

## Colorectal cancer screening in countries of European Council outside of the EU-28

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### Abstract

**AIM:** To provide an update on colorectal cancer (CRC) screening programmes in non-European Union (EU)-28 Council of Europe member states as of December 2015.

**METHODS:** The mission of the Council of Europe is to protect and promote human rights in its 47 member countries. Its 19 non-EU member states are Albania, Andorra, Armenia, Azerbaijan, Bosnia and Herzegovina, Republika Srpska, Georgia, Iceland, Liechtenstein, Republic of Moldova, Monaco, Montenegro, Norway, Russian Federation, San Marino, Serbia, Switzerland, FYR of Macedonia, Turkey, and Ukraine (EU-19). The main data source were GLOBOCAN, IARC, WHO, EUCAN, NORDCAN, ENCR, volume X of the CI5, the ministerial and Public Health Agency websites of the individual countries, PubMed, EMBASE, registries of some websites and the [www.cochranlibrary.com](http://www.cochranlibrary.com), Scopus, [www.clinicaltrials.gov](http://www.clinicaltrials.gov), [www.clinicaltrialsregister.eu](http://www.clinicaltrialsregister.eu), Research gate, Google and data extracted from screening programme results.

**RESULTS:** Our results show that epidemiological data quality varies broadly between EU-28 and EU-19 countries. In terms of incidence, only 30% of EU-19 countries rank high in data quality as opposed to 86% of EU-28 states. The same applies to mortality data, since 52% of EU-19 countries as against all EU-28 countries are found in the high ranks. Assessment of the method of collection of incidence data showed that only 32% of EU-19 countries are found in the top three quality classes as against 89% of EU-28 countries. For the mortality data, 63% of EU-19 countries are found in the highest ranks as opposed to all EU-28 member states. Interestingly, comparison of neighbouring countries offering regional screening shows, for instance, that incidence and mortality rates are respectively 38.9 and 13.0 in Norway and 29.2 and

10.9 in Sweden, whereas in Finland, where a national organised programme is available, they are respectively 23.5 and 9.3.

**CONCLUSION:** Cancer screening should be viewed as a key health care tool, also because investing in screening protects the weakest in the population, decreases the social burden of cancer, and reduces all types of health care costs, including those for radical surgery, long-term hospitalisation, and chemotherapy.

**Key words:** Colorectal cancer; Screening; EU-28; EU-19; European Union; Early detection; European Council

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**Core tip:** In the WHO Europe Region, colorectal cancer (CRC) is the first tumour with 471000 new cases per year and a mortality rate of 28.2 per 100000 population. Large-scale studies have found a reduction in mortality due to the adoption of population-based screening programmes. A 2010 European Parliament resolution called for the adoption of prevention programmes. As a result, some member states have begun enacting programmes, others are organising strategies for CRC screening implementation, and others still are moving from pilot projects to national-scale programmes. The present systematic review provides an update on CRC screening programmes in non EU-28 European Council States.

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## INTRODUCTION

Although cervical, breast and colorectal cancer are the only tumours for which screening has proven efficacy and cost-effectiveness, in several European countries screening implementation is fraught with difficulties. This is especially true of programmes regarding colorectal cancer (CRC)<sup>[1-3]</sup>, a highly common malignancy. According to GLOBOCAN data<sup>[3]</sup>, 1.36 million new cases affecting 17.2 per 100000 population (746000 men and 614000 women) are diagnosed in the world each year, and 693000 people (373000 men and 320000 women) die from CRC, accounting for a yearly mortality rate of 8.4 per 100000. In the World Health Organisation (WHO) Europe Region, CRC is the first tumour by incidence, with 471000 new cases each year and a mean mortality rate of 28.2 per 100000 population<sup>[4]</sup>. In the European Union (EU-28), its mean incidence rate is 31.3 per 100000 population, with 345000 new cases per year and an incidence per

100000 population of 39.5 for men 39.5 and 24.4 for women. The mean CRC incidence rates for men and women in the WHO Europe Region are 35.6 and 22.6 per 100000 population, respectively. In addition, with 228000 deaths per year and a mortality rate of 12.3 per 100000 population, CRC is the second cause of cancer death after lung cancer for men and women in the region<sup>[4]</sup>. The mean mortality rates per 100000 population in EU-28 countries and the WHO Europe Region are respectively 15.2 and 15.7 for men and 9.0 and 9.7 for women<sup>[4]</sup>.

CRC incidence is quite variable in EU-28 countries, and is higher in central and northern member states than in eastern ones. However, the lower rates found in eastern Europe are higher than the world mean<sup>[3]</sup>. This has prompted the Council of Europe to recommend the priority activation of CRC screening programmes<sup>[5]</sup>. According to a 2008 European Commission report on the diffusion of CRC screening programmes in the EU, only 12 of the then 22 member states had population-based screening programmes; the others were recommended to provide to their citizens equal access to cancer prevention<sup>[6]</sup>.

Crucially, more than 95% of CRC cases could benefit from surgical treatment if diagnosed early<sup>[7]</sup>. Several large-scale studies have found a considerable reduction in mortality due to the adoption of population-based screening programmes<sup>[8,9]</sup>.

The first European guidelines on CRC screening and the quality of CRC diagnosis were issued in 2010<sup>[10]</sup>. A European Parliament resolution of 6 May 2010 asked the Commission to promote the adoption of prevention programmes by any means and to encourage member states to allocate further resources to primary prevention and early diagnosis through screening<sup>[11]</sup>. As a result, some member states have begun enacting programmes, others are organising strategies for CRC screening implementation<sup>[3]</sup>, and others still are moving from pilot projects to national-scale programmes<sup>[12-16]</sup>.

The aim of the present systematic review is to provide an update on CRC screening programmes in non EU-28 European Council member states as of December 2015.

