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The Colorectal Cancer Mortality-to-Incidence Ratio as an Indicator of Global Cancer Screening and Care

Vasu Sunkara, MD, PhD[1,2] and **James R. Hébert, MSPH, ScD**[3,4]

[1]Department of Economics, Harvard University, Cambridge, Massachusetts

[2]Saint Vincent Hospital, Erie, Pennsylvania

[3]Cancer Prevention and Control Program, Department of Epidemiology and Biostatistics, Arnold School of Public Health, University of South Carolina, Columbia, South Carolina

[4]Department of Family and Preventive Medicine, University of South Carolina School of Medicine, Columbia, South Carolina

Abstract

BACKGROUND—Disparities in cancer screening, incidence, treatment, and survival are worsening globally. The mortality-to-incidence ratio (MIR) has been used previously to evaluate such disparities.

METHODS—The MIR for colorectal cancer is calculated for all Organisation for Economic Cooperation and Development (OECD) countries using the 2012 GLOBOCAN incidence and mortality statistics. Health system rankings were obtained from the World Health Organization. Two linear regression models were fit with the MIR as the dependent variable and health system ranking as the independent variable; one included all countries and one model had the "divergents" removed.

RESULTS—The regression model for all countries explained 24% of the total variance in the MIR. Nine countries were found to have regression-calculated MIRs that differed from the actual MIR by >20%. Countries with lower-than-expected MIRs were found to have strong national health systems characterized by formal colorectal cancer screening programs. Conversely, countries with higher-than-expected MIRs lack screening programs. When these divergent points were removed from the data set, the recalculated regression model explained 60% of the total variance in the MIR.

CONCLUSIONS—The MIR proved useful for identifying disparities in cancer screening and treatment internationally. It has potential as an indicator of the long-term success of cancer surveillance programs and may be extended to other cancer types for these purposes.

Corresponding author: Vasu Sunkara, MD, PhD, Saint Vincent Hospital, 2314 Sassafras St, Erie, PA 16502; Fax: (814)452-5097; ssunkara@svhs.org.

CONFLICT OF INTEREST DISCLOSURES
Dr. Hebert is the owner of Connecting Health Innovations LLC, which exists to commercialize his inventions (developed as an employee of the University of South Carolina). Currently, Connecting Health Innovations LLC has a grant from the National Institute of Diabetes and Digestive and Kidney Diseases for work related to commercializing the dietary inflammatory index for use in clinical practice. That work has absolutely nothing to do with the current study.

Keywords

colorectal cancer; mass screening; public health; clinical medicine

INTRODUCTION

The worldwide rise in cancer has been dramatic. The International Agency for Research on Cancer's GLOBOCAN 2012 report details an increase in newly incident cancers from 12.7 million in 2008 to 14.1 million in 2012. The annual number of cancer-related deaths likewise has increased from 7.6 million in 2008 to 8.2 million in 2012. This global rise in cancer deaths is coupled with differences in cancer diagnosis and mortality for low-income versus high-income nations.[1]

There are significant questions that remain to be answered to explain these apparent disparities. First among these is the manner in which a country's cancer mortality rate trends compared with its cancer incidence rate. In addition, it is unclear to what extent disparities in health care services affect cancer mortality and incidence. With high-quality economic and health care-related data, the member countries of the Organisation for Economic Cooperation and Development (OECD) provide a unique opportunity to delve into these important issues.

The OECD consists of 34 member countries that collaborate on multiple policy fronts, ranging from education and trade partnerships to a shared advancement of cultural, economic, and humanitarian goals.[2] Many of these are high-income countries. Of these 34 member countries, 26 (76%) have universal health care coverage for their citizens.[3] Previous research has reported inequalities in health care use within OECD countries. For example, the frequency of dental visits, physician visits, and cancer screening appointments is greater among high-income residents compared with low-income residents in the OECD nations studied.[4] Moreover, there are differences in cervical cancer screening rates between selected OECD countries, with certain nations maintaining stable screening rates from 2000 to 2009 versus the fluctuating screening levels of others.[5]

