

**Supplementary of *Effectiveness and safety of colorectal cancer screening: A systematic review, meta-analysis, and network meta-analysis incorporating direct and indirect comparisons***

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## Supplementary File 1: Search strategy

### 1. EMBASE

#13 #6 AND #9 AND #12

#12 #10 OR #11

#11 colonoscop\*:ti,ab OR sigmoidoscop\*:ti,ab OR colonograph\*:ti,ab OR proctosigmoidoscopy:ti,ab OR colonography:ti,ab OR fobt:ti,ab OR ifobt:ti,ab OR gfobt:ti,ab OR 'mt sdna'

#10 (fecal:ti,ab OR stool:ti,ab OR faecal:ti,ab) AND ('occult blood':ti,ab OR guaiac:ti,ab OR 'immunochemical':ti,ab OR dna:ti,ab OR 'deoxyribonucleic acid':ti,ab)

#9 #7 OR #8

#8 screen\*:ti OR surveillance:ti OR 'early detection':ti

#7 'screening'/exp OR 'early cancer diagnosis'/exp

#6 #1 OR #2 OR #5

#5 #3 AND #4

#4 colorectal\*:ti OR colon\*:ti OR crc:ti OR rectal:ti OR rectum:ti OR sigmoid:ti OR rectosigmoid:ti OR anal:ti OR anus:ti

#3 carcinom\*:ti OR cancer:ti OR tumor\*:ti OR tumour:ti OR malignant:ti OR neoplasm:ti OR neoplasm\*:ti

#2 'rectum cancer'/exp

#1 'colorectal cancer'/exp

### 2. MEDLINE

1. exp Colorectal Neoplasms/

2. exp Colonic Neoplasms/

3. exp Sigmoid Neoplasms/

4. exp Rectal Neoplasms/

5. exp Anus Neoplasms/

6. (carcinom\* or cancer or tumor\* or tumour or malignant or neoplasm or neoplasm\*).ti.

7. (colorectal\* or colon\* or crc or rectal or rectum or sigmoid or rectosigmoid or anal or anus).ti.

8. 6 and 7

9. 1 or 2 or 3 or 4 or 5 or 8

10. exp Mass Screening/

11. exp Early Detection of Cancer/

12. (screen\* or surveillance or 'early detection').ti.

13. 10 or 11 or 12

14. (fecal or stool or faecal).ti,ab.

15. ('occult blood' or guaiac or immunochemical or dna or 'deoxyribonucleic acid').ti,ab.

16. 14 and 15

17. (colonoscop\* or sigmoidoscop\* or colonograph\* or proctosigmoidoscopy or colonography or fobt or ifobt or gfobt or mt-sdna).ti,ab.

18. 16 or 17

19. 9 and 13 and 18

### 3. COCHRANE

- #1 [mh "Colorectal Neoplasms"]
- #2 [mh "Colonic Neoplasms"]
- #3 [mh "Sigmoid Neoplasms"]
- #4 [mh "Rectal Neoplasms"]
- #5 [mh "Anus Neoplasms"]
- #6 (carcinom\* or cancer or tumor\* or tumour or malignant or neoplasm or neoplasm\*):ti
- #7 (colorectal\* or colon\* or crc or rectal or rectum or sigmoid or rectosigmoid or anal or anus):ti
- #8 #6 OR #7
- #9 #1 OR #2 OR #3 OR #4 OR #5 OR #8
- #10 [mh "Mass Screening"]
- #11 [mh "Early Detection of Cancer"]
- #12 (screen\* or surveillance or 'early detection'):ti
- #13 #10 OR #11 OR #12
- #14 (fecal or stool or faecal):ti,ab
- #15 ('occult blood' or guaiac or immunochemical or dna or 'deoxyribonucleic acid'):ti,ab
- #16 #14 AND #15
- #17 (colonoscop\* or sigmoidoscop\* or colonograph\* or proctosigmoidoscopy or colonography or fobt or ifobt or gfovt or mt-sdna):ti,ab
- #18 #16 OR #17
- #19 #9 AND #13 AND #18

### 4. Clinicaltrial.gov

245 Studies found for: screen OR screening OR screened OR surveillance OR "early detection" | Completed Studies | "colorectal neoplasm" OR "colorectal cancer" OR "rectum cancer" OR "rectal neoplasm" OR "colonic neoplasm" OR "sigmoid neoplasm" OR "colonic cancer" OR "sigmoid cancer" | colonoscopy OR sigmoidoscopy OR colonography OR proctosigmoidoscopy OR colonography OR fobt OR ifobt OR gfovt OR sdna OR fecal OR stool OR faecal