## MATERIALS AND METHODS

### **Council of Europe member countries**

The Council of Europe is a supranational institution founded in 1949 by the Treaty of London. Its mission is to protect and promote human rights in member countries. There are 47 member countries and a number of states with observer status. All EU-28 States are members (Austria, Belgium, Bulgaria, Croatia, Cyprus, Czech Republic, Denmark, Estonia, Finland, France, Germany, Greece, Hungary, Ireland, Italy, Latvia, Lithuania, Luxembourg, Malta, Poland, Portugal, Romania, Slovakia, Slovenia, Spain, Sweden, the Netherlands, and the United Kingdom). The other

**Table 1** Number of cases and standardized colorectal cancer burden in women and men in EU-19, 2012 (Adapted from Ferlay *et al.*<sup>[4]</sup>)

Country	WOMAN						MAN					
	Incidence		5-yr prevalence		Mortality		Incidence		5-yr prevalence		Mortality	
	Cases	ASR (W)	Cases	%	Cases	ASR (W)	Cases	ASR (W)	Cases	%	Cases	ASR (W)
Albania	167	7.9	501	39.9	90	4.0	175	9.0	526	42.0	97	4.8
Andorra	NR											
Armenia	4.4	17.0	939	68.6	281	9.7	426	22.8	855	77.1	261	13.4
Azerbaijan	346	6.4	209	4.0	755	19.8	313	7.1	661	18.5	187	4.3
Bosnia and Herzegovina	489	13.3	1427	84.8	327	7.7	620	20.7	1811	119.1	422	12.7
Georgia	300	7.5	608	31.3	173	4.0	305	9.9	631	38.3	177	5.5
Iceland	79	28.3	238	183.6	21	5.8	78	28.9	232	177.5	27	9.3
Liechtenstein	NR											
Republic of Moldova	716	23.0	1736	111.0	409	12.6	799	36.0	1963	143.2	491	22.0
Monaco	NR											
Montenegro	107	21.1	314	118.7	67	12.0	157	36.2	465	187.3	95	20.7
Norway	1947	35.8	5665	279.6	779	12.1	1966	42.6	5839	289.8	727	14.3
Russian Fed	33183	21.8	78454	119.1	21791	12.7	26745	30.0	63572	116.4	18116	19.9
San Marino	NR											
Serbia	2143	23.3	6281	151.4	1213	11.5	3370	43.4	9919	248.8	1922	22.8
Switzerland	2167	23.6	6522	193.8	718	6.4	2707	36.3	8340	259.9	1668	12.8
FYR Macedonia'	366	20.5	1070	124.0	213	10.8	421	28.4	1256	147.3	239	15.5
Turkey	5041	13.1	10690	38.2	3030	7.8	6889	20.6	14982	54.7	4128	12.6
Ukraine	9780	19.9	23110	109.6	5704	10.8	6269	29.9	22120	127.8	5929	18.8
EU-28	151920	24.4	417252	189.0	69087	9.0	193426	39.5	535845	257.8	82959	15.2

EU-28: Countries members of European Union; NR: Not Reported; ASR (W): Per 100000.

19 countries (hereafter EU-19) are in the European area: Albania, Andorra, Armenia, Azerbaijan, Bosnia and Herzegovina, Republika Srpska, Georgia, Iceland, Liechtenstein, Republic of Moldova, Monaco, Montenegro, Norway, Russian Federation, San Marino, Serbia, Switzerland, FYR of Macedonia, Turkey, and Ukraine.

**Sources of EU-19 epidemiological data: Search strategy**

The main data source was the GLOBOCAN 2012 website of the International Agency for Research on Cancer (IARC), which provides access to several databases that enable assessing the impact of CRC in 184 countries or territories in the world<sup>[4]</sup>.

Additional sources were the WHO, EUCAN and NORDCAN, the European Network of Cancer Registries (ENCR), volume X of the CI5, and the ministerial and Public Health Agency websites of the individual countries. The PubMed search used "Early Detection of Cancer" or "Colorectal Cancer screening" AND "state name" for each of the 19 countries. A MeSH search was conducted using the same criteria. The EMBASE did not provide further relevant results. The registries of some websites and the www.cochranelibrary.com, Scopus, www.clinicaltrials.gov, www.clinicaltrialsregister.eu, Research gate, and Google databases were also consulted. Other data were extracted from screening programme results.

**Statistical analysis**

Incidence and mortality data, their age-standardised rates per 100000 population (ASR-W), and 5-year

prevalence estimates for 2012 are reported by gender in Table 1. The quality of incidence and mortality data of EU-19 and EU-28 based on Data Sources and Methods<sup>[17]</sup> is compared in Table 2. The information regarding screening programmes in EU-19 is shown in Table 3. Finally mean income, total population, the existence of any registries, the availability of early detection tests at the public primary health care level, and the ranking of CRC incidence and mortality in EU-19 countries are reported in Table 4. The distribution of screening programmes (organised, spontaneous, unknown) in EU-28 and EU-19 countries is shown in Figure 1.

**RESULTS**

The results of the present systematic review are listed by physical geographical area as well as disaggregated by state. The incidence and mortality data are reported as ASR-W per 100000 population.

**Northern Europe**

The only North European countries that are not also EU-28 members are Iceland and Norway. The United Kingdom and Northern Ireland, Ireland, Finland, Denmark, Estonia, and Latvia offer organised national screening programmes and Sweden an organised regional programme; only Lithuania adopts spontaneous screening (Figure 1).

