years, and dietary data available for 1979–81. European countries were also used in a separate analysis.

Dietary supply data were obtained from the Food and Agriculture Food Balance Sheets [41]. The factors included in the analyses were alcohol, beer, wine, cereals, eggs, animal product energy, vegetable product energy, total energy, animal fat, vegetable fat, fish fat, fruit, legumes (beans), meat, nonfat portion of milk, onions, animal protein, vegetable protein, sweeteners (added sugar), tomatoes, UV-B radiation, and vegetables. In addition, the study considered some combinations of individual dietary factors, such as “protective vegetable products” (all vegetable products less alcohol, fats and oils, and sweeteners). Care was taken to ensure that the various factors used in any regression were not included twice; thus, when vegetable products were used with vegetables or onions, they were removed from the protective vegetable product category. The 3-year data for these factors for every five years from 1965 to 1990 as well as 1962 were tabulated. Vegetable product energy divided by total energy supply was also included.

Solar UV-B (280–320 nm) data were obtained from annual average data reported for a number of European ground stations [42]. The spectral sensitivity of the UV-B sensor used is closely linked to the erythemal action spectrum. UV-B data for 11 countries from 28° to 69° latitude were used to generate a graph of dose versus latitude and fit with a quadratic curve. The regression equations are:

\[ UV-B (\text{MJ m}^{-2}) = 9.07 - 0.246 \times \text{lat. (deg.)} + 0.00182 \times (\text{lat. (deg.)})^2 \]

(adjusted \( r^2 = 0.95, \) F-test (ANOVA) = 94, \( p < 0.001 \))

Data on tobacco smoking were obtained from [43].

The minimum, median, mean, and maximum values for the factors used in this study are given in Table 2. Given the large variety of countries included in the study, there are wide ranges for most of the factors, thereby helping to insure that the factors will have sufficient variability to yield significant correlations.

Linear and multiple linear regression analyses were performed. Preliminary results indicated that dietary data from 1979 to 1981 yielded the highest adjusted \( r^2 \) value, which is consistent with the long time lag from cancer initiation to discovery or death [44]. Thus, data for 1979–81 were used for all subsequent analyses, except for tomatoes and onions for which 1984–86 data were the closest data to 1980 available. Generally, a large number of factors were initially included in the analysis; those with low \( p \) values were generally omitted in subsequent analyses. However, when a factor was found to be important for one group of countries and outcome, it was reintroduced into the analysis for other countries and outcomes.

### 3. Results

The most significant regression results for PrCM are given in Tables 3 and 4 and Figs. 1 and 2. For European countries, onions had the highest (inverse) correlation with prostate cancer, with other protective vegetable products having a similar correlation. Energy derived from animal products, animal fat less fish fat, and nonfat milk were weakly correlated with PrCM. Solar UV-B radiation and tomatoes were weakly (inversely) correlated with PrCM. Lung cancer reduces life expectancy, thus plays an indirect role in reducing the risk of PrCM.

For the predominantly Caucasian countries, animal products had the highest correlation as a risk factor for...
Table 2
Ranges of the variables used in this study for both predominantly Caucasian and European countries