Applied Filters: Completed

### 5. CNKI

SU=("结直肠癌"+"结直肠肿瘤")\*(("筛查"+"监测"+"早期检测")\*(("粪便隐血"+"免疫法粪便隐血"+"愈创木脂粪便隐血"+"多靶点粪便 DNA 检测"+"结肠镜"+"软式乙状结肠镜"+"CT 结肠镜成像"+"CT 仿真结肠镜"))

### 6. Wanfang Database

主题: ("结直肠癌"+"结直肠肿瘤")\*主题: ("筛查"+"监测"+"早期检测")\*主题: ("粪便隐血"+"免疫法粪便隐血"+"愈创木脂粪便隐血"+"多靶点粪便 DNA 检测"+"结肠镜"+"软式乙状结肠镜"+"CT 结肠镜成像"+"CT 仿真结肠镜")

### 7. CQVIP

(M=结直肠癌 OR M=结直肠肿瘤) AND (M=筛查 OR M=监测 OR M=早期检测) AND (M=粪便隐血 OR M=免疫法粪便隐血 OR M=愈创木脂粪便隐血 OR M=多靶点粪便 DNA 检测 OR M=结肠镜 OR M=软式乙状结肠镜 OR M= CT 结肠镜成像 OR M= CT 仿真结肠镜)

### 8. Sinomed

- #1 "结直肠肿瘤"[核心字段] OR "结直肠癌"[核心字段]
- #2 "筛查"[常用字段] OR "监测"[常用字段] OR "早期检测"[常用字段]
- #3 "粪便隐血"[常用字段] OR "免疫法粪便隐血"[常用字段] OR "愈创木脂粪便隐血"[常用

字段] OR "多靶点粪便 DNA 检测"[常用字段] OR "结肠镜"[常用字段] OR "软式乙状结肠镜"[常用字段] OR "CT 结肠镜成像"[常用字段] OR "CT 仿真结肠镜"[常用字段]

# 4 (#7) AND (#6) AND (#5)

#### 9. Web of science

	检索式	结果
# 10	#9 AND #4 AND #3	<a href="#">4019</a>
# 9	#8 OR #7	<a href="#">15424</a>
# 8	主题： (colonoscop*) OR 主题： (sigmoidoscop*) OR 主题： (colonograph*) OR 主题： (proctosigmoidoscopy) OR 主题： (colonography) OR 主题： (fobt) OR 主题： (ifobt) OR 主题： (gfobt) OR 主题： ("mt sdna") OR 主题： ("mt-sdna") OR 主题： (sdna)	<a href="#">11829</a>
# 7	#6 AND #5	<a href="#">4777</a>
# 6	主题： ("occult blood") OR 主题： (guaiac) OR 主题： (immunochemical) OR 主题： (dna) OR 主题： ("deoxyribonucleic acid")	<a href="#">288017</a>
# 5	主题： (fecal) OR 主题： (stool) OR 主题： (faecal)	<a href="#">39619</a>
# 4	TS=("Mass Screening") OR TS=("Early Detection of Cancer") OR TS=(screen*) OR TS=(surveillance) OR TS=("early detection") OR TS=("early cancer diagnosis")	<a href="#">382774</a>
# 3	#2 AND #1	<a href="#">115385</a>
# 2	主题： (colorectal*) OR 主题： (colon*) OR 主题： (crc) OR 主题： (rectal) OR 主题： (rectum) OR 主题： (sigmoid) OR 主题： (rectosigmoid) OR 主题： (anal) OR 主题： (anus)	<a href="#">269246</a>
# 1	主题： (carcinom*) OR 主题： (cancer) OR 主题： (tumor*) OR 主题： (tumour) OR 主题： (malignant) OR 主题： (neoplasm) OR 主题： (neoplasm*)	<a href="#">1052772</a>
	索引 =SCI-EXPANDED, SSCI, A&HCI, CPCI-S, CPCI-SSH, ESCI, CCR-EXPANDED, IC 时间跨度=最近 5 年	

#### 10. Google scholar

allintitle:(("colorectal" OR "rectum" OR "colonic" OR "rectal" OR "anus" OR "sigmoid") AND ("screen" OR "surveillance" OR "early detection"))

