BIOLOGY HIGHER LEVEL INTERNAL ASSESSMENT
AN INVESTIGATION ON THE CORRELATION BETWEEN THE HUMAN DEVELOPMENT INDEX (HDI) AND THE (AGE-STANDARDIZED) MORTALITY RATE OF CERVICAL CANCER FOR 27 COUNTRIES IN EUROPE

Research Question:

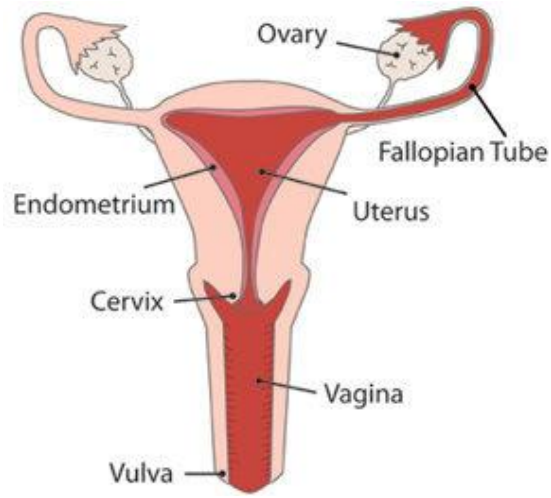
What is the correlation between European countries' HDI (Human Development Index) and the age-standardized mortality rate due to cervical cancer, per 100.000 people?

Background Information:

Cancer, a group of diseases that is one of the leading causes of mortality in the world is defined as the "rapid creation of abnormal cells"[1]. What makes these cells abnormal is due to their features such as continuing to grow despite the opposing signals, tricking the immune system into not destroying these cells, potentially growing into cancerous tumors and spreading into new areas in the body (metastasis)[2].

The focus organ of this investigation, the cervix, is an organ in the reproductive system of the people assigned female at birth (AFAB). Cervix connects the vagina and the uterus (Figure 1). This connective organ takes part in the menstrual cycle, pregnancy and vaginal birth, as well as protecting the uterus[3]. The focus of this investigation, cervical cancer, is a type of cancer that initializes in the cervix.

Figure 1: The female reproductive system



The main cause of cervical cancer is human papilloma virus (HPV), a group of viruses. This virus is usually transmitted via sexual intercourse. Even though most sexually active people encounter the virus, a smaller percentage actually turns into cancer[4]. The other factors that may contribute to the development of the cancer are smoking, having another sexually-transmitted disease (STD), having more than one sexual partner, taking contraceptive pills[5].

The first prevention of cervical cancer is the HPV vaccination. It provides immunity for the specific types of HPV virus which cause 70% of the cervical cancer incidents in the world. It is usually recommended for girls aged 9-14. WHO recommends 2 doses of the vaccine for those under 15 years of age, and 3 doses for

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[1] "Cancer - WHO," World Health Organization, accessed September 20, 2022, https://www.who.int/news-room/fact-sheets/detail/cancer.
[2] "What Is Cancer? - NCI," cgvArticle, National Cancer Institute, September 17, 2007, nciglobal,ncienterprise, https://www.cancer.gov/about-cancer/understanding/what-is-cancer.
[3] "Cervix: Anatomy, Function, Changes & Conditions," Cleveland Clinic, accessed September 20, 2022, https://my.clevelandclinic.org/health/body/23279-cervix.
[4] "Cervical Cancer," World Health Organization, February 22, 2022, https://www.who.int/news-room/fact-sheets/detail/cervical-cancer.
[5] Poonam Sachdev, "Cervical Cancer," WebMD, accessed September 21, 2022, https://www.webmd.com/cancer/cervical-cancer/cervical-cancer.

those over 15[6]. Because, the vaccine is found to be more effective when the person has not yet encountered the virus/ isn't yet sexually active[7].

Since the cancer develops slowly (in 15-20 years) it is possible to take precautions before the cancer further spreads. Testing for infection for the virus (cervical cancer screening) also is an important way of prevention of cervical cancer. These tests are recommended to (healthy) women over 30, every 5-10 years[8].