The mortality-to-incidence ratio (MIR) is a novel measure that can be used to evaluate cancer mortality in relation to incidence, as a proxy for 1-survival. It is used in this study to identify whether a country has a higher mortality than might be expected based on its incidence. Other information must be gathered to determine the causes for departures from expectation. Parkin and Bray have shown in a single-country setting that the MIR, approximately equivalent to 1-(cancer survival), is a useful measure of the completeness of a cancer registry, especially when considering the quality of cancer care and cancer reporting in a country.[6] In addition, Asadzadeh Vostakolaei et al have extended the validity of the MIR to a multiple-country setting. They demonstrated a strong association between 5-year cancer survival data and the MIR.[7] Moreover, the MIR has been used by Hebert et al to describe cancer disparities in African Americans versus European Americans in South Carolina,[8] and has now been applied in an other state within the United States to examine associations with additional attributes of the health care system.[9]

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Using the MIR, the current study sought to detail the differences in colorectal cancer outcomes in the OECD countries based on the performance of each country's health care system. Colorectal cancer was selected because it is very successfully prevented by the use of competent screening, especially via colonoscopy. This information is further supplemented with evaluation of the cancer screening programs for those nations for which the MIR is not as well predicted by the regression modeling. By having a detailed analysis of MIR values across the OECD, we believe this study has the potential to provide a more comprehensive overview of colorectal cancer outcomes in this major economic zone.

MATERIALS AND METHODS

Mortality and incidence rate data per 100,000 population per year were obtained from the GLOBOCAN 2012 database for all 34 OECD countries. Different methods were used to calculate the mortality and incidence rates by country, ranging from the national rates for 2012, the most recent rates extended to the 2012 population, the application of quantitative models using the most recent rates, to aggregating the most recent rates across neighboring countries. The methodology in calculating the incidence and mortality for a given country is generally not the same. In addition, there is a wide range with regard to the quality of collected data for GLOBOCAN. For incidence data, the quality standard ranges from No Data (grade G) to High Quality Data Exceeding 50% of the Population (grade A). Similarly for mortality data, measures range from No Data (score of 6) to High Quality Complete Registration (score of 1).

The MIR was calculated by dividing the reported mortality rate for a given OECD nation by its incidence rate. To evaluate the association between MIR and the health system ranking, data from the 2000 World Health Organization (WHO) health system ranking for all OECD countries were obtained. The numerical ranking is for 191 countries and is a composite measure of 5 different national indices: health, health care financing, health inequality, level of health care responsiveness, and the distribution of health care services. The score is a weighted average of the 5 measures, in the following percentages: 25% for equity in financing, 12.5% for distribution in health care responsiveness, 12.5% for the health care responsiveness level, 25% for the level of heath inequality, and 25% for overall health.[10]

A scatterplot of the WHO health system ranking versus the MIR value was thereafter generated. A simple linear regression based on these data was obtained using the formula: MIR =Health Systems Ranking * Beta + Alpha. Next, divergent points were identified. Divergent points were defined as countries with an MIR >|0.07| from their actual versus regression-predicted MIR value (corresponding to a 20% discrepancy). A second scatter-plot was generated with the new edited data set (ie, excluding these divergent points). An additional simple linear regression was obtained with the formula MIR_{edited} = Health $Systems\ Ranking_{edited}$ * $Beta_{edited}$ + $Alpha_{edited}$. Finally, a description of the health care characteristics of divergent countries was further provided.

RESULTS

Figure 1 includes the full data sample and demonstrates a weak positive association between a lower health system ranking and a higher colorectal cancer MIR, with an R^2 (R-squared value) of 0.24 (meaning that 24% of the total variability in the MIR was explained by the model). The regression formula is Y =0.0019*×+0.3324 (*P* =.003). That is, for a 1-unit change in the health system ranking, there is a 0.0019 increment rise in the MIR. Based on the criterion of a 20% discrepancy in the predicted and actual MIR, 9 countries were identified as divergent. Iceland, Israel, Canada, and South Korea each demonstrated a negative difference from the predicted MIR (ie, a lower MIR than predicted), whereas Chile, Greece, Poland, Mexico, and Turkey each demonstrated a positive difference from the regression-predicted MIR value.

Table 1 shows the full data for the selected countries sorted by the health system ranking. The residual is the actual MIR value subtracted from the regression-predicted MIR. For the 34-country sample, there was a range in the residual of −0.20 to +0.20. The averaged residual for all the data points was 0.00, whereas the median was −0.02.

