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# Badanie wzorów żywienia w kontekście ryzyka raka płuc u mężczyzn z regionu Polski północno-wschodniej

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# A study of dietary patterns in the context of lung cancer risk in men from the region of northeastern Poland

PhD thesis

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Olsztyn 2023

*Składam serdeczne podziękowania*
*Pani prof. dr hab. Lidii Wądołowskiej*
*za opiekę merytoryczną, poświęcony czas i cenne wskazówki*
*w przygotowaniu niniejszej pracy*
*oraz za możliwość doskonalenia warsztatu badawczego.*

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*oraz za wsparcie*
*udzielone mi podczas realizacji badań.*

*Pragnę podziękować wszystkim uczestnikom badań,*
*bez których ich wykonanie nie byłoby możliwe.*

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2. **Hawrysz I.**, Wadolowska L., Slowinska M.A., Biernacki M., Czerwinska A., Golota J.J. Lung cancer risk in men and compliance with 2018 WCRF/AICR cancer prevention recommendations. *Nutrients* 2022, *14*(20), 4295; doi.org/10.3390/nu14204295 (**140 pkt.; IF=6,706**).

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## 1. Streszczenie

Celem pracy była kompleksowa ocena współzależności między wzorami żywieni oraz przestrzeganiem rekomendacji dotyczących profilaktyki raka płuc i ryzykiem raka płuc u mężczyzn.

Badanie typu kliniczno-kontrolnego zrealizowano u 439 mężczyzn w wieku 45-80 lat z północno-wschodniej Polski. Próbę kliniczną stanowiło 187 mężczyzn z nowo zdiagnozowanym rakiem płuc, a próbę kontrolną 252 mężczyzn bez tego rodzaju raka. Dane zbierano w latach 2013-2017.

Dane żywieniowe dotyczące spożycia 62 grup żywności zebrano za pomocą zwalidowanego kwestionariusza częstotliwości spożycia żywności o akronimie FFQ-6® w wywiadzie przeprowadzonym indywidualnie. Do identyfikacji wzorów żywienia (DP) zastosowano dwa podejścia – oparte na danych i oparte na założeniach wstępnych (predefiniowane). Wzory żywienia oparte na danych zidentyfikowano za pomocą analizy głównych składowych (PCA-DP). Zastosowano dwa rodzaje predefiniowanych wzorów żywienia: (i) wskaźnik dostosowania diety do diety śródziemnomorskiej (MED) w polskiej adaptacji ('Polish-aMED®'), opracowany przez Krusińską i in. [1], (ii) wskaźnik dostosowania diety do rekomendacji WCRF/AICR z roku 2018 dotyczących profilaktyki raka ('Wskaźnik WCRF/AICR'), który zaadaptowano do rekomendacji profilaktyki raka płuc ('Wskaźnik Ad-LC WCRF/AICR'), opracowany na potrzeby niniejszych badań.

PCA-DP zidentyfikowano przez włączenie do analizy danych dotyczących częstotliwości spożycia 62 grup żywności po ich logicznym połączeniu w 23 grupy żywności. Wzory nazwano adekwatnie do najczęściej spożywanych grup żywności, tj. tych, które wykazywały największą korelację ze wzorem żywienia jako zbiorem cech. Zidentyfikowano trzy PCA-DP: 'Rozsądny', 'Zachodni-tradycyjny' i 'Słodki-mleczny'. Dla każdego PCA-DP oddzielnie określono dostosowanie diety mężczyzn do wzoru w oparciu o podział tercylowy, w pierwszym tercylu znalazły się osoby o małym dostosowaniu do wzoru, w drugim tercylu – o średnim, a w trzecim tercylu – o dużym dostosowaniu do wzoru.

Wskaźnik diety śródziemnomorskiej obejmował wyróżniki tradycyjnej diety śródziemnomorskiej – skorelowane z nim dodatnio (owoce, warzywa, pełnoziarniste produkty zbożowe, ryby, rośliny strączkowe, orzechy i ziarna, iloraz częstotliwości spożycia tłuszczów roślinnych do tłuszczów zwierzęcych) i ujemnie (mięso czerwone i jego przetwory, nadużywanie alkoholu). Jego adaptacja polegała na zastąpieniu oliwy z oliwek olejami roślinnymi podczas obliczania ilorazu częstotliwości spożycia tłuszczów roślinnych do tłuszczów zwierzęcych, aby odzwierciedlić specyfikę polskiej diety oraz przyjęcia innego systemu wyznaczania progów odcięcia (opartego na medianie), respektując ideę i zasady konstrukcji oryginalnego wskaźnika. Wskaźnik 'Polish-aMED®' obliczono jako sumę punktów. Oryginalny 'Wskaźnik WCRF/AICR' składał się z ośmiu wyróżników stanowiących rekomendacje, a jego adaptacja polegała na usunięciu rekomendacji dotyczącej kobiet i dodaniu rekomendacji dotyczącej palenia tytoniu (wyrażonego w paczko-latach) oraz zmianie wszystkich kryteriów i/lub systemu punktowania ośmiu wyróżników, respektując

ideę i zasady konstrukcji oryginalnego wskaźnika. ‘Wskaźnik Ad-LC WCRF/AICR’ obliczono w obliczono jako sumę punktów. W obu wskaźnikach po ich adaptacji nie zmienił się zakres punktów ('Polish-aMED®' zakres: 0-9 pkt; ‘Ad-LC WCRF/AICR’ zakres: 0-8 pkt) określający stopień dostosowania diety do wskaźnika (predefiniowanego DP). Wyniki intepretowano w następujący sposób: im więcej punktów, tym lepsze dostosowanie diety do predefiniowanego DP.

W analizie statystycznej wykorzystano analizę regresji logistycznej (bez adjustacji i z adjustacją na czynniki zakłócające) do oszacowania ilorazu szans (OR) i 95% przedziału ufności (95%CI) ryzyka raka płuc w zależności od stopnia dostosowania diety mężczyzn do wzorów żywienia. W analizie uwzględniono palenie tytoniu, które było podstawą do pogrupowania mężczyzn na: nigdy nie palących (0 paczko-lat), umiarkowanie palących i dużo palących (>11 paczko-lat).

Wykazano, że u mężczyzn o dużym dostosowaniu diety do wzoru ‘Rozsądnego’ ryzyko raka płuc było mniejsze o 28% (adjustowany OR=0,72; 95%CI 0,53–0,96) w porównaniu z mężczyznami o małym dostosowaniu diety do tego wzoru. U mężczyzn umiarkowanie palących i o dużym dostosowaniu diety do wzoru ‘Rozsądnego’ ryzyko raka płuc było mniejsze o 41% (adjustowany OR=0,59; 95%CI 0,39–0,90) w porównaniu z mężczyznami niepalącymi i o małym dostosowaniu diety do tego wzoru. Wzory ‘Zachodni-tradycyjny’ i ‘Słodki-mleczny’ nie były istotnie związane z ryzykiem raka płuc u mężczyzn umiarkowanie palących i mężczyzn ogółem (bez uwzględnienia statusu palenia). U mężczyzn dużo palących żaden z trzech PCA-DP nie był istotnie związany z ryzykiem raka płuc. Mniejsze ryzyko raka płuc o 66% (adjustowany OR=0,34; 95%CI 0,15–0,76) mieli mężczyźni umiarkowanie palący z dużym dostosowaniem diety do ‘Polish-aMED®’ (7-9 pkt), a mniejsze o 65% (adjustowany OR=0,35; 95%CI 0,18–0,65) mężczyźni umiarkowanie palący ze średnim dostosowaniem diety do ‘Polish-aMED®’ (4-6 pkt) w porównaniu do mężczyzn niepalących i z małym dostosowaniem diety (0–3 pkt). U mężczyzn dużo palących żaden z poziomów dostosowania ich diety do ‘Polish-aMED®’ nie był istotnie związany z ryzykiem raka płuc.

Ryzyko raka płuc w pełnym modelu, uwzględniającym wszystkie rekomendacje ujęte we ‘Wskaźniku Ad-LC WCRF/AICR’, było mniejsze o 47% (adjustowany OR=0,53; 95%CI 0,32-0,88) u osób o większej zgodności z rekomendacjami w porównaniu do osób o mniejszej zgodności z rekomendacjami. Każdy 1-punktowy wzrost ‘Wskaźnika Ad-LC WCRF/AICR’ zmniejszał ryzyko raka płuc u mężczyzn o 34% (OR=0,66; 95%CI 0,45-0,95).

Jeden wyróżnik ‘Wskaźnika Ad-LC WCRF/AICR’, tj. rekomendacja „Ogranicz palenie”, był niezależnie związany z mniejszym ryzykiem raka płuc u mężczyzn, bez względu na zestaw czynników zakłócających użyty do adjustacji. Ryzyko raka płuc u mężczyzn nigdy nie palących było mniejsze o 87% (adjustowany OR=0,13; 95%CI 0,04–0,37), a u mężczyzn umiarkowanie palących o 45% (adjustowany OR=0,55; 95%CI 0,33–0,91) w porównaniu z mężczyznami dużo palącymi. Analiza związku między ryzykiem raka płuc i różnymi kombinacjami kilku pojedynczych rekomendacji ‘Wskaźnika Ad-LC WCRF/AICR’ wykazała, że większe dostosowanie do kombinacji trzech lub więcej rekomendacji zmniejszało ryzyko raka płuc o 39% do 66% u osób o większej (6-8 pkt) zgodności z rekomendacjami w porównaniu do osób o mniejszej (0-2 pkt) zgodności z rekomendacjami.

Badania wykazały, że prozdrowotne wzory żywienia, w tym dieta śródziemnomorska o polskim profilu, mogą sprzyjać zmniejszeniu ryzyka raka płuc u mężczyzn, w tym u mężczyzn umiarkowanie palących, chociaż nie zostało to potwierdzone u mężczyzn dużo palących. Potwierdzono wcześniejsze dowody, że ograniczenie palenia zmniejsza ryzyko raka płuc u mężczyzn i dostarczono nowych danych, że palenie tytoniu jest niezależnym czynnikiem ryzyka raka płuc, a także współdziałającym z dietą, przy czym w przypadku umiarkowanego poziomu palenia tytoniu prozdrowotna dieta działa protekcyjnie.

Po raz pierwszy wykazano znaczenie przestrzegania wielu rekomendacji jednocześnie w zmniejszaniu ryzyka raka płuc u mężczyzn. Dostarczono mocnych przesłanek wskazujących, że przestrzeganie jednocześnie co najmniej trzech rekomendacji dotyczących profilaktyki raka płuc, odnoszących się do diety, stylu życia lub zawartości tłuszczu w ciele, może zapobiegać rakowi płuc u mężczyzn, pomimo obecności innych niezdrowych zachowań.

## 1. Summary

The aim of the study was to comprehensively assess the association between dietary patterns, adherence to recommendations regarding lung cancer prevention, and the risk of lung cancer in men.

This case-control study was conducted in 439 men aged 45-80 years from north-eastern Poland. The clinical sample consisted of 187 men with newly diagnosed lung cancer, and the control sample consisted of 252 men without lung cancer. Data was collected from 2013 to 2017.

Dietary data on the consumption of 62 food groups was collected using a validated food frequency questionnaire FFQ-6® during individual face-to-face interviews. Two approaches were used to identify dietary patterns (DPs) – data-driven and hypothesis-driven (predefined). Data-driven dietary patterns were identified using the Principal Components Analysis (PCA-DP). Two types of predefined dietary patterns were used: (i) Mediterranean diet (MED) score in the Polish adaptation ('Polish-aMED®'), developed by Krusinska et al. [1], (ii) dietary adherence to WCRF/AICR cancer prevention recommendations ('WCRF/AICR Score'), adapted to the recommendation of lung cancer prevention ('Ad-LC WCRF/AICR Score'), developed for the aim of this study.

The PCA-DPs were identified by including data on the frequency of consumption of 62 food groups after being combined into 23 food groups. These patterns were named adequately to the most frequently consumed food groups, which were most correlated with each dietary pattern. Three dietary patterns were identified: 'Prudent', 'Westernized Traditional' and 'Sweet Dairy'. For each of PCA-DPs adherence to the pattern was determined separately based on the tertile distribution; with the bottom tertile representing low adherence to the pattern and the upper tertile representing high adherence to the pattern.

The Mediterranean diet score included the characteristics of the traditional Mediterranean diet - positively correlated with fruits, vegetables, wholegrain cereal products, fish, legumes, nuts and grains, the ratio of the frequency of consumption of vegetable fats to animal fats, and negatively correlated with red meat and meat products, abuse of alcohol. The Polish adaptation regarding replacing olive oil with vegetable oils when calculating the quotient of the frequency of consumption of vegetable fats to animal fats to reflect the specificity of the Polish diet and adopting a different system for determining cut-off thresholds (based on the median), respecting the idea and construction principles of the original score. The 'Polish-aMED®' score was calculated as a sum of points. The original 'WCRF/AICR Score' consisted of eight components expressing recommendations. It was adapted by removing recommendations regarding women, adding a recommendation regarding smoking (expressed in pack-years), and changing all criteria and/or the scoring system of eight components, respecting the idea and construction principles of the original score. 'Ad-LC WCRF/AICR Score' was calculated as a sum of points. In both component's scores, after their adaptation, the range of points did not change ('Polish-aMED®' range: 0-9 points; 'Ad-LC WCRF/AICR' range: 0-8 points) defining the degree of adherence to the diet to the score (predefined DP). The results were interpreted as follows: the higher the score indicates the better adherence of the diet to the predefined DP.

In the statistical analysis, logistic regression analysis (with and without adjustment for confounding factors) was used to estimate the odds ratio (OR) and the 95% confidence interval (95% CI) of lung cancer risk, depending on the degree of the adherence of men's diet to dietary patterns. The analysis included smoking, which was the basis for grouping men into: never smokers (0 pack-years), moderate smokers and heavy smokers (>11 pack-years).

Men with a high dietary adherence to the 'Prudent' pattern were shown to have a 28% lower risk of lung cancer (adjusted OR=0.72; 95%CI 0.53–0.96) compared to men with a low dietary adherence to the 'Prudent' pattern. Moderate smokers with a high 'Prudent' dietary adherence had a 41% lower risk of lung cancer (adjusted OR=0.59; 95%CI 0.39–0.90) compared to non-smokers and a low adherence to this pattern. The 'Western-Traditional' and 'Sweet-dairy' patterns were not significantly associated with the risk of lung cancer in moderate smokers and men overall (without taking into account smoking status). In heavy smokers, none of the three PCA-DPs were significantly associated with lung cancer risk. The risk of lung cancer was lower by 66% (adjusted OR=0.34; 95%CI 0.15–0.76) in moderate smokers with a high adherence of the diet to 'Polish-aMED®' (7-9 points), and lower by 65% (adjusted OR=0.35; 95%CI 0.18–0.65) in moderate smokers with moderate dietary adherence to 'Polish-aMED®' (4-6 points) compared to non-smokers with low dietary adherence (0-3 points). In heavy smokers, none of the levels of adherence of their diet to 'Polish-aMED®' was significantly associated with the risk of lung cancer.

The risk of lung cancer in the full model, taking into account all recommendations included in the 'Ad-LC WCRF/AICR Score', was lower by 47% (adjusted OR=0.53; 95%CI 0.32-0.88) in men with higher compliance with recommendations compared to people with lower compliance with recommendations. Each 1-point increase in the 'Ad-LC WCRF/AICR Score' reduced the risk of lung cancer in men by 34% (OR=0.66; 95%CI 0.45-0.95).

The recommendation 'limit smoking' of the as one of components 'Ad-LC WCRF/AICR Score' was independently associated with a lower risk of lung cancer in men, regardless of the set of confounding factors used for adjustment. The risk of lung cancer was by 87% lower in men who never smoked (adjusted OR=0.13; 95%CI 0.04–0.37) and by 45% lower in men who were moderate smokers (adjusted OR=0.55; 95% CI 0.33–0.91) compared to heavy smokers. An analysis of the association between the risk of lung cancer and various combinations of several single recommendations of the 'Ad-LC WCRF/AICR Score' showed that greater adherence to a combination of three or more recommendations reduced the risk of lung cancer by from 39% to 66% in men with higher (6-8 points) compliance to the recommendations compared to men with lower (0-2 points) compliance to the recommendations.

Studies have shown that healthy dietary patterns, including the Polish Mediterranean diet, may help reduce the risk of lung cancer in men, including moderate smokers, although this has not been confirmed in heavy smokers. Previous evidence has been confirmed that reducing smoking reduces the risk of lung cancer in men, and new evidence has been provided that smoking is an independent risk factor for lung cancer and also interacts with diet, with moderate levels of smoking being protected by a healthy diet. For the first time, the importance of adhering to multiple recommendations has been demonstrated in reducing the risk of lung cancer in men. There is strong evidence that adhering to at least three lung cancer

prevention recommendations related to diet, lifestyle or body fat can prevent lung cancer in men despite the presence of other unhealthy behaviors.

## 2. Wstęp

Szacuje się, że w 2018 roku na świecie 18 milionów ludzi zachorowało na nowotwory złośliwe, z tego 9,5 miliona dotyczyło mężczyzn i 8,5 miliona kobiet [2]. Rak jest drugą najczęstszą przyczyną zgonów na świecie (pierwsza to choroby układu krążenia) [3]. Rak płuc jest najczęstszą przyczyną zgonów z powodu raka u mężczyzn powyżej 40 roku życia oraz kobiet powyżej 60 roku życia [4]. Głównym powodem dużej śmiertelności tego rodzaju nowotworu jest późna diagnoza wynikająca z względnie długiego okresu bezobjawowego i dlatego jest on najczęściej wykrywany w zaawansowanym stadium choroby [5].

Etiologia raka jest wieloczynnikowa i obejmuje czynniki, które nie są modyfikowalne, takie jak: wiek, predyspozycje genetyczne i niektóre czynniki środowiskowe, podczas gdy styl życia, w tym: palenie tytoniu, aktywność fizyczna i dieta, są możliwe do zmiany [3, 4, 6, 7, 8]. Zarówno modyfikowalne, jak i niemodyfikowalne czynniki mogą zwiększać ryzyko wystąpienia raka płuc [8, 9]. Związek między paleniem tytoniu a rakiem płuc jest zdecydowanie najsilniejszym i najdłużej znanym modyfikowalnym czynnikiem stylu życia [10, 11]. Szacuje się, że około 90% przypadków raka płuc na świecie przypisuje się paleniu tytoniu (w tym również biernemu paleniu) [4, 7]. Palenie generuje ogromną ilość wolnych rodników i jest jednym z kluczowych źródeł stanu zapalnego oraz stresu oksydacyjnego. Skutki palenia można w pewnym stopniu zneutralizować poprzez spożywanie składników o właściwościach przeciwutleniających i przeciwzapalnych lub żywności zawierającej takie składniki [12]. Spożywanie żywności o wysokiej zawartości witamin antyoksydacyjnych, związków fenolowych, składników mineralnych i błonnika pokarmowego wpływa korzystnie na układ oddechowy [13, 14].

Według Światowego Funduszu Badań nad Rakiem (WCRF) [5, 15] istnieją mocne dowody na to, że przyjmowanie dużych dawek suplementów beta-karotenu (u obecnych i byłych palaczy) zwiększa ryzyko raka płuc. Natomiast spożywanie warzyw i owoców (u obecnych palaczy i byłych palaczy), żywności zawierającej retinol, beta-karoten i witaminę C (u obecnych palaczy) oraz żywności bogatej w izoflawony (u osób nigdy nie palących) może zmniejszać ryzyko raka płuc [5, 16, 17]. Dalsze dowody sugerują, że spożywanie czerwonego mięsa oraz produktów mięsnych i napojów alkoholowych może zwiększać ryzyko raka płuc [5, 18]. Wpływ innych grup żywności lub składników odżywczych na ryzyko raka płuc jest ograniczony i do tej pory nie wyciągnięto jednoznacznych wniosków o ich działaniu [5]. Dlatego WCRF/AICER postuluje, że ważna jest identyfikacja czynników żywieniowych, które mogą mieć znaczenie w profilaktyce raka, w tym raka płuc [5, 18]. Wiele wcześniejszych badań dotyczyło pojedynczych produktów lub składników odżywczych w celu oceny związku z rakiem płuc [18-25]. Jako że pojedyncze produkty lub składniki odżywcze są spożywane w kombinacjach i wchodzą ze sobą w interakcje w złożony sposób, ważna jest kompleksowa ocena wpływu całej diety na ryzyko choroby. W ocenie tej wykorzystuje się najczęściej analizę opartą na danych, w tym analizę głównych składowych (PCA) tworząc wzory żywienia (DP) [7, 28]. Drugim podejściem w ocenie wpływu całej diety są predefiniowane wzory żywienia, oparte na wcześniejszej wiedzy na temat wpływu składników żywności i stylu życia na zdrowie, czego przykładem może być wskaźnik diety śródziemnomorskiej (MED) oraz ‘Wskaźnik WCRF/AICR’. Światowy Fundusz Badań nad

Rakiem zwraca uwagę, że należy uzupełnić dotychczasową wiedzę na rzecz badań przesiewowych dotyczących czynników żywieniowych i stylu życia oraz ich wpływu na nowotwory złośliwe. Szczególnie ważne jest poznanie tej zależności w przypadku nowotworów uważanych za nie-dietozależne, tj. raka skóry czy raka płuc [8, 15]. W związku z tym niezwykle potrzebne są badania mające na celu poznanie przyczyn raka i zdefiniowanie skutecznych strategii wdrażania i utrzymywania zdrowego stylu życia w społeczeństwie.

## 3. Cel badań

W wielu badaniach analizowano związek między żywieniem i stylem życia a występowaniem raka, jednak żadne z nich nie dotyczyło mężczyzn z rakiem płuc mieszkających w Europie Środkowej i Wschodniej. Przeprowadzenie badań wśród tej grupy mężczyzn może wypełnić lukę wiedzy i dostarczyć nowych unikatowych informacji. Celem pracy była kompleksowa ocena współzależności między wzorami żywienia, przestrzeganiem rekomendacji dotyczących profilaktyki raka płuc i ryzykiem raka płuc u mężczyzn.

## 4. Metodyka badań

### *4.1. Pozwolenie Komisji Bioetycznej*

Protokół badania został zatwierdzony przez Komisję Bioetyczną Wydziału Nauk Medycznych Uniwersytetu Warmińsko-Mazurskiego w Olsztynie w dniu 2.10.2013 r. (Uchwała nr 29/2013). Przed przystąpieniem do badań każdy mężczyzna został poinformowany o celu badania i wyraził pisemną świadomą zgodę na udział w badaniu.

### *4.2. Organizacja badań i charakterystyka próby*

Badanie kliniczno-kontrolne przeprowadzono od października 2013 r. do sierpnia 2017 r. Kryteriami włączenia do badań były: (i) płeć męska, (ii) wiek ≥18 lat, zamieszkanie w północno-wschodniej Polsce, (iii) wykonana tomografia płuc i/lub badanie rentgenowskie oraz (iv) zgoda na udział w badaniu. Kompletne dane uzyskano od 439 mężczyzn w wieku od 45 do 80 lat (średnia 62,6; SD 7,2).

Próbę kliniczną stanowiło 187 mężczyzn z nowo zdiagnozowanym i potwierdzonym histologicznie pierwotnym rakiem płuc. Okres rozpoznania występowania raka, rekrutacji przypadków do badań i zbierania danych wynosił od 7 do 14 dni od diagnozy. Osoby chore w trakcie lub po aktywnym leczeniu raka płuc nie zostały zakwalifikowane do badania, ponieważ mogły nastąpić u tych osób zmiany nawyków żywieniowych lub stylu życia. Do badania nie kwalifikowali się mężczyźni, u których rozpoznano inny rodzaj raka, wtórnego raka płuc lub zmiany łagodne.

Próbę kontrolną stanowiło 252 mężczyzn, u których wykonano cyfrowe zdjęcie rentgenowskie (RTG) i/lub tomografię komputerową (TK) klatki piersiowej z wynikiem: braku zmian w płucach. Okres od wykluczenia raka do udziału w badaniu nie przekraczał 6 miesięcy. Osoby z grupy kontrolnej nie miały żadnych objawów klinicznych ani podejrzeń jakiegokolwiek innego rodzaju raka w swojej historii medycznej. Próba kontrolna składała się z mężczyzn rekrutowanych spośród tych, którzy uczestniczyli w krajowych programach badań przesiewowych w celu wczesnej diagnozy raka płuc.

### *4.3. Zbieranie danych*

Techniką wywiadu zebrano dane socjoekonomiczne oraz dotyczące żywienia, stosowania suplementów witaminowo-mineralnych i stylu życia (palenia tytoniu, spożywania alkoholu, aktywności fizycznej, narażenia zawodowego na czynniki ryzyka, np. w miejscu pracy), występowania raka płuc w rodzinie oraz innych czynników mających znaczenie w etiologii raka płuc. Wszystkie pytania dotyczące żywienia i stylu życia dotyczyły okresu 12 miesięcy przed rozpoznaniem raka płuc. Pytania dotyczące palenia tytoniu odnosiły się do przeszłości i teraźniejszości. Wywiad został przeprowadzony osobiście przez badacza, był szczegółowy i standaryzowany (użyto kwestionariuszy typu zamkniętego), a wszelkie niejasności były natychmiast wyjaśniane.

