A Feasibility Study of Machine Learning Models for Cancer Rate Prediction

Shan Chen [1], Yuanzhao Ding [2,*]

[1] Department of Applied Social Sciences, The Hong Kong Polytechnic University, 11 Yuk Choi Rd, Hung Hom, Hong Kong, China. ORCID: 0000-0002-5434-4883. chenshan1893@gmail.com
[2] Social Sciences Division, University of Oxford, South Parks Road, Oxford, OX1 3QY, United Kingdom. ORCID: 0000-0003-0116-3648. armstrongding@163.com
* Correspondence: armstrongding@163.com

Abstract: Cancer is a major concern for people, and accurately predicting the probability of cancer incidence and mortality is an important research topic. With the development of big data and artificial intelligence technology, a new machine learning model has emerged. Using 72,591 pieces of data, including age, case count, population size, race, gender, site, and year of discovery, we built a machine learning model. Through calculations, we found that the decision tree, random forest, logistic regression, support vector machine, and neural network achieved testing accuracies of 62.11%, 61.68%, 54.53%, 55.72%, and 63.10%, respectively. With the help of this model, scientists and policymakers can accurately predict future cancer incidence and mortality rates through databases, allowing them to make relevant policies (such as timely allocating doctors and medical resources) to better serve the people.

Keywords: Cancer; Incidence; Mortality; Artificial Intelligence; Machine learning; Neural network

1. Introduction

Cancer is a pervasive and devastating disease that poses a significant threat to human health and wellbeing [1]. It is estimated that globally, there are approximately 18.1 million new cases of cancer and 9.6 million cancer-related deaths annually [2,3]. Notably, males have a higher incidence and mortality rate than females, with around 20% of males and 17% of females experiencing cancer at some point in their lifetime, while 13% of males and 9% of females will die from it [2,3]. In cancer research, accurately predicting the incidence and mortality rates of cancer is a crucial research topic. Various factors influence the incidence rates, including demographic, lifestyle, environmental, and genetic factors. On the other hand, mortality rates are additionally impacted by healthcare accessibility and quality [4]. Therefore, the precise prediction of cancer incidence and mortality rates is of vital importance, as it can empower policymakers and healthcare providers with the necessary information to develop targeted and effective policies and interventions to combat cancer's pervasive and devastating impact on individuals and communities [5].

Traditional cancer prediction relies on mathematical calculations [6,7]. The first step involves collecting relevant data, followed by using the collected data to calculate and fit a formula that establishes connections between cancer occurrence and factors such as family history, age, height, BMI, and age at first childbirth. The third step involves using the formula for cancer prediction, while the fourth step involves examining the accuracy of the predictions [6]. However, the accuracy of the prediction is heavily reliant on the accuracy of the formula, which depends on the assumptions made (such as BMI affecting cancer) and the researchers' experience. To mitigate the risk of incorrect assumptions and biases from researchers, a novel technique is being developed - machine learning (ML). ML models directly connect the input data and cancer prediction output, without considering the formula. The accuracy of the prediction depends on the quality and quantity of data, making it a promising technique for predicting cancer incidence and mortality rates.

Table 1. Comparison between traditional cancer and new ML model on cancer prediction.

	Breast cancer prediction model	ML model
Rationales	Use of mathematic formula to predict the cancer	Prediction of cancer via the ML algorithm
Methods	Use of data to build formula, connecting factors (e.g., age, height, BMI) and cancer;	Prediction via the "black box" without considering the connections
Accuracy of prediction	Assumptions and connections	Quality and quantity of data
Advantages	Matured methods with clear process	Convenient and fact prediction
Limitations	Incorrect assumption and researchers' bias	"Black swan" effect
Reference	[6,7]	[8-13]

The purpose of this study is to investigate the feasibility of using ML models to predict cancer incidence and mortality rates. The specific objectives are as follows: (1) to collect large datasets of cancer and perform data cleaning; (2) to construct ML models using the collected data; (3) to predict cancer outcomes using the ML models; and (4) to validate the prediction results and calculate the accuracy. The significance of this study is that, following the validation of the feasibility of ML models, policymakers may employ these models to forecast cancer outbreaks and better plan for medical resource allocation in advance.