To eliminate the effect of divergent points, MIR values >|0.20| of the predicted value were removed. As shown in Table 2, the 9 countries with divergent MIRs were removed in this process. With data points from 25 countries, the averaged residual decreased to −0.01, whereas the median remained unchanged at −0.02. The revised data set in which the divergent points were removed was replotted. A new regression line was fit, and demonstrated a strong positive association between a weaker health system ranking and a higher MIR, with an R^2 of 0.60 (corresponding to 60% of total variability explained by the model). The R^2 value was found to change by +0.36 with the data set edited by removing these divergent points. The regression formula for fitting these data was Y =0.0016*× +0.3301 (*P* <.0001). A 1-unit change in the health system ranking was found to have a more pronounced MIR-lowering effect than the previous regression equation, with an MIR increase of 0.0016 per 1-unit ranking change (Fig. 2).

DISCUSSION

The results of the current study demonstrated a strong linear relationship between country-specific MIR and health system ranking. Furthermore, the removal of divergent points (ie, those countries with much lower or much higher than predicted MIRs), appeared to greatly improve the predictive ability. Reanalysis with the excluded divergent points produced results accounting for >60% of the total variability in MIRs across countries. Case studies of these divergent points corroborated interesting differences in screening policy and behavior from the typical pattern.

We also evaluated the role of the MIR in helping to elucidate suspected discrepancies in care across different geographic locales within the OECD. The majority of the data were found to cluster between an MIR of 0.30 and 0.40. Qualitatively, a linear relationship was apparent between the health system ranking and the MIR, although the R^2 was modest when the data from all countries were included in analyses. Removal of the divergent points was found to strengthen the linear association while dramatically increasing the R^2 from 0.24 to 0.60 (ie, from explaining approximately 25% of variance to explaining well over 50% of the variance). Simultaneously, the extent of the MIR change for a given decrease in the health system ranking was found to decrease with the divergent points removed, declining from a change of +0.0016 in the MIR per unit change in ranking (edited data set) to a change of +0.0019 in the MIR per unit change in ranking (full data set).

As shown in Table 3, those countries with an MIR below the regression-predicted MIR appear to be more likely to have formal colorectal cancer screening guidelines that are acted on across a variety of health care settings. For example, South Korea has an MIR that is 0.20 below its regression-predicted value. As per the Korean Central Cancer Registry, the country has an age-standardized colorectal cancer incidence per 100,000 population that increased from 27.0 in 1999 to 50.2 in 2009. It is during this period, starting in 2004, that the Korean National Cancer Screening Program unveiled a nationwide colorectal cancer screening initiative. Since that time, screening levels have substantially increased, with lifetime screening rates increasing from 25.3% in 2004 to 54.2% in 2010.[11]

Likewise, Canada, Israel, and Iceland have MIR values 0.08, 0.08, and 0.10, respectively, below their regression-predicted MIR. These countries have formal screening recommendations in place, although the institution of these guidelines differs across countries. The Canadian Cancer Society has recommended fecal occult blood testing (FOBT) or fecal immunochemical testing (FIT) every 2 years for all Canadian men and women between the ages of 50 to 75 years, with flexible sigmoidoscopy being offered every 10 years to those with an average-risk profile.[12] However, screening rates vary by province, with Manitoba reported to have a rate of 18% in 2008, whereas Ontario was reported to have a rate of 30% in 2010.[13] Israel promotes annual FOBT for screening.[14] In comparison, Iceland has instituted pilot FOBT screening.[15]

Those countries with MIR values that are much higher than expected also present distinctive trends. These nations have a lower likelihood of having formal screening guidelines in place, and a lower percentage of the population being comprehensively screened. For example, Greece has an MIR that is 0.20 higher than its regression-predicted value. Triantafillidis et al reported a low level of screening in Greece, and recommended a concerted system-wide effort to increase access to routine colorectal cancer screening.[16] Focusing on a select study group, Kamposioras et al reported especially low colorectal cancer screening rates among 7012 individuals in 30 Greek locales. Fewer than 2% had undergone FOBT or sigmoidoscopy for routine screening, although 88% of males and 93% of females sought comprehensive cancer screening services.[17] In Chile, in which the actual MIR of 0.18 is higher than the regression-predicted value, Silva et al emphasized the need for greater awareness of colorectal cancer prevention.[18] Such awareness can make an appreciable impact, with the authors reporting the effectiveness of a local Chilean colorectal cancer prevention campaign for identifying polyps in 45% of the 1158 individuals enrolled in a single-clinic study.[18]