The detected pre-cancerous cells (the cells that can develop into cancerous cells) in the area can be removed. If an abnormal tissue of cancer cells is detected, there are a variety of treatment options considering various factors like the stage of the cancer, the age and health condition of the patient and whether or not staying fertile is crucial post-operation. The treatment can be done by removing the tissue/ related organs (ex. hysterectomy, trachelectomy)[9], chemotherapy (medication to eliminate the cancerous cells), or radiotherapy[10].

As stated in a 2018 study, cervical cancer "is the 4th most common cause of cancer incidence and mortality in women worldwide"[11]. The same study also mentions that 85% of the incidents of cervical cancer has been in less developed countries in 2008. It can be deduced from this that the development of the countries can be related to the cervical cancer incidents/ deaths. For this reason, human development index is utilized in this investigation.

The Human Development Index (HDI), lets the countries in the world be compared on the level of development. A number of 3 decimal places between 0 and 1 is calculated for every country for this purpose, indicating how developed the country is, considering 3 main features of the countries:

- Health dimension considering the expected life span,
- Education dimension considering the number of schooling years,
- The standard of living dimension considering the gross national income (GNI).[12]

Using all the information above, it was deduced that a more developed country (according to their HDI) could potentially provide better precautions/ treatments for cervical cancer, hence have a less mortality rate.

Personal Engagement

The significance of this topic for me is about my personal experience with HPV vaccine as a teenage girl living in a developing country. A couple years ago, when I visited my pediatrician with my mother for a throat infection, she also informed us about how she had just got the HPV vaccine and explained the significance of the vaccine to prevent cervical cancer. After some more research, we decided that I should get the

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[6] "Human Papillomavirus (HPV)," accessed September 21, 2022, https://www.who.int/teams/immunization-vaccines-and-biologicals/diseases/human-papillomavirus-vaccines-(HPV).

[7] "Human Papillomavirus (HPV) Vaccines - NCI," cgvArticle, National Cancer Institute, June 18, 2021, nciglobal,ncienterprise, https://www.cancer.gov/about-cancer/causes-prevention/risk/infectious-agents/hpv-vaccine-fact-sheet.

[8] "Cervical Cancer," February 22, 2022.

[9] Healthdirect Australia, "Cervical Cancer," http://purl.org/ontology/nhccn#text_html, Healthdirect (Healthdirect Australia, August 16, 2022), https://www.healthdirect.gov.au/cervical-cancer.

[10] "How Is Cervical Cancer Diagnosed and Treated? | CDC," December 15, 2021, https://www.cdc.gov/cancer/cervical/basic_info/diagnosis_treatment.htm.

[11] Marc Arbyn et al., "Estimates of Incidence and Mortality of Cervical Cancer in 2018: A Worldwide Analysis," *The Lancet Global Health* 8, no. 2 (February 1, 2020): e191–203, https://doi.org/10.1016/S2214-109X(19)30482-6.

[12] United Nations, "Human Development Index," *Human Development Reports* (United Nations), accessed September 24, 2022, https://hdr.undp.org/data-center/human-development-index.

vaccine. I eventually could get the 3 doses; however, it was extremely hard to obtain the vaccines because they are low in demand and they were also quite expensive. We had to pre-order the vaccines months ago from the providers. This made me think that the development of the country might be related to its vaccination coverage among women and also the other prevention techniques hence affecting the mortality rate due to the cancer which HPV causes.

Hypothesis:

The mortality rate (age-standardized rate) and the HDI of the countries in Europe should have a negative correlation.

This prediction is supported by advanced healthcare systems present in more developed countries, more attention to such cancer and more funds provided in those countries.

Data Sources:

It was essential that data from reliable sources were used for this investigation. This factor led me to choose data from these resources:

- United Nations Development Programme (HDI data)[13]
- World Health Organization/ International Agency for Research on Cancer (IARC) (Database on the mortality rate due to cancer of the cervix uteri)[14]

Variables:

Independent variable: The HDI values from different countries.
Dependent variable: The mortality rates (age-standardized rate) due to cervical cancer
Controlled variables are explained below.