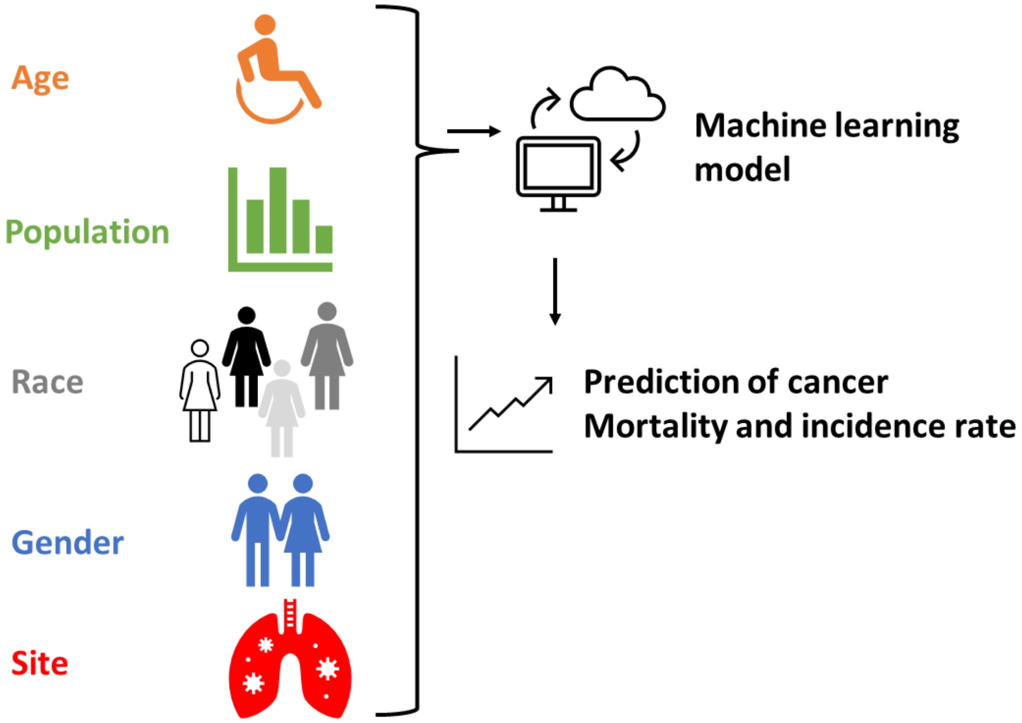


Figure 1. Schematic illustration showing the process of ML model setup and prediction.

2. Material and Methods

2.1. Data collection and clear

This study utilized data from the Centers for Disease Control and Prevention (CDC), United States Cancer Statistics (USCS), unless otherwise specified (https://www.cdc.gov/cancer/uscs/dataviz/download_data.htm, accessed on 1 March 2023). Prior to analysis, all incomplete records were removed from the dataset. Specifically, we extracted the following categories: "age", "count", "population", "race", "gender", "site", "year", "incidence rate", and "mortality rate". To facilitate analysis, a relationship matrix was generated to compare the different categories. To ensure consistency in data formatting, all data were converted to positive integers based on the classification presented in **Table 2**.

Table 2. Classification method for data treatment.

Age	Approximate number	Site	Assigned number	Year	Assigned number
≤ 1	1	Testis	1	2019	1
1-4	3	Hodgkin Lymphoma	2	2018	2
5-9	7	Thyroid	3	2017	3
10-14	12	Mesothelioma	4	2016	4
15-19	17	Cervix	5	2015	5
20-24	22	Brain and Other Nervous System	6	2014	6
25-29	27	Larynx	7	2013	7
30-34	32	Melanomas of the Skin	8	2012	8
35-39	37	Oral Cavity and Pharynx	9	2011	9
40-44	42	Kidney and Renal Pelvis	10	2010	10
45-49	47	Leukemias	11	2009	11
50-54	52	Esophagus	12	2008	12
55-59	57	Corpus and Uterus, NOS	13	2007	13
60-64	62	Myeloma	14	2006	14
65-69	67	Ovary	15	2005	15
70-74	72	Non-Hodgkin Lymphoma	16	2004	16
75-79	77	Stomach	17	2003	17
80-84	82	Urinary Bladder	18	2002	18
85+	87	Liver and Intrahepatic Bile Duct	19	2001	19
		Pancreas	20	2000	20
		Female Breast	21	1999	21
		Colon and Rectum	22		
		Lung and Bronchus	23		
		Prostate	24		

Gender	Assigned number	Race	Approximate number	Event type	Assigned number
Female	1	Non-Hispanic White	1	Incidence	1
Male	2	Non-Hispanic Asian/Pacific Islander	2	Mortality	2
		Non-Hispanic American Indian/Alaska Native	3		
		Non-Hispanic Black	4		
		Hispanic of any race	5		

CIlower/CIupper	Approximate number	Incidence/Mortality Rate	Assigned number
[0-0.5)	0	[0-5)	0
[0.5-1.5)	1	[5-15)	10
[1.5-2.5)	2	[15-25)	20
[2.5-3.5)	3	[25-35)	30
…	…	…	…

2.2. ML models

The application of machine learning (ML) models in cancer prediction has been a topic of interest for researchers in recent years [8,9]. In this study, we built upon previous studies by making slight modifications to the ML models used. A total of 72591 records were utilized for the ML calculations, with 75% of the records being used for training the models, and the remaining 25% for testing. The ML models were implemented on the Anaconda 3 and Jupyter 6.3.0 platform using programming tools such as Scikit-learn, Graphviz, Numpy, Pandas, Matplotlib, and SciPy, as detailed in Tables S1 and S2. We employed five different ML methods to make the calculations - decision tree, random forest, logistic regression, support vector machine (SVC), and neural network. In the case of the random forest model, we employed a hyper-tuning process via the random search method (Table S3 and S4). Our neural network model consisted of a total of 100 hidden layers, with each layer containing 100 nodes.

After the models were trained, we conducted an analysis of the testing accuracy and confirmed the ML model that showed the highest accuracy. We then conducted a detailed investigation into the two significant factors - "age" and "site" - and their influence on the incidence and mortality rates of cancer. Our analysis yielded important insights into the factors that contribute to the incidence and mortality rates of different types of cancer. Finally, based on the results of our study, we provided recommendations to improve the ML models and control the most lethal cancers identified. These recommendations could help policymakers and healthcare providers develop targeted and effective policies and interventions to combat cancer's pervasive and devastating impact on individuals and communities. Overall, this study underscores the potential of ML models to aid in cancer prediction and the importance of continued research in this area.