**Iceland:** The incidence rate of CRC in Iceland is 28.9 and 28.3 in men and women, respectively, with

**Table 2** Quality assessment of Epidemiological data source and methods according to Mathers *et al*<sup>[17]</sup>

Data source	EU-19	EU-28	EU-28
Incidence	Mortality	Incidence	Mortality
A: Iceland Norway, Ukraine	1: Iceland, Republic of Moldova	A: Austria, Belgium, Bulgaria, Croatia, Czech Republic, Denmark, Estonia, Ireland, Latvia, Lithuania, Malta, Sweden, Slovenia, Slovakia, The Netherlands, United Kingdom, Finland, France (Martinique)	1: Estonia, Hungary, Ireland, Latvia, Lithuania, Malta, Slovenia, Slovakia, Romania, United Kingdom, Finland
B: Serbia, Switzerland	2: Azerbaijan, Norway, Russian Federation, Serbia, Switzerland	B: France, Germany, Italy, Spain	2: Austria, Belgium, Bulgaria, Croatia, Czech Republic, Denmark, France, Germany, Italy, Luxembourg, Spain, Sweden, The Netherlands, France (Guadalupe), (La Reunion), France (Martinique), France (Guiana)
C: Turkey	3: Albania, Armenia, FYR Macedonia	C: Portugal, Poland	3: Greece, Portugal, Poland
D: Bosnia Herzegovina, Russian Federation	4: -	D: Luxembourg, France (La Reunion)	4: - 5: - 6: -
E: -	5: Bosnia Herzegovina	E: Romania	
F: -	6: Georgia, Montenegro, Turkey	F: -	
G: Albania, Armenia, Azerbaijan, FYR Macedonia, Georgia, Montenegro, Republic of Moldova		G: Greece, Hungary, France (Guadalupe), France (Guiana)	
Methods			
EU-19	EU-28	EU-19	EU-28
Incidence	Mortality	Incidence	Mortality
1: Iceland, Norway	1: Albania, FYR Macedonia, Iceland, Norway, Republic of Moldova, Serbia, Switzerland	1: Austria, Bulgaria, Croatia, Czech Republic, Denmark, Estonia, Finland, Germany, Ireland, Latvia, Lithuania, Malta, Slovakia, Slovenia, Sweden The Netherlands, United Kingdom, France (La Reunion), France (Martinique)	1: Austria, Bulgaria, Croatia, Czech Republic, Denmark, Estonia, Finland, France (metropolitan) Germany, Greece, Hungary, Ireland, Italy, Latvia, Lithuania, Luxembourg, Malta, Poland, Portugal, Slovakia, Slovenia, Spain, Sweden, The Netherlands, United Kingdom, France (Martinique)
2: Bosnia Herzegovina, Ukraine	2: Armenia, Azerbaijan, Bosnia Herzegovina, Georgia, Republic of Moldova, Ukraine	2: Belgium, Cyprus	2: Belgium, Cyprus, France (Guadalupe)
3: Turkey, Switzerland	3: - 4: -	3: France (metropolitan), Germany, Italy, Poland, Spain	3: Greece, Portugal, Poland
4: Albania, FYR Macedonia, Republic of Moldova, Serbia	5: Turkey	4: Greece, Hungary, Luxembourg, Portugal	4: -
5: Armenia, Azerbaijan, Georgia	6: Montenegro	5: Romania, France (Guadalupe),	5: France (La Reunion)
6: Turkey		6: - 7: - 8: - 9: -	6: -
7: - 8: -			
9: Montenegro			

Comparison between EU-19 and EU-28 countries, as defined in the main text. -: No country classified in that category.

a mortality rate of 9.3 for men and 5.8 for women (Table 1). The national cancer registry, linked to the NORDCAN project, covers the whole population and provides high-quality data (Table 2). Iceland has no active organised CRC screening programme (Table 3). The decision to adopt one, made in 2008<sup>[18]</sup>, was postponed due to the economic crisis. According to a recent congress communication<sup>[19]</sup>, a programme offering screening with the iFOBT at 2-year intervals to 55 to 75 year olds is due to start soon (Table 3). Until then, only spontaneous screening with the iFOBT will be available at the level of public primary health care (Table 4). CRC is the third most common tumour in both genders in the country and the fourth and second cause of cancer death in Iceland (Table 4).

**Norway:** In this country the incidence of CRC is 42.6 among men and 35.8 among women, with a mortality rate - 12.1 in men and 14.3 in women (Table 1). High data quality is ensured by a national cancer registry linked to the NORDCAN that covers the whole population (Table 2). A pilot study offering the iFOBT at 2-year intervals was activated in 2012 in the Ostfold region<sup>[20]</sup>. In a randomised controlled study (NORCCAPP) conducted in the Oslo and Telemark areas

in 1999-2001 the population was assigned to three groups that were tested with the iFOBT, received the iFOBT + sigmoidoscopy, or were just asked to report if they had had a diagnosis of CRC in the course of the study<sup>[21]</sup> (Table 3). CRC is the second most common tumour in both sexes and the second cause of cancer death for both sexes in Norway (Table 4).

**Balkan countries**

Several of these countries are EU-19 States: Albania, Republika Srpska, Bosnia and Herzegovina, Montenegro, and Serbia. Slovenia and Croatia are EU-28 Member states offering organised screening programmes (Figure 1).

**Albania:** Albania has a low CRC incidence rate, 9.0 among men and 7.9 among women, and an equally low mortality rate, respectively 4.8 and 4.0 (Table 1). Hospital-based disease registries provide non-excellent data quality (Table 2). Neither spontaneous nor organised screening is available<sup>[22]</sup>. The most recent data are for 2011. A 2015 paper<sup>[23]</sup> that first measured the frequency of gastrointestinal polypoid lesions in the Albanian population stressed the absence of a screening programme. According to the