## Supplementary File 2: Definition of outcomes

Outcomes of effectiveness were defined as follow:

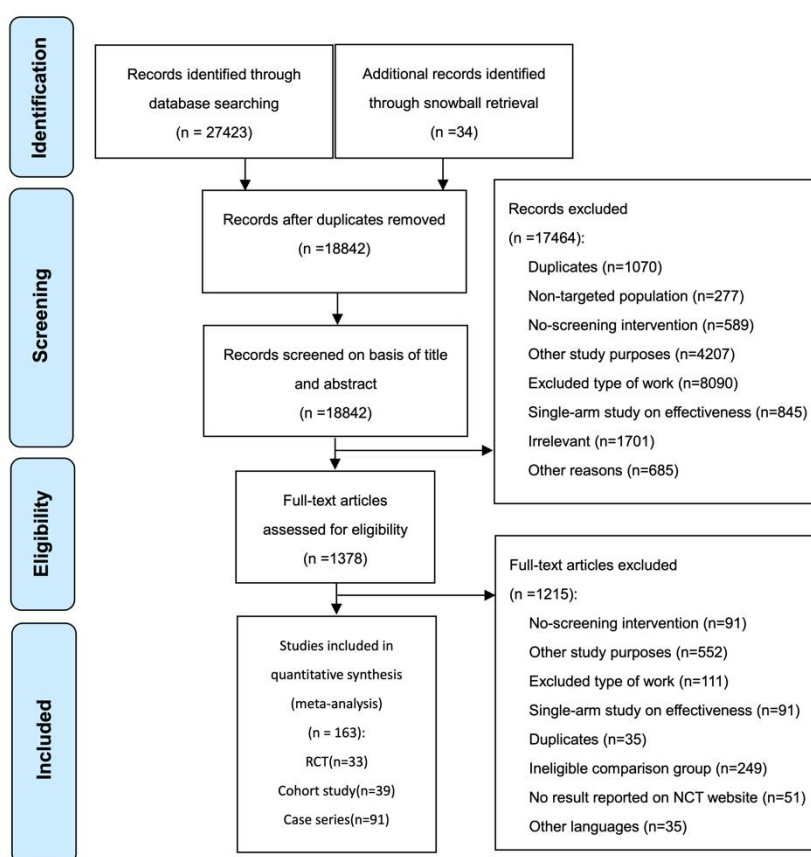
- a) Colorectal cancer mortality (CRC mortality): the number of deaths from colorectal cancer during the follow-up period divided by the total number of observations.

- b) All-cause mortality: the number of all-cause deaths during follow-up divided by the total number of observations.
- c) Colorectal cancer incidence (CRC incidence): the number of new patients with colorectal cancer during the follow-up period divided by the total number of observations.

Safety outcomes were defined as follow:

- a) Severe bleeding: bleeding required blood transfusion or hospitalization.
- b) Perforation: accidental piercing or tearing of the gut as a result of screening measures.
- c) Death caused by screening complications: Only deaths caused by the screening procedure were counted to determine the safety outcome, and deaths without specific causes or caused by other reasons were excluded.

### Supplementary File 3: Flow diagram of study selection



### Supplementary File 4: Characteristic table of included studies

Study	Follow-up	Country	screening population	Intervention	Number of screening	Female (%)	Age range
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## Case Series