3. Results

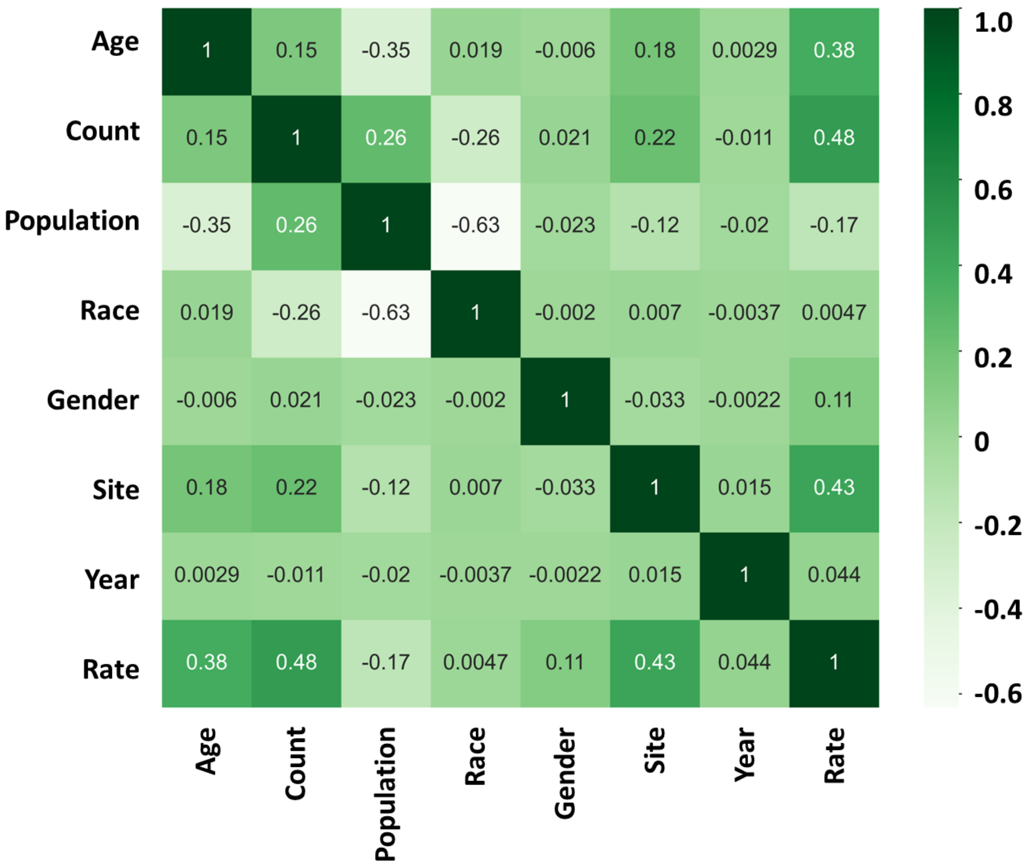
3.1. Factors affecting the cancer

After conducting a comprehensive analysis of the data, our findings revealed that the risk of developing cancer is highly influenced by two major factors: "age" and "site". We used a heatmap analysis to evaluate the relationship between these factors and the cancer incidence rate. Our results indicate that the correlation coefficient between "age" and cancer incidence rate was found to be +0.38 (**Figure 2**). This suggests that as individuals age, they become more susceptible to developing cancer.

Furthermore, our analysis also showed that the "site" of cancer is another crucial factor that affects the incidence rate of cancer. The correlation coefficient between "site" and cancer incidence rate was found to be +0.43 (**Figure 2**). This implies that the location or the specific organ where the cancer is found has a significant impact on its progression.

In contrast, our study found that factors such as "race", "gender", and "year of discovery" have relatively low impact on the incidence rate of cancer. The correlation coefficient between race and cancer incidence rate was found to be +0.0047, while that between gender and cancer incidence rate was found to be +0.11. Similarly, the correlation coefficient between year of discovery and cancer incidence rate was found to be +0.044. Although these factors are important, their influence on the incidence rate of cancer is comparatively low.

Our study underscores the importance of identifying and understanding the factors that affect the incidence rate of cancer. By recognizing the significant impact of "age" and "site", health professionals and policymakers can develop more targeted prevention and treatment strategies. Our findings provide a foundation for further research to identify additional factors that may influence the incidence rate of cancer, ultimately leading to more effective prevention and treatment methods.



	Age	Count	Population	Race	Gender	Site	Year	Rate
Age	1	0.15	-0.35	0.019	-0.006	0.18	0.0029	0.38
Count	0.15	1	0.26	-0.26	0.021	0.22	-0.011	0.48
Population	-0.35	0.26	1	-0.63	-0.023	-0.12	-0.02	-0.17
Race	0.019	-0.26	-0.63	1	-0.002	0.007	-0.0037	0.0047
Gender	-0.006	0.021	-0.023	-0.002	1	-0.033	-0.0022	0.11
Site	0.18	0.22	-0.12	0.007	-0.033	1	0.015	0.43
Year	0.0029	-0.011	-0.02	-0.0037	-0.0022	0.015	1	0.044
Rate	0.38	0.48	-0.17	0.0047	0.11	0.43	0.044	1

Figure 2. Heatmap analysis showing the relationship between "age", "count", "population", "race", "gender", "site", "year", and "rate" in cancer incidence rate.

The mortality rate analysis of the study further confirmed the significance of age and site in influencing the outcome of cancer. The heatmap analysis revealed that "age" and "site" have a high positive correlation coefficient with the mortality rate, indicating that they are important predictors of cancer death. The correlation coefficient for "age" was found to be +0.39 (Figure 2), which implies that the likelihood of cancer death increases with age. Similarly, the correlation coefficient for "site" was +0.40 (**Figure 3**), indicating that the location of cancer significantly affects its progression and outcome.