<table>
<thead>
<tr>
<th>Factor</th>
<th>Minimum Eur/Cauc</th>
<th>Median Eur/Cauc</th>
<th>Mean Eur/Cauc</th>
<th>Maximum Eur/Cauc</th>
</tr>
</thead>
<tbody>
<tr>
<td>Prostate cancer mortality (cases/100k/year)</td>
<td>7.3/1.9</td>
<td>18.7/17.9</td>
<td>17.7/14.9</td>
<td>27.3/27.3</td>
</tr>
<tr>
<td>Alcohol (kcal/day)</td>
<td>95/0</td>
<td>208/180</td>
<td>203/156</td>
<td>301/301</td>
</tr>
<tr>
<td>Cereals (kcal/day)</td>
<td>602/592</td>
<td>765/859</td>
<td>906/944</td>
<td>1602/1835</td>
</tr>
<tr>
<td>Energy, animal (kcal/day)</td>
<td>556/214</td>
<td>1163/1067</td>
<td>1108/1012</td>
<td>1521/1812</td>
</tr>
<tr>
<td>Energy, vegetable/total</td>
<td>0.56/0.55</td>
<td>0.64/0.66</td>
<td>0.67/0.71</td>
<td>0.81/0.93</td>
</tr>
<tr>
<td>Fat, animal (g/day)</td>
<td>40/15</td>
<td>92/76</td>
<td>86/72</td>
<td>134/134</td>
</tr>
<tr>
<td>Nonfat milk (kcal/day)</td>
<td>61/22</td>
<td>152/137</td>
<td>161/143</td>
<td>262/262</td>
</tr>
<tr>
<td>Onions (kcal/day)</td>
<td>0/0</td>
<td>77</td>
<td>7/9</td>
<td>21/23</td>
</tr>
<tr>
<td>Protein, animal (g/day)</td>
<td>37/11</td>
<td>60/57</td>
<td>57/51</td>
<td>75/75</td>
</tr>
<tr>
<td>Protein, vegetable (g/day)</td>
<td>30/30</td>
<td>37/39</td>
<td>41/43</td>
<td>61/70</td>
</tr>
<tr>
<td>Skin reflectance at 425 nm (%)</td>
<td>29/15</td>
<td>35/28</td>
<td>34/31</td>
<td>39/39</td>
</tr>
<tr>
<td>Sweeteners (kcal/day)</td>
<td>280/255</td>
<td>397/376</td>
<td>380/377</td>
<td>455/573</td>
</tr>
<tr>
<td>Tomatoes (kcal/day)</td>
<td>4/4</td>
<td>9/13</td>
<td>16/17</td>
<td>73/73</td>
</tr>
<tr>
<td>Vegetable products less alcohol, fats,</td>
<td>884/884</td>
<td>1086/1204</td>
<td>1220/1308</td>
<td>1827/2099</td>
</tr>
<tr>
<td>sweeteners (kcal/day)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Vegetable products less alcohol, fats,</td>
<td>880/880</td>
<td>1212/1190</td>
<td>1082/1312</td>
<td>1818/2099</td>
</tr>
<tr>
<td>onions, sweeteners (kcal/day)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>UV-B radiation (MJ m$^{-2}$/year)</td>
<td>0.8/0.8</td>
<td>1.3/1.6</td>
<td>1.4/1.8</td>
<td>2.3/3.6</td>
</tr>
</tbody>
</table>

The dietary supply data are for 1979–81 except for onions and tomatoes, which are for 1984–6.

Table 3
Regression results for prostate cancer for 20 European countries

<table>
<thead>
<tr>
<th>Adj. $r^2$, $F$, $*$</th>
<th>1st term ($t$, $p$)</th>
<th>2nd term ($t$, $p$)</th>
<th>3rd term ($t$, $p$)</th>
</tr>
</thead>
<tbody>
<tr>
<td>0.83, 46, * fail CV</td>
<td>Onions, −5.2, *</td>
<td>V-AFOS, −4.1, *</td>
<td>Lung cancer, −0.8, 0.423</td>
</tr>
<tr>
<td>0.82, 30, *</td>
<td>Onions, −5.1, *</td>
<td>V-AFOS, −3.9, *</td>
<td></td>
</tr>
<tr>
<td>0.81, 41, *</td>
<td>Onions, −5.9, *</td>
<td>Cereals, −3.7, 0.002</td>
<td></td>
</tr>
<tr>
<td>0.77, 32, *</td>
<td>Onions, −4.6, *</td>
<td>Energy: vegetable/total, −2.9, 0.010</td>
<td></td>
</tr>
<tr>
<td>0.72, 26, *</td>
<td>Onions, −5.3, *</td>
<td>Animal fat − fish fat, 2.1, 0.052</td>
<td></td>
</tr>
<tr>
<td>0.67, 40, *</td>
<td>Onions, −6.3, *</td>
<td></td>
<td></td>
</tr>
<tr>
<td>0.59, 28, *</td>
<td>V-AFS, −5.3, *</td>
<td></td>
<td></td>
</tr>
<tr>
<td>0.55, 13, *</td>
<td>Energy, vegetable, −2.6, 0.017</td>
<td>Energy, animal, 1.1, 0.282</td>
<td></td>
</tr>
<tr>
<td>0.40, 14, 0.002</td>
<td>UV-B, −3.7, 0.002</td>
<td></td>
<td></td>
</tr>
<tr>
<td>0.32, 17, 0.006</td>
<td>Log(tomatoes), −3.1, 0.006</td>
<td></td>
<td></td>
</tr>
<tr>
<td>0.30, 9, 0.007</td>
<td>Animal fat − fish fat, 3.0, 0.007</td>
<td></td>
<td></td>
</tr>
<tr>
<td>0.30, 9, 0.008</td>
<td>Nonfat milk, 3.0, 0.008</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