#### *4.3.1. Dane socjoekonomiczne*

Dane dotyczące miejsca zamieszkania, poziomu edukacji i sytuacji ekonomicznej mężczyzn zebrano korzystając z pytań kwestionariusza KomPAN® [28]. Na tej podstawie

określono ich status socjoekonomiczny (SES), który wyrażono jako wskaźnik SES. Wskaźnik SES obliczono jako sumę wartości liczbowych przypisanych kategoriom odpowiedzi każdej składowej SES, następnie zlogarytmowano. Mężczyzn podzielono na trzy grupy na podstawie rozkładu tercylowego w celu rozróżnienia respondentów o niskim, średnim i wysokim SES.

*4.3.2. Dane dotyczące stylu życia*

Korzystając z pytań kwestionariusza KomPAN® [28], mężczyźni zostali poproszeni o określenie swojej aktywności fizycznej w pracy i czasie wolnym przez wybranie jednej z trzech kategorii aktywności (niskiej, umiarkowanej, wysokiej). Każda z kategorii była szczegółowo objaśniona w kwestionariuszu i dostosowana do kontekstu (praca zawodowa vs rekreacja). Oba rodzaje aktywności fizycznej zostały połączone zgodnie z procedurą opracowania danych pochodzących z kwestionariusza KomPAN® [28] – utworzono trzy kategorie ogólnej aktywności fizycznej (niska, umiarkowana, wysoka).

Aby określić status palenia tytoniu, zebrano dane dotyczące aktualnego palenia, czasu trwania i intensywności palenia oraz czasu, jaki upłynął od zaprzestania palenia. Status palenia wyrażono w paczko-latach, który obliczono jako iloczyn liczby paczek papierosów wypalanych dziennie i liczby lat palenia przez daną osobę [29]. Mężczyzn podzielono na trzy grupy: osoby nigdy niepalące (0 paczko-lat), umiarkowanie palące i dużo palące (>11 paczko-lat). Podział ten uwzględniono w ocenie związku między wzorami żywienia a ryzykiem raka płuc.

*4.3.3. Czynniki zakłócające, masa i skład ciała*

Czynniki zakłócające zostały wybrane na podstawie literatury, jako czynniki odgrywające rolę w etiologii raka płuc [8]. Do tych czynników należały: wiek, wskaźnik masy ciała, status socjoekonomiczny, aktywność fizyczna, występowanie raka płuc w rodzinie, narażenie w miejscu pracy na czynniki ryzyka, np. azbest, stosowanie suplementów witaminowo-mineralnych.

Wykonano pomiary masy i wysokości ciała i obliczono wskaźnik masy ciała (BMI, $kg/m^2$). Pomiaru zawartości tkanki tłuszczowej (%) dokonano z wykorzystaniem interakcji w bliskiej podczerwieni (Futrex 6100/XL).

*4.4. Częstotliwość spożycia żywności*

Dane żywieniowe zebrano za pomocą zwalidowanego kwestionariusza częstotliwości spożycia żywności o akronimie FFQ-6® [30]. Pytania dotyczyły częstotliwości spożycia 62 grup żywności (z sześcioma kategoriami do wyboru) w ciągu ostatnich 12 miesięcy przed badaniem. Kategorie częstotliwości spożycia żywności przekształcono na częstotliwość dzienną (krotność/dzień) na podstawie wartości liczbowych przyporządkowanych poszczególnym kategoriom: „nigdy lub prawie nigdy" = 0 razy/dzień; „raz w miesiącu lub rzadziej" = 0,025 razy/dzień; „kilka razy w miesiącu" = 0,1 razy/dzień; „kilka razy w tygodniu" = 0,571 razy/dzień; „codziennie" = 1 razy/dzień; „kilka razy dziennie" = 2 razy/dzień [30]. Po przekształceniu danych uzyskanych dla 62 grup

żywności zagregowano je do 23 logicznych grup żywności (przez sumowanie częstotliwości spożycia).

W odniesieniu do alkoholu stworzono trzy kategorie spożycia etanolu (g) na podstawie danych o zwyczajowym spożyciu napojów alkoholowych: 0 etanolu dziennie (0 drinków/dzień), >0–≤28 g etanolu dziennie (do 2 drinków/dzień) oraz >28 etanolu dziennie (powyżej 2 drinków/dzień). Punkty odcięcia ustalono na podstawie literatury [9].

*4.5. Identyfikacja wzorów żywienia*

Do identyfikacji wzorów żywienia (DP) zastosowano dwa podejścia – oparte na danych i oparte na założeniach wstępnych (predefiniowane).

*4.5.1. Oparte na danych wzory żywienia*

Wzory żywienia oparte na danych (PCA-DP) zidentyfikowano za pomocą analizy głównych składowych (PCA). Do PCA włączono dane dotyczące częstotliwości spożycia 23 grup żywności. Składowe tworzące poszczególne wzory żywienia wybrano w oparciu o wartości ładunków czynnikowych >|0,3|. Wzory żywienia nazwano adekwatnie do najczęściej spożywanych grup żywności, tj. tych, które wykazywały największą korelację ze wzorem żywienia jako zbiorem cech. Zidentyfikowano trzy PCA-DP: 'Rozsądny', 'Zachodni-tradycyjny' i 'Słodki-mleczny', wyjaśniające łącznie 31% wariancji.

Wzór 'Rozsądny' charakteryzował się większą częstotliwością spożycia: produktów pełnoziarnistych, owoców, orzechów/ziaren, warzyw, ryb, roślin strączkowych i soków owocowych/warzywnych/warzywno-owocowych oraz mniejszą częstotliwością spożycia: rafinowanych produktów zbożowych, cukru/miodu/słodyczy. Wzór 'Zachodni-tradycyjny' charakteryzował się większą częstotliwością spożycia: czerwonego mięsa i jego przetworów, białego mięsa, ziemniaków, innych tłuszczów (np. margaryny, majonezu), warzyw, rafinowanych produktów zbożowych, słodzonych napojów/napojów energetyzujących, cukru/miodu/słodyczy. Wzór 'Słodki-mleczny' charakteryzował się większą częstotliwością spożycia: tłuszczów zwierzęcych, mleka, fermentowanych napojów mlecznych/twarogów, słodzonych napojów mlecznych/smakowych, serków homogenizowanych, jaj, serów, cukru/miodu/słodyczy, płatków śniadaniowych, rafinowanych produktów zbożowych, olejów roślinnych oraz suszonych owoców/przetworów owocowych, a mniejszą częstotliwością spożycia innych tłuszczów.

Dla każdego PCA-DP oddzielnie określono dostosowanie diety mężczyzn do wzoru w oparciu o podziały tercylowe. W pierwszym tercylu były osoby o małym dostosowaniu diety do wzoru, w drugim tercylu – o średnim, a w trzecim tercylu – o dużym dostosowaniu diety do wzoru.

*4.5.2. Predefiniowane wzory żywienia*

*4.5.2.1. Wskaźnik diety śródziemnomorskiej w polskiej adaptacji ('Wskaźnik Polish-aMED® ')*

Wskaźnik dostosowania diety do diety śródziemnomorskiej (MED) w polskiej adaptacji ('Wskaźnik Polish-aMED®') został opracowany przez Krusińską i in. [1]. MED obejmował wyróżniki tradycyjnej diety śródziemnomorskiej – skorelowane z nim dodatnio (owoce, warzywa, pełnoziarniste produkty zbożowe, ryby, rośliny strączkowe, orzechy/ziarna, iloraz częstotliwości spożycia tłuszczów roślinnych do tłuszczów

zwierzęcych) i ujemnie (mięso czerwone i jego przetwory, nadużywanie alkoholu). Jego adaptacja polegała na zastąpieniu oliwy z oliwek olejami roślinnymi podczas obliczania ilorazu częstotliwości spożycia tłuszczów roślinnych do tłuszczów zwierzęcych, aby odzwierciedlić specyfikę polskiej diety oraz przyjęcia innego systemu wyznaczania progów odcięcia (opartego na medianie), respektując ideę i zasady konstrukcji oryginalnego wskaźnika.

'Wskaźnik Polish-aMED®' obliczono jako sumę punktów (zakres 0-9), które przyznawano za częstotliwość spożycia powyżej mediany (po 1 pkt.) dla wymienionych powyżej sześciu grup żywności i ilorazu częstotliwości spożycia tłuszczów roślinnych do tłuszczów zwierzęcych. Dodatkowe punkty przyznano za częstotliwość spożycia czerwonego mięsa i jego przetworów poniżej mediany (1 pkt.) oraz za nie nadużywanie alkoholu (1 pkt.). Po adaptacji nie zmienił się zakres punktów określający stopień dostosowania diety do 'Wskaźnika Polish-aMED®'. Wyniki intepretowano w następujący sposób: im więcej punktów, tym lepsze dostosowanie diety do diety śródziemnomorskiej. Wyróżniono trzy poziomy dostosowania diety mężczyzn do 'Wskaźnika Polish-aMED®': małe (0-3 pkt.), średnie (4-6 pkt.) i duże (7-9 pkt.).

*4.5.2.2. Adaptowany wskaźnik profilaktyki raka płuc ('Wskaźnik Ad-LC WCRF/AICR')*

Oryginalny 'Wskaźnik WCRF/AICR' składał się z ośmiu wyróżników stanowiących rekomendacje, a jego adaptacja ('Wskaźnik Ad-LC WCRF/AICR') polegała na usunięciu rekomendacji dotyczącej kobiet i dodaniu rekomendacji dotyczącej palenia tytoniu (wyrażonego w paczko-latach) oraz zmianie wszystkich kryteriów i/lub systemu punktowania ośmiu wyróżników, respektując ideę i zasady konstrukcji oryginalnego wskaźnika. 'Wskaźnik Ad-LC WCRF/AICR' obejmował następujące wyróżniki, stanowiące rekomendacje w profilaktyce raka płuc:

(1) prawidłowa ilość tkanki tłuszczowej (która zastąpiła wyróżnik: prawidłowa masa ciała),
(2) aktywność fizyczna,
(3) spożywanie produktów pełnoziarnistych/warzyw/owoców/zbóż,
(4) ograniczenie spożycia żywności typu fast food/innej przetworzonej żywności bogatej w tłuszcze/skrobię/cukry,
(5) ograniczenie spożycia czerwonego/przetworzonego mięsa,
(6) ograniczenie spożycia napojów słodzonych cukrem,
(7) ograniczenie spożycia alkoholu,
(8) ograniczenie palenia.

'Wskaźnik Ad-LC WCRF/AICR' obliczono w następujący sposób: 1 pkt. przyznawano za spełnienie każdej rekomendacji, 0,5 pkt. za jej częściowe spełnienie i 0 pkt. za niespełnienie rekomendacji, postępując zgodnie z zasadami obliczania 'Wskaźnika WCRF/AICR' [9]. Po adaptacji nie zmienił się zakres punktów 'Wskaźnika Ad-LC WCRF/AICR' (0-8 pkt) określający stopień dostosowania diety do tego wskaźnika i przestrzegania rekomendacji odnoszących się do profilaktyki raka płuc. Wyniki intepretowano w następujący sposób: im więcej punktów, tym lepsze dostosowanie diety do rekomendacji. Wyróżniono trzy poziomy dostosowania diety mężczyzn do rekomendacji odnoszących się do profilaktyki raka płuc: małe (0-3 pkt.), średnie (4–5 pkt.), duże (6-8 pkt.).

### 4.6. Analiza statystyczna

Dane ilościowe przedstawiono jako średnią i odchylenie standardowe (SD), a dane jakościowe wyrażono jako liczbę i procent (n, %). Do oceny różnic między grupami zastosowano test Kruskala-Wallisa dla danych ilościowych oraz test $chi^2$ dla danych jakościowych. Różnice uznano za statystycznie istotne gdy $p \leq 0,05$. Do weryfikacji współzależności między wzorami żywienia a ryzykiem raka płuc wykonano regresję logistyczną. Obliczono iloraz szans (OR) wystąpienia raka płuc i 95% przedział ufności (95%CI), a poziom istotności OR zweryfikowano testem Walda [31]. W analizie regresji logistycznej zastosowano dwa modele: (i) bez adjustacji, (ii) z adjustacją na czynniki zakłócające. Analizę statystyczną przeprowadzono za pomocą pakietu statystycznego STATISTICA (wersja 13.3 PL; StatSoft Inc., Tulsa, OK, USA; Kraków, StatSoft Polska).

## 5. Wyniki

### *5.1. Czynniki socjoekonomiczne i styl życia*

Większość mężczyzn z rakiem płuc była starsza, miała niższy poziom wykształcenia, niższy status socjoekonomiczny, niższą aktywność fizyczną ogólną i podczas pracy oraz niższą masę ciała w porównaniu z grupą bez raka płuc (grupa kontrolna). Więcej mężczyzn z rakiem w przeszłości paliło przez dłuższy czas (>10 lat) i zostali sklasyfikowani jako mężczyźni dużo palący (>11 paczko-lat).

### *5.2. Oparte na danych wzory żywienia a ryzyko raka płuc*

U mężczyzn o średnim dostosowaniu diety do wzoru 'Rozsądnego' (w środkowym tercylu) ryzyko raka płuc było mniejsze o 37% (nie adjustowany OR=0,63; 95%CI 0,39–1,00; p=0,0472) w porównaniu z mężczyznami o małym dostosowaniu diety do tego wzoru (w dolnym tercylu). Zależność ta była jednak nieistotna po adjustacji na czynniki zakłócające. U mężczyzn o dużym dostosowaniu diety do wzoru 'Rozsądnego' (w górnym tercylu) ryzyko raka płuc było mniejsze o 43% w modelu bez adjustacji (nie adjustowany OR=0,57; 95%CI 0,44–0,72; p<0,0001) oraz mniejsze o 28% w modelu z adjustacją na czynniki zakłócające (adjustowany OR=0,72; 95%CI 0,53–0,96; p=0,0432) w porównaniu z mężczyznami o małym dostosowaniu diety do tego wzoru.

U mężczyzn umiarkowanie palących i wykazujących duże dostosowanie diety do wzoru 'Rozsądnego' ryzyko raka płuc było mniejsze o 49% w modelu bez adjustacji (nie adjustowany OR=0,51; 95% CI 0,37–0,71; $p < 0,0001$) oraz mniejsze o 41% w modelu z adjustacją na czynniki zakłócające (adjustowany OR=0,59; 95%CI 0,39–0,90; p<0,05) w porównaniu z mężczyznami niepalącymi i o małym dostosowaniu diety do tego wzoru.

Wzory żywienia 'Zachodni-tradycyjny' i 'Słodki-mleczny' nie były istotnie związane z ryzykiem raka płuc u mężczyzn ogółem (bez uwzględnienia statusu palenia) oraz u mężczyzn umiarkowanie palących. U mężczyzn dużo palących żaden z trzech PCA-DP nie był istotnie związany z ryzykiem raka płuc.

### *5.3.* Predefiniowane *wzory żywienia a ryzyko raka płuc*

#### *5.3.1. 'Wskaźnik Polish-aMED®' a ryzyko raka płuc*

W modelu bez adjustacji mniejsze ryzyko raka płuc o 59% i 50% mieli mężczyźni o dużym (7-9 pkt) i średnim (4-6 pkt) dostosowaniu diety do 'Wskaźnika Polish-aMED®' (odpowiednio nie adjustowany OR=0,41; 95%CI 0,27–0,64; p<0,0001 i OR=0,50; 95%CI 0,30–0,74; p<0,001) w porównaniu z mężczyznami o małym dostosowaniu diety (0-3 pkt) do tego wskaźnika. W modelu z adjustacją na czynniki zakłócające mniejsze ryzyko raka płuc o 49% mieli mężczyźni zarówno z dużym (7-9 pkt), jak i średnim (4-6 pkt) dostosowaniu diety do 'Wskaźnika Polish-aMED®' (odpowiednio adjustowany OR=0,51; 95%CI 0,31–0,81; p<0,05 i OR=0,51; 95%CI 0,32–0,81; p<0,05) w porównaniu z małym dostosowaniem diety do tego wskaźnika.

Biorąc pod uwagę status palenia w modelu bez adjustacji mniejsze ryzyko raka płuc o 72% (nie adjustowany OR=0,28; 95%CI 0,13–0,61; p<0,01) mieli mężczyźni umiarkowanie palący i wykazujący duże dostosowanie diety do 'Wskaźnika Polish-aMED®' w porównaniu

z mężczyznami niepalącymi i o małym dostosowaniu diety do tego wskaźnika. Mniejsze ryzyko raka płuc o 60% (nie adjustowany OR=0,40; 95%CI 0,23–0,68; p<0,001) mieli mężczyźni umiarkowanie palący i wykazujący średnie dostosowanie diety do tego wskaźnika w porównaniu z mężczyznami niepalącymi i o małym dostosowaniu diety do tego wskaźnika. W modelu z adjustacją na czynniki zakłócające ryzyko raka płuc było mniejsze o 66% (adjustowany OR=0,34; 95%CI 0,15–0,76; p<0,05) u mężczyzn umiarkowanie palących i wykazujących duże dostosowanie diety do 'Wskaźnika Polish-aMED®' oraz o 65% (adjustowany OR=0,35; 95%CI 0,18–0,65; p<0,05) u mężczyzn umiarkowanie palących i wykazujących średnie dostosowanie diety do tego wskaźnika w porównaniu z mężczyznami niepalącymi i o małym dostosowaniu diety do tego wskaźnika.

Żaden poziom dostosowania diety mężczyzn do 'Wskaźnika Polish-aMED®' nie był istotnie związany z ryzykiem raka płuc u mężczyzn dużo palących.

*5.3.2. 'Wskaźnik Ad-LC WCRF/AICR' a ryzyko raka płuc*

Biorąc pod uwagę pojedyncze rekomendacje 'Wskaźnika Ad-LC WCRF/AICR' tylko jedna rekomendacja była niezależnie związana z mniejszym ryzykiem raka płuc u mężczyzn, niezależnie od zestawu zastosowanych czynników zakłócających. W modelu 2 (z adjustacją) stosowanie się do rekomendacji „Ogranicz palenie" wiązało się z mniejszym ryzykiem raka płuc o 87% (OR=0,13; 95%CI 0,04–0,37; p=0,0002) u mężczyzn nigdy nie palących (którym przypisano 1 pkt. za spełnienie rekomendacji) oraz o 45% (OR=0,55; 95%CI 0,33–0,91; p=0,0189) u mężczyzn umiarkowanie palących (0,5 pkt.) w porównaniu z mężczyznami dużo palącymi (0 pkt.).

W modelu częściowo skorygowanym (model 1) dwie pojedyncze rekomendacje osiągnęły istotność statystyczną (dodatnią lub ujemną). Przestrzeganie rekomendacji „Jedz produkty pełnoziarniste/warzywa/owoce/fasolę" wiązało się z mniejszym ryzykiem raka płuc o 31% (częściowo adjustowany OR=0,69; 95%CI 0,53–0,90; p=0,0057) u mężczyzn często spożywających tą grupę żywności (1 pkt. za spełnienie rekomendacji) w porównaniu z mężczyznami spożywającymi tą grupę żywności okazjonalnie (0 pkt.). Przestrzeganie rekomendacji „Ogranicz spożycie czerwonego/przetworzonego mięsa" wiązało się z ponad dwukrotnie większym ryzykiem raka płuc (częściowo adjustowany OR=2,04; 95%CI 1,16–3,58; p=0,0129) u mężczyzn umiarkowanie często spożywających tą grupę żywności (0,5 pkt.) i 1,4 razy większym (OR=1,40; 95%CI 1,07–1,97; p=0,0152) u mężczyzn rzadko spożywających tą grupę żywności (1 pkt.) w porównaniu do mężczyzn często spożywających tę grupę żywności (0 pkt.). W modelu z pełną adjustacją (model 2) dla obu rekomendacji, tj. „Jedz produkty pełnoziarniste/warzywa/owoce/fasola" i „Ogranicz spożycie czerwonego/przetworzonego mięsa", współzależność z ryzykiem raka płuc była nieistotna.

W pełnym modelu uwzględniającym wszystkie rekomendacje ujęte we 'Wskaźniku Ad-LC WCRF/AICR' ryzyko raka płuc dla było mniejsze o 47% (adjustowany OR= 0,53; 95%CI 0,32-0,88; p=0,0129) u mężczyzn o większej (6-8 pkt) zgodności diety z rekomendacjami w porównaniu do mężczyzn o mniejszej (0-2 pkt) zgodności diety z rekomendacjami. Każdy 1-punktowy wzrost 'Wskaźnika Ad-LC WCRF/AICR' zmniejszał ryzyko raka płuc u mężczyzn o 34% (adjustowany OR=0,66; 95%CI 0,45-0,95; p=0,0267).

Analiza związku między ryzykiem raka płuc i różnymi kombinacjami kilku pojedynczych rekomendacji ‘Wskaźnika Ad-LC WCRF/AICR’ wykazała korzyści wynikające z przestrzegania trzech lub więcej rekomendacji. Ryzyko raka płuc było mniejsze o 45% do 78% u mężczyzn o średnim przestrzeganiu trzech lub więcej rekomendacji (z wyjątkiem jednego modelu z siedmiu) i mniejsze o 39% do 66% u mężczyzn o dużym przestrzeganiu trzech lub więcej rekomendacji w porównaniu do mężczyzn w małym stopniu przestrzegających tych rekomendacji.

## 6. Dyskusja

W prezentowanym badaniu dokonano po raz pierwszy kompleksowej oceny współzależności między dwoma rodzajami wzorów żywienia (opartych na danych i predefiniowanych) i ryzykiem raka płuc. Ogólnie rzecz biorąc, wykazano korzystny wpływ prozdrowotnych wzorów żywienia na ryzyko raka płuc u mężczyzn z północno-wschodniej Polski, który był widoczny również u mężczyzn umiarkowanie palących tytoń.

W badaniu duże dostosowanie diety mężczyzn do wzoru „Rozsądnego'' wiązało się z mniejszym ryzykiem raka płuc. W pracach innych autorów opisywano prozdrowotne wzory żywienia, ale zawierające mniejszą liczbę komponentów żywieniowych niż w badaniach własnych. Były to na przykład wzory złożone wyłącznie z owoców i warzyw [32, 33] lub białego mięsa i serów [34], dla których wykazano współzależność z mniejszym ryzykiem raka płuc. Składowymi tych wzorów żywienia były w większości produkty o potwierdzonym działaniu przeciwnowotworowym, np. warzywa i owoce, które dzięki wysokiej zawartości składników bioaktywnych mogły neutralizować reaktywne formy tlenu i w efekcie zmniejszać stan zapalny w organizmie [12, 14].

Zaktualizowany przegląd systematyczny i metaanaliza dowodzą, że ścisłe przestrzeganie diety śródziemnomorskiej zmniejsza ryzyko nowotworów układu oddechowego o 16% [35]. Podobny, silny związek stwierdzono w niniejszym badaniu po adaptacji diety śródziemnomorskiej do warunków diety polskiej, mimo że Polska nie jest krajem śródziemnomorskim. We wcześniejszych doniesieniach z innych krajów, raportowano korzystny wpływ diety śródziemnomorskiej na ryzyko raka płuc [36, 37]. W badaniu holenderskim (NLCS) wysokie dopasowanie diety do alternatywnej diety śródziemnomorskiej (z wyłączeniem alkoholu) wiązało się ze zmniejszonym ryzykiem raka płuc u mężczyzn o 9% [36]. W szwedzkim badaniu stwierdzono, że przestrzeganie diety śródziemnomorskiej zmniejszało ryzyko raka płuc o 14%, podczas gdy we Włoszech przestrzeganie zaleceń tej diety zmniejszało ryzyko raka płuc o 80% [38, 39]. Ze względu na różnice między krajami w zwyczajach żywieniowych i spożyciu żywności, nie istnieje jeden uniwersalny wzorzec diety śródziemnomorskiej – w różnych krajach ma ona lokalny profil, który może w innym stopniu wpływać na zmniejszenie ryzyka raka płuc [40].

Dwa prozdrowotne wzory żywienia zidentyfikowane w niniejszym badaniu – 'Rozsądny' i 'Wskaźnik Polish-aMED®' – były skorelowane z ryzykiem raka płuc u umiarkowanych palaczy. Mężczyźni umiarkowanie palący, których dieta była lepiej dopasowana do tych wzorów żywienia, mieli mniejsze ryzyko zachorowania na raka płuc, podczas gdy u mężczyzn dużo palących nie odnotowano tej zależności. W przeciwieństwie do uzyskanych wyników, we włoskim badaniu z udziałem osób dużo palących (≥20 paczko-lat), w którym uwzględniono stosowanie suplementów zawierających witaminy, większe dopasowanie diety do wzoru 'Witaminy i błonnik' było związane z mniejszym o 43% ryzykiem raka płuc [41]. Chociaż włoski wzór żywienia można zakwalifikować jako prozdrowotny, to nie był on jednak podobny do wzoru 'Rozsądnego' zidentyfikowanego w obecnym badaniu.