On the other hand, the study found that the impact of race, gender, and year of discovery on cancer mortality rate is relatively low, with correlation coefficients of +0.043, +0.13, and +0.05 respectively. These findings suggest that although these factors may have some influence on cancer mortality, their effect is much weaker compared to age and site.

The results of the mortality rate analysis reinforce the importance of age and site as key predictors of cancer outcome. The findings can have significant implications for the development of effective strategies for cancer prevention and treatment. Based on these results, healthcare professionals may prioritize screening and early detection programs for individuals with a higher risk of developing cancer due to age or site factors. Additionally, this study highlights the need for further research to better understand the underlying mechanisms linking age and site to cancer development and progression, which can inform the development of more targeted and personalized treatment approaches.

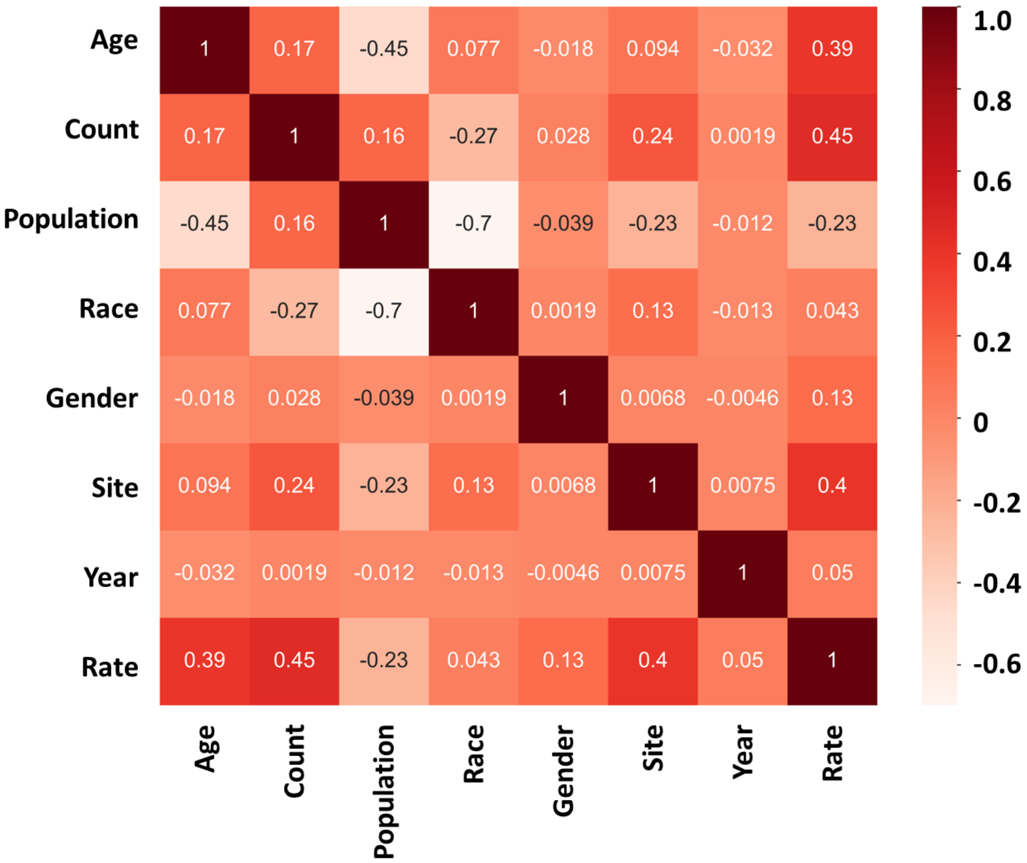


Figure 3. Heatmap analysis showing the relationship between "age", "count", "population", "race", "gender", "site", "year", and "rate" in cancer mortality rate.

3.2. Different ML models and prediction accuracy.

In this study, we utilized five different machine learning (ML) methods, namely decision tree, random forest, logistic regression, support vector machine (SVC), and neural network, to evaluate and compare their effectiveness in predicting cancer incidence and mortality rates. After training the models, we assessed their performance by analyzing the testing accuracy. The results showed that the neural network model achieved the highest accuracy with 60.82% for incidence rate and 63.10% for mortality rate, surpassing the other four models.

Comparing the neural network with the other models, the decision tree, random forest, logistic regression, and SVC models showed relatively lower testing accuracy, indicating that they are less effective in predicting cancer incidence and mortality rates. **Table 3** provides a summary of the testing accuracy of each model.

It is worth noting that the selection of ML methods should consider various factors, such as the data characteristics, model complexity, and computational resources. Therefore, future studies may need to further evaluate and compare different ML methods with larger datasets and more complex models to improve the prediction accuracy of cancer incidence and mortality rates.

Table 3. Comparison of ML prediction method.

	Method	Classifier	Testing Accuracy
Incidence rate prediction	Decision tree	DecisionTreeClassifier	57.22%
	Random forest	RandomForestClassifier	57.80%
	Logistic regression	LogisticRegression	50.11%
	SVC	SupportVectorClassifier	49.99%
	Neural network	MLPClassifier	60.82%
	Method	Classifier	Testing Accuracy

Mortality rate prediction	Decision tree	DecisionTreeClassifier	62.11%
	Random forest	RandomForestClassifier	61.68%
	Logistic regression	LogisticRegression	54.53%
	SVC	SupportVectorClassifier	55.72%
	Neural network	MLPClassifier	63.10%

4. Discussion

4.1. Age affecting incidence and mortality rate

Our analysis of the heatmap (**Figure 2** and **Figure 3**) revealed that age has a greater impact on the incidence and mortality rates of cancer than race, gender, and year of discovery. Specifically, most cancer cases occurred after the age of 40, with the highest incidence rate frequency in the "60-64" age category and the highest mortality rate frequency in the "70-74" age category (**Figure 4**). These results are consistent with previous studies that have shown that cancer rates increase as people age [14]. Moreover, the incidence of breast cancer, for example, is known to be extremely low before the age of 30 and reaches its highest level at the age of 80 [15]. While it is possible for cancer to occur at any age, most patients with invasive cancer are over 65, which may be due to the accumulation of protein-altering mutations [16].