**Table 3** Distribution of colorectal cancer screening programmes in EU-19 as of December 2015

Country	Program			Test	Screening interval (yr)	Age (yr)	Program start	Pop target	Level of participation (%)
	Type	Status	Region						
Federation of Bosnia and Heregovina <sup>[22]</sup>	Spontaneous Organised	NatW	All country	FOBT	-	> 50	-	-	-
Republika Srpska <sup>[22]</sup>	Spontaneous Organised	NatW	All country	FOBT	-	> 50	-	-	-
Georgia <sup>[51]</sup>	Organised	NatW	Tblisi	gFOBT	2	50-69	-	25388	53
Iceland <sup>[18]</sup>	Programmed as organised	NatW	OutsideTblisi	gFOBT	2	50-69	-	71364	84
			All country	FOBT	2	55-75 <sup>[19]</sup>	-	86000 <sup>[19]</sup>	
Iceland <sup>[19]</sup>	Spontaneous	NatW	All country	Colonoscopy		50-59			30
Monaco <sup>[55]</sup>	PB	Natw	All country	iFOBT (from 2015) gFOBT	2	50-80	2006	16000 <sup>[55]</sup>	60
Montenegro <sup>[22,28]</sup>	None	-	-	-	-	-	-	-	-
Montenegro <sup>[28]</sup>	Not PB	PilotStudy	Daniligrav, municipality of Podgorica	iFOBT	-	50-74	2010-2011	4500	33.3
Norway <sup>[20]</sup>	PB	Pilot Study	Østfold, Akershus and Buskerud	iFOBT	2		2012		
Norway <sup>[21]</sup>	PB	Pilot Study RCT	Oslo and Telemark in 1999-2001 NORCAPP	FOBT and FOBT + Sigmoidoscopy	-	55-64	1999-2000	13823	64.8
Russian Fed <sup>[42]</sup>	PB	Pilot Study	Sant Petersburg, all 18 town district	iFOBT		48-75	November 15 2010	20000	
Russian Fed <sup>[43]</sup>	NPB	Pilot Study	Kazan, Tatarstan Republic	FOBT, DRE, questionnaire	-			1071	
San Marino <sup>[36,37]</sup>	PB	Natw	All country	iFOBT	2	50-79	2009		65 <sup>[37]</sup>
Serbia <sup>[51]</sup>	PB	Natw	All country	iFOBT	2	50-74		789330	58.38
Switzerland <sup>[32]</sup>	Spontaneous	NatW	All country	FOBT or Colonoscopy	2, 10	50-80	2013	13170	22
Switzerland <sup>[33]</sup>	PB	Pilot Study RCT	Glarus, Vallée du Joux Uri	FOBT and or Colonoscopy	-	50-80	2001	20000	
Switzerland <sup>[34]</sup>	PB	Pilot Study, NRCT	Vaud	iFOBT or Colonoscopy		50-69	2015		
Turkey <sup>[44]</sup>	Organised Spontaneous	NatW		FOBT		50-69	2009	11681513	30 <sup>[44]</sup>
Ukraine <sup>[46,54]</sup>	PB	NatW		Not available	Not available	Not available	2002-2006		Not available

gFOBT: Guaiac test; iFOBT: Immunological test; FOBT: Not specified if gFOBT or iFOBT; DRE: Digital rectal exam; NPB: Not population-based.

WHO report<sup>[24]</sup>, neither the FOBT nor colonoscopy are available at the level of public primary health care (Table 4).

**Bosnia and Herzegovina, Republika Srpska:** In the Federation of Bosnia and Herzegovina the incidence of CRC is 20.7 among men and 13.3 among women, with a mortality rate of 12.7 in men and 7.7 in women. Data quality is not excellent (Table 2). According to Giordano *et al.*<sup>[22]</sup>, spontaneous and organised screening based on the FOBT is available for those aged more than 50 years. However, Buturovic reports that in the Konjic area colonoscopy is not available<sup>[25]</sup>. As shown in Table 4, the WHO has no data on the availability of screening tests (FOBT, colonoscopy) at the level of public primary health care<sup>[26]</sup>. The tumour represents the third and second most common cancer and the second and third cause of death in the country (Table 4).

In the Republika Srpska only spontaneous screening is available to subjects older than 50 years<sup>[22]</sup>. Again,

there is no clear information on screening programmes.

**FYR Macedonia:** In this country CRC incidence is moderately high in men (28.4) as well as women (20.5) (Table 1) and mortality rates of 15.5 and 10.8, respectively. Data quality is mediocre (Table 2). There seem to be no organised screening programmes, even though the iFOBT is available at the public primary health care level<sup>[27]</sup> (Table 4). CRC is the third most common tumour in the country for both sexes and the second cause of cancer death (Table 4).

**Montenegro:** The incidence of CRC in Montenegro is 36.2 among men and 21.1 among women, with a mortality rate of 20.7 in men and 12.0 in women. Data quality is poor (Table 2). A population-based screening programme using the iFOBT and involving subjects aged 50 to 74 years was conducted from February 2010 to March 2011 in Daniligrav municipality (Podgorica)<sup>[28]</sup>, while neither organised nor opportunistic screening is available in the other areas<sup>[22]</sup>. According