W prezentowanym badaniu oceniono zależność między przestrzeganiem rekomendacji dotyczących profilaktyki raka płuc a ryzykiem raka płuc u mężczyzn. Wykazano, że

mężczyźni przestrzegający wszystkich lub co najmniej 3 rekomendacji stanowiących komponenty ‘Wskaźnika Ad-LC WCRF/AICR’, mieli mniejsze ryzyko raka płuc o 47%, przy czym nie musiały być przestrzegane wszystkie rekomendacje. Wśród pojedynczych składowych tego wskaźnika dwie rekomendacje wyróżniły się istotnym wpływem na ryzyko raka płuc u mężczyzn. Jedna z nich „Ogranicz palenie’ jest najsilniejszym i najdłużej znanym modyfikowalnym czynnikiem ryzyka raka płuc związanym ze stylem życia [4, 9, 10, 42], co również zaobserwowano w obecnym badaniu. Wpływ drugiej rekomendacji „Ogranicz spożycie czerwonego/przetworzonego mięsa” na ryzyko raka płuc jest mniej poznany. W niniejszy badaniu w częściowo skorygowanym modelu zaobserwowano zwiększone ryzyko zachorowania na raka płuc u osób, które przestrzegały tej rekomendacji. Wynik ten różni się od wcześniejszych doniesień wiążących spożycie czerwonego mięsa ze zwiększonym ryzykiem raka płuc [5, 8, 11, 41, 43-45]. Analiza pozostałych komponentów diety mężczyzn pozwala stwierdzić, że mniejszej częstotliwości spożycia mięsa czerwonego/przetworzonego (tj. lepszemu przestrzeganiu rekomendacji) towarzyszyła bardzo mała częstotliwość spożycia warzyw i owoców. Mężczyźni o większym dostosowaniu do rekomendacji ograniczającej spożycie mięsa czerwonego/przetworzonego (spożywali je średnio 0,9 razy/dzień), rzadko spożywali warzywa i owoce (średnio 1,1 razy/dzień), zatem te dwie cechy odżywiania mogły być wspólnie przyczyną braku ochronnego działania warzyw i owoców, o którym donosiły inne badania [13, 14]. Badanie *European Prospective Investigation into Cancer and Nutrition* (EPIC) [23] nie wykazało związku między spożyciem mięsa/przetworzonego mięsa a ryzykiem raka płuc. Natomiast wykazano, że połączenie kilku pojedynczych czynników żywieniowych i stylu życia wiązało się ze zmniejszonym o około połowę ryzykiem raka płuc, pomimo większej częstotliwości spożycia mięsa czerwonego i jego przetworów.

Kobiety z reguły częściej niż mężczyźni prowadzą zdrowy styl życia i dokonują lepszych wyborów żywieniowych [46]. Uważa się, że mężczyźni rzadziej przestrzegają zasad zdrowej diety [47]. To spostrzeżenie można poprzeć wynikami badań własnych, w których wykazano, że tylko 9% mężczyzn (39 z 439) przestrzegało wszystkich rekomendacji uzyskując maksymalną liczbę punktów ‘Wskaźnika Ad-LC WCRF/AICR’, z pełną świadomością faktu, że w badaniach własnych nie istnieje możliwość porównania z kobietami.

Obecne badanie wykazało, że ryzyko raka płuc było mniejsze dla pełnego modelu uwzględniającego wszystkie komponenty ‘Wskaźnika Ad-LC WCRF/AICR’ i wykazało ochronny związek wobec raka płuc z każdym jednopunktowym wzrostem tego wskaźnika. Do chwili obecnej w literaturze przedmiotu nie opisano korzyści dla ryzyka raka płuc wynikających z przestrzegania rekomendacji WCRF/AICR opracowanych w 2018 r. Dostępne analizy odnoszą się wyłącznie do rekomendacji opracowanych przez WCRF/AICR w 2007 r. – wykazano w nich, że przestrzeganie rekomendacji wiązało się ze zmniejszonym ryzykiem raka płuc [48-50]. Wadą tych prac, utrudniającą interpretację i przeprowadzenie analizy porównawczej, jest brak znormalizowanej metody punktacji dla rekomendacji opracowanych przez WCRF/AICR w 2007 r., dlatego w każdym z badań opracowano własny system punktowania. Obecne badanie jest pierwszym (i jak dotąd jedynym) oceniającym związek między przestrzeganiem rekomendacji odnoszących się do zaleceń WCRF/AICR z 2018 r. (po adaptacji wskaźnika do ryzyka raka płuc) a ryzykiem raka płuc u mężczyzn. Do

tej pory przeprowadzono niewiele badań oceniających związek między rekomendacjami z roku 2018 a ryzykiem innych nowotworów. W badaniach dotyczących ryzyka całkowitej zachorowalności na nowotwory złośliwe [51], raka jelita grubego, raka piersi [52-55] oraz raka prostaty [56], podobnie jak w obecnym badaniu, stwierdzono pozytywny związek z przestrzeganiem rekomendacji WCRF/AICR z 2018 r. Z kolei inne badanie dotyczące raka piersi [57] oraz badanie kliniczno-kontrolne dotyczące przewlekłej białaczki limfatycznej [58] nie wykazało istotnego związku między tymi nowotworami a przestrzeganiem rekomendacji WCRF/AICR z 2018 r.

*6.1. Mocne i słabe strony badania*

Obecne badanie ma kilka ograniczeń. Ze względu na wieloczynnikową etiologię raka, w analizie związku między dietą i ryzykiem raka płuc uwzględniono wiele potencjalnych czynników zakłócających [1, 8, 59] nie było możliwe uwzględnienie ich wszystkich. Kolejnym ograniczeniem jest brak danych dotyczących ilości spożywanej żywności, ponieważ wzory żywienia tworzono na podstawie danych dotyczących częstotliwości spożycia żywności. Takie podejście jest wprawdzie uprawnione i było stosowane przez innych badaczy, jako że istnieje korelacja między ilością i częstotliwością spożycia żywności, co jednak nie wyklucza związanego z tym błędu [60, 61]. Wiele danych, w tym związanych z dietą i stylem życia, pochodziło z deklaracji uzyskanej od uczestników, co może odpowiadać za stronniczość danych. Z drugiej strony nie istnieje złoty standard w ocenie żywienia, a metoda częstotliwości spożycia żywności obejmująca jeden rok jest rozsądnym wyborem w ocenie jakości diety [62]. Ponadto, długoterminowy pomiar zwyczajowej codziennej aktywności fizycznej lub palenia tytoniu jest trudny. Nie można także wykluczyć, że niektóre elementy stylu życia mogły ulec zmianie przed rozpoznaniem raka, z powodu wczesnych objawów. W tym badaniu wielowymiarowa analiza statystyczna (PCA) ma zarówno ograniczenia, jak i mocne strony. W przypadku trzech zidentyfikowanych wzorów żywienia opartych na PCA skumulowany odsetek wyjaśnionej wariancji nie był wysoki (31%). Jednakże, podczas identyfikacji wzorów żywienia opartych na danych nie jest możliwe osiągnięcie wysokiego poziomu całkowitej wyjaśnionej wariancji, ponieważ zmienne żywieniowe ‘z natury’ cechuje duża zmienność [63]. Zgodnie z literaturą przedmiotu, typowy zakres całkowitej wyjaśnionej wariancji dla 2-3 wzorów żywienia wynosi od 20% do 30%. W tym świetle, obecny wynik (31% dla trzech wzorów żywienia) jest lepszy niż w innych badaniach [64-67].

Badanie ma kilka mocnych stron. Osoby z rakiem płuc i bez raka płuc zostały wybrane zgodnie z kryteriami włączenia obejmującymi wyniki tomografii i/lub badania rentgenowskiego płuc [68]. Osoby z rakiem płuc rekrutowano w momencie diagnozy i przed leczeniem, dzięki czemu dane żywieniowe nie zostały zakłócone przez ewentualną zmianę diety po rozpoznaniu raka. Główną zaletą badania jest identyfikacja wzorów żywienia z zastosowaniem dwóch podejść (opartego na danych i predefiniowanego) [69]. To pozwoliło na identyfikację kilku różnych wzorów żywienia, a odrębna analiza zależności między ryzykiem raka i każdym ze wzorów żywienia pozwoliła na wszechstronną ocenę współzależności dieta–rak płuc. Po drugie, przeprowadzono dodatkową analizę regresji logistycznej na danych, w których podgrupę kontrolną (n=238) dopasowano pod względem

wieku do grupy mężczyzn chorych na raka płuc, aby upewnić się, że wnioski z badania nie różnią się, gdy dwie grupy są dopasowane wiekowo. Po trzecie, do kolekcji danych żywieniowych użyto kwestionariusza FFQ-6®, który cechuje odpowiednia do wysokiej zgodność wewnętrzna [30, 70], a jego zastosowanie w wersji administrowanej przez badacza zmniejsza stronniczość danych. Wreszcie, chociaż w kilku poprzednich badaniach analizowano związek między wzorami żywienia a rakiem płuc, to w żadnym z nich nie przedstawiono wyników dotyczących osób dorosłych mieszkających w Europie Środkowej lub Wschodniej, biorąc pod uwagę historię palenia tytoniu. Niniejsze badania wypełniają ważną lukę, badając współzależność między różnymi wzorami żywienia, w tym wskaźnikami 'Polish-aMED®' i 'Ad-LC WCRF/AICR' a ryzykiem raka u mężczyzn z północno-wschodniej Polski.

## 7. Podsumowanie i wnioski

Badania wykazały, że prozdrowotne wzory żywienia, w tym dieta śródziemnomorska o polskim profilu, mogą sprzyjać zmniejszeniu ryzyka raka płuc u mężczyzn, w tym u mężczyzn umiarkowanie palących, chociaż nie zostało to potwierdzone u mężczyzn dużo palących. Potwierdzono wcześniejsze dowody, że ograniczenie palenia zmniejsza ryzyko raka płuc u mężczyzn i dostarczono nowych danych, że palenie tytoniu jest niezależnym czynnikiem ryzyka raka płuc, a także współdziałającym z dietą, przy czym w przypadku umiarkowanego poziomu palenia tytoniu prozdrowotna dieta działa protekcyjnie.

Po raz pierwszy wykazano znaczenie przestrzegania wielu rekomendacji jednocześnie w zmniejszaniu ryzyka raka płuc u mężczyzn. Dostarczono mocnych przesłanek wskazujących, że przestrzeganie jednocześnie co najmniej trzech rekomendacji dotyczących profilaktyki raka płuc, odnoszących się do diety, stylu życia lub zawartości tłuszczu w ciele, może zapobiegać rakowi płuc u mężczyzn, pomimo obecności innych niezdrowych zachowań.

## 8. Piśmiennictwo


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## 9. Publikacji wraz z materiałami uzupełniającymi

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# Adherence to Prudent and Mediterranean Dietary Patterns Is Inversely Associated with Lung Cancer in Moderate But Not Heavy Male Polish Smokers: A Case-Control Study

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**Abstract:** Lung cancer is the most commonly diagnosed cancer in men worldwide. Studies regarding dietary patterns (DPs) and lung cancer are limited, with results remaining inconclusive, and the association of DPs with lung cancer in smokers is unclear. This study analyzed the associations between DPs, including the Polish-adapted Mediterranean diet (Polish-aMED) score, and lung cancer risk in Polish adult male smokers. This case-control study involved 439 men aged 45–80 years from northeastern Poland, including 187 newly diagnosed lung cancer cases. Dietary data was collected with a 62-item food frequency questionnaire (FFQ-6). Two approaches were applied to identify dietary patterns. The Polish-aMED score was calculated (hypothesis-driven approach) and a principal component analysis (PCA) was used to identify PCA-driven DPs (data-driven approach). A logistic regression analysis was performed to estimate the odds ratio (OR) and 95% confidence interval (95% CI) of the lung cancer risk associated with the adherence to DPs overall as well as for moderate (2.5–11 pack-years) and heavy (>11 pack-years) smokers. Among moderate smokers, the risk of lung cancer was lower by 41% (OR: 0.59; 95% CI: 0.39–0.90; $p < 0.05$; adjusted model) in the higher adherence to the prudent DP when compared to the lower adherence, and by 66% (OR: 0.34; 95% CI: 0.15–0.76; $p < 0.05$; adjusted model) in the high adherence (7–9 points) to the Polish-aMED score when compared to the low adherence (0–3 points). No significant association between the westernized traditional DP or the sweet dairy DP and lung cancer was revealed. In conclusion, the current study suggests that pro-healthy dietary patterns, including the Mediterranean pattern, may favour lower risk of lung cancer in moderate smokers, although it was not confirmed in heavy smokers.

**Keywords:** lung cancer; men; smoking; smokers; dietary patterns; prudent diet; Mediterranean diet; diet quality score

## 1. Introduction

There were an estimated 18 million cancer cases around the world in 2018; of these, 9.5 million cases were in men and 8.5 million in women [1]. Cancer is the second most common cause of death globally (cardiovascular diseases were the most common) [2]. In 2018, GLOBOCAN [1] estimated that the most common cancers in the world were lung cancer in men and breast cancer in women,

each representing 12.3% of the total number of new cases diagnosed. Lung cancer has become the most common cause of cancer death in men aged 40 and older and women aged 60 and older [3].

In Poland, the number of cases of malignant cancer in the last three decades has grown more than twice, in 2013 reaching over 156 thousand cases (equally 78 thousand in men and women). Lung cancer is the most commonly diagnosed cancer and the most common cancer cause of death in men in Poland and across the world. Lung cancer accounts for approximately 18.7% and 30.7% of the total number of cancer cases and deaths in men in Poland, respectively [4]. In Poland, longevity for men over the past few decades has been lower than in more developed European countries. This is partly due to the higher likelihood of unhealthy lifestyle behaviours of Polish men, e.g., tobacco use, alcohol abuse, and an unhealthy diet, resulting in more deaths from heart disease, cancer, and other diseases [5]. Cancer aetiology is multi-factorial, and includes some predictors that cannot be modified, such as age, genetic predisposition, and some environmental factors (including air pollution), whereas lifestyle factors, such as smoking, physical activity, and diet are modifiable and can be changed [2,3,6–8].

Tobacco smoking remains the predominant risk factor for lung cancer development [3]. It is estimated that about 90% of lung cancer cases worldwide are attributable to tobacco use (including passive smoking) [3,7]. Smoking generates thousands of free radical particles, and is one of the key sources of inflammation and oxidative stress, which can be neutralized by a dietary intake of antioxidants and/or anti-inflammatory foods, leading to a protective effect on lung function [9]. The consumption of fruits and vegetables with a high content of antioxidant vitamins, phenolic compounds, minerals, and dietary fiber has a beneficial effect on respiratory health [10,11]. Incidence rates of lung cancer vary among world regions as a reflection of different historic patterns of tobacco exposure, which includes exposure intensity and duration, cigarette type and degree of inhalation, and the evolution of these patterns over time, commonly called the tobacco epidemic [12]. It should be noted that lung cancer in inactive smokers, i.e., passive smokers (25% of lung cancer cases worldwide), is a disease different from the more common forms of lung cancer associated with active smoking [12–14]. Because tobacco remains the leading risk factor for lung cancer, prevention of this disease is focused on smoking avoidance and cessation. Other prevention measures include healthy diet choices and maintaining a physically active lifestyle [3]. However, research on the association of dietary patterns and lung cancer risk that takes into consideration smoking is still limited. There are suggestions that diet may act independently or in concert with tobacco smoking in shaping the descriptive epidemiology of lung cancer [8,15].

According to the World Cancer Research Fund [7,16], there is strong evidence that taking high doses of beta-carotene supplements (in current and former smokers) increases the risk of lung cancer. Contrarily, there is some evidence that consuming vegetables and fruit (in current smokers and former smokers), foods containing retinol, beta-carotene or carotenoids, foods containing vitamin C (in current smokers), and foods rich in isoflavones (in never smokers) might decrease the risk of lung cancer [7,17,18]. Further evidence suggests that the consumption of red meat, processed meat, and alcoholic drinks might also increase the risk of lung cancer [7,19]. Evidence for the impact of other food groups or nutrients of the risk of lung cancer is limited, and to date, no explicit conclusions have yet been drawn [7].

It is important to identify dietary factors that might be useful in lung cancer prevention [7]. Many previous studies have investigated single foods or nutrients to assess the association with lung cancer [19–26]. Since different foods are consumed in combinations, and they interact with each other in a complex way, a comprehensive dietary pattern analysis can better reflect dietary habits and provide an evaluation of the overall effects of diet on human health [27,28].

The research in the world on the relationship between dietary patterns (DPs) and lung cancer, particularly the effects of the Mediterranean diet, is ambiguous and limited. Many studies have investigated the associations between dietary patterns and lung cancer risk [29–37]. Though the findings are not definitive, the majority of these studies suggest that a healthy diet is associated with a decreased risk of lung cancer. A healthy diet (also known as a prudent diet) is usually characterized by

high consumption of vegetables, fruit, white meat, fish, and whole grains, and low consumption of red meat, high-fat foods, and refined grains [30,38].

The Mediterranean diet (MD) has long been recognized as the optimal diet responsible for longer life and reduced cancer risk [39–43], and a few studies have demonstrated a strong and inverse relationship between high adherence to the Mediterranean diet and lung cancer [35,44–47]. There are many variants of the MD; each Mediterranean country has its own gastronomy habits [48,49]. However, this dietary pattern in different countries is characterized by some common features, i.e., high consumption of whole grains, fruit, and vegetables, moderate consumption of dairy products, olive oil, poultry, and fish, and low consumption of red meat and sweets. A final characteristic of this diet is the moderate consumption of alcohol (mainly red wine during meals) [50–52]. The MD is rich among others in fiber, vitamins, phenolic compound (polyphenol), and PUFA n-3 [53–55].

The results of the meta-analysis and reviews confirm that high adherence to the prudent pattern and the Mediterranean diet reduces the risk of many cancers [39,55], including lung cancer [30,47]. Certainly, the effect is not due to single nutrients, but to a complex of components with synergistic and antagonistic interactions [47]. However, the evidence is still limited, because there are still only a few studies (including one study of Polish men) focusing on dietary patterns [29–37] and the Mediterranean diet [34,44–47] and the risk of lung cancer. To the authors' knowledge, no studies have so far been published assessing the relationship between dietary patterns and the risk of lung cancer in Polish men who smoked moderately or heavily.

The current study analyzed the associations between dietary patterns, including Polish-adapted Mediterranean diet (Polish-aMED) score and lung cancer risk in Polish adult male smokers.

## 2. Materials and Methods

### *2.1. Ethical Considerations*

The study protocol was approved by the Bioethics Committee of the Faculty of Medical Sciences, University of Warmia and Mazury in Olsztyn on 2 October 2013 (resolution no. 29/2013). All of the subjects gave their written informed consent to participate in the study.

### *2.2. Study Design and Sample Characteristics*

A case-control study was carried out from October 2013 to August 2017. The total sample screened consisted of 439 adult men aged 45 to 80 (mean = 62.6, SD = 7.2) years. The subjects were residents of northeastern Poland.

The cancer sample consisted of 187 men with a newly primarily diagnosed (with digital X-ray examination (RTG) and computed tomography (CT) of the chest) and histologically confirmed lung cancer. The period from cancer diagnosis to case recruitment for study and data collection ranged from seven days to 14 days (Figure 1a). Cases during or after active treatment were not qualified for the study, since they may have involved changes in dietary habits or other behaviors. Therefore, the dietary data have not been disturbed by a possible change of diet after the diagnosis of cancer. The exclusion criteria of the cancer sample collection were described previously [34]. In brief, cases diagnosed with other cancer or secondary lung cancer, or with benign changes, after active treatment (e.g., chemotherapy, radiotherapy) or surgical intervention were not eligible for participation in the study.

The control sample consisted of 252 men who received a negative result from a digital X-ray examination (RTG) and/or computed tomography (CT) of the chest. The period since the cancer exclusion until participation in the study did not exceed six months (Figure 1b). Control subjects did not have any clinical symptoms or suspicion of any type of cancer in their medical history. The control sample was comprised of men recruited from those who attended national screening programs for the early diagnosis of lung cancer. Details regarding the enrollment are presented in Figure 2.

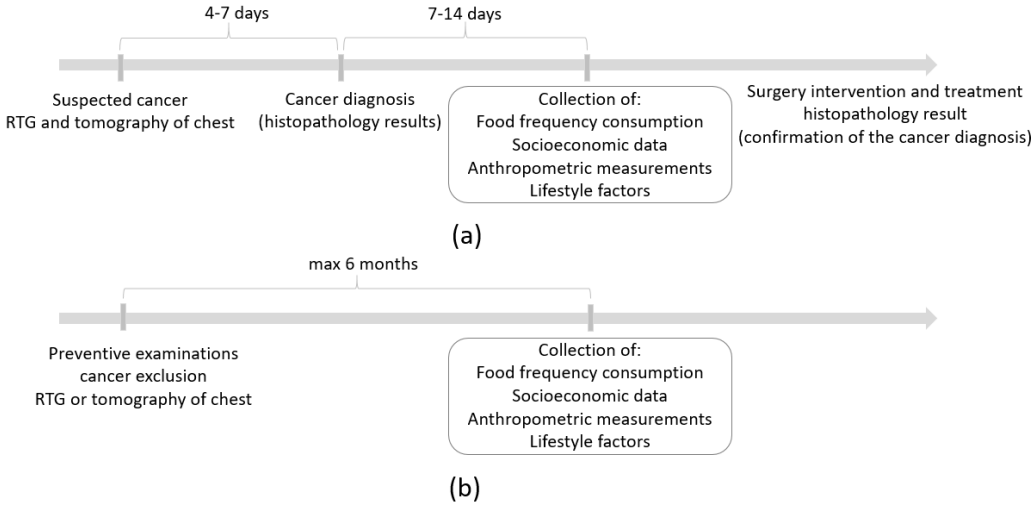



**Figure 1.** Time schemes of the study design for (**a**) the cancer sample and (**b**) the control sample. RTG digital X-ray examination.

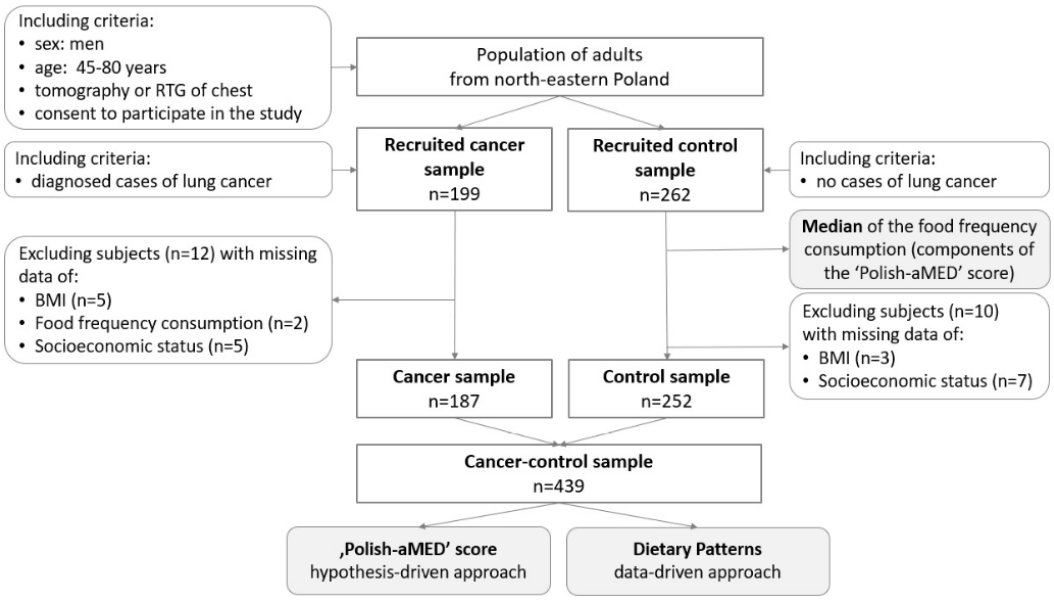



**Figure 2.** Flow chart of the sample collection and study design. Notes: RTG: digital X-ray examination; BMI: body mass index; Polish-aMED: Polish-adapted Mediterranean diet score.

### *2.3. Dietary Data Collection and Dietary Pattern Identification*

The dietary data collection methods have been previously described in detail [34]. Briefly, the subjects' diets were studied using data from a validated food frequency questionnaire (FFQ-6) [56]. The FFQ-6 provided data regarding the consumption frequency of 62 food items. A qualified dietitian asked the participants during face-to-face interviews how frequently, on average, during the past year they had consumed the specific food items. The subjects could choose one of six categories (next converted into daily frequency): never or almost never (0 times/day), once a month or less (0.25 times/day), several times a month (0.1 times/day), several times a week (0.571 times/day), daily (1.0 time/day), or several times a day (2.0 times/day) [57].

Two approaches were applied to identify DPs. The Polish-adapted Mediterranean diet (Polish-aMED) score was calculated (hypothesis-driven approach), while the principal component analysis (PCA) was used to identify PCA-driven DPs (data-driven approach) [58].