Adeyemo.2014 <sup>1</sup>	NR	United States	general population	colonoscopy	118004	53.67	≥18(mean(sd)=60.58(13.60))
Ankur.2002 <sup>2</sup>	NR	United States	general population	FS	5017		
Arana-Arri.2018 <sup>3</sup>	30d	Spain	general population	colonoscopy	39254	29.8	50-69(mean=61.7)
Bair.2009 <sup>4</sup>	NR	Canada	general population	colonoscopy	3741	51.86	mean=57.1
Berhane.2009 <sup>5</sup>	30d	United States	general population	colonoscopy	11808		50-90
Bielawska.2014 <sup>6</sup>	NR	Canada	general population	colonoscopy	54474		
Binefa.2013 <sup>7</sup>	NR	Spain	high risk population	colonoscopy	1806		50-69
Blotière.2014 <sup>8</sup>	3d	France	general population	colonoscopy	947061	55.6	
Bokemeyer.2009 <sup>9</sup>	4w	Germany	general population	colonoscopy	269144	55.7	55-99
Bowles.2004 <sup>10</sup>	30d	United Kingdom	general population	colonoscopy	9223	49.65	16-95
Castro.2013 <sup>11</sup>	30d	United States	general population	colonoscopy	3355	74	50-64(mean=55.9)
Cheng.2002 <sup>12</sup>	NR	Taiwan, China	general population	colonoscopy	7411	45	mean=46.8
Chukmaitov.2013 <sup>13</sup>	30d	United States	general population	colonoscopy	2315126	54.2	≥19
Cotterill.2005 <sup>14</sup>	NR	Canada	general population	colonoscopy	152	44.1	22-80
Crispin.2009 <sup>15</sup>	NR	Germany	general population/high risk	colonoscopy	236078	56.7	18-100
Ko.2007 <sup>16</sup>	30d	United States	general population	colonoscopy	502	50.8	≥40
De Jonge.2012 <sup>17</sup>	30d	Netherland	general population	colonoscopy	1144	50.6	mean=58.6
Denis.2013 <sup>18</sup>	NR	France	general population	colonoscopy	10277	42.4	50-74(mean=62.7)
Denters.2013 <sup>19</sup>	NR	Netherland	general population	colonoscopy	273	46.9	50-74(mean(sd)=62.8(6.7))
Derbyshire.2018 <sup>20</sup>	30d	United Kingdom	general population	colonoscopy	263129	39.5	60-74(mean=65.5)
Edwards. 2004 <sup>21</sup>	NR	Australia	general population	CTC	340	46.4	50-54,65-69
Ellul.2010 <sup>22</sup>	NR	United Kingdom	general population	colonoscopy	1039		60-69
Exbrayat.2010 <sup>23</sup>	NR	France	general population	colonoscopy	2558	54	22-99(mean=58)
Forsberg.2017 <sup>24</sup>	30d	Sweden	general population	colonoscopy	593315	56	18–105(mean=62.7)
Garcia.2012 <sup>25</sup>	NR	Spain	high risk population	colonoscopy	989	43.3	50-69
Cooper.2013 <sup>26</sup>	30d	United States	general population	colonoscopy	165527	48.76	≥66
Gupta.2012 <sup>27</sup>	30d	United Kingdom	general population	colonoscopy	1057		60-69
Hamdani.2013 <sup>28</sup>	NR	United States	general population	colonoscopy	80118	51.3	≥18
Hayman.2013 <sup>29</sup>	7d	United States	general population	colonoscopy	311	1	53-69(median=61)
Hilsden.2015 <sup>30</sup>	NR	Canada	general population/high risk	colonoscopy	18456	54	40-74
Ho.2012 <sup>31</sup>	7d	Canada	general population	colonoscopy	50660	51.85	≥66(median=73)
Hoff.2006 <sup>32</sup>	NR	Norway	general population	colonoscopy	5452		56-65
Horiuchi.2013 <sup>33</sup>	NR	Japan	general population	colonoscopy	2301	36	mean=65.4
Hsieh.2009 <sup>34</sup>	NR	China	general population	colonoscopy	9501	41.6	22-74(mean=51.17)
Iafate.2013 <sup>35</sup>	NR	Italy	general population	CTC	40121		
Ibez J.2018 <sup>36</sup>	30d	Spain	general population	colonoscopy	8831	42.1	50-69
Johnson.2012 <sup>37</sup>	NR	United States	general population	CTC	2531	52.4	≥65
Kang.2009 <sup>38</sup>	NR	Korea	general population	colonoscopy	44534	36	27-84(mean=60)
Kewenter.1996 <sup>39</sup>	NR	Sweden	general population	colonoscopy	190		60-64
			general population	FS	2108		60-64