Approach to the Research Question and Controlled Variables:

The inclusion criteria for the selected countries: These criteria decide which countries should be included in this investigation. It should be noted that data availability for cervical cancer is seen to be somewhat less than other cancer data. In the IARC website (and in reports of any other data collecting organizations), not every country was ever included in the data section, except the recent data from 2020. It was also evident that not every country had data for each year. It was seen that the included countries in general were in Europe and Americas. This might be due to these areas being more developed. This situation also might indicate how relatively undeveloped countries do not/ cannot give the same attention to cervical cancer. Due to these circumstances, I decided to proceed with European countries (defined by UN[15]), because the data availability seemed enough to find a correlation if it existed. Choosing countries from the same geographical area, I tried to control variables like lifestyles and traditions.

Considering the availability of the data, I could have been working with only the year 2020 in order to include more countries; however, in order to minimize the effect of confounding variables it was essential that more than 1 years of data was to be picked. I chose years 2012, 2014, 2016 and 2020 for this purpose. The data for year

[13] "Country Insights," *Human Development Reports* (United Nations), accessed September 19, 2022, https://hdr.undp.org/data-center/country-insights.

[14] "Cancer Over Time," accessed September 19, 2022, https://gco.iarc.fr/overtime.

[15] "Regional Groups of Member States | Department for General Assembly and Conference Management," accessed September 24, 2022, https://www.un.org/dgacm/en/content/regional-groups.

2018 were extremely limited and many countries were missing, so that year was not included in this report.

Among the European countries I could obtain data for 27 European countries. Only 4 of the countries lacked data for only one year, considering the limitations of the data source these countries were still included and the calculations were only a little modified in order to suit the purpose.

In order to further standardize the data, the mortality rates used are per 100.000 people, since each country has different population. Moreover, the data used was also age-standardized, which is defined as "weighted average of the age-specific mortality rates per 100 000 persons"[16] by WHO. The benefit of this data comes from the fact that the age distribution of the population in different countries may be different. For example, if population A has more proportion of women aged 35+ in the population, than population B, the crude mortality rate for population A might be higher than B (since cervical cancer usually occurs later in the life of a woman[17]) when in reality, this is irrelevant to the independent variable (HDI).

Safety, Environmental and Ethical Considerations:

There are no safety or environmental considerations. As for ethical considerations, all the data is taken from a publicly open website and with credits.

Trial Investigation and Methodology:

In order to see if a general trend may exist in these 27 countries, it was essential that a trial investigation is done using only 5 countries. Such investigation will give me an idea whether I can proceed with my actual investigation. In order to select these 5 countries, an online random generator[18] was used. The table below, shows the countries and the data taken from the IARC website for these countries. As the ASR data were already given on the website, the calculations to find these numbers form the crude rate were unnecessary, and the given calculated data was used.

Table 1: Raw data showing the HDI and mortality ASR due to cervical cancer for 5 selected countries for years 2012, 2014, 2016 and 2020

	HDI (Human Development Index)				**ASR for Mortality due to Cervical Cancer**			
Countries	**2012**	**2014**	**2016**	**2020**	**2012**	**2014**	**2016**	**2020**
Austria	0.906	0.909	0.915	0.913	1.9	1.7	1.6	1.8
Estonia	0.874	0.879	0.885	0.892	5.5	4.9	4.4	4.3
Ireland	0.903	0.914	0.929	0.943	2.9	2.8	-	2.8
Slovakia	0.845	0.849	0.854	0.857	4.9	4.8	-	5.3
Switzerland	0.945	0.952	0.956	0.956	1.0	0.8	1.1	1.0

In order to standardize the values, mean values are going to be taken as mentioned before. The means are found by summing up the available values and diving this sum by the number of available values.
Sample calculation for Ireland:

[16] "Age-Standardized Mortality Rate (per 100 000 Population)," World Health Organization, accessed September 24, 2022, https://www.who.int/data/gho/indicator-metadata-registry/imr-details/78.
[17] Sachdev, "Cervical Cancer."
[18] "The Random Choice Generator Online Tool," TextFixer, accessed September 24, 2022, https://www.textfixer.com/tools/random-choice.php.