Table 4 National cancer profiles

Country	Income <sup>1</sup>	Total population	Cancer registry	Availability at public primary health care levels of early detection tests		Ranking CRC incidence <sup>2</sup>		Ranking CRC mortality <sup>2</sup>	
				Faecal occult blood test	Bowel cancer screening by exam or colonoscopy	Man	Woman	Man	Woman
North Europe									
Iceland <sup>2</sup>	High	326000	National, population-based	-	-	3 <sup>rd</sup>	3 <sup>rd</sup>	2 <sup>nd</sup>	4 <sup>th</sup>
Norway <sup>2</sup>	High	4994000	National, population-based	Yes	-	2 <sup>nd</sup>	2 <sup>nd</sup>	3 <sup>rd</sup>	2 <sup>nd</sup>
Central Europe									
Liechtenstein <sup>3</sup>	High non OECD	36925	NA	-	-	2 <sup>nd</sup>	3 <sup>rd</sup>	NR	NR
Monaco	High non OECD	38000	Hospital-based	Yes	Yes	NR	NR	NR	NR
Switzerland <sup>3</sup>	High	7997000	Sub-national, population-based <sup>a</sup>	Yes	Yes	2 <sup>nd</sup>	2 <sup>nd</sup>	3 <sup>rd</sup>	3 <sup>rd</sup>
South Europe									
Andorra	High non OECD	78000	Hospital-based	Yes	Yes	NR	NR	NR	NR
San Marino	High non OECD	31000	National, population-based	Yes	Yes	NR	NR	NR	NR
Balkan countries									
Albania <sup>3</sup>	Upper middle	3162000	Sub-national, hospital-based	-	-	> 5 <sup>th</sup>	5 <sup>th</sup>	> 5 <sup>th</sup>	5 <sup>th</sup>
Bosnia and Herzegovina <sup>3</sup>	Upper middle	3834000	NA	-	-	3 <sup>rd</sup>	2 <sup>nd</sup>	2 <sup>nd</sup>	3 <sup>rd</sup>
Montenegro <sup>3</sup>	Upper middle	621000	NA	-	-	2 <sup>nd</sup>	2 <sup>nd</sup>	2 <sup>nd</sup>	3 <sup>rd</sup>
Serbia <sup>3</sup>	Upper middle	9553000	Sub-national	Yes	Yes	2 <sup>nd</sup>	2 <sup>nd</sup>	2 <sup>nd</sup>	3 <sup>rd</sup>
FYR of Macedonia <sup>3</sup>	Upper middle	2106000	National	Yes	-	3 <sup>rd</sup>	3 <sup>rd</sup>	2 <sup>nd</sup>	2 <sup>nd</sup>
Eastern Europe									
Republic of Moldova <sup>3</sup>	Lower middle	3514000	National, hospital-based	Yes	Yes	2 <sup>nd</sup>	2 <sup>nd</sup>	2 <sup>nd</sup>	2 <sup>nd</sup>
Russian Fed <sup>3</sup>	High non OECD	143000000	Sub-national, population-based <sup>b</sup>	Yes	Yes	3 <sup>rd</sup>	2 <sup>nd</sup>	3 <sup>rd</sup>	2 <sup>nd</sup>
Turkey <sup>3</sup>	Upper middle	73997000	Sub-national, population-based <sup>c</sup>	Yes	Yes	4 <sup>th</sup>	3 <sup>rd</sup>	4 <sup>th</sup>	3 <sup>rd</sup>
Ukraine <sup>3</sup>	Lower middle	45530000	National, population-based	-	-	2 <sup>nd</sup>	2 <sup>nd</sup>	2 <sup>nd</sup>	2 <sup>nd</sup>
Caucasian countries									
Armenia <sup>3</sup>	Lower middle	2969000	National, hospital-based	Yes	-	5 <sup>th</sup>	3 <sup>rd</sup>	4 <sup>th</sup>	2 <sup>nd</sup>
Azerbaijan <sup>3</sup>	Upper middle	9309000	NA	Yes	-	4 <sup>th</sup>	4 <sup>th</sup>	5 <sup>th</sup>	5 <sup>th</sup>
Georgia <sup>3</sup>	Lower middle	4358000	Sub-national, population-based	-	-	5 <sup>th</sup>	> 5 <sup>th</sup>	5 <sup>th</sup>	> 5 <sup>th</sup>

OECD (Organization for Economic Co-operation and Development): <sup>1</sup>It referred to pro capita Gross National Income (current US\$) as indicated by World Bank: High income \$382742014; High Income non OECD: \$18939; Upper middle \$79012014; Lower middle \$2012; <sup>2</sup>Incidence and mortality between different cancers for country: data from <http://www.who.int/cancer/country-profiles/en/adapted> for each country; <sup>3</sup>Data available from: <http://assets.krebsliga.ch/downloads/fl2014.pdf>; <sup>a</sup>Registry in Zurich, Vaud, Valais, Ticino, St Gall-Appenzell, Neuchâtel, Graubünden and Glarus, Geneva, Basel; <sup>b</sup>Registry in Saint Petersburg; <sup>c</sup>Registry in Trabzon, Izmir, Erdine, Antalya. Information about registry existence are available from Ref. [46]. NA: Not available; NR: Not reported; CRC: Colorectal cancer.

to WHO data (Table 4), early detection tests are not available at the public primary health care level<sup>[29]</sup>. CRC ranks respectively as the second and third cause of cancer death in Montenegro (Table 4).

**Serbia:** At 43.3 in men and 23.3 in women, the incidence of CRC in Serbia is fairly high and the tumour is the second most common malignancy in both sexes. The mortality rates are 28.8 in men and 11.5 in women, and CRC is respectively the second and third cause of cancer death in the country. Data quality is good (Table 2). In 2013 Serbia implemented a national screening programme by extending a programmes

that had been active in Vozdovac, Subotica and Zrenjanin since 2005<sup>[30]</sup>. The current programme is offered to 50 to 74 year olds without evidence of CRC and uses the iFOBT. Its results are available online. The rate of participation as of 30 September 2015 was 58.38%<sup>[31]</sup>.