The impact of age on cancer incidence and mortality rates is not surprising, given that aging is a complex process that affects all body systems. With increasing age, cells in the body accumulate genetic mutations and other changes that increase the risk of developing cancer [17,18]. Additionally, the immune system weakens with age, making it less effective in detecting and fighting cancer cells [19,20]. These factors contribute to the higher incidence and mortality rates of cancer in older adults. Overall, our findings highlight the importance of age as a risk factor for cancer and suggest that strategies aimed at preventing and treating cancer should consider the age of the patient. Moreover, our results underscore the need for continued research into the complex interplay between aging and cancer development.

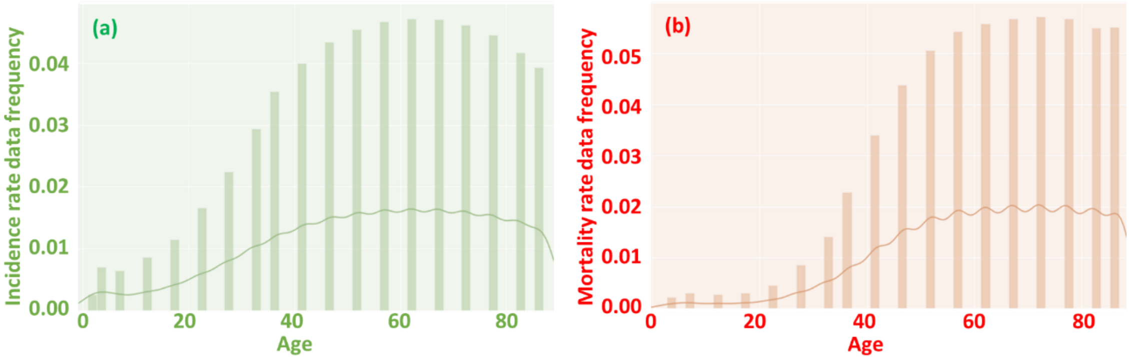


Figure 4. Incidence and mortality by age. Frequency a value from 0 (the lowest possibility) to 1 (the highest possibility).

4.2. Cancer of the lung, bronchus, and prostate and prevention

Our analysis of cancer mortality rates revealed that prostate cancer and lung and bronchus cancer pose the greatest threat, with 170 and 140 reported deaths per 100,000 individuals, respectively. This indicates that these cancers are associated with the highest mortality rates compared to other types of cancer, as presented in Table 4. On the other hand, the incidence of testis cancer, Hodgkin lymphoma cancer, and thyroid cancer had the lowest reported deaths per 100,000 individuals, with rates of 0.416, 1.052, and 2.675, respectively.

It is important to note that our findings corroborate with previous studies that have also reported prostate and lung cancer as the leading causes of cancer deaths worldwide. For instance, according to the World Health Organization, lung cancer is the most common cancer worldwide, with 2.1 million new cases in 2018, representing 11.6% of all new cancer cases, and 1.8 million deaths, accounting for 18.4% of all cancer deaths [21]. Similarly, the American Cancer Society estimates that prostate cancer is the second most common cancer and the second leading cause of cancer death among men in the United States, with an estimated 248,530 new cases and 34,130 deaths in 2021 [22,23].

Considering these findings, it is crucial to prioritize prevention, early detection, and effective treatment of these types of cancer to reduce the associated morbidity and mortality rates. This may involve regular screening, lifestyle modifications, such as smoking cessation and physical activity, and the development of novel therapies for advanced-stage cancers. Our analysis of cancer mortality rates highlights the significance of cancer type in predicting cancer-related outcomes. While prostate and lung cancer are associated with the highest mortality rates, testis cancer, Hodgkin lymphoma cancer, and thyroid cancer have the least reported deaths. By identifying these patterns, we can better understand the risk factors and implement effective strategies to improve cancer prevention and treatment outcomes.

Table 4. Average mortality rate by different sites of cancer.

Scheme 100.	Reported incidence rate per 100’000	Reported death rate per 100’000
Testis	6.109	0.416
Hodgkin Lymphoma	3.357	1.052
Thyroid	15.838	2.675
Mesothelioma	5.771	5.176
Cervix	14.571	6.23
Brain and Other Nervous System	7.758	7.599
Larynx	14.946	7.642
Melanomas of the Skin	26.591	8.439
Oral Cavity and Pharynx	21.866	9.773
Kidney and Renal Pelvis	34.078	15.238
Leukemias	20.492	15.742
Esophagus	16.881	16.278
Corpus and Uterus, NOS	46.417	16.556
Myeloma	25.058	18.811
Ovary	20.202	19.706
Non-Hodgkin Lymphoma	33.855	19.849
Stomach	31.179	21.067
Urinary Bladder 18	58.880	23.543
Liver and Intrahepatic Bile Duct	31.211	28.477
Pancreas	40.685	40.167
Female Breast	137.875	51.988
Colon and Rectum	113.632	55.407
Lung and Bronchus	169.056	139.842
Prostate	429.041	169.678

According to recent research, one of the emerging factors that can lead to the development of prostate cancer and lung cancer is bacteria and biofilm infection [24-27]. Bacteria and biofilms are known to play a critical role in the genesis of prostate calcifications [26,28,29], which can cause inflammation and ultimately lead to prostate cancer. Similarly, biofilm formation can lead to lung infections caused by microorganisms such as *Pseudomonas aeruginosa* and *Enterococcus faecalis* [30-32], which can further develop into lung cancer.