The factors are ordered by their relative importance (adjusted $r^2$, then the $F$-test). The $t$ and $p$ values for each factor are given. The relative importance of each factor in the multiple regression is proportional to $t^2$.* $p < 0.001$; CV: constant variance test; UV-B: solar UV-B dose; V-AF(O)S: vegetable products less alcohol, fat, (onions), sweeteners.

Table 4
Regression results for prostate cancer for 32 countries (31 when alcohol or onions are included) with predominantly Caucasian inhabitants, as in Table 3

<table>
<thead>
<tr>
<th>Adj. $r^2$, $F$, *</th>
<th>1st term ($t$, $p$)</th>
<th>2nd term ($t$, $p$)</th>
<th>3rd term ($t$, $p$)</th>
<th>4th term ($t$, $p$)</th>
</tr>
</thead>
<tbody>
<tr>
<td>0.87, 68</td>
<td>Energy, animal, 4.1, *</td>
<td>Onions, −3.8, *</td>
<td>V-AFOS, −2.4, 0.023</td>
<td></td>
</tr>
<tr>
<td>0.87, 65</td>
<td>Onions, −4.2, *</td>
<td>Energy, animal, 3.8, *</td>
<td>Cereals, −2.2, 0.038</td>
<td></td>
</tr>
<tr>
<td>0.87, 49</td>
<td>Onions, −3.7, *</td>
<td>Nonfat milk, 3.2, 0.004</td>
<td>Alcohol, 2.8, 0.009</td>
<td>V-AFOS, −2.7, 0.011</td>
</tr>
<tr>
<td>0.86, 94</td>
<td>Energy: vegetable/total, −8.0, 0.001</td>
<td>Onions, −4.2, *</td>
<td></td>
<td></td>
</tr>
<tr>
<td>0.85, 59 fail N</td>
<td>Onions, −3.7, 0.001</td>
<td>Animal fat − fish fat, 3.5, 0.002</td>
<td>V-AFOS, −3.1, 0.004</td>
<td></td>
</tr>
<tr>
<td>0.78, 111 fail N</td>
<td>Energy, vegetable/total, −11, *</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>0.78, 55 fail N</td>
<td>Energy, animal, 5.6, *</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>0.52, 34</td>
<td>Nonfat milk, 5.9, *</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>0.51, 33</td>
<td>UV-B, −5.8, *</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>0.47, 27</td>
<td>Log(alcohol), 5.2, *</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>0.46, 27</td>
<td>Sweeteners, 5.2, *</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>0.34, 17</td>
<td>Log(tomatoes), −4.1, *</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

$p < 0.001$; N: normality test; UV-B: solar UV-B dose; V-AFOS: vegetable products less alcohol, fat, (onions), sweeteners.
4. Discussion

These regression results are in general agreement with the literature but deviate in some important ways, such as relative importance. The most important factors in this study, animal products, nonfat milk and calcium, onions, and protective vegetables, are supported in the literature: animal products [5–11]; NFM and calcium [33,34,45,46]; vegetable products [9,11,47–53], and allium family vegetables [22,23,54]. The role of animal products in the etiology of prostate cancer is likely largely mediated through IGF-I. IGF-I is an important risk factor for prostate cancer [55,56] and other cancers [57].

The strength of onions in this study is very interesting given that allium family vegetables have received little attention as a risk reduction factor for prostate cancer [22,23]. If the result is not due to confounding with other factors, it would suggest that one or more compounds found in allium family vegetables can be very effective in reducing the risk of prostate cancer. A quick check of the correlation between onions and cancers at other sites found two other cancers with statistically significant results—multiple myeloma and pancreatic cancer, both of which have strong positive latitudinal gradients. These findings warrant further investigation.

However, the protective role of lycopene-rich vegetables such as tomatoes [24–28,46] was found to be relatively unimportant, even though it was found in a previous ecologic study by the author [45]. A recent cohort study also failed to find a significant inverse correlation between serum lycopene and prostate cancer incidence [30]. What is particularly interesting in this regard is that while lycopene and/or tomatoes have been linked to prostate cancer in 108 papers according to PubMed (July 20, 2003), there are only 12 reports of garlic or allium family vegetables in relation to prostate cancer, yet they may be much more effective in reducing the risk of prostate cancer.