### Central Europe

France, Poland, Hungary, and the Netherlands offer national organised programmes, and Belgium a regional programme. Austria, Germany, the Czech Republic, Slovakia, and Luxembourg provide for spontaneous screening (Figure 1). The other countries



■ EU-28 Countries with organised screening	ASW-R	Inc.	Mort.	■ EU-28 Countries with spontaneous screening	ASW-R	Inc.	Mort.	■ EU-19 Countries with organised screening	ASW-R	Inc.	Mort.
Belgium[r]	36.7	11.8		Austria	26.0	9.9		Bosnia[r]	16.6		9.8
Croatia	32.9	18.7		Czech Republic	38.9	15.4		Georgia	8.5		4.6
Cyprus	24.5	6.9		Luxembourg	31.5	11.2		Monaco	NA		NA
Denmark	40.5	14.5		Lithuania	23.4	13.7		Norway[r]	38.9		13.0
Estonia	27.2	12.3		Germany	30.9	10.4		San marino	NA		NA
Finland	23.5	8.3		Greece	13.5	7.5		Sebia	32.6		16.6
France	30.0	10.2		Slovakia	42.7	18.0		Turkey[r]	16.6		10.0
Hungary	42.3	20.8		■ EU-28 Countries with unknown screening status				■ EU-19 Countries with unknown screening status			
Ireland	34.9	12.2		ASW-R	Inc.	Mort.		ASW-R	Inc.	Mort.	
Italy	33.9	10.8		Bulgaria	31.5	16.0		Albania	8.4		4.4
Latvia	23.7	19.9		Romania	26.4	13.4		Andorra	NA		NA
Malta	31.9	12.2		■ EU-19 Country with spontaneous screening				Armenia	19.3		11.1
Netherlands	40.2	13.4		ASW-R	Inc.	Mort.		Azerbaij	6.7		4.1
Poland	27.0	14.5		Iceland	28.4	7.4		Liechtenstein	NA		NA
Portugal[r]	31.7	13.6		Russia	24.5	15.2		Monteneg	28.2		15.9
Slovenia	37.0	16.2		Switzerland	29.4	9.3		Macedonia	24.3		13.0
Spain	33.1	12.3						Moldova	28.3		16.5
Sweden[r]	29.2	10.9						Ukraine	23.4		13.7
United Kingdom	30.2	10.7									

Figure 1 Comparison between EU-28 and EU-19 according to distribution of screening programmes. Inc: Incidence; Mort.: Mortality; [r]: Regional screening; NA: Not available.

in the area are Switzerland, Liechtenstein, and the Principality of Monaco.

**Switzerland:** The incidence rate of CRC is 36.3 in men and 23.3 in women; CRC is the second most common neoplasm in the country (Table 4). With a mortality rate of 28.8 in men and 6.4 in women, CRC ranks as the third cause of cancer death in both sexes (Table 4). Data quality is good and in line with that of neighbouring countries (Italy, France, and Germany). Since 2002, the Swiss Federal Statistical Office has been conducting a telephone survey, the Swiss Health Interview Survey (SHIS). In 2007, it assessed for the first time the date and reason for the use of the iFOBT and/or colonoscopy and asked detailed questions on screening<sup>[32]</sup>. The 2007 results found a rate of participation of 18.9% for both methods. In 2012 participation rose to 22.2% ( $P = 0.036$ )<sup>[33]</sup>; colonoscopy rose from 8.2% in 2007 to 15% ( $P < 0.001$ ) and the iFOBT fell from 13% to 9.8% ( $P = 0.002$ ). In 2007 the prevalence of CRC screening among respondents was 24.5% among higher-income respondents ( $> \$6000$  a month) and 10.5% in those with a low income ( $< \$2000$ ); the 2012 survey found a similar difference (respectively 28.6% and 16.0%). There was no association with education or occupation<sup>[32]</sup>. Since 1 July 2013 the test (colonoscopy every 10 years and iFOBT every 2 years) is partially covered by the mandatory insurance for those aged 50 to 69 years. In Uri Canton an organised programme is offered to 50-80 year olds without a past or current history of CRC. The programme was introduced in 2000 and the results of the first round have been published<sup>[33]</sup>; the patient could choose among colonoscopy, sigmoidoscopy, and iFOBT + sigmoidoscopy, and more than 70% opted for colonoscopy. Another programme in Vaud Canton offers screening to individuals aged 50 to 69 years having no risk factors or a past or current history of CRC; they can choose between the iFOBT every 2 years and colonoscopy every 10 years; the excess is paid for by the Cantonal administration, the remaining expenses are sustained by the patient. The programme is co-ordinated by the Fondation Vaudoise pour le Dépistage du Cancer<sup>[34]</sup>.

**Liechtenstein:** In this tiny state the incidence data are provided by the National Bureau of Statistics. CRC is the second most common cancer in men and the third in women. No data are available on CRC screening programmes, neither through institutional websites nor through the WHO (Table 4).

**Principality of Monaco:** Official incidence and mortality data validated by the WHO are not available for this city-state, but they are probably similar to those of France. The Centre Monégasque de Dépistage has been coordinating the CRC screening campaign

since 2006. The programme uses the iFOBT. Subjects receiving a letter of invitation can choose between picking up the examination kit at their general practitioner (GP) or at the screening centre. Those with a positive test are referred to the Centre Hospitalier Princesse Grace, where digestive endoscopy is performed to establish the cause of the bleeding. The service is offered to residents and foreign workers aged 50-80 years. Participation is about 60%. In March every year, the Blue March is organised in France and the Principality to promote CRC awareness and focus the attention of the population on the value of CRC prevention<sup>[35]</sup>.

### **Southern Europe**

In this region, Italy, Spain, Malta, and Cyprus offer national organised programmes, and Portugal a regional organised programme. In Greece screening is spontaneous (Figure 1). There are also two tiny states, Andorra and San Marino.

**San Marino:** Official incidence and mortality data are not available; however, since San Marino is nestled in the Italian region of Emilia-Romagna, they should be similar to those of Italy. A national programme, offered to individuals aged 50 to 75 years and managed by the Screening Centre of the Istituto per la Sicurezza Sociale, has been in place since 2009. The test is delivered home by mail and the recipient is asked to take it to the relevant Health Centre. Failure to do so in three months results in a reminder. Subjects with a positive test are referred to the State Hospital for a second-level examination, usually colonoscopy<sup>[36]</sup>. Participation rates (65%) have been illustrated at a press conference and are encouraging<sup>[37]</sup>.