Khalid-de.2011 <sup>40</sup>	1m	Netherland	general population	colonoscopy	214	60.7	mean=54
Kim.2010 <sup>41</sup>	NR	United States	general population	CTC	577	48.2	65-79(mean=69.2)
Ko.2010 <sup>42</sup>	30d	United States	general population	colonoscopy	21375	45	≥40
Korman.2003 <sup>43</sup>	NR	United States	general population	colonoscopy	116000		39-87(median=75)
Kozbial.2014 <sup>44</sup>	NR	Australia	general population	colonoscopy	59901	51.1	mean=61.2
Laanani.2019 <sup>45</sup>	30d	France	general population	colonoscopy	4088799	55.2	≥30
Lee.2012 <sup>46</sup>	NR	United Kingdom	general population	colonoscopy	38168	38.4	60-92(mean=66)
Levin.2002 <sup>47</sup>	4w	United States	general population	FS	109534	48.8	50-79
Levin.2006 <sup>48</sup>	30d	United States	general population	colonoscopy	109534	48.8	50-79(median=61)
Lieberman.2000 <sup>49</sup>	NR	United States	general population/high risk	colonoscopy	3121	3.2	50-75(mean(sd)=62.9(0.13))
Loffeld.2011 <sup>50</sup>	NR	Netherland	general population	colonoscopy	19135		33-89(mean=74.9)
Lorenzo.2010 <sup>51</sup>	NR	Spain	general population	colonoscopy	25214		36-89(mean=64.3)
Mansmann.2008 <sup>52</sup>	NR	Germany	general population	colonoscopy	236087	56.75	≥55(mean=60.7)
Marbet.2008 <sup>53</sup>	5y	Switzerland	general population	colonoscopy	2044	47.3	50-80
McClellan.2015 <sup>54</sup>	NR	United States	general population	colonoscopy	1101		17-85(mean=54.7)
Meagher. 1994 <sup>55</sup>	4.4y	Australia	general population	colonoscopy	645		≥25
Mikkelsen.2018 <sup>56</sup>	30d	Denmark	general population	colonoscopy	286	37.1	50-74(mean=67)
Nagata.2017 <sup>57</sup>	NR	Japan	general population	CTC	147439		
Nelson.2002 <sup>58</sup>	30d	United States	general population	colonoscopy	3196	3.2	50-75(mean=63)
Pace.2016 <sup>59</sup>	NR	Canada	general population	colonoscopy	3235	55.8	mean=59
Parente.2013 <sup>60</sup>	NR	Italy	general population	colonoscopy	4373		50-69
Pickhardt.2003 <sup>61</sup>	NR	United States	general population	CTC	1233	40.96	50-79(mean=57.8)
Portillo.2018 <sup>62</sup>	30d	Spain	general population	colonoscopy	48759	40.4	49-69
Pox.2012 <sup>63</sup>	NR	Germany	general population	colonoscopy	2821392	55.6	≥55(mean=65)
Quallick.2009 <sup>64</sup>	NR	United States	general population	colonoscopy	39054		
Quyn.2018 <sup>65</sup>	NR	Scotland	general population	colonoscopy	50967	41.7	60-74
Rabeneck.2008 <sup>66</sup>	30d	Canada	general population	colonoscopy	97091	54.2	50-75(mean=60.9)
Randall. 2013 <sup>67</sup>	3.9y	United Kingdom	high risk population	colonoscopy	3982	60	≥40(median=51)
Rutter.2012 <sup>68</sup>	30d	United States	general population	colonoscopy	43456	51	40-85
Rutter.2014 <sup>69</sup>	30d	United Kingdom	general population	colonoscopy	130831	39.3	59-92(mean=65.7)
Sagawa.2012 <sup>70</sup>	NR	Japan	general population	colonoscopy	10826		
Samalavicius.2013 <sup>71</sup>	NR	Republic of Lithuania	general population	colonoscopy	56882		39-85(mean=70)
Saraste.2016 <sup>72</sup>	30d	Sweden	general population	colonoscopy	2984		60-69
Sawatzki.2015 <sup>73</sup>	4-12w	Switzerland	general population	colonoscopy	104	45.2	33-80(median=59)
Sewitch. 2018 <sup>74</sup>	30d	Canada	general population	colonoscopy	420	45.7	40-75(mean=58.7)
Sieg.2001 <sup>75</sup>	NR	Germany	general population	colonoscopy	82416		
Singh.2009 <sup>76</sup>	NR	Canada	general population	colonoscopy	24509	56	>16(mean=59)
Sosna.2006 <sup>77</sup>	NR	Isreal	general population	CTC	11870	42.4	38-90
Steele.2009 <sup>78</sup>	NR	United Kingdom	general population	colonoscopy	8631		50-69
Strul.2006 <sup>79</sup>	NR	Isreal	general population	colonoscopy	1177	53	40-80
Suissa.2012 <sup>80</sup>	NR	Isreal	general population	colonoscopy	6584	49.6	mean=57.7