The methods of deriving PCA-driven DPs have been previously described in detail [28,29]. After aggregating some food items collected with the FFQ-6, a total of 23 food groups were included in the PCA (Table S1). The data were checked using the Kaiser–Meyer–Olkin (KMO) index to measure the sampling adequacy [59], and Bartlett's test of sphericity was used [60]. The PCA performance is justified when the KMO is greater than 0.5 and Bartlett's test is statistically significant ($p < 0.05$). In this dataset, the Kaiser–Meyer–Olkin (KMO) value was 0.716 and Bartlett's test had a significance of $p < 0.001$. For the statistical analysis, the sample size was sufficient for the PCA performance because the subject-to-item ratio was 19:1 (439 subjects and 23 items) [61]. Before the analysis, input variables were standardized. During the identification of the number of DPs, the following criteria were considered: (i) the eigenvalues of the variable correlations > 1.0, (ii) the plot of eigenvalues, and (iii) the total variance explained [58]. Rotated factor loadings with an absolute value > |0.30| were considered to be specific to the given pattern and used to label the patterns accordingly [62]. For each subject and each pattern, DP scores were calculated as a product of factor loading and food consumption frequency (for dietary variables). Next, for each DP, tertile intervals were calculated, which aimed to categorize subjects' adherence to the patterns; subjects that were located in the upper tertile were characterized as those with higher adherence to the pattern, while subjects located in the bottom tertile were characterized as those with lower adherence.

The Polish-aMED score is a Polish version of the Mediterranean diet (MED) score, modified and described earlier by Fung et al. [63]. Briefly, the Polish-aMED score was calculated based on the qualitative data of the frequency of consumption (times/day) of nine selected dietary items. The methods of calculation of the Polish-aMED score have been previously described in detail [34]. In this study, alcohol was included as a component of the Polish-aMED score because there is no definitive evidence that it is a risk factor for lung cancer [7,64,65]. Detailed calculation of the Polish-aMED is shown in Supplementary Table S2. Possible scores for the Polish-aMED ranged from 0 (minimal adherence) to 9 (maximal adherence). Next, the adherence to the Polish-aMED was categorized as low (0–3 points), moderate (4–6 points), and high (7–9 points).

### *2.4. Smoking*

Data regarding smoking status was collected for all subjects, including current smoking status, duration, the intensity of smoking, and time since cessation. The pack-years of smoking were calculated by multiplying the average number of packs of cigarettes smoked per day (intensity) by the number of years the person had smoked [66]. Smoking status pack-years were classified into two groups: moderate (2.5–11 pack-years) or heavy (>11 pack-years) smokers. These categories were based on the median value, which in this sample was equal to 11 pack-years (at enrollment).

Example of calculation:

A man reported smoking 30 cigarettes a day for 10 years.
The calculated number of pack-years is: $10 \times 30/20 = 15$ pack-years
10—years of smoking
30—number of cigarettes per day
20—number of cigarettes in one pack

### *2.5. Confounders*

Data regarding socioeconomic, lifestyle, and medical factors were collected during an individual interview with each subject. The confounding factors were selected based on data analysis and a literature search. These factors included variables with a significantly differing distribution between the cancer and control samples, and the factors that were previously indicated as playing a role in lung cancer aetiology [7]: age, weight (body mass index), smoking, socioeconomic status, physical activity, the occurrence of lung cancer in a relative, workplace exposure to asbestos, chemical compounds (radon,

uranium, chromium, arsenic, nickel, zinc, and polycyclic aromatic hydrocarbons), and hardwood dust. The potential confounders considered in this study have been described previously [33,34].

To describe socioeconomic status, the SES index was calculated using three variables: place of residence (three categories), education level (three categories), and economic status (three categories). The SES index was calculated as the sum of the values assigned to the individual response categories to each SES factor. All variables that were components of the SES index were standardized, and the tertiles of the SES index were then created to identify subjects with low, average, and high SES.

Subjects were asked about their physical activity at work and in leisure time. These data were combined, and three categories of overall physical activity were established (Table S3). Measurements of weight and height were taken, and body mass index (BMI, kg/m$^2$) was calculated and used as an indirect measure of energy balance.

### *2.6. Statistical Analysis*

The data are presented as percentages of the sample for categorical variables, or means and standard deviations (SDs) for continuous variables with normal distribution. Differences between groups were verified with Pearson's chi-squared test for categorical variables or the Kruskal–Wallis test for continuous variables, and were considered statistically significant when $p < 0.05$. Logistic regression was used to verify the associations between DPs or Polish-aMED, lung cancer, and smoking. The odds ratios (ORs) and 95% confidence intervals (95% CIs) were calculated [67]. Two models were created and adjusted for potential confounders: age (categories), sex, BMI (categories), current smoking status (never smokers, current smokers, former smokers), socioeconomic status (low, average, high), overall physical activity (low, moderate, high), the occurrence of lung cancer in relatives (yes, no, I do not know), and occupational exposure in the workplace (yes, no) (see Section 2.5). The reference categories (OR = 1.00) were the control sample and the lowest level of each DP (the bottom tertile or low level). The level of significance of the OR was verified with Wald's test [67]. The statistical analysis was performed using STATISTICA software (version 13.3 PL; StatSoft Inc., Tulsa, OK, USA; Kraków, StatSoft Polska).

## 3. Results

The distribution of the general characteristics of the cases and controls is shown in Table 1. Most subjects with lung cancer cases were slightly older and had lower body weight compared to the non-cancer group (controls). When compared to the controls, more cases of lung cancer had a lower education level and socioeconomic status, and were less physically active at work and overall. A higher proportion of cases were former smokers who smoked for a long time (>10 years) and were classified as heavy smokers (>11 pack-years). The frequency of food consumption by smoking status is shown in Supplementary Table S4.

**Table 1.** Characteristics of the lung cancer sample and control sample.

| Variable | Cancer Control Sample | | Cancer Sample | | Control Sample | | *p*-Value |
|---|---|---|---|---|---|---|---|
| | *n* | % | *n* | % | *n* | % | |
| **Sample size** | 439 | 100.0 | 187 | 100.0 | 252 | 100.0 | |
| Age (years *) | 62.6 (7.2) | | 63.0 (7.1) | | 62.3 (7.3) | | 0.2586 |
| 45.0–49.9 | 12 | 2.8 | 3 | 1.6 | 9 | 3.6 | |
| 50.0–54.9 | 41 | 9.3 | 12 | 6.4 | 29 | 11.5 | |
| 55.0–59.9 | 76 | 17.3 | 24 | 12.8 | 52 | 20.6 | |
| 60.0–64.9 | 133 | 30.3 | 51 | 27.3 | 82 | 32.5 | <0.0001 |
| 65.0–69.9 | 97 | 22.1 | 42 | 22.5 | 55 | 21.8 | |
| 70.0–74.9 | 47 | 10.7 | 29 | 15.5 | 18 | 7.1 | |
| 75.0–80.0 | 33 | 7.5 | 26 | 13.9 | 7 | 2.8 | |

**Table 1.** *Cont.*

| Variable | Cancer Control Sample | | Cancer Sample | | Control Sample | | *p*-Value |
|---|---|---|---|---|---|---|---|
| | *n* | % | *n* | % | *n* | % | |
| BMI (kg/m$^2$ *) | 27.7 (4.8) | | 27.3 (4.9) | | 28.0 (4.7) | | 0.1354 |
| <18.5 | 10 | 2.3 | 10 | 5.4 | 0 | 0.0 | <0.0001 |
| 18.5–24.9 | 125 | 28.5 | 86 | 46.0 | 39 | 15.5 | |
| 25.0–29.9 | 160 | 36.4 | 55 | 29.4 | 105 | 41.7 | |
| ≥30 | 144 | 32.8 | 36 | 19.2 | 108 | 42.8 | |
| Place of residence | | | | | | | |
| rural | 152 | 34.6 | 67 | 35.8 | 85 | 33.7 | 0.5981 |
| sub-urban | 202 | 46.0 | 81 | 43.3 | 121 | 48.0 | |
| urban | 85 | 19.4 | 39 | 20.9 | 46 | 18.3 | |
| Education level | | | | | | | |
| primary | 104 | 23.7 | 72 | 38.5 | 32 | 12.7 | <0.0001 |
| secondary | 258 | 58.8 | 104 | 55.6 | 154 | 61.1 | |
| higher | 77 | 17.5 | 11 | 5.9 | 66 | 26.2 | |
| Economic situation | | | | | | | |
| below average | 91 | 20.7 | 53 | 28.3 | 38 | 15.1 | <0.0001 |
| average | 278 | 63.3 | 118 | 63.1 | 160 | 63.5 | |
| above average | 70 | 16.0 | 16 | 8.6 | 54 | 21.4 | |
| Socioeconomic status (SES index) [a] | | | | | | | |
| low | 235 | 53.5 | 121 | 64.7 | 114 | 45.2 | 0.0002 |
| average | 87 | 19.,8 | 25 | 13.4 | 62 | 24.6 | |
| high | 117 | 26.6 | 41 | 21.9 | 76 | 30.2 | |
| Physical activity at work [b] | | | | | | | |
| low | 223 | 50.8 | 115 | 61.5 | 108 | 42.9 | 0.0003 |
| moderate | 154 | 35.1 | 48 | 25.7 | 106 | 42.0 | |
| high | 62 | 14.1 | 24 | 12.8 | 38 | 15.1 | |
| Physical activity in leisure time [c] | | | | | | | |
| low | 148 | 33.7 | 71 | 38.0 | 77 | 30.6 | 0.2570 |
| moderate | 236 | 53.8 | 95 | 50.8 | 141 | 55.9 | |
| high | 55 | 12.5 | 21 | 11.2 | 34 | 13.5 | |
| Overall physical activity [d] | | | | | | | |
| low | 227 | 51.7 | 113 | 60.4 | 114 | 45.2 | 0.0069 |
| moderate | 165 | 37.6 | 57 | 30.5 | 108 | 42.9 | |
| high | 47 | 10.7 | 17 | 9.1 | 30 | 11.9 | |
| Current smoking status | | | | | | | |
| never smokers | 50 | 12.5 | 1 | 0.5 | 49 | 19.5 | <0.0001 |
| current smokers | 157 | 34.6 | 69 | 36.9 | 88 | 45.6 | |
| former smokers | 232 | 52.9 | 117 | 62.6 | 115 | 34.9 | |
| Smoking period | | | | | | | |
| never smokers | 55 | 12.5 | 1 | 0.5 | 54 | 21.4 | <0.0001 |
| <5 years | 27 | 6.1 | 5 | 2.7 | 22 | 8.7 | |
| 5–10 years | 13 | 3.0 | 2 | 1.1 | 11 | 4.4 | |
| >10 years | 344 | 78.4 | 179 | 95.7 | 165 | 65.5 | |
| Number of cigarettes smoked | | | | | | | |
| 0 pcs | 55 | 12.5 | 1 | 0.5 | 54 | 21.4 | <0.0001 |
| <10 pcs | 28 | 6.4 | 6 | 3.2 | 22 | 8.7 | |
| 11–20 pcs | 217 | 49.4 | 104 | 55.6 | 113 | 44.9 | |
| 21–40 pcs | 104 | 23.7 | 50 | 26.8 | 54 | 21.4 | |
| >40 pcs | 35 | 8.0 | 26 | 13.9 | 9 | 3.6 | |
| Smoking (pack-years) | | | | | | | |
| 0 pack-years (never smoker) | 55 | 12.5 | 1 | 0.5 | 54 | 21.4 | <0.0001 |
| 2.5–11 pack-years (moderate smoker) | 252 | 57.4 | 112 | 59.9 | 140 | 55.6 | |
| >11 pack-years (heavy smoker) | 132 | 30.1 | 74 | 39.6 | 58 | 23.0 | |

**Table 1.** *Cont.*

| Variable | Cancer Control Sample | | Cancer Sample | | Control Sample | | *p*-Value |
|---|---|---|---|---|---|---|---|
| | *n* | % | *n* | % | *n* | % | |
| Family history of lung cancer among relatives | | | | | | | |
| yes | 91 | 20.7 | 39 | 20.9 | 52 | 20.6 | |
| no | 324 | 73.8 | 138 | 73.8 | 186 | 73.8 | 0.9945 |
| I do not know | 28 | 5.5 | 10 | 5.3 | 14 | 5.6 | |
| Occupational exposure in the workplace | | | | | | | |
| yes | 137 | 31.2 | 64 | 34.2 | 73 | 28.9 | 0.2399 |
| no | 302 | 68.8 | 123 | 65.8 | 179 | 71.1 | |

* Mean and *standard deviation* (SD); [a] SES index was calculated based on place of residence, educational level, and declared economic situation (description in the Materials and Methods section); [b] physical activity at work: low—more than 70% of working time spent sedentary or retired, moderate—approx. 50% of working time spent sedentary and 50% of working time spent in an active manner, high—approx. 70% of working time spent in an active manner or physical work related to great exertion [64]; [c] physical activity in leisure time: low—sedentary for most of the time, watching TV, reading books, walking 1–2 h per week, moderate—walking, bike riding, gymnastics, gardening, light physical activity performed 2–3 h per week, high—bike riding, jogging, gardening, sport activities involving physical exertion performed more than 3 h weekly [68]; [d] after combining data based on declared physical activity at work and physical activity in leisure time [69]; details in Supplementary Table S3; *n*—number; %—percentage of the sample; *p*—level of significance assessed by chi$^2$ test (categorical variables) or Kruskal–Wallis' test (continuous variables).

### 3.1. Food Consumption Frequency and Dietary Patterns

Using three PCA-driven DPs, three dietary patterns were derived: prudent DP, westernized traditional DP, and sweet dairy DP. The total explained variation of these three dietary patterns was 31%. Each dietary pattern explained 15%, 10%, and 6% of the consumption variance of 23 food groups, respectively. The concise names of the patterns represented the most prominent features and were labelled as follows: prudent DP—was positively loaded by the consumption frequency of whole grain products (0.65), fruits (0.64), nuts and seeds (0.57), vegetables (0.49), fish (0.48), legumes (0.47), and fruit, vegetable, and vegetable-fruit juices (0.32), and was negatively loaded by the consumption frequency of refined grain products (−0.54), sugar, honey and sweets (−0.45); westernized traditional DP—was positively loaded by the consumption frequency of red and processed meats (0.63), white meat (0.56), potatoes (0.51), other fats (0.45), vegetables (0.43), refined grain products (0.39), sweetened beverages and energy drinks (0.38), and sugar, honey, and sweets (0.37); sweet dairy—was positively loaded by the consumption frequency of animal fats (0.66), milk, fermented milk drinks, and curd cheese (0.49), sweetened milk drinks and flavored homogenized cheese (0.45), eggs (0.43), cheese (0.38), sugar, honey, and sweets (0.37), breakfast cereals (0.37), refined grain products (0.35), vegetable oils (0.33), and dried fruit and preserves (0.32), and was negatively loaded by the consumption frequency of other fats (−0.39) (Table 2). The frequency of food consumption by different dietary patterns is shown in Supplementary Table S5.

For the Polish-aMED, a significantly positive correlation was found between the Polish-aMED score with the consumption frequency of seven (out of nine) components: whole grains products (r = 0.49), fruits (r = 0.25), nuts and seeds (r = 0.54), vegetables (r = 0.50), legumes (r = 0.41), alcohol (r = 0.21), and the ratio of vegetable oils to animal fat (r = 0.11) (Table 2).

### 3.2. Dietary Patterns and Lung Cancer

The association between dietary patterns and the risk of lung cancer are presented in Table 3 (distributions) and Table 4; Table 5 (odds ratios).

Within the cancer-control sample, one out of the three PCA-driven dietary patterns, prudent, showed a significant association with the prevalence of lung cancer in a logistic regression analysis. The risk of lung cancer was lower by 37% (OR: 0.63; 95% CI: 0.39–1.00; $p < 0.05$; crude model) in subjects with moderate adherence to the prudent DP when compared to the lower adherence as a

reference. This association was not significant after adjustment. The risk of lung cancer was lower by 43% (OR: 0.57; 95% CI: 0.44–0.72; $p < 0.0001$; crude model) and 28% (OR: 0.72; 95% CI: 0.53–0.96; $p < 0.05$; adjusted model) in subjects with higher adherence to the prudent DP when compared to the lower adherence as a reference (Table 3). The westernized traditional DP and sweet dairy DP were not significantly associated with the risk of lung cancer. For the Polish a-MED DP, the risk of lung cancer was lower by 49% (OR: 0.51; 95% CI: 0.31–0.81; $p < 0.05$, adjusted model and OR: 0.51; 95% CI: 0.32–0.81; $p < 0.05$; adjusted model) in subjects with moderate adherence (4–6 points) and high adherence (7–9 points) to the Polish-aMED score when compared to the low adherence (0–3 points).

For moderate smokers, the risk of lung cancer was lower by 49% (OR: 0.51; 95% CI: 0.37–0.71; $p < 0.0001$; crude model) and 41% (OR: 0.59; 95% CI: 0.39–0.90; $p < 0.05$; adjusted model) for higher adherence to the prudent DP when compared to the lower adherence. The westernized traditional DP and sweet dairy DP were not significantly associated with the risk of lung cancer in moderate smokers. For moderate smokers, the risk of lung cancer was lower by 65% (OR: 0.35; 95% CI: 0.18–0.65; $p < 0.05$; adjusted model) and 66% (OR: 0.34; 95% CI: 0.15–0.76; $p < 0.05$; adjusted model) in the moderate adherence (4–6 points) and the high adherence (7–9 points) to the Polish-aMED score when compared to the low adherence (0–3 points).

No dietary pattern was significantly associated with the risk of lung cancer among heavy smokers.

**Table 2.** Factor loadings for food groups in principal component analysis (PCA)-derived dietary patterns and the Pearson's correlation coefficients for food groups in the Polish-aMED score ($n$ = 439).

| Food Groups | PCA-Derived Dietary Patterns | | | Polish-aMED Score |
|---|---|---|---|---|
| | Prudent | Westernized Traditional | Sweet Dairy | |
| Whole grain products | **0.65** | −0.04 | −0.03 | **0.49** * |
| Fruits | **0.64** | 0.16 | 0.24 | **0.25** * |
| Nuts and seeds | **0.57** | 0.05 | 0.12 | **0.54** * |
| Vegetables | **0.49** | **0.43** | 0.20 | **0.50** * |
| Fish | **0.48** | 0.23 | 0.08 | **0.41** |
| Legumes | **0.47** | 0.04 | 0.26 | **0.41** * |
| Fruit, vegetable, vegetable-fruit juices | **0.32** | 0.20 | 0.26 | **0.21** * |
| Refined grains products | **−0.54** | **0.39** | **0.35** | **−0.21** * |
| Sugar, honey, and sweets | **−0.45** | **0.37** | **0.37** | −0.09 |
| Red and processed meats | 0.08 | **0.63** | 0.07 | **−0.00** |
| White meat | 0.19 | **0.56** | −0.01 | **0.13** * |
| Potatoes | −0.13 | **0.51** | 0.13 | −0.02 |
| Other fats | −0.18 | **0.45** | **−0.39** | **−0.13** * |
| Sweetened beverages and energy drinks | 0.10 | **0.38** | 0.23 | **0.14** * |
| Animal fats | −0.11 | 0.01 | **0.66** | 0.06 |
| Milk, fermented milk drinks, and curd cheese | 0.13 | 0.12 | **0.49** | **0.17** * |
| Sweetened milk drinks and flavored homogenized cheese | −0.02 | 0.01 | **0.45** | 0.07 |
| Eggs | 0.12 | 0.17 | **0.43** | **0.14** * |
| Cheese | 0.12 | 0.15 | **0.38** | **0.19** * |
| Breakfast cereals | 0.10 | −0.25 | **0.37** | **0.10** * |
| Vegetable oils | 0.11 | 0.24 | **0.33** | **0.11** * |
| Dried fruit and preserves | 0.23 | 0.02 | **0.32** | **0.15** * |
| Alcohol | 0.05 | 0.12 | 0.01 | **0.21** * |
| Ratio of vegetable oils to animal fat | NA | NA | NA | 0.11 * |
| Share in explaining the variance (%) | 15 | 10 | 6 | NA |

Polish-aMED—Polish-adapted Mediterranean diet (range of points: 0–9); bolded values are marked for the main components of PCA-derived dietary patterns with absolute loadings > |0.3| and for nine components of the Polish-aMED score; * $p < 0.05$, test of significance for Pearson's correlation coefficients; NA—not applied.

**Table 3.** Distribution of lung cancer cases by adherence to the dietary patterns and smoking status.

| Adherence to the Dietary Pattern | Cancer Control Sample ($n$ = 439) | | | | Smoking Status | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | Never Smoker ($n$ = 55) | | | | Moderate Smoker ($n$ = 252) | | | | Heavy Smoker ($n$ = 132) | | | |
| | Sample Size | Cancer Cases | | $p$ | Sample Size | Cancer Cases | | $p$ | Sample Size | Cancer Cases | | $p$ | Sample Size | Cancer Cases | | $p$ |
| | | $n$ | % | | | $n$ | % | | | $n$ | % | | | $n$ | % | |
| Prudent | | | | <0.0001 | | | | 0.6742 | | | | 0.0046 | | | | 0.6541 |
| lower | 146 | 81 | 55.5 | | 7 | 0 | 0.0 | | 90 | 51 | 56.7 | | 49 | 30 | 61.2 | |
| moderate | 146 | 64 | 43.8 | | 17 | 0 | 0.0 | | 85 | 41 | 48.3 | | 44 | 23 | 52.3 | |
| higher | 147 | 42 | 28.6 | | 30 | 1 | 3.3 | | 77 | 20 | 25.9 | | 40 | 21 | 52.5 | |
| Westernized Traditional | | | | 0.8912 | | | | 0.4102 | | | | 0.9861 | | | | 0.1221 |
| lower | 147 | 63 | 42.9 | | 20 | 1 | 5.0 | | 84 | 37 | 44.0 | | 43 | 25 | 58.1 | |
| moderate | 146 | 64 | 43.8 | | 19 | 0 | 0.0 | | 82 | 37 | 45.1 | | 45 | 27 | 60.0 | |
| higher | 146 | 60 | 41.1 | | 16 | 0 | 0.0 | | 86 | 38 | 44.2 | | 44 | 22 | 50.0 | |
| Sweet Dairy | | | | 0.4017 | | | | 0.4101 | | | | 0.9054 | | | | 0.8343 |
| lower | 146 | 62 | 42.5 | | 17 | 0 | 0.0 | | 85 | 37 | 43.5 | | 44 | 25 | 56.8 | |
| moderate | 147 | 57 | 38.8 | | 20 | 1 | 5.0 | | 89 | 37 | 41.6 | | 38 | 19 | 50.0 | |
| higher | 146 | 68 | 46.6 | | 18 | 0 | 0.0 | | 78 | 38 | 48.7 | | 50 | 30 | 60.0 | |
| Polish–aMED score | | | | <0.0001 | | | | 0.4102 | | | | 0.0003 | | | | 0.8254 |
| low (0–3 points) | 177 | 97 | 51.9 | | 15 | 0 | 0.0 | | 106 | 63 | 59.4 | | 56 | 34 | 60.7 | |
| moderate (4–6 points) | 221 | 83 | 44.4 | | 27 | 1 | 3.7 | | 127 | 47 | 37.1 | | 67 | 35 | 52.2 | |
| high (7–9 points) | 41 | 7 | 3.7 | | 13 | 0 | 0.0 | | 19 | 2 | 10.5 | | 9 | 5 | 55.6 | |

Polish-aMEDscore—Polish-adapted Mediterranean diet score (range of points: 0–9); $n$—number; %—percentage of the sample; $p$—the level of significance verified with the $chi^2$ test (cancer cases vs. controls).

**Table 4.** Odds ratios (95% confidence intervals) of lung cancer risk by adherence to the dietary patterns.

| Adherence to the Dietary Pattern | Cancer-Control Sample ($n$ = 439) | | | |
|---|---|---|---|---|
| | **Crude Model** | ***p*** | **Adjusted Model** | ***p*** |
| Prudent | | | | |
| lower (ref.) | Ref. | | Ref. | |
| moderate | 0.63 (0.39; 1.00) | 0.0472 | 0.63 (0.37; 1.08) | 0.1394 |
| higher | 0.57 (0.44; 0.72) | <0.0001 | 0.72 (0.53; 0.96) | 0.0432 |
| Westernized Traditional | | | | |
| lower (ref.) | Ref. | | Ref. | |
| moderate | 1.04 (0.65; 1.66) | 0.8667 | 0.79 (0.45; 1.37) | 0.5123 |
| higher | 0.96 (0.76;1.22) | 0.7601 | 0.81 (0.60; 1.08) | 0.1495 |
| Sweet Dairy | | | | |
| lower (ref.) | Ref. | | Ref. | |
| moderate | 0.86 (0.54; 1.37) | 0.5203 | 0.68 (0.39; 1.20) | 0.1495 |
| higher | 1.09 (0.86; 1.37) | 0.4803 | 0.99 (0.75; 1.30) | 0.7999 |
| Polish–aMED score | | | | |
| low (0–3 points; ref.) | Ref. | | Ref. | |
| moderate (4–6 points) | 0.50 (0.33; 0.74) | 0.0004 | 0.51 (0.31; 0.81) | 0.0048 |
| high (7–9 points) | 0.41 (0.27; 0.64) | <0.0001 | 0.51 (0.32; 0.81) | 0.0046 |

Ref.—reference category; Polish-aMEDscore—Polish-adapted Mediterranean diet score (range of points: 0–9); *p*—the level of significance assessed by Wald's test; model adjusted for: age (categories), BMI (categories), current smoking status (never smokers, current smokers, former smokers), socioeconomic status (low, average, high), overall physical activity (low, moderate, high), the occurrence of lung cancer in relatives (yes, no, I do not know), and occupational exposure in the workplace (yes, no); reference category in the PCA: controls.