- ✓ For the ASR for mortality due to cervical cancer: $\frac{2.9+2.8+2.8}{3} = 2.83$
- ✓ For the HDI: $\frac{0.903+0.914+0.929+0.943}{4} = 0.922$

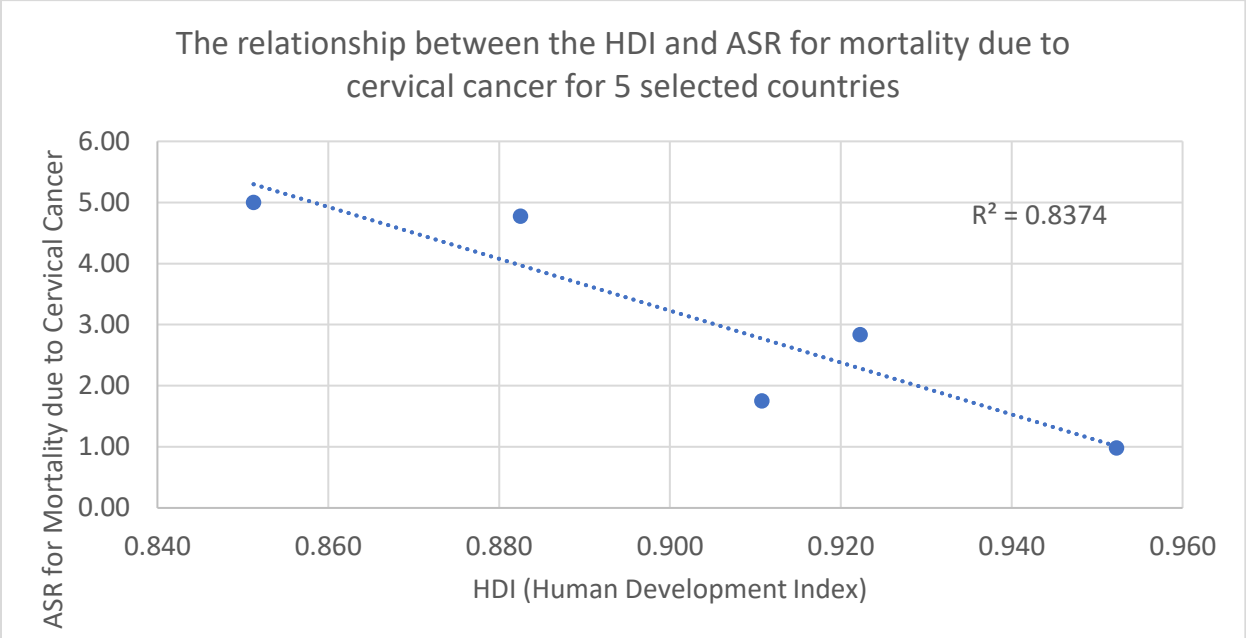
Doing similar calculations for each 5 countries, the processed data can be obtained.

Table 2: Processed data showing the HDI and mortality ASR due to cervical cancer for 5 selected countries for years 2012, 2014, 2016 and 2020

Countries	HDI (Human Development Index)	ASR for Mortality due to Cervical Cancer
Austria	0.911	1.75
Estonia	0.883	4.78
Ireland	0.922	2.83
Slovakia	0.851	5.00
Switzerland	0.952	0.98

Now, it is essential that I put these on a graph in order to observe the correlations. I put the HDI (the independent variable) on the x-axis, and the ASR for mortality due to cervical cancer (the dependent variable) on the y-axis.

Graph 1: Scatter diagram displaying the relationship between the HDI and ASR for mortality due to cervical cancer for trial investigation.



As seen, I denoted the trendline on the graph which indicates a negative correlation. This idea is also supported by the high value of coefficient of determination, $R^2 = 0.8374$, which indicates the existence of a correlation.

This trial investigation means that I can further continue my investigation and do the same steps with 27 countries in Europe.