Sung.2003 <sup>81</sup>	NR	China	general population	colonoscopy	505	55.64	50-79(mean(sd)=56.4(5.4))
Telford.2016 <sup>82</sup>	30d	Canada	general population	colonoscopy	1597		50-74(mean=62)
Tepeš.2017 <sup>83</sup>	NR	Slovenia	general population	colonoscopy	13919	44.32	50-69
Vanaclochai.2019 <sup>84</sup>	NR	Spain	high risk population	colonoscopy	48730	41.7	50-70
Waldmann.2016 <sup>85</sup>	30d	Austria	general population	colonoscopy	159246	49.1	≥50(mean=61.1)
Wan.2002 <sup>86</sup>	NR	China	general population	colonoscopy	8298	5.87	60-90(mean=70.5)
Wang.2018 <sup>87</sup>	30d	United States	general population	colonoscopy	2802388	55.55	mean=60.4
Wong.2019 <sup>88</sup>	2y	Australia, New Zealand,	high risk population	colonoscopy	323		35-74
Xirasagar.2010 <sup>89</sup>	NR	United States	general population	colonoscopy	9815	52	>50(mean=58.3)
Zwink.2017 <sup>90</sup>	4w	Germany	general population	colonoscopy	5252	52	50-69(median=61)
Cao.2011 <sup>91</sup>	NR	China	general population	colonoscopy	2200	41.2	13-86(mean=51.8)

#### Cohort Studies

Kistler.2011 <sup>92</sup>	NR	United States	general population	colonoscopy	118	0	≥70
			general population	usual care	94	1.1	≥70
B, Strum W.2006 <sup>93</sup>	NR	Germany	high risk population	FS	210	57	40-89(mean=58.5)
			general population	FS	2937	51	40-89(mean=58.5)
Ferlitsch.2011 <sup>94</sup>	NR	Austria	general population	colonoscopy	22598	100	≥30
			general population	colonoscopy	21752	0	≥30
Gatto.2003 <sup>95</sup>	7d	United States	general population/high risk	colonoscopy	39286	57	≥60(mean=74)
			general population/high risk	FS	35298	56	≥60(mean=74)
Johnson.2008 <sup>96</sup>	NR	United States	general population	colonoscopy	2531	52	52-62(mean=58)
			general population	CTC	2531	52	52-62(mean=58)
Kim.2007 <sup>97</sup>	NR	United States	general population	CTC	3120	56	mean=57
			general population	colonoscopy	2163	55.8	mean=58.1
Kim.2013 <sup>98</sup>	NR	Korea	general population/high risk	FS	20653		≥18(mean=67.5)
			general population/high risk	colonoscopy	94632		≥18(mean=67.5)
Kubisch.2016 <sup>99</sup>	NR	Germany	high risk population	colonoscopy	524954	57.8	≥55
Pabby.2005 <sup>100</sup>	NR	United States	general population	FS	420	55.2	≥75(mean=78)
				FS	6968	52.8	50-74(mean=58.2)
Senore.2011 <sup>101</sup>	30d	Italy	general population	FS	1502	50.2	55-64
				colonoscopy	1198	67.2	55-64
Stock.2013 <sup>102</sup>	30d	Germany	general population	colonoscopy	8658	56	≥20(mean=66)
				usual care	24428	56	≥20(mean=66)
Tam.2013 <sup>103</sup>	30d	United States	general population/high risk	colonoscopy	86101		
				FS	46158		
Tran.2014 <sup>104</sup>	30d	United States	high risk population	colonoscopy	4834	44.2	≥75
				colonoscopy	22929	42.3	50-74
Viiiala.2007 <sup>105</sup>	8.2y	Australia	general population	FS	1992	0	55-64
				FS	1410	100	
Warren.2009 <sup>106</sup>	30d	United States	general population	colonoscopy	53220	58.3	66-95
				usual care	53220	58.3	66-95