Similar to Greece and Chile, Turkey has an MIR that is 0.14 higher than expected. Kaya et al reported the need to expand the clinical infrastructure for comprehensive colorectal cancer screening in a country in which there is no formal screening program in place: "Turkey is in a great need for developing and implementing CRC screening programs. Nurses and other auxiliary health personnel have to be encouraged to take active roles in these programs."[19] Portugal, with an MIR that is 0.07 higher than expected, has limited colorectal cancer surveillance data available, with no comprehensive nationwide screening program in place.[20] Finally, the prevention and treatment of colorectal cancer in Mexico varies based on whether care is obtained from the public health care system, as well as the geographic region.[21]

The high R^2 value in the edited data set points to the significant effect of health system ranking on cancer diagnosis and mortality. Because these OECD countries are widely distributed across different continents, this analysis highlights the role of health care in affecting MIR values as well as the potential to study other putative risk factors such as diet and genetics in relation to cancer risk. In addition, examination of divergent points produces results that are intuitively appealing. For example, those countries that fare particularly well (those with MIR values that are lower than predicted) have better than average cancer-related screening and care. Likewise, those countries that perform poorly (those that have MIR values that are higher than predicted) have worse than average cancer-related screening and care.

As shown in Table 3, among the remaining 25 non-divergent countries, a much higher percentage appeared to have screening policies that include FOBT, FIT, or colonoscopy. Overall, approximately two-thirds of the 25 remaining countries appear to have some form of national-level screening in place. FOBT or FIT screening appears to be used more often. Colonoscopy alone is rare. At the same time, there is substantial room to expand coverage. Quite a few countries are experimenting with pilot programs, or do not have the resources allocated for national screening. Nevertheless, those without the necessary resources, including Norway, Switzerland, Denmark, and Belgium, nevertheless happen to be in the top 25 rankings for the WHO health system ranking. Potentially, for countries such as Norway and Denmark that have low MIR values, there might be a compensatory mechanism in place that enables these lower values (eg, more regular outpatient visits with a medical provider, and expedited referrals to gastroenterologists if a concerning gastrointestinal symptom arises).

Colorectal cancer is one of the most preventable of cancers, including through the use of competent screening colonoscopy.[22] It is also one of the most expensive to treat when diagnosed at a later stage, when prognosis is generally poor. The MIR provides important information relevant to local and global cancer surveillance. It provides a unique perspective on the relationship between cancer incidence and mortality rates in a given geographic locale. In addition, it has the additional benefit of being calculable in a quick and efficient manner. Although previous literature has applied the MIR as a relative marker of cancer care disparities and cancer survival, [7,8] we believe the current study extends that work by further demonstrating an association between the MIR and a country's overall health system performance.

Despite its strengths, there are several limitations to the current study. These include the finding that incomplete cancer registry reporting can skew the mortality and incidence results, and in the process affect the calculated MIR. Divergent countries in particular might represent especially skewed results, in which the credibility of the data collection is under question. Furthermore, due to the unavailability of the raw data for the indices constituting the WHO health system ranking, there are limitations in assessing the degree of discrepancy that exists between countries with regard to their health system performance. Finally, a focus on OECD countries biases the results toward nations that in aggregate have a higher gross domestic product, better data collection methods, and a stronger overall health infrastructure. As a result, it might be challenging to extend the MIR findings to low-income countries.

Despite these limitations, we suspect that OECD countries with strikingly high MIR values will derive a substantial public health benefit by reforming their health care financing and policies toward increasing access to high-quality colorectal cancer screening. Strengthening the health care infrastructure in these countries requires a multipronged approach that includes collaboration between national governments, on-the-ground primary care providers, medical subspecialists, and the wider public health community. This will help to ensure that the citizenry are not only aware of the risks of colorectal cancer, but also have the services afforded to them to have it diagnosed and treated early. In so doing, many lives can be saved from this harrowing, preventable disease. Because of the high costs associated with treatment, it should also prove to be very cost-effective.[23–25]

