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Forecasting and Public Health Implications of Cervical Cancer Mortality in Canada: A Time-Series and Machine Learning Study

Pinyi Zhen

Department of Statistics, University of California, Los Angeles, USA
pinyi0108@ucla.edu

Abstract. Cervical cancer, a highly preventable disease primarily caused by HPV, remains a critical global health issue. In Canada, its incidence rate grew fastest among all cancers from 2015 to 2023, highlighting a pressing public health challenge. To inform future planning, this study forecasts national cervical cancer mortality by comparing traditional and machine learning time-series models. The author analyzed annual age-standardized mortality data (1950-2022) from the Public Health Agency of Canada, evaluating the Exponential Smoothing (ETS), ARIMA, Neural Network Autoregression (NNAR), and eXtreme Gradient Boosting (XGBoost) models using rolling-window cross-validation. Results showed that traditional models outperformed their machine learning counterparts in predictive accuracy. The ETS and ARIMA models achieved lower Root Mean Square Errors (RMSEs of 0.45 and 0.44, respectively) compared to NNAR (0.65) and XGBoost (1.39), indicating that simpler methods better captured the linear historical trend. Despite its lower overall accuracy, XGBoost provided a crucial epidemiological insight: it identified a strong 16-18 year lag in mortality rates, which accounted for over 83% of the model's feature importance, suggesting deep-seated cohort effects or the long-term impact of prevention programs. These forecasts offer actionable data for Canadian health authorities to optimize screening and vaccination strategies. Moreover, the demonstrated lag between intervention and outcome provides a vital evidence-based framework for other countries, supporting the global goal of reducing cervical cancer mortality through timely, data-driven policy.

Keywords: Cervical Cancer Mortality Forecasting, Time-Series Analysis, Model Comparison (ETS, ARIMA, XGBoost), Public Health Policy, Canada

1. Introduction

1.1. Cervical cancer: epidemiology, diagnosis and treatment

Despite being one of the most preventable cancers, cervical cancer remains a significant public health concern in Canada, with mortality rates showing unexpected fluctuations in recent years [1,2]. Cervical cancer, one of the prevailing gynecologic cancers worldwide, can be mainly attributed to persistent human papillomavirus (HPV) infection [1]. Among the many HPV types, HPV types 16,

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18, 6, and 11 were discovered to be responsible for over three-quarters of cervical cancer cases [1]. Cancer-related HPV types manifest in genital lesions or warts that may later progress into cervical cancer [1]. HPV is transmitted between humans via skin contact during sexual activities, for instance, vaginal sex, oral sex, and genital contact [1]. Sexual activities at an early age, non-monogamous sexual interactions, and taking contraceptive pills are positively associated with cervical cancer diagnosis [1]. Fortunately, preventive measures like HPV vaccination combined with screening, as implemented in developed countries, can effectively relieve global mortality and morbidity of cervical cancer [1]. Since early-stage cervical cancer may not manifest any symptoms discoverable by mere physical examination of the genital area, it is paramount to incorporate Papanicolaou (Pap) smears and HPV-DNA lab tests for the purpose of cervical cancer diagnosis [1]. Patients with unusual screening results should proceed with colposcopy for invasive cervical cancer diagnosis, and if diagnosed, cancer stage assessment following the International Federation of Gynecology and Obstetrics (FIGO) evaluation standards [1]. Treatment options for cervical cancer largely depend on cervical cancer staging and the development of the disease [1]. Surgical treatment, either non-invasive or invasive, would be appropriate for treating patients with early-stage or recurrent cervical cancer in some cases [1]. The most important treatment for both early and later stages of cervical cancer is radiotherapy, attributable to its relatively high 5-year survival rates compared to radical hysterectomy [1]. Chemotherapeutic treatment and immunotherapy may be used to treat patients whose conditions do not allow surgery or radiotherapy [1]. Despite its treatability and preventability, cervical cancer still poses a severe global threat to women's health, fertility, and quality of life in general [1]. As recent data suggest, cervical cancer is considered the 14th most prevalent cancer of all cancers and the 4th most prevalent cancer for women across the globe [1]. Moreover, cervical cancer treatment can lead to health complications in both the short term and long term [1]. Despite treatment advances, cervical cancer management is associated with significant short- and long-term complications [1]. Regardless of age, rectal bleeding and urinary tract infection (UTI) that affects the bladder can occur in patients who underwent radiotherapy in just a few weeks [1]. Secondary cancers caused by radiotherapy can occur even decades post-treatment, not to mention ovarian failure, vaginal stenosis, and bone fracture as potential treatment complications [1].