Biofilm is essentially a community of microorganisms that attach to a surface and are embedded in extracellular polymeric substances, such as extracellular DNA, proteins, and polysaccharides [33-37]. In recent years, researchers have been able to engineer biofilms for various purposes, including electricity generation [38-40], pollutant removal [34-36], and concrete enhancements [41-43]. Given the negative effects of biofilm on human health, it is important to explore ways to decrease biofilm in the environment. For example, researchers can develop anti-biofilm cementitious materials [44-46] that could help to create a cleaner environment and reduce the risk of cancer. By developing effective strategies to combat biofilm, we may be able to reduce the incidence of prostate cancer and lung cancer and improve overall public health.

4.3. Future improvement on ML models

This paper proposes a promising direction for the use of machine learning (ML) models in predicting cancer incidence and mortality rates. As with any statistical model, the accuracy of the predictions is influenced by various factors. The accuracy of ML models in cancer prediction is mainly affected by the number of input factors and the quantity of records.

The number of input factors is crucial in determining the accuracy of the prediction. This feasibility study uses six factors ("age", "count", "population", "race", "gender", "site", "year") to predict cancer incidence and mortality rates. However, due to computation power limitations, the number of input factors is restricted. If higher computation power is available in the future, it will be possible to use more factors (e.g., height, weight, smoking habit, drinking habit, family inheritance, migration history, current city, and living environment) to build up the ML model, leading to higher prediction accuracy. Increasing the number of input factors will advance the ML methods, and consequently, the prediction accuracy will also increase [47].

The quantity of records is another factor that determines the accuracy of prediction. This study uses 72591 records to calculate cancer incidence and mortality rates. In the future, if we can use more records (e.g., 1 million), we will have a more accurate prediction of cancer incidence and mortality rates [48,49]. By using a larger amount of data, the ML models can learn better and discover hidden patterns, leading to more accurate predictions.

Furthermore, this study only compares five ML methods (decision tree, random forest, logistic regression, support vector machine (SVC), and neural network) and finds that neural network makes the highest prediction accuracy rate. However, it is possible that there are other ML methods that may perform better. For example, k-means [50], nearest neighbour [51], linear discriminant analysis [52], hidden Markov [53] are other ML methods that can be used to compare prediction accuracy. By employing these additional methods, it may be possible to identify the most accurate method.

In conclusion, the use of ML models in cancer prediction holds great promise. However, there is still room for improvement in the accuracy of the predictions. In the future, by increasing the number of input factors and the quantity of records and exploring other ML methods, we can make more accurate predictions of cancer incidence and mortality rates.

Reference

1. Siegel, R.L.; Miller, K.D.; Wagle, N.S.; Jemal, A. Cancer statistics, 2023. *CA: a cancer journal for clinicians* **2023**, *73*, 17-48.
2. Qawoogha, S.S.; Shahiwala, A. Identification of potential anticancer phytochemicals against colorectal cancer by structure-based docking studies. *Journal of Receptors and Signal Transduction* **2020**, *40*, 67-76.
3. Zhang, R.; Meng, Z.; Wu, X.; Zhang, M.; Zhang, S.; Jin, T. Mortalin promotes breast cancer malignancy. *Experimental and Molecular Pathology* **2021**, *118*, 104593.
4. Kolonel, L.N.; Altshuler, D.; Henderson, B.E. The multiethnic cohort study: exploring genes, lifestyle and cancer risk. *Nature Reviews Cancer* **2004**, *4*, 519-527.
5. Ferlay, J.; Colombet, M.; Soerjomataram, I.; Mathers, C.; Parkin, D.M.; Piñeros, M.; Znaor, A.; Bray, F. Estimating the global cancer incidence and mortality in 2018: GLOBOCAN sources and methods. *International journal of cancer* **2019**, *144*, 1941-1953.
6. Tyrer, J.; Duffy, S.W.; Cuzick, J. A breast cancer prediction model incorporating familial and personal risk factors. *Statistics in medicine* **2004**, *23*, 1111-1130.
7. Antoniou, A.C.; Easton, D.F. Risk prediction models for familial breast cancer. **2006**.
8. Chen, S.; Ding, Y. Machine Learning and Its Applications in Studying the Geographical Distribution of Ants. *Diversity* **2022**, *14*, 706.