The likely reason that animal products, nonfat milk, and alcohol had significant correlations with PrCM for Caucasian countries but not European countries is that the range of values for these factors is much higher for all the Caucasian countries than for the European countries: increases of 20% for nonfat milk; 46% for alcohol; and 68% for animal products. The range of PrCM was 27% greater for Caucasian countries than for European countries. The Caucasian country results are considered more reliable than those for the European countries since any epidemiologic approach is limited by statistical variations in the values of the factors as well as by any unmodeled factors.
Note, too, that some factors such as sweeteners, tomatoes and UV-B radiation have positive or negative correlations with PrCM when considered alone but not in multiple linear regressions with the most important factors. While these factors have been associated with prostate cancer in case-control and/or cohort studies, these factors appear to correlated with other factors that are more important in the etiology of prostate cancer, thus masking their roles in this ecologic study.

The inverse correlation between other protective vegetable products, the bulk of which is cereals, and PrCM is interesting. A number of papers exist discussing vegetable products, the bulk of which is cereals, and prostate cancer, thus masking their roles in this ecologic study. However, such papers generally examine the role of potentially anticarcinogenic micronutrients in whole grains. It is interesting to note that one paper combining the results of three case-control studies found an inverse relation between refined cereals and prostate cancer, but a positive correlation with whole grains [63]. A likely reason that cereals are protective against PrCM is that carbohydrates generate less IGF-I than do fat and protein [64–67]. Recent studies also found that IGF-I is correlated with dietary milk protein [68,69].

Solar UV-B radiation, through production of vitamin D, has been identified as a risk reduction factor for prostate cancer since the early 1990s [16], and confirmed in a number of studies [17–21,43,44], but not all [70]. The prostate gland is also able to convert serum 25(OH)D3 to the active form 1,25(OH)2D3 [71]. The mechanisms whereby vitamin D may reduce the risk of prostate cancer have been discussed [72–76]. They include blocking cell progression and metastasis, increasing cell differentiation and apoptosis of cancer cells, reducing angiogenesis, and reducing parathyroid hormone related peptide secretion (see [76]). Solar UV-B radiation, through production of vitamin D, has also been identified as risk reduction factors for over a dozen cancers in all [20; Grant, submitted]. Parathyroid hormone has been identified as a possible prostate cancer risk factor [77], which is reduced by vitamin D. Microscopic cancer is found in the prostate beginning by age 30 in about 20% of men [78]. This fact may explain why the amount of solar UV-B radiation exposure early in life [21] and diet 15 years prior to mortality play roles in the etiology of prostate cancer.

Note that serum vitamin D has several sources including solar UV-B radiation, diet (e.g., fatty fish and fortified milk), and supplements. Supplement users in the U.S. Prostate Cancer Prevention Trial obtained 61-64% of vitamin D from supplements [79]. Men in the U.S. who do not use supplements obtain the vast majority of their vitamin D from solar UV-B radiation [80]. In some countries, such as Japan, most of the vitamin D comes from seafood [81]. In Scandinavian countries, a large fraction of vitamin D comes from diet and supplements, as judged by wintertime serum vitamin D insufficiency in Europe that decreases with latitude [82]. Finally, lifestyle, urban or rural residence, occupation, and skin pigmentation affect the generation of vitamin D from solar UV-B radiation.

The correlation of nonfat portion of milk with PrCM is in agreement with previous cohort [33,34,83,84] and ecologic [6,45] studies. However, the mechanism of milk’s effect remains elusive. It has been hypothesized that calcium is the component linking dairy products as a risk factor for prostate cancer [33,34]; bone mass was nearly significantly associated with prostate cancer incidence in a recent study [85]. However, the mechanism involved is elusive. The suggestion that calcium leads to increased risk of prostate cancer through reduction of circulating serum vitamin D metabolites [10,84,86] seems to be incorrect. Why, for example, would this mechanism apply to prostate cancer but not to digestive tract cancers as well? Calcium is a risk reduction factor for digestive tract cancers [87,88], as is vitamin D [20,87]. A more likely explanation is that milk and calcium increase the production of IGF-I. Recent studies also found that IGF-I is correlated with dietary milk protein [65,66,89] and calcium [89] and inversely correlated with lycopene [89].