1.2. The Canadian context and research gap

Despite the well-established prevention and treatment protocols outlined above, Canada faces significant challenges in achieving cervical cancer elimination targets [1,2]. The Canadian Partnership Against Cancer (CPAC) aimed to achieve nationwide cervical cancer elimination by 2040, while the World Health Organization (WHO) proposed the same goal for Canada by 2030 [2]. Cervical cancer elimination is defined as an annual incidence rate of less than or equal to 4 cases for every 100,000 females. Still, Canadian nationwide HPV vaccination coverage was estimated to be 26% lower than expected by 2025, making cervical cancer elimination seem unattainable by 2030 [2]. More alarmingly, cervical cancer incidence rate was the number one most rapidly increasing incidence rate among all cancers for Canada from 2015 to 2023, leading to a 2025 Canada health professional convention aimed to increase government and public awareness for HPV screening and vaccination [2,3]. Low vaccination rate and high cervical cancer incidence urge for improved HPV vaccination and screening uptake. Health experts proposed regionalized public education on cervical cancer preventative measures [2,3]. They also recommended establishing centralized data collection registries to forecast future cervical cancer prevention needs [2,3]. Accurate cervical cancer mortality forecasting is essential for the following reasons. Federal and provincial departments can reference accurate cervical cancer mortality forecasts for medical resource allocation. For instance,

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Canadian public health agencies can plan medical center construction, establish HPV screening sites, and prepare HPV vaccination inventory. This relieves the national cervical cancer burden in a timely manner. Forecasting cervical cancer mortality also benefits the Canadian public by encouraging the uptake of proven preventive measures [2,3]. As a result, population-level reproductive health outcomes could be better. Moreover, public cervical cancer mortality surveillance raises reproductive healthcare awareness. This could, in turn, increase public funding for nationwide HPV vaccination and screening programs. Moreover, other countries may follow the Canadian initiative to publicize cervical cancer mortality forecasts. Thus, cervical cancer mortality forecasting may even positively impact the global cervical cancer context. By raising worldwide reproductive health awareness, cervical cancer mortality forecasts potentially reduce global incidences. However, recent cervical cancer research has mainly focused on immunotherapy [4]. Researchers focused on immune checkpoint inhibitor efficacy and immunotherapy integration into traditional cancer treatment [4]. The author did not find sufficient recent research intended to forecast Canadian cervical cancer deaths. This study aimed to fill this critical gap by employing advanced time series analysis. In this way, the study could offer useful recommendations relevant to cancer prevention planning.

1.3. Study objectives and framework

This study aimed to conduct traditional and machine-learning-based time-series analysis to forecast Canadian cervical cancer deaths [5,6]. Extreme gradient boosting (XGBoost) was selected for its superior time-series forecasting accuracy, given a small number of observations [5]. In a prior study by German researchers, the XGBoost model obtained high accuracy in predicting thyroid cancer recurrence [5]. Neural Network Autoregression (NNAR) was chosen because it allowed robust mapping of non-linear complex patterns with impressive predictive performance [6]. This paper plans to take advantage of NNAR and XGBoost's predictive ability to forecast cervical cancer mortality [5,6]. In this way, the study could provide suggestions on forecasting model selection for Canadian public health agencies. Comparative predictive performance analysis could inform HPV screening program planning and vaccination campaign promotion. This article sought to answer three research questions. What are the Canada's historical trends in cervical cancer mortality? How accurately can time series models forecast future mortality rates? What are the implications of these forecasts for Canada's cervical cancer elimination objectives [2]?