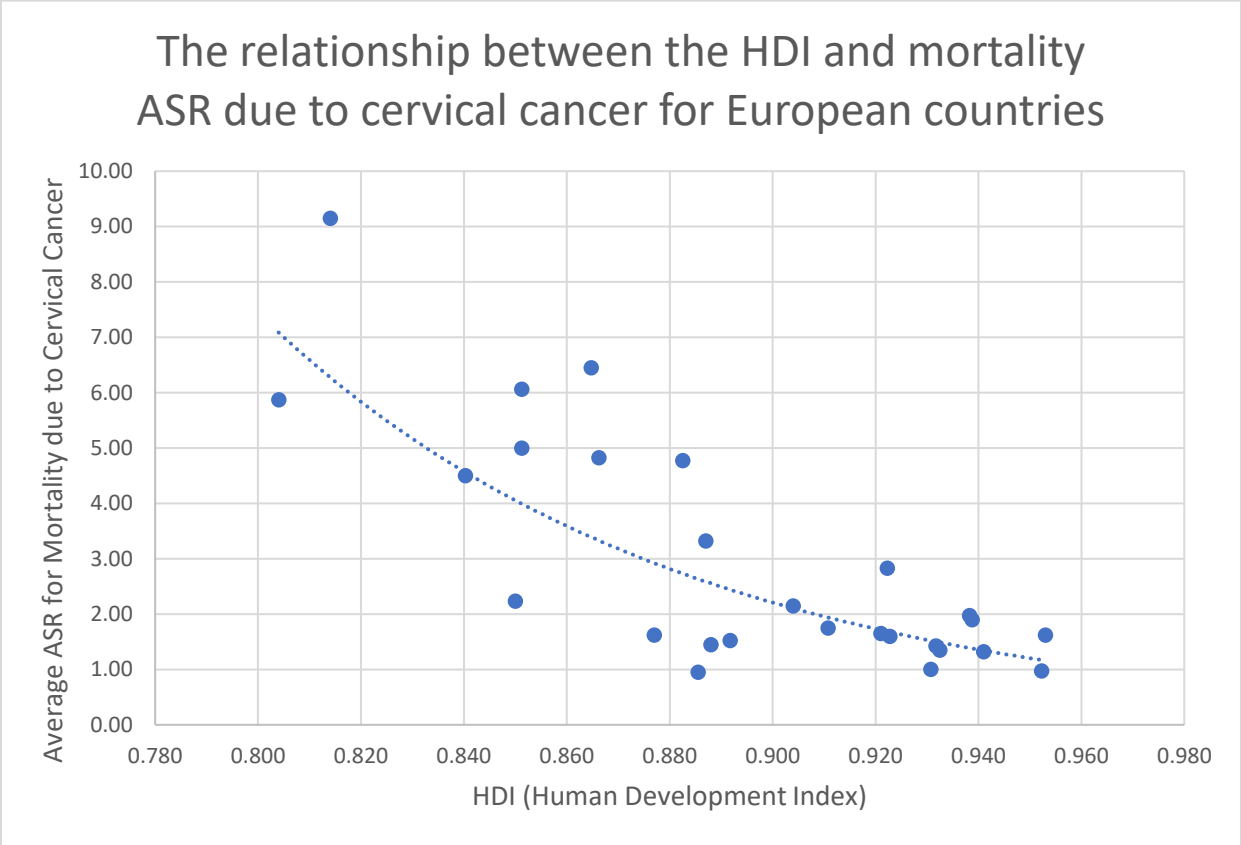
Investigation and Results:

Table 3: The HDI and average ASR for mortality due to cervical cancer given for 27 countries in Europe.

Countries	HDI (Human Development Index)	Average ASR for Mortality due to Cervical Cancer
Austria	0.911	1.75
Belgium	0.923	1.60
Bulgaria	0.804	5.88
Czechia	0.887	3.33
Denmark	0.938	1.98
Estonia	0.883	4.78
Finland	0.931	1.00
France	0.892	1.53
Germany	0.939	1.90
Greece	0.877	1.63
Hungary	0.840	4.50
Iceland	0.941	1.32
Ireland	0.922	2.83
Italy	0.886	0.96
Latvia	0.851	6.07
Lithuania	0.865	6.45
Norway	0.953	1.63
Poland	0.866	4.83
Portugal	0.850	2.23
Romania	0.814	9.15
Slovakia	0.851	5.00
Slovenia	0.904	2.15
Spain	0.888	1.45
Sweden	0.932	1.43
Switzerland	0.952	0.98
The Netherlands	0.933	1.35
United Kingdom	0.921	1.65

It is appropriate to note these values on a graph to see the correlation:

Graph 2: The scatter diagram displaying the relationship between the HDI and ASR for mortality due to cervical cancer for European countries



I can see the negative correlation by eye, looking at the trendline which is chosen to be logarithmic instead of linear by eye. However, a suitable statistical testing is still necessary. Before that, the two possible hypotheses should be stated. The results of the statistical test will indicate which hypothesis to accept.