9. Chen, S.; Ding, Y. A Machine Learning Approach to Predicting Academic Performance in Pennsylvania's Schools. *Social Sciences* **2023**, *12*, 118.
10. Chen, S.; Ding, Y.; Liu, X. Development of the growth mindset scale: Evidence of structural validity, measurement model, direct and indirect effects in Chinese samples. *Current Psychology* **2021**, 1-15.
11. Wabartha, M.; Durand, A.; Francois-Lavet, V.; Pineau, J. Handling black swan events in deep learning with diversely extrapolated neural networks. 2021; pp. 2140-2147.
12. Cruz, J.A.; Wishart, D.S. Applications of machine learning in cancer prediction and prognosis. *Cancer informatics* **2006**, *2*, 117693510600200030.
13. Wang, G.; Lam, K.-M.; Deng, Z.; Choi, K.-S. Prediction of mortality after radical cystectomy for bladder cancer by machine learning techniques. *Computers in biology and medicine* **2015**, *63*, 124-132.
14. Jemal, A.; Bray, F.; Center, M.M.; Ferlay, J.; Ward, E.; Forman, D. Global cancer statistics. *CA: a cancer journal for clinicians* **2011**, *61*, 69-90.
15. Singletary, S.E. Rating the risk factors for breast cancer. *Annals of surgery* **2003**, *237*, 474.
16. Vogelstein, B.; Papadopoulos, N.; Velculescu, V.E.; Zhou, S.; Diaz Jr, L.A.; Kinzler, K.W. Cancer genome landscapes. *science* **2013**, *339*, 1546-1558.
17. Preston-Martin, S.; Pike, M.C.; Ross, R.K.; Jones, P.A.; Henderson, B.E. Increased cell division as a cause of human cancer. *Cancer research* **1990**, *50*, 7415-7421.
18. Rubin, J.B.; Lagas, J.S.; Broestl, L.; Sponagel, J.; Rockwell, N.; Rhee, G.; Rosen, S.F.; Chen, S.; Klein, R.S.; Imoukhuede, P. Sex differences in cancer mechanisms. *Biology of sex Differences* **2020**, *11*, 1-29.
19. Marasco, V.; Carniti, C.; Guidetti, A.; Farina, L.; Magni, M.; Miceli, R.; Calabretta, L.; Verderio, P.; Ljevar, S.; Serpenti, F. T-cell immune response after mRNA SARS-CoV-2 vaccines is frequently detected also in the absence of seroconversion in patients with lymphoid malignancies. *British journal of haematology* **2022**, *196*, 548-558.
20. Mellman, I.; Coukos, G.; Dranoff, G. Cancer immunotherapy comes of age. *Nature* **2011**, *480*, 480-489.
21. Bray, F.; Ferlay, J.; Soerjomataram, I.; Siegel, R.L.; Torre, L.A.; Jemal, A. Global cancer statistics 2018: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. *CA: a cancer journal for clinicians* **2018**, *68*, 394-424.
22. Berglund, A.; Matta, J.; Encarnación-Medina, J.; Ortiz-Sanchéz, C.; Dutil, J.; Linares, R.; Marcial, J.; Abreu-Takemura, C.; Moreno, N.; Putney, R. Dysregulation of DNA Methylation and Epigenetic Clocks in Prostate Cancer among Puerto Rican Men. *Biomolecules* **2022**, *12*, 2.
23. Spieker, A.J.; Gordetsky, J.B.; Maris, A.S.; Dehan, L.M.; Denney, J.E.; Arnold Egloff, S.A.; Scarpato, K.; Barocas, D.A.; Giannico, G.A. PTEN expression and morphological patterns in prostatic adenocarcinoma. *Histopathology* **2021**, *79*, 1061-1071.
24. Li, S.; Konstantinov, S.R.; Smits, R.; Peppelenbosch, M.P. Bacterial biofilms in colorectal cancer initiation and progression. *Trends in molecular medicine* **2017**, *23*, 18-30.
25. Mirzaei, R.; Sabokroo, N.; Ahmadyousefi, Y.; Motamedi, H.; Karampoor, S. Immunometabolism in biofilm infection: lessons from cancer. *Molecular medicine* **2022**, *28*, 10.
26. Parsonnet, J. Bacterial infection as a cause of cancer. *Environmental health perspectives* **1995**, *103*, 263-268.
27. Uemura, N.; Okamoto, S.; Yamamoto, S.; Matsumura, N.; Yamaguchi, S.; Yamakido, M.; Taniyama, K.; Sasaki, N.; Schlemper, R.J. Helicobacter pylori infection and the development of gastric cancer. *New England journal of medicine* **2001**, *345*, 784-789.
28. Cai, T.; Santi, R.; Tamanini, I.; Galli, I.C.; Perletti, G.; Bjerklund Johansen, T.E.; Nesi, G. Current knowledge of the potential links between inflammation and prostate cancer. *International journal of molecular sciences* **2019**, *20*, 3833.
29. Cai, T.; Tessarolo, F.; Caola, I.; Piccoli, F.; Nollo, G.; Caciagli, P.; Mazzoli, S.; Palmieri, A.; Verze, P.; Malossini, G. Prostate calcifications: A case series supporting the microbial biofilm theory. *Investigative and Clinical Urology* **2018**, *59*, 187-193.
30. Chudzik-Rząd, B.; Zalewski, D.; Kasela, M.; Sawicki, R.; Szymańska, J.; Bogucka-Kocka, A.; Malm, A. The Landscape of Gene Expression during Hyperfilamentous Biofilm Development in Oral Candida albicans Isolated from a Lung Cancer Patient. *International Journal of Molecular Sciences* **2023**, *24*, 368.
31. Vijayakumar, S.; Vaseeharan, B.; Malaikozhundan, B.; Gopi, N.; Ekambaram, P.; Pachaiappan, R.; Velusamy, P.; Murugan, K.; Benelli, G.; Kumar, R.S. Therapeutic effects of gold nanoparticles synthesized using Musa paradisiaca peel extract against multiple antibiotic resistant Enterococcus faecalis biofilms and human lung cancer cells (A549). *Microbial pathogenesis* **2017**, *102*, 173-183.
32. Bjarnsholt, T.; Buhlin, K.; Dufrêne, Y.F.; Gomelsky, M.; Moroni, A.; Ramstedt, M.; Rumbaugh, K.P.; Schulte, T.; Sun, L.; Åkerlund, B. Biofilm formation–what we can learn from recent developments. **2018**, *284*, 332-345.
33. Wu, Y.; Ding, Y.; Cohen, Y.; Cao, B. Elevated level of the second messenger c-di-GMP in Comamonas testosteroni enhances biofilm formation and biofilm-based biodegradation of 3-chloroaniline. *Applied microbiology and biotechnology* **2015**, *99*, 1967-1976.
34. Ding, Y.; Peng, N.; Du, Y.; Ji, L.; Cao, B. Disruption of putrescine biosynthesis in Shewanella oneidensis enhances biofilm cohesiveness and performance in Cr (VI) immobilization. *Applied and environmental microbiology* **2014**, *80*, 1498-1506.
35. Ding, Y.; Zhou, Y.; Yao, J.; Szymanski, C.; Fredrickson, J.; Shi, L.; Cao, B.; Zhu, Z.; Yu, X.-Y. In situ molecular imaging of the biofilm and its matrix. *Analytical chemistry* **2016**, *88*, 11244-11252.
36. Ding, Y.; Zhou, Y.; Yao, J.; Xiong, Y.; Zhu, Z.; Yu, X.-Y. Molecular evidence of a toxic effect on a biofilm and its matrix. *Analyst* **2019**, *144*, 2498-2503.