Andorra: WHO incidence and mortality data are not available, but they can reasonably be considered to resemble those of Cataluña. According to the 2014 WHO report - Cancer Country Profiles, CRC screening with the iFOBT and colonoscopy are generally available at the public primary health care level in this small Pyrenean state<sup>[38]</sup> (Table 4). However, unlike the case of breast cancer, the institutional website provides no information on CRC prevention.

### **Eastern Europe**

In this area, Romania and Bulgaria do not offer organised screening (Figure 1). The other states in the region include the Republic of Moldova, the Russian Federation, Turkey and Ukraine.

**Republic of Moldova:** In this country CRC is the second most common neoplasm in men and women alike (Table 4) with an incidence of 36.0 and 23.0 respectively. The mortality rate is 22.0 and 12.6, respectively; CRC is the second cause of cancer mortality in the country (Table 4). The literature provides



no information on screening programmes, but the FOBT and colonoscopy are both available at the public primary health care level<sup>[39]</sup> (Table 4).

**Russian Federation:** CRC is the third tumour by incidence and mortality among men (respectively 30.0 and 19.9) and the second among women (respectively 21.8 and 11.5) (Tables 1 and 4). Data quality is mediocre (Table 2). No national screening programmes are in place<sup>[40]</sup>. The poor awareness regarding CRC involves a high rate of late diagnoses (25.6% in stage IV vs 18.8% in the United States) despite the fact that the iFOBT and colonoscopy are largely available at the public primary health care level<sup>[41]</sup> (Table 4). A screening campaign launched in November 2015 in the Saint Petersburg area, which hosts the sole cancer registry in the Federation<sup>[42]</sup>, follows an earlier, small-scale programme set up in the Kazan region<sup>[43]</sup> (Table 3).

**Turkey:** In Turkey CRC incidence is 20.6 and 13.1 in men and women, respectively (Table 1). The mortality rate is 12.6 and 10.8, respectively (Table 1). Data quality is mediocre (Table 2). The national Cancer Control Department has been promoting cancer prevention campaigns since 2003. In 2009 there were no active population-based programmes, but merely some sporadic pilot studies<sup>[44]</sup>. However, a KETEM centre per province (including 2 in Istanbul and 3 in Ankara) supervise the execution of cancer screening (breast and cervical cancer) according with national guidelines; CRC was added in 2009. Screening is not covered by Social Security provisions and is sustained by the Health Ministry only for older and poorer people. Screening is largely spontaneous, but some centres like Ankara have started population-based programmes<sup>[44]</sup> (Table 3). In the future, GPs will be given the task of encouraging patients to pursue early CRC detection<sup>[44]</sup>. Both the FOBT and colonoscopy are available at the public primary health care level, as reported by the WHO country cancer profile<sup>[45]</sup>. CRC is the third and fourth cause of cancer death in the country (Table 4).

**Ukraine:** In Ukraine, the incidence rate of CRC is 29.9 in men and 19.9 in women and the tumour ranks second as a cause of cancer death. The mortality rate is 18.8 in men and 10.8 in women. Data quality is excellent (Table 2). According to the cancer registry, the 2002-2006 cancer plan included prevention programmes for cervical, breast, colorectum, prostate, skin, and oral cavity<sup>[46]</sup>. Based on WHO data, screening tests are not available at the public primary health care level<sup>[47]</sup> (Table 4).

### Caucasian countries

These states lie on the extreme eastern boundary of Europe, where the Caucasus traditionally represents

the geographical border with the Middle East.

**Armenia:** In Armenia CRC is the fifth most common tumour among men (22.8) and the third among women (17.0); it is the fourth cause of cancer death among men (13.4) and the second among women (9.7) (Tables 1 and 4). Data quality is fairly poor (Table 2). The literature supplies no information on screening, but the FOBT is available at the level of public primary health care<sup>[48]</sup>.

**Azerbaijan:** In Azerbaijan CRC incidence is fairly low in both sexes (7.1 in men and 6.4 in women) and is the fourth most common tumour. CRC mortality is lower in men (4.3) than in women (19.8) and the tumour is the fifth cause of cancer death in the country (Tables 1 and 4). Data quality is poor (Table 2). Although there are no published data on screening, the WHO report indicates that the FOBT is available at the public primary health care level<sup>[49]</sup>.

**Georgia:** In this country CRC incidence is low: 9.9 in men and 7.5 in women. The mortality figures are 5.5 in men and 4.0 in women. Data quality is poor (Table 2). Even though according to the WHO reports neither the FOBT nor colonoscopy is available for first-level screening<sup>[50]</sup>, the literature and the official websites mention a CRC screening campaign and report its results<sup>[51]</sup>. These data are summarised in Table 2.

## DISCUSSION

Improvements in the health status of populations and the progressive increase in life expectancy call for the promotion and diffusion of healthy lifestyles, to reduce the impact of non-communicable diseases; in particular, cancer entails an extremely high social and psychological burden. The chief mission of the Council of Europe is to promote and protect human rights in member states by issuing orientation papers and guidelines. In particular, art. 11 of the Social Charter, "The Right to Protection of Health", explicitly mentions the promotion of the health of the citizens of member states<sup>[52]</sup> and art. 3 of the Convention on Human Rights and Biomedicine makes reference to equal and appropriate access to health care<sup>[53]</sup>.

Interestingly, comparison of neighbouring countries offering regional screening shows, for instance, that incidence and mortality rates are 38.9 and 13.0 in Norway and 29.2 and 10.9 in Sweden, whereas in Finland, where a national organised programme is available, they are respectively 23.5 and 9.3<sup>[54]</sup>.

Epidemiological data quality varies broadly between EU-28 and EU-19 countries. In terms of incidence, only 30% of EU-19 countries rank high in data quality (A, B and C), as opposed to 86% of EU-28 states. The same applies to mortality data: 52% of EU-19 countries as against all EU-28 countries are found in the high ranks

(1, 2, or 3) (Table 2).