**Table 5.** Odds ratios (95% confidence intervals) of lung cancer risk by adherence to the dietary patterns in smokers.

| Adherence to the Dietary Pattern | Moderate Smoker ($n$ = 252) | | | | Heavy Smoker ($n$ = 132) | | | |
|---|---|---|---|---|---|---|---|---|
| | **Crude Model** | ***p*** | **Adjusted Model** | ***p*** | **Crude Model** | ***p*** | **Adjusted Model** | ***p*** |
| Prudent | | | | | | | | |
| lower (ref.) | Ref. | | Ref. | | Ref. | | Ref. | |
| moderate | 0.67 (0.37; 1.21) | 0.2579 | 0.68 (0.34; 1.34) | 0.2579 | 0.80 (0.34; 1.90) | 0.6226 | 0.82 (0.30; 2.26) | 0.6958 |
| higher | 0.51 (0.37; 0.71) | < 0.0001 | 0.59 (0.39; 0.90) | 0.0154 | 0.88 (0.57; 1.37) | 0.5758 | 1.10 (0.64; 1.88) | 0.7187 |
| Westernized Traditional | | | | | | | | |
| lower (ref.) | Ref. | | Ref. | | Ref. | | Ref. | |
| moderate | 1.09 (0.59; 2.00) | 0.8320 | 0.92 (0.43; 1.96) | 0.8320 | 0.95 (0.40; 2.33) | 0.9147 | 0.79 (0.28; 2.27) | 0.6574 |
| higher | 1.03 (0.76; 1.40) | 0.8131 | 0.95 (0.65; 1.40) | 0.8131 | 0.77 (050; 1.21) | 0.2505 | 0.69 (0.40; 1.19) | 0.1495 |
| Sweet Dairy | | | | | | | | |
| lower (ref.) | Ref. | | Ref. | | Ref. | | Ref. | |
| moderate | 0.96 (0.53; 1.76) | 0.5139 | 0.78 (0.38; 1.64) | 0.5139 | 0.68 (0.27; 1.69) | 0.3944 | 0.49 (0.16; 1.46) | 0.1496 |
| higher | 1.14 (0.84;1.56) | 0.8109 | 1.05 (0.72; 1.51) | 0.8109 | 0.98 (0.64; 1.50) | 0.9244 | 0.92 (0.56; 1.50) | 0.7999 |
| Polish–aMED score | | | | | | | | |
| low (0–3 points; ref.) | Ref. | | Ref. | | Ref. | | Ref. | |
| moderate (4–6 points) | 0.40 (0.23; 0.68) | 0.0007 | 0.35 (0.18; 0.65) | 0.0010 | 0.71 (0.34; 1.46) | 0.3462 | 0.64 (0.27; 1.55) | 0.2485 |
| high (7–9 points) | 0.28 (0.13; 0.61) | 0.0010 | 0.34 (0.15; 0.76) | 0.0079 | 0.77 (0.90; 0.44) | 0.7692 | 1.17 (0.53; 2.61) | 0.3462 |

Ref.—reference category; Polish-aMEDscore—Polish-adapted Mediterranean diet score (range of points: 0–9); moderate smoker—smoker who smoked 2.5 to 11 pack-years; heavy smoker—smoker who smoked more than 11 pack-years; *p*—the level of significance assessed by Wald's test; adjusted model for: age (categories), BMI (categories), socioeconomic status (low, average, high), overall physical activity (low, moderate, high), the occurrence of lung cancer in relatives (yes, no, I do not know), and occupational exposure in the workplace (yes, no); reference category in the PCA: never smoker in controls.

## 4. Discussion

The current study found that men from northeastern Poland had higher adherence to the prudent DP and that the Polish-aMED score was associated with a significantly lower risk of lung cancer, independent of confounders. This inverse association between both pro-healthy dietary patterns and lung cancer in men was visible even in moderate smokers, although it was not confirmed among heavy smokers. The westernized traditional DP and sweet dairy DP were not significantly associated with the risk of lung cancer.

The study showed that the risk of lung cancer was 28% lower in men with higher adherence to the prudent DP, independent of confounders, which were taking into consideration. This prudent DP included whole grain products, fruits, nuts and seeds, vegetables, fish, legumes, fruits, vegetables, and vegetable-fruit juices, while it was negatively loaded by the consumption frequency of refined grain products, sugar, honey, and sweets. A beneficial effect was previously shown for many pro-healthy dietary patterns, which were rich, similar to the prudent DP, in fruits and vegetables [29], milk [32], low-fat foods [14], fish [70], pasta, rice, poultry, and oils [31].

High and moderate adherence to the Polish-aMED score reduced lung cancer risk at the same level (by 49%), independent of confounders. This strong association was found even though Poland is a non-Mediterranean country and the dietary habits of the Polish population do not closely resemble the traditional Mediterranean diet. This result is consistent with previous outcomes from other countries, which found a beneficial effect of the Mediterranean pattern on lung cancer risk [44,68]. In a Dutch study (NLCS), high adherence to the alternate Mediterranean diet (without alcohol) was associated with a reduced risk of lung cancer in men by 9% and women by 27% [44]. In a study (both sexes) in Sweden, it was found that following the Mediterranean diet reduces the risk of lung cancer by 14%, while, in Italy, following the recommendations of this diet reduces the risk by as much as 80% [71,72]. While there were similarities between the countries, there are also important differences in dietary habits and food consumption [49]. An updated systematic review and meta-analysis confirm that high adherence to the Mediterranean diet reduces the risk of respiratory cancers by 16% [73].

An inverse association between lung cancer and both pro-healthy dietary patterns was visible even in moderate smokers. Moderate smokers with higher adherence to the prudent DP had a lower risk of lung cancer by 41%, independent of confounders. Previous studies from China [32], USA [29], and the Netherlands [31] revealed that the pro-healthy patterns rich in fruits and vegetables were associated with reduced risk of lung cancer risk among smokers. Case studies among smokers (both genders) found that the fruits and vegetables pattern was associated with the reduced risk of lung cancer by 46% in Americans and 73% in Chinese people [29,32]. For Dutch males, higher adherence to the salad vegetables pattern was associated with a 10% lower risk of lung cancer among male smokers and 23% lower risk among former smokers [31]. This result was partly confirmed in the current study, showing that for moderate smokers, a higher adherence to the prudent DP, characterized by a higher consumption frequency of vegetables and fruit, was associated with a lower risk of lung cancer.

The current study found that moderate smokers (including current smokers) with higher and moderate adherence to the Polish-aMED score had a lower risk of lung cancer (66% and 65%, respectively), independent of confounders, which were taken into consideration. Previous studies from Australia [45] found that high adherence to the Mediterranean diet score was associated with lower lung cancer risk (by 36% overall and by 62% for current smokers). The European Prospective Investigation into Cancer and Nutrition (EPIC) study [74] found that higher adherence to the Mediterranean dietary pattern was associated with a 12% reduction in the risk of tobacco-related cancers among smokers. Thus, the current results reinforce previous reports and confirm the pro-health effect of the Mediterranean diet in relation to the risk of lung cancer, even for moderate smokers.

The two pro-healthy dietary patterns considered in this study—the prudent pattern and the Polish a-MED score—were inversely associated with healthy outcomes in moderate smokers. Moderate male smokers with higher adherence to these dietary patterns had a lower risk of lung cancer (by 41% and 66%, respectively), whereas, among heavy male smokers, this relationship disappeared, and no

pro-healthy dietary patterns were significantly associated with the risk of lung cancer. In contrast to the current findings, in an Italian study involving heavy smokers (≥20 pack-years), adherence to the vitamin and fiber diet regimen was associated with a 43% lower risk of lung cancer [75]. Although this pattern can be classified as pro-healthy, it was not similar to the prudent pattern in the current study because the vitamin and fiber formula included vitamin supplementation, so the possibility of comparing both results is limited. This finding documents the positive potential of pro-healthy dietary patterns. It may be speculated that these DPs could modulate the negative impact of moderate smoking, but not heavy smoking. Further studies are needed in both sexes and in other countries to determine if it is a general rule or a specific relationship for Polish males.

The study found no association between the westernized traditional pattern and lung cancer, which can be explained by the opposite influence of food components of this pattern. The westernized traditional pattern reflects the diet of many Poles, which consists of traditional staple foods (e.g., meat, potatoes, refined grain products) and vegetables prepared in a traditional manner, which are combined with western dietary influences, e.g., the consumption of sweetened beverages and energy drinks, sugar, honey, and sweets [76,77]. Contrary to the current results, a higher adherence to dietary patterns labelled as Western was associated with an increased risk of lung cancer in American [29] and Uruguayan men [36], although components of these Western patterns slightly differed from the westernized traditional pattern of Polish men. In previous Polish studies [33] regarding the risk of breast cancer in women and lung cancer in men, no significant relationship between the traditional Polish pattern and both cancers was obtained. The components of the westernized Polish pattern coincide with the characteristics reported in previous Polish studies, in which the westernized traditional pattern was positively associated with lipid disorders and high blood pressure in adolescents [76], and the westernized traditional pattern with premature coronary artery disease in young men [78].

In the current study, no association between the sweet dairy pattern and lung cancer risk was found. This pattern included foods with a potentially beneficial effect on health (vegetable oils, dried fruit, and preserves) and foods with potentially negative effects on health (sugar, honey, sweets, and breakfast cereals) [76,79,80]. Such a combination may have influenced the neutral character of the final results regarding lung cancer risk. Other studies on dietary patterns and lung cancer have not identified a similar pattern, so a direct comparison of the current results is limited. The components of the sweet dairy pattern coincide with the characteristics reported in previous health-related studies, in which the pattern was neutral for health outcomes. In elderly Italians from the EPIC study, more hyperlipidemic subjects were found in those with lower adherence to the sweet and dairy pattern than those with normal blood lipids [81].

In the current study, in moderate and heavy male smokers, the westernized traditional and the sweet dairy patterns were not significantly associated with the risk of lung cancer. No previous studies involved male smokers to investigate the risk of lung cancer in this cohort with similar dietary patterns, so a direct comparison of the current results with other studies cannot be provided.

To the authors' best knowledge, this is the first Polish study in men regarding the association between lung cancer risk and dietary patterns, including the Polish-aMED score, considering the time of tobacco smoking. Overall, the data highlight the beneficial effect of a healthy diet on lung cancer risk in men from northeastern Poland. These findings could be helpful in preventing lung cancer, which was the most common cause of death from cancer in 14 regions of the world in 2018 (including in Eastern Europe) [82].

*Strength and Limitations*

The current study has several limitations. Due to the multifactorial aetiology of cancer, an adjusted model for the diet–cancer association, including many potential confounders [7,33,34], was calculated. However, it was not possible to include all potential confounders. Thus, the possibility of residual confounding by factors that were not evaluated cannot be ruled out. The next limitation is a lack of quantitative data regarding food consumption and nutrient intake, although current evidence shows the

limitations in concluding when single foods or nutrient components are considered [80]. In this study, an informational bias regarding lifestyle factors (e.g., diet, physical activity, smoking) is possible—it is a general limitation when subject-reported data are collected and interpreted. On the other hand, there is no golden method, and the food frequency method covering one year is a reasonable choice in dietary assessment [83]. Furthermore, the measurement of long-term usual daily physical activity or smoking is difficult. It cannot be ruled out that some of these lifestyle factors may have changed close to the cancer diagnosis due to early symptoms. Although retrospective data has been collected (for diet: 12 months before to data collection and diagnosis; for smoking: many years before). Thus, it can be speculated that the association between retrospective, long-time exposure (lifestyle) and cancer risk was identified, not short-term exposure as a result of health impairment. With respect to smoking, the cumulative exposure (in pack-years) can be interpreted with caution. Without a doubt, the longer one smokes and the more cigarettes one smokes per day (pack-years), the greater one's chances of getting lung cancer and other smoking-related diseases. Even though the problem of how to summarize the effects of extended and variable exposures is a universal one in epidemiology and is still open, the cumulative dose has been widely used in analyses of numerous other exposures, including smoking [84]. In this study, a multidimensional statistical analysis (PCA) has both limitations and strengths. For the three PCA-driven dietary patterns that have been identified, the cumulative percentage of variance explained was not too high (31%). Since dietary data are variables with high variability [85], it is not possible to achieve a high level of the total variance explained while data-driven dietary patterns were identified. According to the literature on nutrition, the typical range is 20% to 30% of the total variance explained by two or three dietary factors (dietary patterns). In this light, the current result (31% for three factors) is better than many previously reported [86–89]. The strength of a statistical analysis is the sample size—sufficient for PCA performance (the subject-to-item ratio 19:1) [61].

A major strength of the study is the identification of dietary patterns (hypothesis-driven approach and data-driven approach) [58], which represents the overall combination of commonly consumed food and a consideration of the health outcome (synergistic or opposed) of many single dietary items [90]. Secondly, an additional logistic regression analysis was performed on the data, including an age-matched control sub-sample ($n$ = 238), to ensure that study outcomes do not differ when the two groups are age-matched (Tables S6 and S7). Thirdly, to collect dietary data, an interviewer-administrated FFQ with adequate to high internal repeatability [91] was used. Finally, although several studies have explored the association between dietary patterns and lung cancer, none have reported results from adults living in Central or Eastern Europe, considering the history of tobacco smoking. The current paper fills this important gap by exploring the link between different dietary patterns, including the Polish-aMED score, and cancer risk in male smokers from northeastern Poland.

## 5. Conclusions

The current study suggests that pro-healthy dietary patterns, including the Mediterranean pattern, may favour a lower risk of lung cancer in men. This beneficial association was found in moderate smokers, although it was not confirmed in heavy smokers. It can be speculated that a higher consumption frequency of foods with components of a pro-healthy diet can, to some extent, reduce the negative effect of moderate smoking and lower the risk of lung cancer. Given the limited number of participants, prospective studies with close control of confounding factors are needed, especially in northeastern European countries, to confirm the link between pro-healthy dietary patterns and the lower risk of lung cancer in moderate smokers.

**Supplementary Materials:** The following are available online at http://www.mdpi.com/2072-6643/12/12/3788/s1, Table S1: Food groups used in the dietary pattern analysis. Table S2: The Polish-aMED score (0–9 points) calculation and reference medians of food consumption frequency—data for 262 subjects of the control sample. Table S3: Estimation of the overall physical activity after combining data based on self-reported physical activity at work and physical activity in leisure time. Table S4: The mean (95% confidence interval) of the frequency of food consumption by smoking status for the cancer control sample (times/day). Table S5: The mean (95% confidence interval) of the frequency of food consumption by dietary patterns (times/day). Table S6: Characteristics of the

lung cancer sub-sample and the control sub-sample after age matching. Table S7: Odds ratios (95% confidence interval) of lung cancer risk by adherence to the dietary patterns in smokers after age matching of controls.

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**Table S1.** Food groups used in the dietary pattern analysis.

| Food Groups | Dietary Items |
|---|---|
| Whole grain products | Wholemeal wheat or rye bread, seeded loaves, pumpernickel, wholemeal cracker bread, buckwheat groats, barley, brown rice, wholemeal pasta, etc. |
| Fruits | All kinds of fruits |
| Nuts and seeds | Peanuts, hazelnuts, walnuts, cashews, coconuts, chestnuts, peanut butter, chocolate-nut spread, pumpkin seeds, sesame seeds, sunflower seeds, wheat germs, wheat bran, etc. |
| Vegetables | All kinds of vegetables (potatoes not included) |
| Fish | Pollock, cod, perch, hake, carp to 1 kg, tuna, panga, trout, salmon, sardines, herring, mackerel, eel, large carp, etc. |
| Legumes | Corn, green peas, green beans, etc. |
| Fruit, vegetable, vegetable-fruit juices | Mixed fruit juice, orange, grapefruit, apple, pear, grape, blackcurrant, cherry juice, mixed vegetable juice, tomato, carrot and carrot-fruit juice, etc. |
| Refined grain products | White bread, rye, wheat-rye bread, toast bread, white bread rolls, brioche, bagels, semolina, milled barley, pasta, white rice, rice flakes, etc. |
| Sugar, honey and sweets | Sugar added to beverages, such as tea, coffee. Honey added to dishes and beverages. Chocolate, chocolate sweets and chocolate bars, boiled sweets, hard caramels, jellied sweets, fudge, biscuits, cream cakes, fruit cakes, sponge cakes, cheesecakes, doughnuts, poppy-seed cakes, muffins, croissants, ice-creams and custard etc. |
| Red and processed meats | Pork, beef, veal, wild boar, venison, quail, mallard, hare, etc. |
| White meat | Poultry and rabbit |
| Potatoes | Boiled, baked, French fries, potato rosti, gnocchi, etc. |
| Other fats | Margarine for baking, frying, spreading. Mayonnaise and salad dressings |
| Sweetened beverages and energy drinks | Sweetened beverages and energy drinks |
| Animal fats | Lard, pork fat, etc. |
| Milk, fermented milk drinks and curd cheese | Milk and natural milk beverages (yoghurt, kefir, buttermilk), porridge, cheese curd, natural cottage cheese, soft cheese, mozzarella, cottage cheese with herbs, etc. |
| Sweetened milk drinks and flavoured homogenized cheese | Fruit yoghurts, yoghurts with chocolate flakes, flavoured buttermilk, hot chocolate, flavoured curds (with fruit, chocolate, vanilla), etc. |
| Eggs | Scrambled eggs, omelette, egg salad, cooked eggs |
| Cheese | Hard cheese, blue cheese, processed cheese, cheese spreads, etc. |
| Breakfast cereals | Muesli, cornflakes, other cereals - sweetened or unsweetened, etc. |
| Vegetable oils | Vegetable-based oil |
| Dried fruit, fruit preserves and fruit condiments | Raisins, dried apricots, figs, apples, prunes, fruit compote, jams, marmalades, dates, dried bananas, etc. |
| Alcohol | Beer, wine and cocktails, vodka and other spirits |

**Table S2.** The 'Polish-aMED' score (0–9 points) calculation and reference medians of food consumption frequency–data for 262 subjects of the control sample.

| Food Groups | Frequency of consumption (times/day)* | | Criteria for 1 point |
|---|---|---|---|
| | Mean (95% Cl) | Median[#] | |
| Vegetables | 0.831 (0.758; 0.903) | 0.704 | Greater than median intake |
| Fruit | 0.625 (0.583; 0.666) | 0.565 | Greater than median intake |
| Whole grains | 0.711 (0.633; 0.789) | 0.671 | Greater than median intake |
| Fish | 0.233 (0.198; 0.268) | 0.200 | Greater than median intake |
| Legumes | 0.207 (0.171; 0.244) | 0.125 | Greater than median intake |
| Nuts and seeds | 0.258 (0.201; 0.316) | 0.050 | Greater than median intake |
| Ratio of vegetable oils to animal fat | 1.334 (0.824; 1.844) | 0.444 | Greater than median intake |
| Red and processed meat | 1.998 (1.856; 2.214) | 1.913 | Less than median intake |
| Alcohol | - | - | Do not abuse[&] |

* food consumption frequency was expressed as times/day after assigning the values for categories of frequencies as follows: 'never or almost never' = 0; 'once a month or less' = 0.025; 'several times a month' = 0.1; 'several times a week' = 0.571; 'daily' = 1; 'several times a day' = 2. 95% CI—95% confidence interval; [#] reference median of food consumption frequency; [&] the men were asked about their alcohol consumption and, based on the literature, two classifications were created: (i) abuse, (ii) do not abuse alcohol [63, 64, 65].

**Table S3**. Estimation of the overall physical activity after combining data based on self-reported physical activity at work and physical activity in leisure time [69].

| | | Physical activity at work | | |
|---|---|---|---|---|
| | | **low** | **moderate** | **high** |
| **Physical activity in leisure time** | **low** | low | low | moderate |
| | **moderate** | low | moderate | moderate |
| | **high** | moderate | moderate | high |

**Table S4**. The mean (95% Confidence Interval) of the frequency of food consumption by smoking status* for cancer-control sample (times/day).

| Food groups | Moderate smoker | | | Heavy smoker | | |
|---|---|---|---|---|---|---|
| | Cancer Sample | Control Sample | *p* | Cancer Sample | Control Sample | *p* |
| Sample size (n) | 112 | 140 | - | 74 | 58 | - |
| Sugar, honey and sweets | 2.0 (1.9; 2.0) | 1.9 (1.7; 2.0) | 0.012 | 2.0 (1.9; 2.0) | 2.0 (1.7; 2.0) | 0.910 |
| Red and processed meats | 1.9 (1.7; 2.0) | 2.0 (1.8; 1.9) | 0.130 | 1.6 (1.4; 1.9) | 2.0 (1.7; 2.2) | 0.044 |
| Animal fats | 1.4 (1.2; 1.5) | 1.1 (1.0; 1.3) | 0.071 | 1.4 (1.2; 1.6) | 1.3 (1.0; 1.5) | 0.447 |
| Refined grain products | 1.3 (1.2; 1.5) | 1.0 (0.9; 1.1) | 0.001 | 1.3 (1.8; 1.4) | 1.2 (1.0; 1.4) | 0.508 |
| Milk, fermented milk drinks and curd cheese | 0.9 (0.7; 0.9) | 1.0 (0.9; 1.1) | 0.113 | 1.0 (0.8; 1.1) | 1.0 (0.8; 1.2) | 0.532 |
| Vegetables | 0.5 (0.4; 0.5) | 0.6 (0.6; 0.7) | < 0.001 | 0.5 (0.4; 0.6) | 0.5 (0.4; 0.6) | 0.733 |
| Fruits | 0.6 (0.5; 0.6) | 0.7 (0.6; 0.8) | 0.024 | 0.6 (0.5; 0.7) | 0.6 (0.5; 0.7) | 0.846 |
| Potatoes | 0.6 (0.6; 0.7) | 0.6 (0.6; 0.7) | 0.998 | 0.6 (0.6; 0.7) | 0.8 (0.7; 0.9) | 0.009 |
| Whole grain products | 0.4 (0.3; 0.5) | 0.7 (0.6; 0.8) | < 0.001 | 0.5 (0.4; 0.6) | 0.6 (0.4; 0.7) | 0.378 |
| Vegetable oils (including olive oil) | 0.5 (0.4; 0.6) | 0.5 (0.5; 0.6) | 0.238 | 0.5 (0.4; 0.5) | 0.5 (0.4; 0.6) | 0.414 |
| Other fats (margarine, mayonnaise, dressings) | 0.4 (0.3; 0.5) | 0.4 (0.3; 0.5) | 0.657 | 0.4 (0.2; 0.5) | 0.5 (0.3; 0.6) | 0.211 |
| Cheese | 0.4 (0.3; 0.5) | 0.4 (0.4; 0.5) | 0.582 | 0.4 (0.3; 0.4) | 0.3 (0.2; 0.4) | 0.566 |
| White meat | 0.4 (0.3; 0.4) | 0.4 (0.4; 0.5) | 0.068 | 0.3 (0.3; 0.4) | 0.4 (0.4; 0.5) | 0.086 |
| Sweetened beverages and energy drinks | 0.4 (0.3; 0.5) | 0.4 (0.3; 0.5) | 0.838 | 0.4 (0.3; 0.5) | 0.3 (0.2; 0.4) | 0.036 |
| Dried fruit and preserves | 0.1 (0.1; 0.1) | 0.1 (0.1; 0.2) | 0.295 | 0.1 (0.1; 0.1) | 0.1 (0.1; 0.2) | 0.146 |
| Eggs | 0.3 (0.2; 0.3) | 0.4 (0.3; 0.4) | 0.022 | 0.3 (0.3; 0.4) | 0.4 (0.3; 0.4) | 0.366 |
| Alcohol | 0.4 (0.3; 0.5) | 0.4 (0.3; 0.5) | 0.610 | 0.2 (0.1; 0.3) | 0.2 (0.1; 0.4) | 0.981 |
| Sweetened milk drinks and flavoured homogenized cheese | 0.2 (0.1; 0.2) | 0.1 (0.1; 0.2) | 0.476 | 0.2 (0.1; 0.3) | 0.2 (0.1; 0.2) | 0.168 |
| Fish | 0.2 (0.1; 0.2) | 0.2 (0.2; 0.3) | 0.229 | 0.2 (0.1; 0.3) | 0.2 (0.1; 0.3) | 0.915 |
| Nuts and seeds | 0.1 (0.0; 0.1) | 0.3 (0.2; 0.4) | < 0.001 | 0.1 (0.0; 0.2) | 0.1 (0.1; 0.2) | 0.504 |
| Legumes | 0.1 (0.1; 0.1) | 0.2 (0.2; 0.3) | 0.002 | 0.2 (0.1; 0.3) | 0.2 (0.1; 0.2) | 0.705 |
| Fruit, vegetable, vegetable-fruit juices | 0.2 (0.1; 0.2) | 0.1 (0.1; 0.2) | 0.290 | 0.1 (0.1; 0.2) | 0.1 (0.0; 0.2) | 0.396 |
| Breakfast cereals | 0.0 (0.0; 0.1) | 0.1 (0.0; 0.1) | 0.287 | 0.0 (0.0; 0.1) | 0.0 (0.0; 0.1) | 0.545 |

* Data for never smokers were not presented due to the small number of subjects (n = 55) especially within the cancer sample (n = 1); *p* – level of significance verified with a Kruskal-Wallis test.