2. Method

2.1. Data source and collection

The study dataset was assessed for missing values, consistency, and temporal coverage before analysis. No missing entries were identified in mortality rates from 1950 to 2022 [7]. The study data were downloaded from Health Infobase, the Public Health Agency of Canada's (PHAC) official health research database [7]. Health Infobase aggregated data from many administrative databases and surveys [7]. Provinces, territories, and survey participants consented to de-identified data release [7]. Age-standardized rates per 100,000 females would be abbreviated to age-standardized rates for brevity in later paper sections [7]. Time-dependent data features were annual age-standardized cervical cancer case rates (1950-2019) and annual age-standardized mortality rates (1950-2022) [7]. The 73-year cervical cancer mortality rates were the primary data analysis focus [7]. Time-invariant variables in the database included age-standardized new cervical cancer case rates, cervical cancer

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mortality by province, cervical cancer mortality by age group, stage at cancer diagnosis by age group, age-standardized new case rates by rural/urban residence, age-standardized new case rates by household income quintile, and age-standardized mortality rates by ethnicity [7]. Data analysis in this paper was conducted in R 4.4.3 [8].

2.2. Statistical models

The author employed four distinct modeling approaches to forecast cervical cancer mortality rates: (1) traditional time series models (ETS and ARIMA), (2) NNAR, and (3) XGBoost [5,6]. This multi-model approach allowed for an informative forecasting performance comparison across various statistical methodologies. Exponential smoothing state-space (ETS) model, autoregressive integrated moving-average (ARIMA) model, NNAR model, and XGBoost model were used to forecast annual age-standardized cervical cancer mortality rates [5,6]. Mathematical transformation of the data was unnecessary as the variance was relatively constant. The data were not scaled or normalized, as XGBoost models were not greatly affected by scaling [5].

2.3. Model evaluation

The XGBoost algorithm was proven for high time-series predictive accuracy, its ability to handle non-linear relationships, and to rank feature importance [5]. Feature engineering involved creating lagged variables up to 18 years based on autocorrelation analysis. Model hyperparameters were tuned via 5-fold cross-validation with a grid search, optimizing for the smallest root mean squared error (RMSE). Model performance comparison was based on two metrics: average root mean squared error and mean absolute error (MAE) on the validation sets. RMSE and MAE were selected for their interpretability and for their prior use in the time series forecasting literature [5,6]. Cross-validation with a rolling window was implemented to accommodate the ordered nature of time series data. The initial training window included the first 10 years (1950-1959). Subsequent windows expanded by one year at each iteration. Models were fit to the expanding training set and tested on the subsequent year's mortality rate at each step. This procedure was repeated until reaching the final year of the time series, resulting in 63 validation sets.

3. Result

This section presents the key findings from analyzing Canada's cervical cancer mortality. The section first describes the exploratory data analysis results, followed by detailed model fitting and forecasting outcomes for each of the four approaches (ETS, ARIMA, NNAR, and XGBoost). Model performance is evaluated based on cross-validation metrics.

3.1. Exploratory data analysis

The minimum and maximum age-standardized cervical cancer mortality rates were 1.90% and 14.20% respectively. The first quartile (Q1) and third quartile (Q3) of the response variable were 2.40% and 9.70% respectively. The interquartile range (IQR) for age-standardized mortality was 7.30%. The mean age-standardized mortality rate was 5.86% and the median was 4.00%. Despite the right-skewed distribution evident in the histogram, Tukey's fence method (using 1.5×IQR thresholds) identified no statistical outliers in the time series data. The standard deviation for the age-standardized mortality rate was 3.95%. These descriptive statistics indicated relatively stable variability in mortality rates and a right-skewed distribution (mean > median) in the 73-year time

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series data. According to Figure 1, annual age-standardized cervical cancer mortality showed a fast-decreasing trend from 1950 to 2022. Figure 1 showed no obvious seasonal or cyclic behavior in the data. The sustained downward trend likely reflected improvements in screening, vaccination, and treatment over the past seven decades. The ggseasonplot() function in the ggplot2 package supported this hypothesis by indicating the presence of no seasonality in the data. The Augmented Dickey-Fuller (ADF) test confirmed the visual impression of non-stationarity (p = 0.99). The author would attempt to experiment with differencing the non-stationary time series before applying certain modeling techniques.