Another hypothesis regarding the role of calcium in the etiology of prostate cancer was presented in [15]. It is hypothesized that prostate cancer cells are osteo-mimetic [90] potentially explaining why prostate cancer metastasizes preferentially to the skeleton and elicits osteoblastic reactions [91]. Recent research has shown that osteoblasts produce soluble factors that contribute to the progression of prostate cancer skeletal metastases [92]. Bisphosphonates inhibit tumor induced osteoclastic bone resorption and have been shown to be effective in reducing the risk of prostate cancer metastases [93]. See, too, recent reviews [94,95]. Elevated extracellular calcium concentrations stimulate parathyroid hormone-related protein (PTHrP) secretion form normal and malignant cells [96]. In addition, PTHrP increases prostate tumor growth in vivo [97] through both autocrine/paracrine and intracrine pathways [98] and stimulates the production of interleukin-8, which may stimulate prostate cancer growth by promoting angiogenesis [99]. Note that vitamin D can down regulate PTHrP gene transcription [100].
In this study, alcohol consumption is weakly correlated with PrCM for the Caucasian countries, but not for the European countries. The Caucasian countries include some Middle-Eastern countries where alcohol is not consumed. While a meta-analysis of 33 studies regarding alcohol consumption and prostate cancer published prior to July 1998 concluded that the relative risk of 1.02 per drink was not statistically significant [101], several papers published since then have reported that alcohol was a significant risk factor for prostate cancer [102–104]. Thus, this study provides modest support for alcohol as a risk factor.

4.1. Evaluation of the ecologic approach

The ecologic approach is considered the least reliable epidemiologic approach [1], which may not be entirely justified. Any epidemiologic approach is subject to error due to whether such factors as the important dietary, environmental, genetic, healthcare, and lifestyle parameters are included, and whether the values are accurate and appropriate for those considered. For example, dietary fiber was identified as an important risk reduction factor for colon cancer by the ecologic approach in the early 1970s [105] and confirmed in the late 1990s [106]. Data from the Nurses’ Health Study have been reported with the conclusion that dietary fiber does not reduce the risk of colon cancer [107]. Two recent studies concluded that dietary fiber does, indeed, reduce the risk of colon cancer, but that about 30 g of fiber per day are required for optimal results [108,109]. The likely reason that the Nurses’ Health Study is unable to confirm findings from other studies is that the range of dietary variables is too limited, along with some possible error associated with the dietary recall approach [110].

While the ecologic approach generally does well regarding macronutrients, it does not do as well with micronutrients such as selenium and vitamin E, for pesticides [111], or for exercise and obesity since the data are not generally available. Also, genetic factors that vary within racial groups of populations, e.g., polymorphism of the insulin gene [112], are difficult. However, recent studies of genetic factors and prostate cancer have concluded that it is likely that a number of genetic factors, each contributing a small amount to PrCM risk, are involved [113–115], so there is, perhaps, a lesser chance that a latitudinal gradient exists. Even for a disease with a large genetic component with a latitudinal gradient [116], Alzheimer’s disease, an ecologic study was first to identify the dietary factors that were important risk and risk reduction factors [117], later confirmed in a cohort study [118].

In summary, the ecologic approach can yield results of quality comparable to those of case-control and cohort approaches; each has certain strengths and limitations that are becoming better appreciated.

5. Conclusions

A number of dietary and environmental links to prostate cancer mortality rates were determined and their relative importance assessed. Animal products, the nonfat portion of milk, and alcohol were associated with risk, while onions, other protective vegetable products (primarily cereals), and solar UV-B radiation were associated with risk reduction. IGF-I seems to be the primary way dietary factors are mediated for prostate cancer risk, and are related to the roles of carbohydrate, fat, protein and total energy consumption in its production. Various compounds in vegetables and vitamin D reduce the risk of prostate cancer.

The results presented in this paper can be checked using data from ongoing case control or cohort studies or dietary modification studies. There are dietary modification studies in progress that may help to confirm or refute the present findings such as one regarding a low-fat diet [119]. However, since the lag between diet and disease outcome appears to be about 15–20 years for prostate cancer, dietary modification studies may be slow in yielding definitive results.

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