**Table S5.** The mean (95% Confidence Interval) of the frequency of food consumption by dietary patterns (times/day).

| Food groups | Total | Adherence to the dietary pattern | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | 'Prudent' | | | 'Westernized Traditional' | | | 'Sweet Dairy' | | | 'Polish-a MED' score | | |
| | | lower | moderate | higher | lower | moderate | higher | lower | moderate | higher | low | moderate | high |
| Sample size (n) | 439 | 146 | 146 | 147 | 147 | 146 | 146 | 146 | 147 | 146 | 177 | 221 | 41 |
| Sugar, honey and sweets | 2.0 (1.9;2.2) | 3.0 (2.8;3.1) | 2.0 (1.8;2.1) | 1.2 (1.0;1.4) | 1.2 (1.1;1.4) | 2.0 (1.8;2.1) | 2.9 (2.7;3.1) | 1.3 (1.1;1.4) | 2.0 (1.7;2.1) | 2.9 (2.7;3.1) | 2.4 (1.1;1.4) | 2.0 (1.2;1.4) | 1.0 (0.8;1.3) |
| Red and processed meats | 1.9 (1.8;2.0) | 1.9 (1.8;2.1) | 1.9 (1.7;2.1) | 2.0 (1.8;2.2) | 1.1 (1.0;1.2) | 1.9 (1.7;2.0) | 2.9 (2.7;3.1) | 1.6 (1.4;1.7) | 1.9 (1.7;2.1) | 2.4 (2.2;2.6) | 1.8 (1.0;1.2) | 2.1 (1.1;1.3) | 2.1 (0.9;1.5) |
| Animal fats | 1.3 (1.2;1.3) | 1.4 (1.2;1.5) | 1.3 (1.1;1.4) | 1.2 (1.0;1.2) | 1.1 (1.0;1.2) | 1.2 (1.1;1.3) | 1.5 (1.4;1.7) | 0.6 (0.5;0.6) | 1.2 (1.1;1.3) | 2.0 (1.9;2.1) | 1.3 (0.8;1.0) | 1.3 (0.8;1.0) | 0.8 (0.5;0.8) |
| Refined grain products | 1.1 (1.0;1.2) | 1.8 (1.7;1.8) | 1.1 (1.0;1.2) | 0.5 (0.5;0.6) | 0.7 (0.6;08) | 1.1 (1.0;1.2) | 1.6 (1.5;1.7) | 0.8 (0.7;0.9) | 1.0 (0.9;1.1) | 1.6 (1.5;1.7) | 1.3 (0.7;0.9) | 1.1 (0.7;0.8) | 0.7 (0.5;0.7) |
| Milk, fermented milk drinks and curd cheese | 0.9 (0.9;1.0) | 0.9 (0.7;1.0) | 0.9 (0.8;1.0) | 1.1 (1.0;1.2) | 0.8 (0.7;0.9) | 0.9 (0.8;1.0) | 1.1 (1.0;1.2) | 0.6 (0.5;0.6) | 1.0 (0.9;1.1) | 1.2 (1.1;1.4) | 0.8 (0.6;0.7) | 1.0 (0.6;0.7) | 1.0 (0.5;0.8) |
| Vegetables | 0.8 (0.8;0.9) | 0.8 (0.7;0.9) | 0.8 (0.7;0.8) | 0.9 (0.8;1.0) | 0.7 (0.6;0.7) | 0.8 (0.7;0.9) | 1.0 (0.9;1.1) | 0.7 (0.6;0.7) | 0.8 (0.7;0.9) | 1.0 (0.9;1.1) | 0.7 (0.4;0.5) | 0.9 (0.4:0.5) | 1.0 (0.3;0.5) |
| Fruits | 0.8 (0.7;0.8) | 0.6 (0.6;0.7) | 0.7 (0.7;0.8) | 0.9 (0.8;1.0) | 0.6 (0.6;0.7) | 0.7 (0.6;0.8) | 0.9 (0.9;1.0) | 0.6 (0.5;0.7) | 0.8 (0.7;0.8) | 0.9 (0.9;1.0) | 0.5 (0.4;0.5) | 0.9 (0.4;0.5) | 1.2 (0.4;0.6) |
| Potatoes | 0.7 (0.6;0.7) | 0.7 (0.7;0.7) | 0.7 (0.6;0.7) | 0.6 (0.5;0.7) | 0.5 (0.4;0.6) | 0.7 (0.7;0.8) | 0.8 (0.7;0.8) | 0.6 (0.5;0.6) | 0.7 (0.6;0.7) | 0.7 (0.7;0.8) | 0.7 (0.3;0.4) | 0.7 (0.3;0.4) | 0.6 (0.2;0.4) |
| Whole grain products | 0.6 (0.5;0.6) | 0.2 (0.1;0.2) | 0.5 (0.4;0.5) | 1.2 (1.1;1.2) | 0.7 (0.6;0.8) | 0.6 (0.5;0.7) | 0.5 (0.4;0.6) | 0.6 (0.5;0.7) | 0.7 (0.6;0.7) | 0.5 (0.4;0.6) | 0.3 (0.4;0.5) | 0.7 (0.6;0.7) | 1.2 (0.4;0.7) |
| Vegetable oils (including olive oil) | 0.5 (0.5;0.5) | 0.5 (0.4;0.5) | 0.5 (0.4;0.5) | 0.6 (0.5;0.6) | 0.4 (0.3;0.5) | 0.5 (0.5;0.6) | 0.5 (0.5;0.6) | 0.4 (0.3;0.4) | 0.5 (0.5;0.6) | 0.6 (0.6;0.7) | 0.4 (0.3;0.4) | 0.5 (0.3;0.4) | 0.6 (0.3;0.4) |
| Other fats (margarine, mayonnaise, dressings) | 0.4 (0.3;0.4) | 0.5 (0.4;0.6) | 0.4 (0.3;0.5) | 0.2 (0.2;0.3) | 0.2 (0.1;0.2) | 0.4 (0.3;0.5) | 0.6 (0.4;0.7) | 0.6 (0.5;0.7) | 0.4 (0.3;0.5) | 0.2 (0.1;0.3) | 0.4 (0.6;0.7) | 0.4 (0.5;0.6) | 0.4 (0.5;0.7) |
| Cheese | 0.4 (0.4;0.4) | 0.3 (0.3;0.4) | 0.4 (0.3;0.5) | 0.4 (0.4;0.5) | 0.3 (0.3;0.4) | 0.4 (0.3;0.4) | 0.5 (0.4;0.5) | 0.2 (0.2;0.3) | 0.4 (0.4;0.5) | 0.5 (0.5;0.6) | 0.3 (0.3;0.3) | 0.4 (0.2;0.3) | 0.4 (0.3;0.4) |
| White meat | 0.4 (0.4;04) | 0.3 (0.3;0.4) | 0.4 (0.4;0.4) | 0.4 (0.4;0.5) | 0.3 (0.2;0.3) | 0.4 (0.4;0.4) | 0.5 (0.5;0.5) | 0.3 (0.3;0.3) | 0.4 (0.4;0.5) | 0.4 (0.4;0.5) | 0.3 (0.4;0.3) | 0.4 (0.2;0.3) | 0.5 (0.2;0.3) |
| Sweetened beverages and energy drinks | 0.4 (0.3;0.4) | 0.4 (0.3;0.4) | 0.4 (0.3;0.5) | 0.4 (0.3;0.5) | 0.2 (0.2;0.3) | 0.3 (0.3;0.4) | 0.6 (0.5;0.7) | 0.3 (0.2;0.3) | 0.3 (0.3;0.4) | 0.6 (0.5;0.6) | 0.3 (0.4;0.5) | 0.4 (0.4;0.5) | 0.4 (0.4;0.7) |
| Dried fruit and preserves | 0.3 (0.4;0.4) | 0.2 (0.3;0.4) | 0.3 (0.3;0.4) | 0.3 (0.4;0.5) | 0.3 (0.4;0.5) | 0.3 (0.3;0.4) | 0.3 (0.3;0.4) | 0.2 (0.3;0.4) | 0.3 (0.4;0.5) | 0.3 (0.4;0.4) | 0.2 (0.3;0.4) | 0.3 (0.3;0.4) | 0.4 (0.4;0.6) |
| Eggs | 0.3 (0.3;0.3) | 0.3 (0.2;0.3) | 0.3 (0.3;0.3) | 0.4 (0.3;0.4) | 0.2 (0.2;0.3) | 0.3 (0.3;0.4) | 0.4 (0.3;0.4) | 0.2 (0.2;0.3) | 0.3 (0.3;0.4) | 0.4 (0.4;0.5) | 0.2 (0.2;0.2) | 0.3 (0.3;0.3) | 0.4 (0.2;0.3) |
| Alcohol | 0.3 (0.3;0.4) | 0.4 (0.3;0.5) | 0.2 (0.2;0.3) | 0.4 (0.3;0.5) | 0.2 (0.2;0.2) | 0.4 (0.3;0.5) | 0.4 (0.3;0.5) | 0.3 (0.2;0.4) | 0.4 (0.3;0.4) | 0.3 (0.3;0.4) | 0.4 (0.3;0.4) | 0.3 (0.3;0.4) | 0.3 (0.1;0.4) |
| Sweetened milk drinks and flavoured homogenized cheese | 0.2 (0.1;0.2) | 0.2 (0.1;0.2) | 0.1 (0.1;0.2) | 0.2 (0.1;0.2) | 0.1 (0.1;0.1) | 0.2 (0.1;0.2) | 0.2 (0.2;0.3) | 0.1 (0.0;0.1) | 0.2 (0.1;0.2) | 0.3 (0.2;0.3) | 0.1 (0.2;0.3) | 0.2 (0.3;0.4) | 0.1 (0.2;0.3) |
| Fish | 0.2 (0.2;0.2) | 0.1 (0.1;0.2) | 0.2 (0.2;0.2) | 0.3 (0.3;0.4) | 0.2 (0.1;0.2) | 0.2 (0.2;0.3) | 0.3 (0.2;0.3) | 0.2 (0.1;0.2) | 0.2 (0.2;0.3) | 0.2 (0.2;0.3) | 0.1 (0.1;0.1) | 0.2 (0.2;0.3) | 0.5 (0.4;0.6) |
| Nuts and seeds | 0.2 (0.1;0.2) | 0.1 (0.1;0.1) | 0.1 (0.1;0.1) | 0.4 (0.3;0.5) | 0.2 (0.1;0.2) | 0.2 (0.1;0.2) | 0.2 (0.1;0.3) | 0.2 (0.1:0.2) | 0.2 (0.1;0.2) | 0.3 (0.2;0.3) | 0.1 (0.2;0.2) | 0.2 (0.4;0.5) | 0.6 (0.5;0.8) |
| Legumes | 0.2 (0.1;0.2) | 0.1 (0.1;0.2) | 0.1 (0.1;0.2) | 0.3 (0.2;0.3) | 0.2 (0.1;0.2) | 0.2 (0.1;0.2) | 0.2 (0.2;0.3) | 0.1 (0.1;0.2) | 0.2 (0.1;0.2) | 0.2 (0.2;0.3) | 0.1 (0.1;0.2) | 0.2 (0.2;0.3) | 0.4 (0.3;0.5) |
| Fruit, vegetable, vegetable-fruit juices | 0.1 (0.1;0.2) | 0.1 (0.1;01) | 0.1 (0.1;0.2) | 0.2 (0.1;0.2) | 0.1 (0.1;0.1) | 0.1 (0.1;0.2) | 0.2 (0.1;0.2) | 0.1 (0.1;0.1) | 0.1 (0.1;0.2) | 0.2 (0.1;0.2) | 0.1 (0.2;0.2) | 0.1 (0.2;0.3) | 0.3 (0.3;0.4) |
| Breakfast cereals | 0.0 (0.0;0.1) | 0.0 (0.0;0.0) | 0.0 (0.0;0.0) | 0.7 (0.0;0.1) | 0.1 (0.0;0.1) | 0.0 (0.0;0.0) | 0.0 (0.0;0.1) | 0.0 (0.0;0.0) | 0.0 (0.0;0.1) | 0.1 (0.0;0.1) | 0.0 (0.1;0.1) | 0.0 (0.1;0.2) | 0.1 (0.2;0.2) |

**Table S6.** Characteristics of the lung cancer sub-sample and the control sub-sample after age matching.

| Variable | Cancer-control sample | | Cancer sample | | Control sub-sample | | *p* |
|---|---|---|---|---|---|---|---|
| | n | % | n | % | n | % | |
| *Sample size* | 406 | 100.0 | 168 | 100.0 | 238 | 100.0 | |
| *Age (years*)* | 62.3 (6.4) | | 63.4 (6.7) | | 61.6 (6.2) | | 0.5580 |
| 45.0-49.9 | 7 | 1.7 | 3 | 1.8 | 4 | 1.7 | |
| 50.0-54.9 | 37 | 9.1 | 12 | 7.1 | 25 | 10.5 | |
| 55.0-59.9 | 72 | 17.8 | 24 | 14.3 | 48 | 20.2 | |
| 60.0-64.9 | 132 | 32.5 | 51 | 30.3 | 81 | 34.0 | 0.0590 |
| 65.0-69.9 | 97 | 23.9 | 42 | 25.0 | 55 | 23.1 | |
| 70.0-74.9 | 47 | 11.6 | 29 | 17.3 | 18 | 7.6 | |
| 75.0-80.0 | 14 | 3.4 | 7 | 4.2 | 7 | 2.9 | |

*mean and standard deviation (SD); n—number; %—percentage of the sample; *p*—level of significance assessed by chi$^2$ test

**Table S7**. Odds ratios (95% Confidence Interval) of lung cancer risk by adherence to the dietary patterns in ever smokers after age matching of controls.

| Adherence to the dietary pattern | Cancer-control sample (n=406) | | | | Moderate smoker (n=168) | | | | Heavy smoker (n=238) | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | Crude model | *p* | Adjusted model | *p* | Crude model | *p* | Adjusted model | *p* | Crude model | *p* | Adjusted model | *p* |
| **'Prudent'** | | | | | | | | | | | | |
| lower (ref.) | Ref. | | Ref. | | Ref. | | Ref. | | Ref. | | Ref. | |
| moderate | 0.61 (0.37; 0.99) | 0.0438 | 0.71 (0.41; 1.21) | 0.2044 | 0.60 (0.33; 1.12) | 0.1064 | 0.73 (0.37; 1.45) | 0.3732 | 0.84 (0.34; 2.07) | 0.7004 | 0.80 (0.88; 2.24) | 0.6662 |
| higher | 0.54 (0.42; 0.70) | <0.0001 | 0.74 (0.55; 0.99) | 0.0411 | 0.46 (0.33; 0.66) | <0.0001 | 0.64 (0.42; 0.96) | 0.0313 | 0.62 (0.89; 0.57) | 0.6244 | 1.04 (0.60; 1.80) | 0.8823 |
| **'Westernized Traditional'** | | | | | | | | | | | | |
| lower (ref.) | Ref. | | Ref. | | Ref. | | Ref. | | Ref. | | Ref. | |
| moderate | 1.06 (0.66; 1.72) | 0.0518 | 0.82 (0.47; 1.41) | 0.4648 | 1.15 (0.61; 2.19) | 0.6649 | 0.84 (0.40; 1.77) | 0.6485 | 0.92 (0.37; 2.29) | 0.8570 | 0.91 (0.33; 2.52) | 0.8581 |
| higher | 0.98 (0.77; 1.26) | 0.9034 | 0.83 (0.62; 1.11) | 0.1999 | 1.07 (0.78; 1.47) | 0.6625 | 0.94 (0.63; 1.39) | 0.7514 | 0.81 (0.51; 1.28) | 0.3571 | 0.75 (0.44; 1.28) | 0.2899 |
| **'Sweet Dairy'** | | | | | | | | | | | | |
| lower (ref.) | Ref. | | Ref. | | Ref. | | Ref. | | Ref. | | Ref. | |
| moderate | 0.85 (0.52; 1.39) | 0.5161 | 0.79 (0.46; 1.36) | 0.3966 | 0.88 (0.47; 1.66) | 0.7031 | 0.87 (0.43; 1.76) | 0.6876 | 0.77 (0.30; 2.01) | 0.5903 | 0.66 (0.22; 1.98) | 0.4504 |
| higher | 1.09 (0.86; 1.39) | 0.4631 | 1.02 (0.78; 1.34) | 0.8444 | 1.12 (0.82; 1.55) | 0.4641 | 0.98 (0.68; 1.43) | 0.9317 | 1.02 (0.66; 1.58) | 0.0056 | 1.06 (0.65; 1.73) | 0.8068 |
| **'Polish–aMED' score** | | | | | | | | | | | | |
| low (0-3 points; ref.) | Ref. | | Ref. | | Ref. | | Ref. | | Ref. | | Ref. | |
| moderate (4-6 points) | 0.45 (0.29; 0.69) | 0.0002 | 0.53 (0.33; 0.83) | 0.0062 | 0.33 (0.19; 0.57) | <0.0001 | 0.35 (0.19; 0.66) | 0.0009 | 0.68 (0.31; 1.50) | 0.3376 | 0.70 (0.29; 1.68) | 0.4139 |
| high (7-9 points) | 0.41 (0.27; 0.64) | <0.0001 | 0.52 (0.32; 0.82) | 0.0053 | 0.28 (0.13; 0.61) | 0.0012 | 0.36 (0.16; 0.80) | 0.0109 | 0.88 (0.42; 1.84) | 0.7298 | 1.15 (0.50; 2.62) | 0.7347 |

Ref.—reference category; 'Polish-aMED'score—'Polish-adapted Mediterranean Diet' score (range of points: 0–9); Moderate smoker—smoker who smoked 2.5 to 11 pack-years; Heavy smoker—smoker who smoked more than 11 pack-years; *p*—the level of significance was assessed by Wald's test; Adjusted model for: status smoking currently only cancer-control sample (never smokers, current smokers, former smokers), BMI (categories), socioeconomic status (low, average, high), overall physical activity (low, moderate, high), the occurrence of lung cancer in relatives (yes, no, I do not know), occupational exposure in the workplace (yes, no); reference category in the PCA: never smoker in controls.

*nutrients*

MDPI

*Article*

# Lung Cancer Risk in Men and Compliance with the 2018 WCRF/AICR Cancer Prevention Recommendations

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**Abstract:** Lung cancer is the most common and deadly form of cancer worldwide, especially in men. The 2018 World Cancer Research Fund/American Institute for Cancer Research (WCRF/AICR) updated cancer prevention recommendations, and a standard scoring system (2018 WCRF/AICR Score) was published. The purpose of this study was to develop the adapted version of the 2018 WCRF/AICR Score with respect to lung cancer prevention recommendation (Ad-LC WCRF/AICR Score) and to examine the association between lung cancer risk in men and the Ad-LC WCRF/AICR Score as well as its single components. A case–control study was conducted among 439 men aged 45–80 years (187 controls, 252 primary lung cancer cases). Lifestyle and dietary data were collected with a questionnaire including the 62-item food frequency questionnaire (FFQ-6®). The Ad-LC WCRF/AICR Score was used as a categorized and continuous variable. Odds ratios (ORs) and 95% confidence intervals (95% CIs) for lung cancer risk were calculated with the partly and fully adjusted model. One component of the score was independently associated with a lower risk of lung cancer in men, regardless of the set of confounders used. In the fully adjusted model following the recommendation "Limit smoking" was associated with a lower risk of lung cancer—in the never smokers by 87% (OR: 0.13; 95% CI: 0.04–0.37; $p = 0.0002$) and in the moderate smokers by 45% (OR: 0.55; 95% CI: 0.33–0.91; $p = 0.0189$) compared with the heavy smokers as a reference. By adding the single components making up the Ad-LC WCRF/AICR Score, the combination of three components or more, reducing the risk of lung cancer compared to lower compliance as a reference by 45% to 78% and by 39% to 66% for intermediate compliance (except two models out of seven) and higher compliance, respectively. In the fully adjusted model, the risk of lung cancer for the total Ad-LC WCRF/AICR Score was lower by 47% (OR: 0.53; 95% CI: 0.32–0.88; $p = 0.0129$) in higher compliance with the score compared to those with the lower compliance. Each one-point increase in the Ad-LC WCRF/AICR Score reduced lung cancer risk by 34% (OR: 0.66; 95% CI: 0.45–0.95; $p = 0.0267$). The results support previous evidence that limiting smoking reduces the risk of lung cancer in men. It also provides an insight into cancer research by showing that following the combined 2018 cancer prevention recommendations related to diet, lifestyle and body fatness was associated with a lower risk of lung cancer in men.

**Keywords:** lung cancer; prevention; compliance with recommendations; the 2018 WCRF/AICR Score; food-based guidelines; dietary guidelines; case–control study

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## 1. Introduction

Men usually have a shorter life expectancy compared to women and significantly higher mortality with regard to chronic diseases such as cancers [1]. Lung cancer is the world's leading cause of cancer death, including in Poland [2,3]. This is largely because it is initially asymptomatic and typically discovered at advanced stages [4]. Both modifiable

and non-modifiable risk factors may increase the risk of lung cancer [5,6]. The link between tobacco smoking and lung cancer is by far the strongest and longest-known risk association of a modifiable lifestyle factor with a specific type of cancer [7,8]. Poor diet, occupational exposures, and air pollution may act independently or jointly with tobacco smoking in shaping the descriptive epidemiology of lung cancer [9].

Most of the available studies have focused on the analysis of the relationship between single dietary components and the risk of lung cancer [9–16]. The influence of lifestyle factors (in addition to smoking and occupational exposure in the workplace) [7,17] and the combined impact of diet [18–26] on the risk of lung cancer is still limited. An approach that combines lifestyle and dietary factors can be very useful in developing a primary lung cancer prevention strategy.

Given that an estimated 40% of all cancer cases are preventable [27], the World Cancer Research Fund (WCRF) and American Institute for Cancer Research (AICR) published a report in 2018 entitled *Diet, Nutrition, Physical Activity, and Cancer: A Global Perspective* [28]. This report was the basis for the development of the Standardized Scoring System Cancer Prevention Recommendations, which was developed in collaboration with scientists from the US National Cancer Institute (NCI) with members of AICR and WCRF International, and in consultation with the WCRF/AICR Panel Expert and other researchers [7,28]. The proposed 2018 WCRF/AICR Score focuses on eight key lifestyle components, including body weight, physical activity, diet, breastfeeding (optional), and smoking, recommended for some models [7,29]. The WCRF/AICR Continuous Update Project Expert Panel encourage researchers to implement this standardized score in their epidemiologic and clinical studies to enhance the comparability of findings across populations and countries [7,28].

The 2018 WCRF/AICR Score is an a priori approach based on prior knowledge of the health effects of dietary and lifestyle components. To date, there are publications regarding lung cancer risk versus the Mediterranean diet index or healthy eating index [23,30–32]. To the authors' knowledge, no studies have so far been published assessing the relationship between these updated recommendations and lung cancer risk. Furthermore, it is not clear to what extent the total effect of lifestyle factors contributes to the incidence of lung cancer.

Therefore, it seems reasonable to hypothesize that the 2018 WCRF/AICR cancer prevention recommendations may be considered for lung cancer prevention. The purpose of this study was twofold: (i) to develop the adapted version of the 2018 WCRF/AICR Score with respect to lung cancer prevention recommendation (Ad-LC WCRF/AICR Score), and (ii) to examine the association between lung cancer risk in men and the Ad-LC WCRF/AICR Score as well as its single components.

## 2. Materials and Methods

### *2.1. Ethical Statement*

This study was approved by the Bioethics Committee of the Faculty of Medical Sciences, University of Warmia and Mazury in Olsztyn on 2 October 2013 (resolution no. 29/2013). All of the subjects gave their written informed consent to participate in the study.

### *2.2. Study Design and Participants*

The total case–control sample obtained 439 men (187 lung cancer cases, 252 controls). The inclusion criteria were: (i) men, (ii) age $\geq$18 years, north-eastern Poland (urban and rural areas) living, (iv) lung tomography or X-ray examination, and (v) consent to participate in the study. The sample ranged in age from 45 to 80 years (mean 62.6), although recruiting was among adult males with no age restrictions. The study participants were enrolled in the study between October 2013 and August 2017. In order to avoid changes in dietary habits or other behaviors, newly diagnosed cases of lung cancer (up to a maximum of 14 days after cancer diagnosis) were included in the study. The sample collection and study design have previously been described in detail [22,23].

### *2.3. Data Collection*

All of the lifestyle questions referred to the period 12 months before diagnosis. Some questions, such as about smoking status, referred to a period in the past and present. Since the survey was conducted face-to-face by a trained interviewer, the interview was detailed, and any uncertainties were immediately clarified. The baseline questionnaire gathered data on the following background variables for both cases and controls: current sociodemographic, lifestyles (smoking status, alcohol consumption, physical activity, and occupational exposure in the workplace), family history of lung cancer, and vitamin/mineral supplement use.