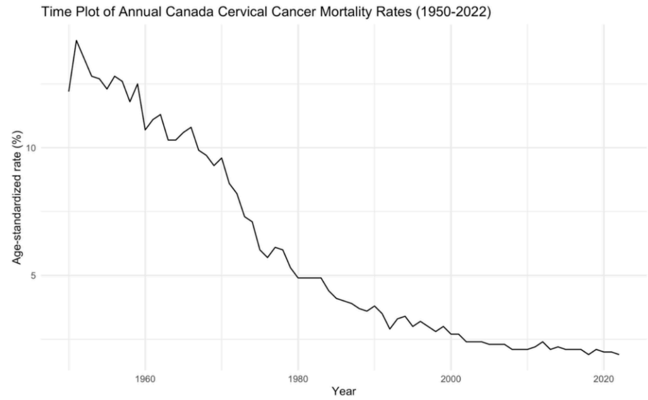

Figure 1. Time plot of annual Canada cervical cancer age-standardized mortality rate (per 100,000 females) from 1950 to 2022 (photo credit: origin)

3.2. Exponential smoothing state space (ETS) model

An ETS(M, Ad, N) model, or Holt's additive damped trend method with multiplicative error, was selected by the ets() function of the forecast package to fit the data. The estimated level smoothing, trend smoothing, and damping parameters for the ETS model were $\alpha = 0.48$, $\beta = 0.068$, and $\phi = 0.94$, respectively. The estimated ETS model initial level and slope were 13.57 and -0.17, respectively. The ETS(M, Ad, N) model yielded AIC and BIC values of 146.73 and 160.47, respectively. As shown in Figure 2, the residual plot of the ETS(M, Ad, N) model demonstrated no apparent trend and a relatively constant variance. The ACF plot of the residuals had no significant lags outside the 95% prediction interval. The residual histogram appeared skewed to the right, but the data distribution was not very far from normal. The Ljung-Box test for the residuals yielded a p-value of 0.68, which is greater than the 0.05 threshold. Hence, the author concluded that the residuals of the ETS(M, Ad, N) model were consistent with white noise and the model fit the data well. The ETS(M, Ad, N) specification with multiplicative error and damped additive trend effectively captured the declining mortality pattern while accounting for changing variability over time. Figure 3 showcased the ETS(M, Ad, N) model forecast for 20 years ahead, where the dark blue bands indicated the 80% prediction intervals (PI) and the light blue band indicated the 95% PIs. The ETS(M, Ad, N) predictions appeared to capture the time series's decreasing trend and rate of change reasonably well. The variability in the prediction was not unreasonable either.

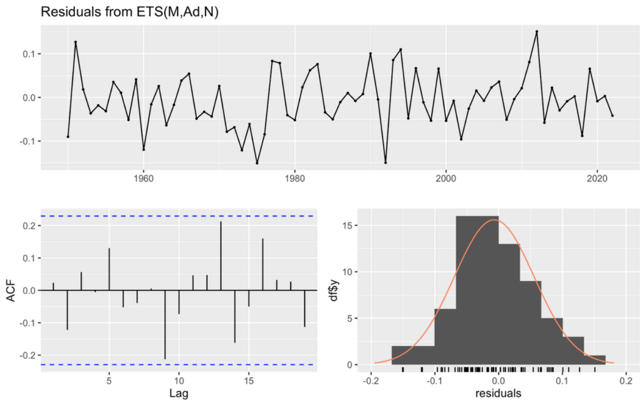

Figure 2. Diagnostic plots of the ETS (M, ad, N) model (photo credit: origin)

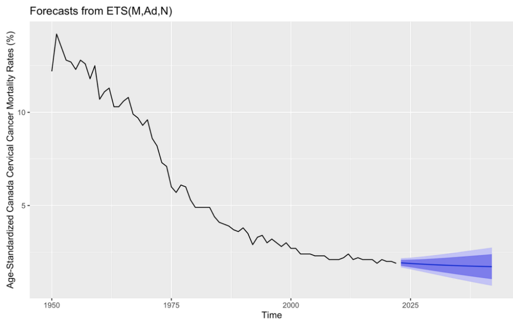

Figure 3. Forecast plot with 80% and 95% prediction intervals for the ETS (M, ad, N) model (photo credit: origin)

Time series cross-validation with a 10-year rolling window yielded an RMSE of 0.45 on one-year-ahead forecasts, establishing a baseline for model comparison.