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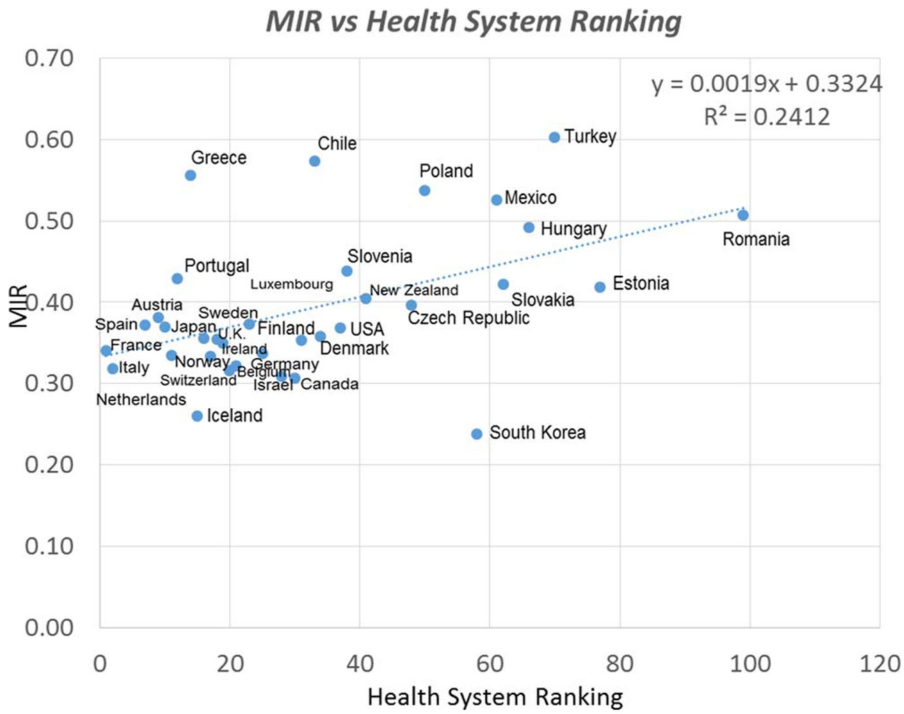

Figure 1.

Full data plot of the mortality-to-incidence ratio (MIR) versus health system ranking is shown. U.K. indicates United Kingdom.

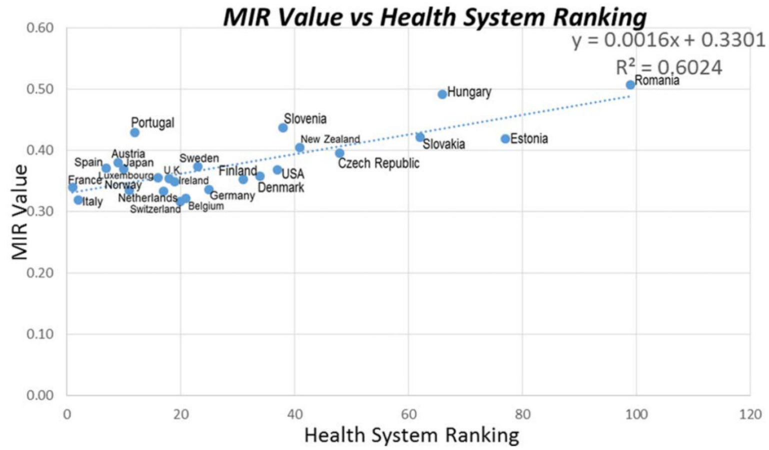

Figure 2.

Edited data plot of the mortality-to-incidence ratio (MIR) versus health system ranking is shown. U.K. indicates United Kingdom.