#### 2.3.1. Sociodemographic Data

Age, place of residence, education level, and economic status were collected in the initial section of the questionnaire through an individual interview with each participant. The respondents were asked about three factors describing their socioeconomic status (SES). The SES index was calculated as the sum of the values (scores) assigned to the response categories for each SES factor (Table 1). SES index values were logarithmized, and SES tertiles were created to distinguish respondents with low, average, and high SES.

**Table 1.** Description of the socioeconomic status factors scoring—values assigned to the response categories.

| Socioeconomic Factors | Categories | Scoring |
|---|---|---|
| Place of residence | rural | 1 |
| | sub-urban | 2 |
| | urban | 3 |
| Education level | primary | 1 |
| | secondary | 2 |
| | higher | 3 |
| Economic situation | below average | 1 |
| | average | 2 |
| | above average | 3 |

#### 2.3.2. Lifestyle Data

The respondents were asked to describe their physical activity at work and physical activity in their leisure time by choosing one of three categories (Table 2). The self-declared data were then combined, and three categories of overall physical activity were created: low, moderate, and high (Table 3).

**Table 2.** Description of the categories of physical activity at work and in leisure time.

| Physical Activity | Categories | Description |
|---|---|---|
| at work | low | more than 70% of working time spent sedentary or retired |
| | moderate | 50% of working time spent sedentary and 50% of working time spent in an active manner |
| | high | 70% of working time spent in an active manner or physical work related to great exertion |
| at leisure time | low | sedentary for most of the time, watching TV, reading books, walking 1–2 h/week |
| | moderate | walking, bike riding, gymnastics, gardening, light physical activity performed 2–3 h/week |
| | high | bike riding, jogging, gardening, and sports activities involving physical exertion performed more than 3 h weekly |

**Table 3.** Estimate the overall physical activity after combining data based on self-reported physical activity at work and physical activity in leisure time.

| | | **Physical Activity at Work** | | |
|---|---|---|---|---|
| | | **Low** | **Moderate** | **High** |
| Physical activity in leisure time | Low | low | low | moderate |
| | Moderate | low | moderate | moderate |
| | High | moderate | moderate | high |

To determine smoking status, data on current smoking status, duration, intensity of smoking, and time since cessation were collected. The smoking status was expressed in pack years. The subjects were classified into three groups: never smoker (0 pack years), moderate smoker (2.5–11 pack years), or heavy smoker (>11 pack years). Smoking categories were based on the median value, which was 11 pack years in this sample (at enrollment). Details on calculation pack years were described previously [29] and are given in Supplementary Material.

#### 2.3.3. Body Composition Data

Trained researchers undertook the measurements of body weight (kg) and height (cm), and body mass index (BMI, kg/m$^2$) was calculated. Professional equipment and measuring tape were used: for weight—electronic digital scale SECA 799, for measuring height—a portable stadiometer SECA 220, for waist and hip circumference—stretch-resistant tape SECA 201. The method of near-infrared interaction with the FUTREX 6100/XL was used to measure the body fat content (%).

#### 2.3.4. Dietary Data

The 62-item food frequency questionnaire (FFQ-6®) in an interviewer-administered version was used [33] to collect data on the frequency of food consumption. The validation procedure of the 62-item FFQ-6® was described by Niedzwiedzka et al. [34]. The respondents were asked about food frequency consumption (6 categories to choose from) within the last 12 months prior to involvement in the study. The frequencies of consumption were recalculated and expressed as times/day as follows: 'never or almost never' = 0; 'once a month or less' = 0.025; 'several times a month' = 0.1; 'several times a week' = 0.571; 'daily' = 1; 'several times a day' = 2 times/day. The frequencies of the consumption of some food items were aggregated, and the following food groups were created: whole grains/vegetables/fruits/beans; fast food/other processed foods high in fat/ starches/sugars; red/processed meats; sugar-sweetened drinks. The sum of the average frequency of food consumption per group (times/day) was then calculated. For these food groups, subjective cut-off points were selected based on tertile distribution within each specific dataset (Table 4). For alcohol consumption, three categories of ethanol consumption were created based on the number of drinks consumed per day: 0 ethanol per day (0 drinks/day), >0–≤28 g of ethanol per day (2 drinks/day), and >28 of ethanol per day (2 drinks/day). All of the cut-offs were made based on the literature-derived components of the proposed 2018 WCRF/AICR Score [7].

**Table 4.** Scoring of the official 2018 WCRF/AICR Score and its adapted version with respect to lung cancer (Ad-LC WCRF/AICR Score).

| 2018 WCRF/AICR Recommendations | Operationalization of Recommendations | Scoring of the 2018 WCRF/AICR Score (Points) | Ad-LC WCRF/AICR Recommendations | Adapted Operationalization of the Recommendations | Scoring of the Ad-LC WCRF/AICR Score (Points) |
|---|---|---|---|---|---|
| 1. Be a healthy weight | **BMI (kg/m$^2$):** | | 1. Have a healthy body fat | **Body fat content (%):** | |
| | 18.5–24.9 | 0.5 | | 11.0–20.0 | 1 |
| | 25–29.9 | 0.25 | | 20.1–24.9 | 0.5 |
| | <18.5 or ≥30 | 0 | | <11.0 or >25.0 | 0 |
| | **Waist circumference (cm (in)):** | | | | |
| | Men: <94 (<37); Women: <80 (<31.5) | 0.5 | | | |
| | Men: 94–<102 (37–<40); Women: 80–<88 (31.5–<35) | 0.25 | | | |
| | Men: ≥102 (≥40); Women: ≥88 (≥35) | 0 | | | |
| 2. Be physically active | **Total moderate-vigorous physical activity (min/wk):** | | 2. Be physically active | **Overall physical activity:** | |
| | ≥150 | 1 | | High | 1 |
| | 75–<150 | 0.5 | | Moderate | 0.5 |
| | <75 | 0 | | Low | 0 |
| 3. Eat a diet rich in whole grains, vegetables, fruit, and beans | **Fruits and vegetables (g/day):** | | 3. Eat whole grains/vegetables/fruits/beans | **Fruits and vegetables [1] (times/day [#]):** | |
| | ≥400 | 0.5 | | Tertile 3 (≥1.435) | 0.5 |
| | 200–<400 | 0.25 | | Tertile 2 (>0.921 < 1.435) | 0.25 |
| | <200 | 0 | | Tertile 1 (≤0.921) | 0 |
| | **Total fibre (g/day):** | | | **Whole grains and beans [2] (times/day [#]):** | |
| | ≥30 | 0.5 | | Tertile 3 (≥1.050) | 0.5 |
| | 15–<30 | 0.25 | | Tertile 2 (>0.200 < 1.050) | 0.25 |
| | <15 | 0 | | Tertile 1 (≤0.200) | 0 |
| 4. Limit consumption of "fast foods" and other processed foods high in fat, starches, or sugars | **Percent of total kcal from ultra-processed foods:** | | 4. Limit consumption of fast foods/other processed foods high in fat/starches/sugars | **"Fast foods" and other processed foods high in fat, starches and sugars [3] (times/day [#]):** | |
| | Tertile 1 | 1 | | Tertile 1 (≤2.421) | 1 |
| | Tertile 2 | 0.5 | | Tertile 2(>2.421 < 4.038) | 0.5 |
| | Tertile 3 | 0 | | Tertile 3 (≥ 4.038) | 0 |
| 5. Limit consumption of red and processed meat | **Total red meat (g/wk) and processed meat (g/wk):** | | 5. Limit consumption of red/processed meats | **Red meat and processed meats [4] (times/day [#]):** | |
| | Red meat <500 and processed meat <21 | 1 | | Tertile 1 (≤1.392) | 1 |
| | Red meat <500 and processed meat 21–<100 | 0.5 | | Tertile 2 (>1.392 < 2.359) | 0.5 |
| | Red meat >500 or processed meat ≥100 | 0 | | Tertile 3 (≥2.359) | 0 |

**Table 4.** *Cont.*

| 2018 WCRF/AICR Recommendations | Operationalization of Recommendations | Scoring of the 2018 WCRF/AICR Score (Points) | Ad-LC WCRF/AICR Recommendations | Adapted Operationalization of the Recommendations | Scoring of the Ad-LC WCRF/AICR Score (Points) |
|---|---|---|---|---|---|
| 6. Limit consumption of sugar-sweetened drinks | **Total sugar-sweetened drinks (g/day):** | | 6. Limit consumption of sugar-sweetened drinks | **Sugar-sweetened drinks [5] (times/day [#]):** | |
| | 0 | 1 | | Tertile 1 (≤0.000) | 1 |
| | >0–≤250 | 0.5 | | Tertile 2 (>0.000 ≤ 0.025) | 0.5 |
| | >250 | 0 | | Tertile 3 (>0.025) | 0 |
| 7. Limit alcohol consumption | **Total ethanol (g/day):** | | 7. Limit alcohol consumption | **Ethanol (g/day):** | |
| | 0 | 1 | | 0 (0 drinks/day) | 1 |
| | >0–≤28 (2 drinks) males and ≤14 (1 drink) females | 0.5 | | >0–≤28 (2 drinks/day) males | 0.5 |
| | >28 (2 drinks) males and >14 (1 drink) females | 0 | | >28 (>2 drinks/day) males | 0 |
| 8. (Optional) For mothers: breastfeed your baby, if you can | **Exclusively breastfed over a lifetime for a total of:** | | 8. (Optional) For mothers: breastfeed your baby, if you can | NA | NA |
| | 6+ months | 1 | | | |
| | >0–<6 months | 0.5 | | | |
| | Never | 0 | | | |
| 9. Limit smoking | NI | NI | 9. Limit smoking | **Smoking pack years:** | |
| | | | | Never (0 pack years) | 1 |
| | | | | Moderate smoker (>0–11 pack years) | 0.5 |
| | | | | Heavy smoker (>11 pack years) | 0 |
| | **Total Score Range 0–8** | | | **Total Score Range 0–8** | |

Food components included into food groups to calculate Ad-LC WCRF/AICR Score: [1] All kinds of fruits and all kinds of vegetables (potatoes not included); [2] Wholemeal wheat or rye bread, seeded loaves, pumpernickel, wholemeal cracker bread, buckwheat groats, barley, brown rice, wholemeal pasta, etc., and beans;; [3] Fast food, fried food, margarine for baking, frying, spreading; mayonnaise and salad dressings; white bread, white bread rolls, semolina, milled barley, white rice and pasta, rice flakes, etc.; chocolate, chocolate sweets and chocolate bars, boiled sweets, hard caramels, jellied sweets, fudge, biscuits, cream cakes, fruit cakes, sponge cakes, cheesecakes, doughnuts, poppy-seed cakes, muffins, croissants, ice-creams and custard, etc.; [4] Pork, beef, veal, wild boar, venison, quail, mallard, hare, etc.; [5] Sweetened beverages and energy drinks; [#] The consumption frequency of food groups (categories) was expressed as times/day (values) as follows: 'never or almost never' = 0; 'once a month or less' = 0.025; 'several times a month' = 0.1; 'several times a week' = 0.571; 'daily' = 1; 'several times a day' = 2 times/day; NI—Not included in the official 2018 WCRF/AICR Recommendations; NA—Not Applicable to men.

### *2.4. Development of the Ad-LC WCRF/AICR Score*

The 2018 WCRF/AICR Score described by Shams-White et al. [7] was modified for this analysis, called the Adapted lung cancer WCRF/AICR Score (Ad-LC WCRF/AICR Score). Of the eight recommendations (single components of the score), the current study included seven components with the modification of one component and the addition of one important lung cancer risk factor: (1) normal body weight modified to normal body fat mass, (2) physical activity, (3) eating whole grains/vegetables/fruits/grains, (4) limiting the consumption of fast food/other processed foods high in fat/starches/sugars, (5) limiting red/processed meat consumption, (6) limiting sugar-sweetened beverage consumption, (7) limiting alcohol consumption, and (8) limiting smoking. The breastfeeding component is not relevant to the current study and was not used in the dietary-lifestyle assessment. The indirect measurement of body fat (BMI) was replaced with the direct measurement of body fat using near-infrared interaction (see Section 2.3.3).

When calculating the Ad-LC WCRF/AICR Score, the scoring weights were equally divided among these components. Each recommendation was assigned a score as follows: 1 point for meeting, 0.5 points for partially meeting, and 0 points for not meeting each recommendation. The total scores ranged from 0 to 8 points, with higher scores indicating greater compliance with the Ad-LC WCRF/AICR Score recommendations for lung cancer prevention (Table 4). The single components and their combinations and the total Ad-LC WCRF/AICR score are also presented. The scores were further categorized according to predefined cut-off points [35]: lower compliance: $\leq$3 points; intermediate compliance: >3–$\leq$5 points; and higher compliance: >5 points.

### *2.5. Statistical Analysis*

The adequacy of the sample size related to the current study was checked. The post hoc statistical power was calculated, taking into consideration variables being components of the Ad-LC WCRF/AICR Score. For example, the data were used to compare two groups with means of body fat content (28.0 SD 8.0% vs. 23.0 SD 6.4%), means of frequency of fruit and vegetable consumption (1.1 SD 0.6 times/day vs. 1.7 SD 1.0 times/day), means of frequency of red/processed meat consumption (2.4 SD 1.2 times/day vs. 1.3 SD 1.0 times/day), the occurrence of low physical activity (65.1% vs. 50.4%) and the occurrence of ethanol consumption >28 g/day (28.8% vs. 12.8%). Assuming a 5% significance level, the statistical power was 98%, 95%, 100%, 82% and 54%, respectively. It was therefore concluded that the sample size was appropriate.

The characteristics of the participants were examined using means and standard deviations (SD) for continuous variables and percentages for categorical variables by categories of the Ad-LC WCRF/AICR Score. A chi-squared test was used to evaluate the level of significance of the differences observed in categorical variables and the Kruskal–Wallis test for continuous variables.

The odds ratios (ORs) were used to assess the association between the Ad-LC WCRF/AICR Score as well as its single components and the risk of lung cancer development. The references (OR = 1.00) were the control sample and the bottom categories (lower compliance with the cancer prevention recommendations). The significance level of OR was verified with Wald's test [36]. The total Ad-LC WCRF/AICR Score was analysed as a categorical variable (for lower, intermediate, and higher compliance) and as a continuous variable (per one point of an increase). Two adjusted models were created for the association between single components, the Ad-LC WCRF/AICR Score and the risk of lung cancer. Model 1 (partly adjusted) included the following as the set of confounders: age (years), BMI (categories: <18.5; 18.5–24.9; 25–29.9; $\geq$30 kg/m$^2$), socioeconomic status (low, average, high), the occurrence of lung cancer in a relative (yes, no, I do not know), occupational exposure in the workplace (yes, no), vitamin/mineral supplement use (no, yes). Model 2 (fully adjusted) included the same confounders as model 1 and single components of the Ad-LC WCRF/AICR Score, excluding the modelled variables as appropriate.

For all tests, the level of statistical significance was considered as $p < 0.05$. Statistical analyses were performed using STATISTICA statistical software (version 13.0 PL; StatSoft Inc., Tulsa, USA; StatSoft, Krakow, Poland).

## 3. Results

The majority of men (254 subjects; 57.9%) had intermediate compliance with the Ad-LC WCRF/AICR Score, while only 39 men (8.9%) had higher compliance. Men with higher compliance with the Ad-LC WCRF/AICR Score compared to men with intermediate or lower compliance were younger, more often lived in urban areas, smoked less, had lower average BMI, waist circumference, and body fat content, as well as a lower frequency of consumption of red/processed meats, sugar-sweetened drinks, fast foods/other processed foods high in fat/starches/sugars and lower ethanol consumption while higher physical activity and frequency of consumption of fruits/vegetables and whole grains/beans (Tables 5 and 6). In the Supplementary Material frequency of food group consumption by categories of compliance with fruit/vegetable consumption, whole grain/beans consumption, and red/processed meats consumption was shown (Tables S1–S3).

**Table 5.** Baseline characteristics of the cancer-control sample by categories of compliance with the Ad-LC WCRF/AICR Score (%).

| Variable | Total (0–8 Points) | Compliance with the Ad-LC WCRF/AICR Score | | | *p*-Value |
|---|---|---|---|---|---|
| | | Lower (≤3 Points) | Intermediate (>3–≤5 Points) | Higher (>5 Points) | |
| Sample size | 439 | 146 | 254 | 39 | |
| Sample percentage | 100 | 33.2 | 57.9 | 8.9 | |
| Age (years), mean (SD) | 62.6 (7.2) | 62.8 (7.3) | 62.9 (7.0) | 60.3 (8.1) | <0.0001 |
| Place of residence | | | | | |
| rural | 34.6 | 43.8 | 30.7 | 25.6 | 0.0258 |
| sub-urban | 46.0 | 41.1 | 49.2 | 43.6 | |
| urban | 19.4 | 15.1 | 20.1 | 30.8 | |
| Education level | | | | | |
| primary | 23.7 | 30.8 | 20.5 | 18.0 | 0.1018 |
| secondary | 58.8 | 54.1 | 61.8 | 56.4 | |
| higher | 17.5 | 15.1 | 17.7 | 25.6 | |
| Economic situation | | | | | |
| below average | 20.7 | 23.3 | 20.5 | 12.8 | 0.3331 |
| average | 63.3 | 65.1 | 61.8 | 66.7 | |
| above average | 16.0 | 11.6 | 17.7 | 20.5 | |
| Socioeconomic status (SES index) [a] | | | | | |
| low | 53.5 | 60.3 | 51.6 | 41.0 | 0.1008 |
| average | 19.8 | 16.4 | 22.0 | 18.0 | |
| high | 26.7 | 23.3 | 26.4 | 41.0 | |
| Family history of lung cancer among relatives | | | | | |
| yes | 20.7 | 21.2 | 18.5 | 33.3 | 0.0925 |
| no | 73.8 | 713.3 | 77.6 | 59.0 | |
| I do not know | 5.5 | 7.5 | 3.9 | 7.7 | |
| Occupational exposure in the workplace | | | | | |
| yes | 31.2 | 29.5 | 32.3 | 30.8 | 0.8394 |
| no | 68.8 | 70.5 | 67.7 | 69.2 | |
| Vitamin/mineral supplements use | | | | | |
| yes | 10.7 | 8.2 | 11.4 | 15.4 | 0.3731 |
| no | 89.3 | 91.8 | 88.6 | 84.6 | |

**Table 5.** *Cont.*

| Variable | Total (0–8 Points) | Compliance with the Ad-LC WCRF/AICR Score | | | *p*-Value |
|---|---|---|---|---|---|
| | | Lower (≤3 Points) | Intermediate (>3–≤5 Points) | Higher (>5 Points) | |
| BMI (kg/m$^2$), mean (SD) | 27.7 (7.2) | 28.5 (5.2) | 27.4 (4.8) | 26.0 (3.4) | <0.0001 |
| <18.5 | 2.3 | 1.4 | 3.1 | 0.0 | |
| 18.5–24.9 | 28.5 | 27.4 | 27.2 | 41.0 | 0.0272 |
| 25.0–29.9 | 36.4 | 30.1 | 38.9 | 43.6 | |
| ≥30.0 | 32.8 | 41.1 | 30.7 | 15.4 | |
| Waist circumference (cm), mean (SD) | 100.6 (12.8) | 102.8 (7.6) | 100.3 (12.6) | 94.1 (10.1) | <0.0001 |
| <94 | 29.6 | 23.9 | 29.9 | 48.7 | |
| 94–<102 | 20.5 | 28.9 | 20.5 | 30.8 | 0.0014 |
| ≥102 | 49.9 | 38.8 | 49.6 | 20.5 | |

SD—standard deviation; [a] SES index was calculated based on place of residence, educational level and declared economic situation (details are given in Section 2.3.1); BMI—Body Mass Index; *p*-Value—level of significance verified with a chi$^2$ test (categorical variables) or a Kruskal–Wallis' test (continuous variable).

**Table 6.** Components of the Ad-LC WCRF/AICR Score by categories of compliance with this score in the cancer-control sample: means (SDs) and sample distribution (%).

| Variable | Total (0–8 Points) | Compliance with the Ad-LC WCRF/AICR Score | | | *p*-Value |
|---|---|---|---|---|---|
| | | Lower (≤3 Points) | Intermediate (3–≤5 Points) | Higher (>5 Points) | |
| Sample size | 439 | 146 | 254 | 39 | |
| Body fat content (%) | 26.6 (7.9) | 28.0 (8.0) | 26.3 (7.8) | 23.0 (6.4) | <0.0001 |
| 11.0–20.0 | 18.4 | 10.3 | 19.7 | 41.0 | |
| 20.1–24.9 | 60.4 | 71.9 | 59.1 | 25.6 | <0.0001 |
| <11.0 or >25.0 | 21.2 | 17.8 | 21.3 | 33.4 | |
| Overall physical activity | | | | | |
| low | 51.7 | 65.1 | 50.4 | 10.3 | |
| moderate | 37.6 | 32.2 | 37.8 | 56.4 | <0.0001 |
| high | 10.7 | 2.7 | 11.8 | 33.3 | |
| Smoking in pack years | 12.4 (7.4) | 14.5 (7.3) | 12.0 (7.0) | 7.3 (6.7) | <0.0001 |
| 0 (never smoker) | 12.5 | 8.2 | 11.4 | 35.9 | |
| >0–11 (moderate smoker) | 57.4 | 49.3 | 62.2 | 56.4 | <0.0001 |
| >11 (heavy smoker) | 30.1 | 42.5 | 26.4 | 7.7 | |
| Fruits and vegetables (times/day) | 1.3 (0.7) | 1.1 (0.6) | 1.3 (0.7) | 1.7 (1.0) | <0.0001 |
| Tertile 1 | 34.4 | 42.5 | 32.3 | 17.9 | |
| Tertile 2 | 32.6 | 34.2 | 31.5 | 33.3 | 0.0065 |
| Tertile 3 | 33.0 | 23.3 | 36.2 | 48.7 | |
| Whole grains and beans (times/day) | 0.8 (0.8) | 0.5 (0.7) | 0.9 (0.8) | 1.2 (0.9) | 0.1070 |
| Tertile 1 | 35.8 | 54.1 | 28.7 | 12.8 | |
| Tertile 2 | 31.0 | 28.8 | 32.3 | 30.8 | <0.0001 |
| Tertile 3 | 33.3 | 17.1 | 39.0 | 56.4 | |
| Fast foods/other processed foods high in fat/starches/sugars (times/day) | 3.3 (1.7) | 4.4 (1.6) | 3.3 (1.5) | 1.7 (1.0) | <0.0001 |
| Tertile 1 | 33.6 | 11.6 | 37.8 | 76.9 | |
| Tertile 2 | 33.5 | 23.3 | 40.9 | 23.1 | <0.0001 |
| Tertile 3 | 33.9 | 65.1 | 21.3 | 0 | |

**Table 6.** *Cont.*

| Variable | Total (0–8 Points) | Compliance with the Ad-LC WCRF/AICR Score | | | *p*-Value |
|---|---|---|---|---|---|
| | | Lower (≤3 Points) | Intermediate (3–≤5 Points) | Higher (>5 Points) | |
| Red/processed meats (times/day) | 2.0 (1.2) | 2.4 (1.2) | 1.8 (1.1) | 1.3 (1.0) | <0.0001 |
| Tertile 1 | 34.6 | 16.4 | 39.8 | 69.2 | |
| Tertile 2 | 32.6 | 33.6 | 33.9 | 20.5 | <0.0001 |
| Tertile 3 | 32.8 | 50.0 | 26.4 | 10.3 | |
| Sugar-sweetened drinks (times/day) | 0.1 (0.3) | 0.2 (0.4) | 0.1 (0.2) | 0.1 (0.2) | <0.0001 |
| Tertile 1 | 50.8 | 24.7 | 61.8 | 76.9 | |
| Tertile 2 | 20.0 | 25.3 | 18.9 | 7.7 | <0.0001 |
| Tertile 3 | 29.2 | 50.0 | 19.3 | 15.4 | |
| Ethanol (g/day) | | | | | |
| 0 | 23.0 | 15.7 | 23.6 | 46.2 | |
| >0–≤28 | 59.5 | 55.5 | 64.6 | 41.0 | <0.0001 |
| >28 | 17.5 | 28.8 | 11.8 | 12.8 | |

SD—standard deviation; Frequencies expressed as times/day are presented after recoding dietary data as follows: 'never or almost never' = 0; 'once a month or less' = 0.025; 'several times a month' = 0.1; 'several times a week' = 0.571; 'daily' = 1; 'several times a day' = 2 times/day; *p*-Value—level of statistical significance verified with a $chi^2$ test (categorical variables) or a Kruskal–Wallis' test (continuous variables).

The odds ratios for the single components of the Ad-LC WCRF/AICR Score are shown in Table 7. One component of the score was independently associated with a lower risk of lung cancer in men, regardless of the set of confounders used. In the fully adjusted model (model 2), following the recommendation "Limit smoking" was associated with a lower risk of lung cancer—in the never smokers (scored with 1 point) by 87% (OR: 0.13; 95% CI: 0.04–0.37; $p = 0.0002$) and in the moderate smokers (scored with 0.5 points) by 45% (OR: 0.55; 95% CI: 0.33–0.91; $p = 0.0189$) compared with the heavy smokers as a reference (scored with 0 points).