3.3. ARIMA model

First-order differencing was performed on the data to remove the trend component. As shown in Figure 4, both the ACF and PACF plots of the first-order differenced time series have only one significant lag at lag 1. This suggests fitting an ARIMA(1, 1, 1) model to age-standardized cervical cancer mortality rates. ARIMA(1, 1, 1) obtained an AIC of 100.11 and a BIC of 109.22. The auto.ARIMA() function in the forecast package selected the ARIMA(2, 1, 2) model with drift. AIC was reduced to 93.16 and BIC to 106.82 for the ARIMA(2, 1, 2) model, so ARIMA(2, 1, 2) was selected as the final ARIMA model. The selected ARIMA(2,1,2) with drift indicates that mortality rates follow a differenced autoregressive-moving-average process with second-order autoregressive and moving-average components, plus a deterministic trend. While residual plots showed constant mean and no significant autocorrelation (Ljung-Box p = 0.28), some heteroscedasticity was evident, suggesting potential limitations in modeling the full variability structure. Ljung-Box test for ARIMA(2, 1, 2) residuals produced a p-value of 0.28, so the author concluded that the residuals were stationary. Cross-validation with a rolling window size of 10 years and a forecast horizon of 1 year yielded a testing dataset RMSE of 0.44, only slightly better than the RMSE of 0.45 for the ETS model.

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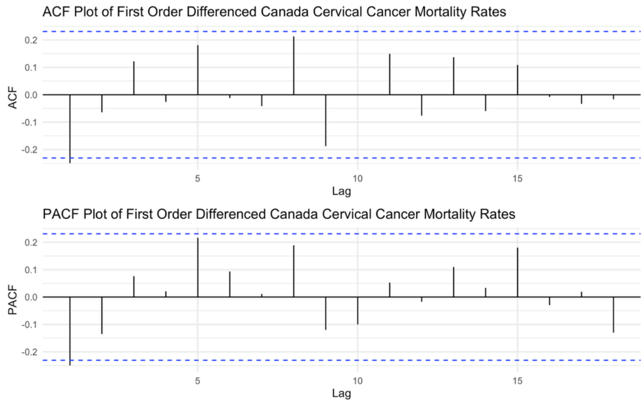

Figure 4. ACF and PACF plots of first-order differenced age-standardized Canada cervical cancer mortality rates (photo credit: origin)

3.4. NNAR model

An NNAR model with a feed-forward architecture and one hidden layer was applied to age-standardized Canada cervical cancer mortality rates [6]. The nnetar() function in the forecast package selected NNAR(1,1) to fit the data. A forecast time plot based on the NNAR(1,1) model was presented in Figure 5. The forecast horizon extended 20 years into the future, beyond the year 2022. The dark blue band indicated the 80% PIs of forecast values, whereas the 95% PIs indicated the 95% PIs. The ETS model and the ARIMA model both predicted a decreasing trend after 2022, but the NNAR model predicted an increasing trend for cervical cancer mortality rate in Canada. The author performed cross-validation for the NNAR model with a 10-year rolling window and a 1-year forecast horizon. The testing set RMSE was 0.65, higher than that of either the ETS or the ARIMA model. The NNAR model had relatively low forecast accuracy and predicted an upward trend, contrary to the historical increasing trend. These may reflect overfitting to recent fluctuations or insufficient data for effective neural network training. This limitation highlights the challenges of applying complex non-linear models to relatively short epidemiological time series.