TABLE 1

Raw Data and Regression Results Based on MIRs for all OECD Countries

Country	Health System Ranking[a]	Mortality Rate[b]	Incidence Rate[c]	Actual MIR (2012)[d]	Regression- Predicted MIR[e]	Residual[f]
France	1	10.2	30	0.34	0.33	0.01
Italy	2	10.8	33.9	0.32	0.34	−0.02
Spain	7	12.3	33.1	0.37	0.35	0.02
Austria	9	9.9	26	0.38	0.35	0.03
Japan	10	11.9	32.2	0.37	0.35	0.02
Norway	11	13	38.9	0.33	0.35	−0.02
Portugal	12	13.6	31.7	0.43	0.36	0.07
Greece	14	7.5	13.5	0.56	0.36	0.20
Iceland	15	7.4	28.4	0.26	0.36	−0.10
Luxembourg	16	11.2	31.5	0.36	0.36	0.00
Netherlands	17	13.4	40.2	0.33	0.36	−0.03
United Kingdom	18	10.7	30.2	0.35	0.37	−0.02
Ireland	19	12.2	34.9	0.35	0.37	−0.02
Switzerland	20	9.3	29.4	0.32	0.37	−0.05
Belgium	21	11.8	36.7	0.32	0.37	−0.05
Sweden	23	10.9	29.2	0.37	0.38	−0.01
Germany	25	10.4	30.9	0.34	0.38	−0.04
Israel	28	11.1	35.9	0.31	0.39	−0.08
Canada	30	10.8	35.2	0.31	0.39	−0.08
Finland	31	8.3	23.5	0.35	0.39	−0.04
Chile	33	8.6	15	0.57	0.40	0.17
Denmark	34	14.5	40.5	0.36	0.40	−0.04
United States	37	9.2	25	0.37	0.40	−0.03
Slovenia	38	16.2	37	0.44	0.40	0.04
New Zealand	41	15.1	37.3	0.40	0.41	−0.01
Czech Republic	48	15.4	38.9	0.40	0.42	−0.02
Poland	50	14.5	27	0.54	0.43	0.11
South Korea	58	10.7	45	0.24	0.44	−0.20

Country	Health System Ranking[a]	Mortality Rate[b]	Incidence Rate[c]	Actual MIR (2012)[d]	Regression- Predicted MIR[e]	Residual[f]
Mexico	61	4.1	7.8	0.53	0.45	0.08
Slovakia	62	18	42.7	0.42	0.45	−0.03
Hungary	66	20.8	42.3	0.49	0.46	0.03
Turkey	70	10	16.6	0.60	0.47	0.13
Estonia	77	11.4	27.2	0.42	0.48	−0.06
Romania	99	13.4	26.4	0.51	0.52	−0.01

Abbreviations: MIR, mortality-to-incidence ratio; OECD, Organisation for Economic Cooperation and Development.

[a]As described/defined in the text.

[b]Deaths per 100,000 population per year, using 2012 data.

[c]Newly incident cases per 100,000 population per year, using 2012 data.

[d]The mortality rate divided by the incidence rate based on 2012 data.

[e]The MIR predicted from the regression equation.

[f]The difference between the actual MIR and the MIR predicted from the regression equation.

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TABLE 2

Residuals of Regression-Predicted MIR Values

Divergent Countries	
MIR moderately higher than prediction (+0.07 to +0.13)	Portugal and Mexico
MIR much higher than prediction (+0.14 to +0.20)	Turkey, Chile, and Greece
MIR moderately lower than prediction (−0.07 to −0.13)	Canada, Israel, and Iceland
MIR much lower than prediction (−0.14 to −0.20)	South Korea

Abbreviation: MIR, mortality-to-incidence ratio.

TABLE 3

Colorectal Cancer Screening Practices by Country and Denoting Health Care System and Divergencies Between Actual and Predicted MIR

Country	Method
No national policy	Luxembourg[a], Switzerland[a], Belgium[a], Denmark[a], Norway[a], Hungary[a], New Zealand[a], Portugal[a], Greece[a,b], Iceland[a,b], Mexico[b], Turkey[b], Estonia, and Romania
FOBT or FIT	France[a], Italy[a], Spain[a], Japan[a], the Netherlands[a], UK[a], Ireland[a], Sweden[a], Finland[a], Slovenia, Slovakia[a], Israel[a,c], Canada[a,c], Chile[b], Czech Republic[a], and South Korea[a,c]
CS	Poland[b], United States, Germany[a,d], and Austria[a,d]

Abbreviations: CS, colonoscopy; FIT, fecal immunochemical testing; FOBT, fecal occult blood testing; MIR, mortality-to-incidence ratio; UK, United Kingdom.

[a] Indicates that the country has some form of universal/single-payer health care.

[b] Indicates a country that demonstrated a positive difference from predicted (ie, higher MIR than predicted).

[c] Indicates a country that demonstrated a negative difference from predicted (ie, lower MIR than predicted).

[d] Indicates that the country has combined CS and FOBT/FIT screening.