In the partly adjusted model (model 1), two single recommendations achieved statistical significance (positive or negative). In model 1, following the recommendation "Eat whole grains/vegetables/fruits/beans" was associated with a lower risk of lung cancer in frequent consumers of these foods (scored with 1 point) by 31% (OR: 0.69; 95% CI: 0.53–0.90; $p = 0.0057$) compared to infrequent consumers as a reference (scored with 0 points). In model 1, following the recommendation "Limit red/processed meat intake" was associated with a higher risk of lung cancer—in moderate frequent consumers (scored with 0.5 points) by more than two-fold (OR: 2.04; 95% CI: 1.16–3.58; $p = 0.0129$ and in infrequent consumers (scored with 1 point) by 1.4-fold (OR: 1.40; 95% CI: 1.07–1.97; $p = 0.0152$) in comparison to frequent consumers (scored with 0 points). In the fully adjusted model (model 2) for both recommendations ("Eat whole grains/vegetables/fruits/beans" and "Limit red/processed meat intake"), the statistical significance disappeared after including single components of the Ad-LC WCRF/AICR Score in the set of confounders.

By adding the single components that make up the Ad-LC WCRF/AICR Score, the combination of three components and more, for both intermediate compliance (except model 6 and full model) and higher compliance (no exception), reduced the risk of lung cancer compared to lower compliance as a reference. In the intermediate compliance group, the risk of lung cancer was lower by 45% to 78% (Model 2 OR: 0.55; 95% CI: 0.21–1.00; $p = 0.0497$; Model 3 OR: 0.22; 95% CI: 0.12–0.39; $p < 0.0001$; Model 4 OR: 0.54; 95% CI: 0.32–0.96; $p = 0.0335$; Model 5 OR: 0.49; 95% CI: 0.29–0.82; $p = 0.0075$). In the higher compliance group, the risk of lung cancer was lower by 39% to 66% (Model 2 OR: 0.53; 95% CI: 0.36–0.78; $p = 0.0013$; Model 3 OR: 0.57; 95% CI: 0.32–0.99; $p < 0.0441$; Model 4 OR: 0.40 95% CI: 0.27–0.59; $p < 0.0001$; Model 5 OR: 0.34; 95% CI: 0.17–0.69; $p = 0.0026$; Model 6 OR: 0.61; 95% CI: 0.43–0.85; $p = 0.0041$) (Table 8). In the full model (7), the risk of lung cancer for the total Ad-LC WCRF/AICR Score was lower by 47% (OR: 0.53; 95% CI: 0.32–0.88; $p = 0.0129$) in

higher compliance with the score compared to those with lower compliance as a reference. Each one-point increase in the Ad-LC WCRF/AICR Score reduced lung cancer risk by 34% (OR: 0.66; 95% CI: 0.45–0.95; $p = 0.0267$) (Table 8).

**Table 7.** Odds ratios (95% confidence intervals) of lung cancer occurrence for single components of Ad-LC WCRF/AICR Score.

| Component Included in the Model | Categories | Scores | Cancer-Control Sample ($n$ = 439) | | | |
|---|---|---|---|---|---|---|
| | | | Model 1 | $p$-Value | Model 2 | $p$-Value |
| 'Have a healthy body fat' | 11.0–20.0% of body fat | 0 | Ref. | | Ref. | |
| | 20.1–24.9% of body fat | 0.5 | 0.69 (0.36; 1.31) | 0.2581 | 0.71 (0.36; 1.41) | 0.3263 |
| | <11.0 or >25.0% of body fat | 1 | 0.86 (0.59; 1.28) | 0.4609 | 0.83 (0.55; 1.25) | 0.3705 |
| 'Be physically active' | Low | 0 | Ref. | | Ref. | |
| | Moderate | 0.5 | 0.70 (0.44; 1.13) | 0.1432 | 0.88 (0.53; 1.47) | 0.6237 |
| | High | 1 | 0.73 (0.49; 1.08) | 0.1110 | 0.82 (0.54; 1.24) | 0.3445 |
| 'Limit smoking' | Heavy smoker | 0 | Ref. | | Ref. | |
| | Moderate smoker | 0.5 | 0.53 (0.33; 0.87) | 0.0116 | 0.55 (0.33; 0.91) | 0.0189 |
| | Never smoker | 1 | 0.14 (0.05; 0.39) | 0.0001 | 0.13 (0.04; 0.37) | 0.0002 |
| 'Eat whole grains/ vegetables/fruits/beans' | Infrequent consumption | 0 | Ref. | | Ref. | |
| | Moderate frequency consumption | 0.5 | 0.76 (0.44; 1.35) | 0.3547 | 0.90 (0.50; 1.63) | 0.7301 |
| | Frequent consumption | 1 | 0.69 (0.53; 0.90) | 0.0057 | 0.77 (0.58; 1.03) | 0.0810 |
| 'Limit consumption of fast foods/other processed foods high in fat/starches/sugars' | Frequent consumption | 0 | Ref. | | Ref. | |
| | Moderate frequency consumption | 0.5 | 1.07 (0.63; 1.81) | 0.8014 | 1.08 (0.60; 1.91) | 0.8150 |
| | Infrequent consumption | 1 | 0.90 (0.69; 1.19) | 0.4830 | 0.93 (0.68; 1.27) | 0.6389 |
| 'Limit consumption of red/processed meats' | Frequent consumption | 0 | Ref. | | Ref. | |
| | Moderate frequency consumption | 0.5 | 2.04 (1.16; 3.58) | 0.0013 | 1.78 (0.98; 3.23) | 0.0575 |
| | Infrequent consumption | 1 | 1.40 (1.07; 1.97) | 0.0152 | 1.18 (0.87; 1.62) | 0.2830 |
| 'Limit consumption of sugar-sweetened drinks' | Frequent consumption | 0 | Ref. | | Ref. | |
| | Moderate frequency consumption | 0.5 | 0.80 (0.41; 1.57) | 0.0512 | 0.56 (1.25; 0.57) | 0.5659 |
| | Infrequent consumption | 1 | 1.10 (0.85; 1.43) | 0.4503 | 0.99 (0.78; 1.26) | 0.9514 |
| 'Limit alcohol consumption' | Frequent consumption | 0 | Ref. | | Ref. | |
| | Moderate frequency consumption | 0.5 | 0.92 (0.50; 1.70) | 0.8013 | 0.89 (0.45; 1.74) | 0.8874 |
| | Infrequent consumption | 1 | 1.13 (0.76; 1.67) | 0.5440 | 0.99 (0.63; 1.53) | 0.9477 |

Model 1 was adjusted for: age (years), BMI (categories: <18.5; 18.5–24.9; 25–29.9; ≥30 kg/m$^2$), socioeconomic status (low, average, high), the occurrence of lung cancer among a relative (yes, no, I do not know), occupational exposure in the workplace (yes, no); vitamin/mineral supplement use (yes, no); Model 2 = Model 1 + an adjustment for single components of the Ad-LC WCRF/AICR Score excluding modelled variable as appropriate; $p$-Value—the level of statistical significance verified with Wald's test.

**Table 8.** Odds ratios (95% confidence intervals) of lung cancer occurrence for the combination of components of Ad-LC WCRF/AICR Score.

| Components Included in the Model | Scores | Cancer-Control Sample ($n$ = 439) | |
|---|---|---|---|
| | | Adjusted Model | $p$-Value |
| Model 1: 'Have a healthy body fat' + 'Be physically active' | ≤0.5 | Ref. | |
| | >0.5–≤1 | 1.04 (0.57; 1.88) | 0.9036 |
| | >1 | 0.69 (0.47; 1.02) | 0.0634 |
| Model 2: Model 1 + 'Limit smoking' | ≤1 | Ref. | |
| | >1–<2 | 0.55 (0.21; 1.00) | 0.0497 |
| | ≥2 | 0.53 (0.36; 0.78) | 0.0013 |
| Model 3: Model 2 + 'Eat whole grains/vegetables/fruits/beans' | <2 | Ref. | |
| | ≥2–<3 | 0.22 (0.12; 0.39) | <0.0001 |
| | ≥3 | 0.57 (0.32; 0.99) | 0.0441 |
| Model 4: Model 3 + 'Limit fast food/other processed foods high in fat/starches/sugars' | ≤3 | Ref. | |
| | >2–<3 | 0.54 (0.32; 0.96) | 0.0335 |
| | ≥3 | 0.40 (0.27; 0.59) | <0.0001 |
| Model 5: Model 4 + 'Limit consumption of red/processed meats' | <3 | Ref. | |
| | >3–≤4 | 0.49 (0.29; 0.82) | 0.0075 |
| | >4 | 0.34 (0.17; 0.69) | 0.0026 |
| Model 6: Model 5 + 'Limit consumption of sugar-sweetened drinks' | ≤3 | Ref. | |
| | >3–≤4 | 0.93 (0.57; 1.53) | 0.0708 |
| | >4 | 0.61 (0.43; 0.85) | 0.0041 |
| Model 7 (full): Model 6 + 'Limit alcohol consumption' | ≤3 | Ref. | |
| | >3–≤5 | 0.87 (0.54; 1.38) | 0.5873 |
| | >5 | 0.53 (0.32; 0.88) | 0.0129 |
| 1-point increase | | 0.66 (0.45; 0.95) | 0.0267 |

Model adjusted for: age (years), BMI (categories: <18.5; 18.5–24.9; 25–29.9; ≥30 kg/m$^2$), socioeconomic status (low, average, high), the occurrence of lung cancer among a relative (yes, no, I do not know), occupational exposure in the workplace (yes, no); vitamin/mineral supplement use (yes, no); $p$-Value—the level of statistical significance verified with Wald's test.

## 4. Discussion

In 2018, the World Cancer Research Fund/American Institute for Cancer Research published the Third Expert Report (Diet, Nutrition, Physical Activity, and Cancer: A Global Perspective) [5]. A year later, a standardized scoring system for the association between adherence to these recommendations and cancer prevention was developed and published [7]. The current findings support these recommendations and highlight the possible importance of the interaction of diet-related components and lifestyle factors with lung cancer risk. Regarding the Ad-LC WCRF/AICR Score, in the current study, higher adherence to the score reduced lung cancer risk. This association was found in both approaches—for categories and per one-point increase in the score.

To the best of the authors' knowledge, this is the first case–control study describing the association between the 2018 WCRF/AICR cancer prevention recommendations and lung cancer risk. The strongest and longest-known modifiable lifestyle risk factor for lung cancer is smoking [7,8,37,38], which was also observed in this study. A protective association was also found between more frequent consumption of whole grains/vegetables/fruits/beans and lung cancer risk in a partially adjusted model. However, this protective association disappeared in the fully adjusted model when other dietary- and lifestyle-related components were included as confounders, including potentially negative components such as red/processed meat [39,40]. Other studies [41,42] have found that the consumption of fruits and vegetables, which are rich in antioxidant vitamins, phenolic compounds, minerals, and fibre, has beneficial effects on respiratory health.

Referring to the single components of the Ad-LC WCRF/AICR Score, one finding must be discussed. In a partially adjusted model, an increased risk of lung cancer in those who

followed the "Limit red/processed meat consumption" recommendation was stated. However, this surprising result has an explanation. As shown in the Supplementary Material (Table S3), the lower frequency of red/processed meat consumption (i.e., higher compliance with the recommendations) was accompanied by a significantly lower frequency of consumption of vegetables and fruits. In particular, in the higher compliance with the red/processed meats consumption group, these foods were consumed nearly once a day (on average 0.9 times/day), while vegetables and fruits were consumed slightly above once a day (on average 1.1 times/day). Thus, despite a lower frequency of red/processed meat consumption, a protective effect of vegetables and fruits did not exist [41,42]. Previous studies [4,5,9,32,43–45] have shown that the consumption of red and processed meat can increase the risk of lung cancer. In contrast, the European Prospective Investigation into Cancer and Nutrition (EPIC) study [14] found no association between meat or processed meat consumption and lung cancer risk.

Due to the complexity of the diet, the approaches assessing associations with cancer that focus on single dietary habits, foods, or nutrients may not be appropriate because it displays only a part of the association [46,47]. An alternative approach is to focus on the overall dietary patterns that express many different aspects of diet [48] and lifestyle [7,49] combined. Such a holistic approach in the cancer prevention recommendations was used by the WCRF/AICR experts [7,28]. An important point of the WCRF/AICR recommendations was that each recommendation was intended to be one part of a comprehensive package of modifiable lifestyle behaviours that together promote a healthy pattern of diet and physical activity conducive to cancer prevention. Thus, a package of lifestyle behaviours should be considered more important in interpretation and conclusion than single ones. Such holistic conclusions were drawn from studies carried out previously [18–26,29–31,49]. For example, a study on cardiometabolic health in Polish men showed that a healthy diet combined with an active lifestyle (healthy diet, activity at work, former smoking pattern) was associated with a reduced risk of obesity and metabolic abnormalities despite some unhealthy components, such as the frequent consumption of fried foods [49]. The authors' previous findings in a cancer-control cohort of men (the same as the current cohort) have shown that health-promoting dietary patterns (Prudent pattern and Mediterranean pattern) may promote a lower risk of lung cancer, even in moderate smokers (smoking 2.5–10 pack years) [29]. The current study casts new light on the association between dietary-lifestyle factors and lung cancer. It showed that a combination of some single dietary-lifestyle factors was associated with reduced lung cancer risk (by approx. a half lower) despite some unhealthy components, for example, higher frequency of red/processed meats consumption, i.e., the beneficial aspects of overall diet and lifestyle prevailed. As in real life, nobody follows all recommendations, and this is good news for lung cancer prevention. A message directed to people can be: "follow as many recommendations as possible"(but it is not necessary to follow all recommendations).

Adherence to a health-promoting lifestyle, including dietary habits, is more common in women than in men [50]. This thesis is supported by the current study, in which only 39 men out of 439 subjects were in the higher adherence score range. Indeed, men seem to have some resistance to following a healthy diet [51]. The current study found that lung cancer risk was lower for total Ad-LC WCRF/AICR Score and demonstrated a protective association between each one-point increase in Ad-LC WCRF/AICR Score and lung cancer risk. To date, the association between adherence to the 2018 WCRF/AICR recommendations and lung cancer incidence has not been assessed, but it has already been examined for the 2007 WCRF/AICR recommendations. A 2007 report: Food, nutrition, physical activity, and the prevention of cancer: a global perspective, presented eight general and two specific recommendations for cancer prevention [52]. Since then, several studies have evaluated the association between adherence to these recommendations and lung cancer risk. In several studies, adherence to the 2007 recommendations for diet, physical activity, and weight control was associated with reduced lung cancer risk [53–55]. However, a standardized scoring method to determine adherence to the 2007 WCRF/AICR recommendations had

not been previously developed, so each study developed its own version of the scoring. To increase the comparability of results across populations and countries, a standardized scoring system for WCRF/AICR cancer prevention recommendations was developed in 2018. The current study is the first (and so far, the only) study to evaluate the association between adherence to the 2018 WCRF/AICR recommendations and lung cancer risk in men. To date, there have been few studies evaluating the association between updated recommendations and the risk of other cancers. Studies on total cancer incidence in Sweden [56] and cancers of the colon in Spain [57] and the USA [58], breast in Spain [59] and the USA [60], and prostate in Spain [61], similarly to the current study, found a positive association with adherence to the 2018 WCRF/AICR recommendations. In contrast, one arm of the EPIC project focused on breast cancer in Europe [35], and a clinical-control study focused on chronic lymphocytic leukaemia in Spain [62] found no association with adherence to the 2018 WCRF/AICR recommendations.

*Strengths and Limitations*

The current study may have some potential limitations that should be noted. This is a case–control design, and the results may be subject to information bias. Lifestyle data, such as dietary and physical activity, were collected through a questionnaire, and the results may also be susceptible to recall bias [62]. Moreover, the use of a food frequency questionnaire is limited by the use of a fixed food list. Furthermore, different interpretations of questions regarding food items and the frequency of consumption by individuals can also be taken into consideration [63,64]. To overcome these limitations, trained interviewers helped participants to answer more accurately while completing the questionnaire. Although the method is not free from measurement error, previous studies using repeated and mixed-method dietary assessment confirmed the utility of food frequency questionnaires in exploring associations between diet and chronic disease risk [64,65]. The use of a simple scoring index (Ad-LC WCRF/AICR Score) should also be considered a potential limitation of the study. The score was based on the sum of several risk factors in the authors' own adaptation or whose association with lung cancer risk is not proven. Such an approach may have weakened the association of scores in the study. Smoking was included as a proven risk factor for lung cancer in the scoring to strengthen the interpretation of the score. Moreover, the indirect measure of body fat (BMI) was replaced with a direct measure of body fat using near-infrared interaction. BMI does not fully account for body composition, such as differences in muscle proportion and different types of fatness in patients with the same BMIs, especially in chronically ill patients [66]. Men who are diagnosed with lung cancer may already exhibit preclinical weight loss.

The current study also has several strengths. It is the first study of its kind in Central Europe to describe the relationship between WCRF/AICR recommendations and lung cancer risk in men. Cases and controls were selected according to the inclusion criteria for the study population described previously [29]; cases were recruited at diagnosis and before treatment. We used the validated FFQ-6® food frequency questionnaire. This type of questionnaire does not provide information on estimated portion size but represents typical eating habits of Poles [22–24,67–69]. In Poland, there has only been one validated semi-quantitative and comprehensive FFQ (165-item FFQ®) [70], but it causes a heavy burden on the respondent (an interview takes 3–4 h). Conducting the 165-item FFQ® among men with lung cancer would have been too difficult. The available data on potential cancer risk factors allowed the survey results to be adjusted for confounders, but unmeasured or residual confounders cannot be ignored.

## 5. Conclusions

The current study provides insight into cancer research by showing that following the combined 2018 cancer prevention recommendations related to diet, lifestyle, and body fatness was associated with a lower risk of lung cancer in men. It also provides new support for previous evidence that limiting smoking reduces the risk of lung cancer in men. The

study found that a combination of some single dietary-lifestyle factors was associated with reduced lung cancer risk despite some unhealthy components. Based on these findings in developing pro-healthy strategies, the message directed to the public can be: "follow as many recommendations as possible to prevent lung cancer".

**Supplementary Materials:** The following supporting information can be downloaded at: https://www.mdpi.com/article/10.3390/nu14204295/s1, Table S1. Frequency of food group consumption (times/day; mean (SD)) by categories of compliance with fruit/vegetable consumption# in the case-control sample; Table S2. Frequency of food group consumption (times/day; mean (SD)) by categories of compliance with whole grain/bean consumption# in the case-control sample; Table S3. Frequency of food group consumption (times/day; mean (SD)) by categories of compliance with red/processed meat consumption# in the case-control sample [71].

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**Lung Cancer Risk in Men and Compliance with the 2018 WCRF/AICR Cancer Prevention Recommendations**

by Iwona Hawrysz, Lidia Wadolowska, Malgorzata Anna Slowinska, Anna Czerwinska and Janusz Jacek Golota

# Supplementary material

**Pack-years of smoking calculation**

Data regarding smoking status was collected for all subjects, including current smoking status, duration, the intensity of smoking, and time since cessation. The pack-years of smoking were calculated by multiplying the average number of packs of cigarettes smoked per day (intensity) by the number of years the person had smoked [71]. Smoking status pack-years were classified into three groups: never smoker (0 pack-years), moderate smoker (2.5–11 pack-years) or heavy smoker (> 11 pack-years). These categories were based on the median value, which, in this sample, was equal to 11 pack-years (at enrolment).

Example of calculation:

A man reported smoking 30 cigarettes a day for ten years.
The calculated number of pack-years is: 10 × 30/20 = 15 pack-years
10—years of smoking
30—number of cigarettes per day
20—number of cigarettes in one pack

**Table S1.** Frequency of food group consumption (times/day; mean (SD)) by categories of compliance with fruit/vegetable consumption [#] in the case-control sample

| Variable | Total (0-8 points) | Compliance with fruit/vegetable consumption | | | *p*-Value |
|---|---|---|---|---|---|
| | | Lower (0 points) | Intermediate (0.25 points) | Higher (0.5 point) | |
| Sample size | 439 | 151 | 143 | 145 | |
| Fruits and vegetables | 1.3 (0.7) | 0.6 (0.2) | 1.2 (0.2) | 2.0 (0.6) | <0.0001 |
| **Other dietary components of the Ad-LC WCRF/AICR Score** | | | | | |
| Whole grains and beans | 0.8 (0.8) | 0.5 (0.6) | 0.7 (0.6) | 1.2 (1.0) | <0.0001 |
| Fast foods/other processed foods high in fat/starches/sugars | 3.3 (1.7) | 3.1 (1.6) | 3.5 (1.8) | 3.5 (1.8) | 0.0866 |
| Red/processed meats | 2.0 (1.2) | 1.6 (1.0) | 2.4 (1.3) | 2.0 (1.3) | <0.0001 |
| Sugar-sweetened drinks | 0.1 (0.3) | 0.1 (0.2) | 0.1 (0.3) | 0.1 (0.3) | 0.9530 |

SD—standard deviation; [#] To determine compliance with the Ad-LC WCRF/AICR Score, the frequency of fruit/vegetable consumption (times/day) was divided according to tertile distribution: tertile 1 (≤0.921), tertile 2 (>0.921 <1.435), tertile 3 (≥1.435).

**Table S2.** Frequency of food group consumption (times/day; mean (SD)) by categories of compliance with whole grain/bean consumption [#] in the case-control sample

| Variable | Total (0-8 points) | Compliance with whole grain/bean consumption | | | |
|---|---|---|---|---|---|
| | | Lower (0 points) | Intermediate (0.25 points) | Higher (0.5 point) | *p*-Value |
| Sample size | 439 | 157 | 139 | 143 | |
| Whole grains and beans | 0.8 (0.8) | 0.1 (0.1) | 0.6 (0.2) | 1.7 (0.7) | <0.0001 |
| **Other dietary components of the Ad-LC WCRF/AICR Score** | | | | | |
| Fruits and vegetables | 1.3 (0.7) | 0.9 (0.5) | 1.3 (0.6) | 1.6 (0.8) | <0.0001 |
| Fast foods/other processed foods high in fat/starches/sugars | 3.3 (1.7) | 3.8 (1.6) | 3.4 (1.8) | 2.7 (1.6) | <0.0001 |
| Red/processed meats | 2.0 (1.2) | 1.9 (1.0) | 1.9 (1.1) | 2.1 (1.0) | 0.6680 |
| Sugar-sweetened drinks | 0.1 (0.3) | 0.2 (0.3) | 0.1 (0.3) | 0.1 (0.3) | 0.6965 |

SD—standard deviation; # To determine compliance with the Ad-LC WCRF/AICR Score, frequency of whole grain/bean consumption (times/day) was divided according to tertile distribution: tertile 1 (≤2.000), tertile 2 (>0.200<1.050, tertile 3 (≥1.050).

**Table S3.** Frequency of food group consumption (times/day; mean (SD)) by categories of compliance with red/processed meat consumption # in the case-control sample

| Variable | Total (0-8 points) | Compliance with red/processed meat consumption | | | |
|---|---|---|---|---|---|
| | | Lower (0 points) | Intermediate (0.5 points) | Higher (1 point) | *p*-Value |
| Sample size | 439 | 144 | 143 | 152 | |
| Red/processed meats | 2.0 (1.2) | 3.3 (1.0) | 1.8 (0.3) | 0.9 (0.4) | <0.0001 |
| **Other dietary components of the Ad-LC WCRF/AICR Score** | | | | | |
| Fruits and vegetables | 1.3 (0.7) | 1.5 (0.7) | 1.2 (0.6) | 1.1 (0.7) | <0.0001 |
| Whole grains and beans | 0.8 (0.8) | 0.8 (0.8) | 0.8 (0.8) | 0.8 (0.8) | 0.9106 |
| Fast foods/other processed foods high in fat/starches/sugars | 3.3 (1.7) | 3.8 (1.8) | 3.5 (1.6) | 2.7 (0.8) | <0.0001 |
| Sugar-sweetened drinks | 0.1 (0.3) | 0.2 (0.4) | 0.1 (0.2) | 0.1 (0.3) | 0.0618 |

SD—standard deviation; # To determine compliance with the Ad-LC WCRF/AICR Score, frequency of red meat/processed meat consumption (times/day) was divided according to tertile distribution: tertile 1 (≤1.392), tertile 2 (>1.392 <2.359), tertile 3 (≥2.359).

## 10. Oświadczenie kontrybucji współautorów publikcji

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**OŚWIADCZENIE**

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A: koncepcja i metodologia badań głównych; B: przeprowadzenie badań; C: źródło danych klinicznych; D: zarządzanie danymi; E: koncepcja i metodologia publikacji; F: analiza statystyczna; G: zarządzanie projektem; H: przygotowanie wizualne publikacji; I: pisanie publikacji; J: krytyczny przegląd i korekta publikacji; K: pozyskiwanie funduszy na realizację badania

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# OŚWIADCZENIE

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