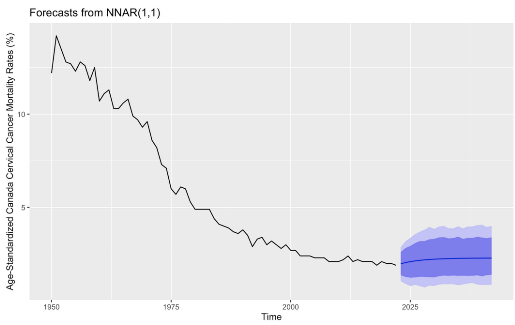

Figure 5. Forecast plot with 80% and 95% prediction intervals for the NNAR(1,1) model; photo credit: origin

3.5. XGBoost model

The XGBoost algorithm can capture complex nonlinear relationships between the response variable and predictor variables [5]. Additionally, XGBoost has gained popularity due to its impressive performance in regression and forecasting [5]. The ACF plot of the undifferenced time series

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showed significant lags up to lag 18, so the author conducted feature engineering using lagged versions of mortality rates up to lag 18. The author trained the XGBoost model using cross-validation with an initial 10-year window size and a 1-year forecast horizon. The optimal parameters selected by the caret package were nrounds = 270, max_depth = 250, eta = 1, gamma = 0.4, tree = 0.6, and subsample = 0.875. The average RMSE and average MAE across the validation sets were both 1.39, respectively. Despite producing the highest RMSE (1.39) among all models, XGBoost provided valuable insights through feature importance analysis. Feature importance analysis revealed that mortality rates from 16-18 years prior (lags 16-18) collectively accounted for 83.1% of prediction accuracy. The prominence of lags 16-18 suggests strong long-term dependencies of cervical cancer mortality patterns. Such long-term dependencies possibly reflect cohort effects or delayed public health intervention impacts.

4. Discussion

4.1. Synthesis of principal findings and model performance

This study aimed to apply traditional time-series models and machine learning methods to predict annual age-standardized cervical cancer mortality rates in Canada. Cervical cancer mortality rates demonstrated an apparent decreasing trend from 1950 to 2022. Traditional time series models (ETS and ARIMA) achieved better predictive performance than machine-learning-based models (NNAR and XGBoost). ARIMA(2,1,2) obtained the lowest validation set RMSE (0.44) among the four models. Although XGBoost had the lowest predictive accuracy (RMSE = 1.39) among all models, it did reveal long-term dependencies in mortality rates 16-18 years apart.

4.2. Interpretation of results: model merits, limitations, and epidemiological insights

Traditional time series models (ETS, ARIMA) outperformed machine-learning methods (NNAR, XGBoost) in terms of prediction accuracy. The time series exhibited relatively simple patterns, as suggested by the monotonic decreasing trend in Figure 1. Thus, linear regression-based models may suffice to capture the main data patterns. The software selected ARIMA(2,1,2) over ARIMA(1,1,1), indicating the need for larger order moving-average and autoregressive components. NNAR(1,1) produced the second-highest testing data RMSE (0.65). It also forecasted an increasing trend, contradicting the prior decreasing trend over decades. The author speculated that this trend reversal occurred because neural networks tend to overfit short-term data fluctuations and underfit long-term trends. Additionally, a small dataset with only 73 observations may not be enough to train effective neural networks. XGBoost produced the highest validation set RMSE (1.39) among all models. Model hyperparameter overfitting and noise introduced by feature engineering might explain XGBoost's high RMSE. However, XGBoost had a strength in revealing long-term dependencies. While not the best for point forecasting in this study, XGBoost was useful for exploratory analysis and hypothesis generation. XGBoost feature importance analysis provided great insights into long-term trend dependencies. Mortality rates lagging at 16-18 years accounted for 83.1% of the prediction accuracy. Cohort effects, such as the long-term impact of HPV vaccination, HPV screening, or the natural history of cervical cancer, may be the cause. ETS and ARIMA both forecasted a continuously decreasing trend after 2022, consistent with the historical trend and public health intervention expectations. On the contrary, NNAR predicted an increasing trend. The author believed this turnabout to be related to model overfitting of recent mortality fluctuations. Complex

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models are sensitive to short-term noise in data. Thus, validating forecast results in an epidemiological context is vital.