Assessment of the method of collection of incidence data showed that only 32% of EU-19 countries were found in the top three quality classes (A, B and C) as against 89% of EU-28 countries. For the mortality data, 63% of EU-19 countries were found in the highest ranks as opposed to all EU-28 member states (Table 2). The continuous improvement in the quality of epidemiological data collection critically supports public health decision-making, in that it represents the phenomena studied in an increasingly accurate manner in all geographical areas. This is all the more important at a time when the European continent is besieged by problems such as the economic downturn, climate change, international tensions and, last but definitely not least, the management of strong migration flows. The economic crisis has hampered the activation of large-scale screening programmes in countries, like Iceland<sup>[19]</sup>, where the recession has had a devastating impact, involving their postponement. In other emerging states and areas, like Serbia<sup>[30,31]</sup>, Georgia<sup>[51]</sup>, and Saint Petersburg<sup>[42]</sup>, population-based programmes have been implemented despite the crisis, making cancer prevention a priority, also to reduce social inequality. Clearly, it is critical to stimulate awareness of the importance of cancer prevention through screening.

In a recent British study, Moffat *et al.*<sup>[55]</sup> found that awareness is crucial where cancer and its early detection are concerned. The authors measured CRC symptom knowledge before and after an awareness campaign directed at lower-income subjects, and showed that the campaign improved the knowledge of suspicious symptoms. Notably, the campaign also increased screening requests to GPs. Another key finding was a greater awareness of CRC among the elderly, suggesting that differential campaigns are not required for different age classes. Large-scale campaigns like the Blue March, organised in France and Monaco Principality, should therefore be encouraged<sup>[35]</sup>.

The absence of organised screening increases the social burden of cancer, delaying the adoption of treatments of proven efficacy that induce as little disability as possible. The situation is especially clear in economically and technologically advanced countries like Switzerland, where a significantly lower demand for testing has been found among low-income than high-income citizens. Conceivably, the problem is even more severe in countries where early detection testing is not provided by the national health care system and is predominantly out of pocket, compounding the vulnerability of the poorer groups in the population. State funding is a problem in several countries, like Turkey, where dedicated cancer screening centres are found in each province and are theoretically easier to reach. In fact, however, the fact that most people have to pay for their tests, since only the poorest and oldest benefit from state help, prevents access by large

swathes of the population. It should be stressed that the activation of organised screening programmes is not a net cost to emerging countries<sup>[56]</sup>, but is actually cost-effective<sup>[57,58]</sup>, also considering that early tumour detection considerably reduces subsequent social and health costs<sup>[43]</sup>.

The situation of these countries contrasts with the one characterising small states like Monaco Principality and San Marino, where the tiny population enables a more effective organisation of health care, including prevention. Monaco Principality deserves high praise for extending screening benefits to foreign workers<sup>[35]</sup>.

### Screening professionals and activity

Finally, gastroenterologists play an important role in CRC screening. They should not view early detection testing as a practice undermining their expertise, but as a resource that adds to their specialist training<sup>[59]</sup>. The same applies to clinical pathologists: in some countries, like Russia, their training is predominantly oriented to necroscopy<sup>[40]</sup>: diagnosing living patients is therefore a challenge for all health care figures. The epidemiologist also has a critical role in local screening co-ordination, patient flow organisation, data management, and data transmission to cancer registries, to improve cancer knowledge and treatment in the various districts. GPs are an essential link in the prevention chain, since they have the task of raising the awareness of those who are at risk and of stimulating those who would benefit from screening to undergo testing, without alarming them. In Turkey, for instance, GPs have the task of directing patients to screening<sup>[44]</sup>. Patient associations and health care professionals should also work to increase the awareness of institutions and law-makers towards screening and its benefits.

In conclusion, cancer screening should be viewed as a key health care tool, also because investing in screening protects the weakest in the population, decreases the social burden of cancer, and reduces all types of health care costs, including those for radical surgery, long-term hospitalisation, and chemotherapy. Finally, screening for those at risk should be stimulated, offered without charge, and adequately publicised irrespective of the health care system organisation in place.

## COMMENTS

### Background

Although colorectal cancer (CRC) is a tumour for which screening has proven efficacy and cost-effectiveness, in several European countries screening implementation is fraught with difficulties. CRC incidence is quite variable among European countries, and the lower rates found in eastern Europe are higher than the world mean.

### Research frontiers

The Council of Europe has recommended the priority activation of CRC screening programmes. According to a 2008 European Commission report on the diffusion of CRC screening programmes in the EU, only 12 of the then 22

member states had population-based screening programmes; the others were recommended to provide to their citizens equal access to cancer prevention.

### Innovations and breakthroughs

The present paper provides a systematic review of the screening programmes that are active in the non-EU 28 members of the Council of Europe, using data collected from institutional websites and from the literature. Besides reviewing the epidemiological data (incidence, 5-year prevalence, and mortality), it undertakes a critical examination of their quality and provides key information on colorectal cancer and the prevention strategies adopted in each country.

### Applications

The absence of organised screening increases the social burden of cancer, delaying the adoption of treatments of proven efficacy that induce as little disability as possible. Conceivably, the problem is even more severe in countries where early detection testing is not provided by the national health care service and is predominantly out of pocket, compounding the vulnerability of the poorer groups in the population. Notably, the activation of organised screening programmes in emerging countries would actually be cost-effective, also considering that early tumour detection considerably reduces subsequent social and health costs.

### Terminology

Fecal occult blood (FOB) refers to blood in the feces that is not visibly apparent. A fecal occult blood test (FOBT) checks for hidden (occult) blood in the stool (feces); immunochemical test (iFOBT) is based on human hemoglobin antibodies.

### Peer-review

This review paper covers recent topics in CRC screening, and is concisely written. The information given is helpful to promote the further advance in the field.

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