- The Null Hypothesis (H_0): There is no statistically significant relationship between the ASR for mortality due to cervical cancer in European countries and their HDI.
- The Alternative Hypothesis (H_1): There is statistically significant negative correlation between the ASR for mortality due to cervical cancer in European countries and their HDI.

Statistical Testing:

One of the most common correlation tests, Pearson's correlation test, requires a normal distribution and a linear data set. These conditions are necessary for the test to be significant, for a meaningful test. However, looking at the graph above, it can be seen that the data set might not be linear. For this reason, I decided to proceed with Spearman's correlation test which does not depend on the data being linear or not[19], to be significant. It is "a statistical measure of the strength of a monotonic relationship between paired data" [20] and it does not need further assumptions unlike Pearson's correlation.

[19] Juhi Ramzai, "Clearly Explained: Pearson V/S Spearman Correlation Coefficient," Medium, May 25, 2021, https://towardsdatascience.com/clearly-explained-pearson-v-s-spearman-correlation-coefficient-ada2f473b8.
[20] "Spearman's Correlation," Statstutor, accessed September 25, 2022, https://www.statstutor.ac.uk/resources/uploaded/spearmans.pdf.

For this statistical test, rank the data for the first variable (let the rank be R_1) and for the second variable (R_2). Then, these 2 ranks are subtracted from each other to find values of d_i. Where n is the population size, correlation coefficient is[21]:

$$\rho = 1 - \frac{6\sum d_i^2}{n(n^2-1)}$$

The values are calculated with the help of the table below (complete data is available upon request):

Countries	**HDI (Human Development Index)**	**Average ASR for Mortality due to Cervical Cancer**	**HDI rank (R_1)**	**ASR rank (R_2)**	**d ($R_1 - R_2$)**	**d^2**
Austria	0.911	1.75	12	15	-3	9
Belgium	0.923	1.60	9	19	-10	100
Bulgaria	0.804	5.88	27	4	23	529
Repeated for all countries						
United Kingdom	0.921	1.65	11	16	-5	25
					SUM:	5593.5

$$\rho = 1 - \frac{6 \cdot 5593.5}{27(27^2-1)} = -0.707$$

This ρ value should be compared with the critical value for Spearman's correlation test, in order to see if there is a significant correlation and the hypothesis is true. If the absolute value of ρ is higher than the critical value, it can be deduced that the correlation is significant and the alternative hypothesis should be accepted. If the reverse is true, the null hypothesis should be accepted. The most commonly used significance level is 0.05, this means that the test gives out 95% probability that the alternative hypothesis is correct. The critical value for this significance level of 0.05 for Spearman's correlation is 0.385[22]. Since $|-0.707| > 0.385$, there is a significant correlation. The fact that ρ is negative indicates the negative correlation[23]. Alternative hypothesis (H_1) is accepted and the null hypothesis is rejected.

[21] "Spearman Rank Correlation in Excel: Formula and Graph," ablebits.com, accessed September 25, 2022, https://www.ablebits.com/office-addins-blog/spearman-rank-correlation-excel/.

[22] "Spearman," University of Washington, n.d.

[23] "Level of Significance (Statistical Significance) | Definition & Steps," BYJUS, accessed September 25, 2022, https://byjus.com/maths/level-of-significance/.

Conclusion

The research question for this investigation was *"What is the correlation between European countries' HDI (Human Development Index) and the age-standardized mortality rate due to the cervical cancer, per 100.000 people?"* In the light of Spearman's ranking correlation test, a statistically significant negative correlation was found as an answer to the research question.

However, the variance of the data can be seen through the $R^2 = 0.618$ value, that this data set indicates some variance. It is evident on the graph that some countries that have similar HDI, may have very different ASR for mortality due to cervical cancer. An example of this situation can be Czechia, Estonia and Italy (HDI are respectively 0.887, 0.883 and 0.886). The mortality rates for these countries are 3.33, 4.78 and 0.96 respectively, when they were expected to be a lot closer to each other. This is clear evidence that there must have been confounding variables that disrupted the results.