37. Flemming, H.-C.; Wingender, J. The biofilm matrix. *Nature reviews microbiology* **2010**, *8*, 623-633.
38. Yang, Y.; Ding, Y.; Hu, Y.; Cao, B.; Rice, S.A.; Kjelleberg, S.; Song, H. Enhancing bidirectional electron transfer of Shewanella oneidensis by a synthetic flavin pathway. *ACS synthetic biology* **2015**, *4*, 815-823.
39. Zhao, C.-e.; Chen, J.; Ding, Y.; Wang, V.B.; Bao, B.; Kjelleberg, S.; Cao, B.; Loo, S.C.J.; Wang, L.; Huang, W. Chemically functionalized conjugated oligoelectrolyte nanoparticles for enhancement of current generation in microbial fuel cells. *ACS Applied Materials & Interfaces* **2015**, *7*, 14501-14505.
40. Zhao, C.e.; Wu, J.; Ding, Y.; Wang, V.B.; Zhang, Y.; Kjelleberg, S.; Loo, J.S.C.; Cao, B.; Zhang, Q. Hybrid conducting biofilm with built-in bacteria for high-performance microbial fuel cells. *ChemElectroChem* **2015**, *2*, 654-658.
41. Zhang, Z.; Liu, D.; Ding, Y.; Wang, S. Mechanical performance of strain-hardening cementitious composites (SHCC) with bacterial addition. *Journal of Infrastructure Preservation and Resilience* **2022**, *3*, 1-11.
42. Zhang, Z.; Weng, Y.; Ding, Y.; Qian, S. Use of Genetically Modified Bacteria to Repair Cracks in Concrete. *Materials* **2019**, *12*, 3912.
43. Zhang, Z.; Ding, Y.; Qian, S. Influence of bacterial incorporation on mechanical properties of engineered cementitious composites (ECC). *Construction and Building Materials* **2019**, *196*, 195-203, doi:https://doi.org/10.1016/j.conbuildmat.2018.11.089.
44. Hamdany, A.H.; Ding, Y.; Qian, S. Visible light antibacterial potential of graphene-TiO2 cementitious composites for self-sterilization surface. *Journal of Sustainable Cement-Based Materials* **2022**, 1-11.
45. Hamdany, A.H.; Ding, Y.; Qian, S. Cementitious Composite Materials for Self-Sterilization Surfaces. *ACI Materials Journal* **2022**, *119*.
46. Hamdany, A.H.; Ding, Y.; Qian, S. Mechanical and antibacterial behavior of photocatalytic lightweight engineered cementitious composites. *Journal of Materials in Civil Engineering* **2021**, *33*, 04021262.
47. Taninaga, J.; Nishiyama, Y.; Fujibayashi, K.; Gunji, T.; Sasabe, N.; Iijima, K.; Naito, T. Prediction of future gastric cancer risk using a machine learning algorithm and comprehensive medical check-up data: A case-control study. *Scientific reports* **2019**, *9*, 12384.
48. Al-Jarrah, O.Y.; Yoo, P.D.; Muhaidat, S.; Karagiannidis, G.K.; Taha, K. Efficient machine learning for big data: A review. *Big Data Research* **2015**, *2*, 87-93.
49. Bzdok, D.; Krzywinski, M.; Altman, N. Machine learning: a primer. *Nature methods* **2017**, *14*, 1119.
50. Zhao, M.; Tang, Y.; Kim, H.; Hasegawa, K. Machine learning with k-means dimensional reduction for predicting survival outcomes in patients with breast cancer. *Cancer informatics* **2018**, *17*, 1176935118810215.
51. Moitra, D.; Mandal, R.K. Automated grading of non-small cell lung cancer by fuzzy rough nearest neighbour method. *Network Modeling Analysis in Health Informatics and Bioinformatics* **2019**, *8*, 1-9.
52. Jessica, E.O.; Hamada, M.; Yusuf, S.I.; Hassan, M. The Role of Linear Discriminant Analysis for Accurate Prediction of Breast Cancer. 2021; pp. 340-344.
53. Nguyen, T.; Khosravi, A.; Creighton, D.; Nahavandi, S. Hidden Markov models for cancer classification using gene expression profiles. *Information Sciences* **2015**, *316*, 293-307.