4.3. Methodological reflections: evaluating analytical choices and future research avenues

This study compared traditional time-series models with machine learning methods. ETS and ARIMA were traditional time-series models. NNAR and XGBoost were machine-learning methods. Rolling window cross-validation (RWCV) assessed a model's ability to capture local trend patterns [9]. This ensures the model can be generalized to unseen observations [9]. RWCV with a 10-year initial window and a 1-year forecast horizon was implemented to quantify out-of-sample forecast accuracy for all four models. Future studies can include RWCV accuracy metrics with varying window sizes and forecasting horizons. The study data came from PHAC's official database [7]. The data quality is high [7]. The study data spanned 73 years from 1950 to 2022. This paper only performed univariate analysis of cervical cancer mortality rates, as other variables had too few observations to be informative [7]. Future studies could include HPV screening and vaccination estimations in multivariate analysis to better support public health policy making [1]. This study computed validation set RMSE and MAE to compare forecast performance because these two metrics are traditionally used in the time series analysis literature [6]. Other accuracy metrics, such as MAPE and MASE, could also be utilized for comprehensive forecast performance comparison [10].

4.4. Translating forecasts into action: public health and policy implications

The study's forecast results could potentially guide public health interventions, medical resource allocation, and public health policy creation. The continuously decreasing trend in forecasts showed population-level cervical cancer intervention effectiveness, including HPV screening and HPV vaccination. Canada aimed to reduce the annual cervical cancer incidence rate to less than or equal to 4 cases for every 100,000 females by 2030 or 2040 [2]. In the long run, mortality forecasting is relevant to Canada's national goal for cervical cancer elimination [2]. This study did not forecast cervical cancer incidence rates, but decreasing mortality rates usually implied disease burden reduction. Based on forecast results, future public health policies could benefit the Canadian public by increasing the HPV vaccination coverage rate, HPV screening participation, and tracking the disease's trend continuously.

5. Conclusion

Historical annual cervical cancer mortality rates decreased sharply between 1950 and 2022, with no detectable seasonality or cyclicity. Traditional time-series models, such as ETS and ARIMA, produced more accurate mortality forecasts than machine-learning models such as NNAR and XGBoost. ETS(M, Ad, N) achieved an average RWCV testing data RMSE of 0.45 while ARIMA(2,1,2) attained an average RWCV testing data RMSE of 0.44. The NNAR(1,1) model and the XGBoost algorithm each produced an average RWCV testing data RMSE of 0.65 and 1.39. Machine learning models produced RMSEs higher than ETS and ARIMA modeling methods. XGBoost acquired the highest RMSE, but feature importance analysis unveiled strong long-term mortality dependencies. Mortality rates 16-18 years apart accounted for 83.1% of XGBoost forecast accuracy.

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This study had public health implications at global, national, and local levels. At the local level, cervical cancer mortality prediction motivates Canadians to take care of their reproductive health. This leads to increased cervical cancer preventative program participation. Better uptake of preventative measures is associated with improved health outcomes. At the national level, public health agencies can plan medical resources making use of cervical cancer mortality forecasts. At the global level, other countries could imitate Canada's initiative for cervical cancer mortality forecasting and improve their national reproductive health outcome. In the long run, mortality forecasting can lead to a global relief of the cervical cancer burden.

There were three shortcomings of this study. Machine learning models could have overfitted short-term data fluctuations. No multivariate analysis was conducted. The forecast accuracy comparison only featured two accuracy metrics. The NNAR(1,1) predicted an increasing trend, contrasting the historical, steadily decreasing trend over the years. This trend reversal could be due to neural networks overfitting short-term cervical mortality rate variability. XGBoost's high RMSE might be related to hyperparameter overfitting and feature engineering-introduced noises. The author only performed univariate time series analysis of cervical cancer mortality rates. Other variables had insufficient observations to permit a multivariate analysis. However, future studies can examine the association between public health interventions and cervical cancer mortality to enhance understanding of this topic. On the last note, this study did not compute accuracy metrics such as MAPE and MASE to generate a more encompassing forecast performance comparison.

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