Overall, this report finds a correlation between the HDI of the European countries and the ASR for mortality due to cervical cancer. This can be supported via many factors. A study by Peters *et al.* suggests that the healthcare systems might improve as the development of the country increases[24]. Even though this report covers low- and middle-income countries unlike this investigation, it is possible to deduce that the healthcare systems correlate with development. It is also possible that the awareness on STDs among the countries may affect the transmission of HPV viruses and cause cervical cancer.

Evaluation:

There are many strengths of this investigation that benefited the accuracy of the results. Using the R-squared values on the graphs let me know the variance of the data, and the Spearman's test and the interpretations of it indicated the statistically significant correlation. I included many European countries and took the average values for 4 different years, the data I used indicated an 8-year time period. These let me investigate the general trends that occurred within the countries. The use of the age-standardized rate (ASR) instead of the crude rate, contributed to minimize the effect of the different distribution of different age groups in each country.

However, the methodology had some weaknesses too. Some countries from the list have much lower population compared to the others (ex. Lithuania, Latvia[25]) and it might have been better to exclude these countries from the calculations because smaller population size yields more inaccuracy and deception[26]. In order to improve the inclusion criteria further, another factor that could be kept in mind was grouping the countries according to the socio-economic groups they are a part of. Moreover, averaging the data of 4 years, could create errors since the outliers were not sought and excluded.

If I look at my data resources, I can say that the IARC which is under the auspice of WHO, had few data for many countries/ years as I mentioned earlier in this report. The most major deficiency of this that affected this investigation is the reasons for these mortalities are unknown. It is unknown to some extent, if the deaths are caused because of the underdevelopment of the country. Maybe some percent of the deaths are caused by late diagnosis, but some are caused regardless of the prevention methods.

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[24] David H. Peters et al., "Poverty and Access to Health Care in Developing Countries," *Annals of the New York Academy of Sciences* 1136 (2008): 161–71, https://doi.org/10.1196/annals.1425.011.

[25] "Country Insights."

[26] Martin Bland, "Some Problems with Sample Size," n.d., 6.

The weaknesses of my second dependent variable, HDI, also reveal many other confounding variables. Firstly; the attention that the government gives to the healthcare system, the budget it has for such diseases can be different and is not necessarily dependent on the HDI of the country. Moreover, the external aids -from many different organizations- that these countries might get is neglected in this investigation. It is possible that some less developed countries (that have lower HDI than the other countries used in this investigation) may get international help (ex. from WHO[27]) that the mortality rates might slightly disrupt. One last factor to consider is the social and educational factors. The lack of sex education at schools (which does not affect countries' HDI directly) may accelerate the spread of STDs. Even though the focus of this investigation was European countries who have similar cultures, the habit of seeing a gynecologist or the outlook of sexually transmitted diseases can vary from culture to culture.

Extensions:

It should be noted that my initial aim before conducting this investigation was to further compare the countries in Europe in two categories: developing and developed countries. However, fewer data for less developed/ developing countries prevented such investigation to present statistically significant results, so this research question was not included.

In order to improve this investigation, it can be possible to study using data from more years and a longer period of time to observe the relationship between the HDI and the mortality rates. This would give a better understanding to the correlation. From another perspective, each country could have been observed individually to pick up patterns while the country's HDI changed over a long period of time.

Instead of using HDI, gross domestic product (GDP) could have been used. This parameter is calculated and is related to a country's size of economy[28]. So, this could be used as an indicator, even though such investigation would still bring many confounding variables with it. It also could have been possible to investigate the death rates in rural and urban areas, as the health services may be limited in undeveloped areas in each country. Moreover, gender inequality index (GII)[29] would have been useful, since cervical cancer is a problem only for those assigned female at birth.

[27] "What We Do," accessed September 26, 2022, https://www.who.int/about/what-we-do.

[28] "Gross Domestic Product: An Economy's All," International Monetary Fund, accessed September 26, 2022, https://www.imf.org/external/pubs/ft/fandd/basics/gdp.htm.

[29] United Nations, "Gender Inequality Index," *Human Development Reports* (United Nations), accessed September 26, 2022, https://hdr.undp.org/data-center/thematic-composite-indices/gender-inequality-index.

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Image 1: "The Human Reproductive System | The Shropshire and Mid Wales Fertility Centre." Accessed September 26, 2022. https://www.shropshireivf.nhs.uk/about-fertility/the-human-reproductive-system/.