Zafar.2014 <sup>107</sup>	30d	United States	general population	CTC	1384	63.6	66-103(mean=76.7)
				colonoscopy	54039	54.7	66-104(mean=74.4)
Lee.2007 <sup>108</sup>	13.1y	Japan	general population	FIT	7179	51.02	40-59
				usual care	34971	51.93	40-59
Jrvinen H. 2000 <sup>109</sup>	14.5y	Finland	high risk population	colonoscopy	133		
	15y			usual care	119		
Eldridge. 2013 <sup>110</sup>	11y	United States	general population	colonoscopy	22780	30.5	50-71
				usual care	45751	46.6	50-71
Chiu H M.2015 <sup>111</sup>	3.09y	China	general population	FIT	1160895	61.55	50-69
				usual care	4256804	50.38	50-69
Bjerrum.2016 <sup>112</sup>	8.9y	Denmark	general population	gFOBT	166277	48.9	50-74
				usual care	1240348	49.5	50-75
Lee.2019 <sup>113</sup>	12y	United States	general population	colonscope	99166	59.1	
				Usual care	1251318	52.9	
Lee.2017 <sup>114</sup>	6y	China	high risk population	colonoscopy	41995	52.7	
				Usual care	10778	53.1	
Niv Y.2002 <sup>115</sup>	11y	Israel	general population	gFOBT	2525	53.7	
				Usual care	2373	45.1	
Lashner B A.1990 <sup>116</sup>	3.9y	United States	high risk population	colonscope	91	41.76	
				Usual care	95	54.74	
Kavanagh.1998 <sup>117</sup>	8y	United States	general population	FS	3195	0	
				Usual care	21549	0	
Manser. 2012 <sup>118</sup>	6y	Switzerland	general population	FS	1912	46.5	50-80
				Usual care	20774		50-80
Nishihara R.2013 <sup>119</sup>	24y	United States	general population	FS			
				colonscope			
				Usual care			
Libby.2012 <sup>120</sup>	8.1y	United Kingdom	general population	colonscope	379655	48.4	50-69
	7.9y			Usual care	379655	48.4	50-69
Hatfield.2018 <sup>121</sup>	30y	Canada	high risk population	colonscope	162		
				Usual care	162		
Morois.2014 <sup>122</sup>	15.4y	France	general population	colonscope	37459	100	
				Usual care	54589	100	
Larsen.2018 <sup>123</sup>	NR	Denmark	general population	FIT	402826	50.5	50-72
				Usual care	956514	50.3	50-72
Lallemand.1984 <sup>124</sup>	2y	United Kingdom	general population <sup>111, 115</sup>	gFOBT	4834		
				Usual care	22929		
				colonoscopy	145	100	
Shen.2015 <sup>125</sup>	6y	China	general population	gFOBT	204504		40-74
				Usual care	35395		40-74
Blom.2008 <sup>126</sup>	9y	Sweden	general population	FS	771	50.06	59-61

				usual care	1215	49.3	59-61
Giorgi Rossi.2015 <sup>127</sup>	8y	Italy	general population	FIT	171785	NR	50-74
				Usual Care	171785	NR	50-74
Hamza.2014 <sup>128</sup>	17.3y	France	general population	gFOBT	45642	55.5	45-74
				Usual Care	45557	55.5	45-74
Kahi.2009 <sup>129</sup>	16y	United States	general population	colonoscopy	715	41	NR
				Usual Care	715	41	NR
Ventura.2014 <sup>130</sup>	11y	Italy	general population	FIT	6961	50.8	50-70
				Usual Care	26285	49.9	50-70
RCTs							
Atkin. 2002 <sup>131</sup>	30d	United Kingdom		FS	40332		
			general population	usual care	2051		
Bretthauer.2016 <sup>132</sup>	NR	Europe	general population	colonoscopy	12574	49.9	55-64
				usual care	62974		
Brevinge.1997 <sup>133</sup>	NR	Sweden	general population	FS	1431		55-56
				FOBT	3183		55-56
Chrissidis.2004 <sup>134</sup>	30m	Greece	general population	colonoscopy	4189		>50
				usual care	4774		>50
Faivre.2004 <sup>135</sup>	11y	France	general population	FOBT	34623	52.48	45-74
				usual care	45557		
Gondal.2003 <sup>136</sup>	30d	Norway	general population	FS	12960	51.36	50-64
				colonoscopy	2524	51.36	50-64
Kobiela.2019 <sup>137</sup>	30d	Poland	general population	colonoscopy	338477		55-64
				usual care	338557		55-64
Mandel.1993 <sup>138</sup>	NR	United States	general population	FOBT	31157		50-80
				usual care	15394		50-80
Quintero.2012 <sup>139</sup>	NR	Spain	general population	colonoscopy	26703	53.5	50-69(mean=59.2)
				FIT	26599	54.3	50-69(mean=59.2)
Rasmussen.1999 <sup>140</sup>	NR	Denmark	general population	FS	2235		50-75
				colonoscopy	502		50-76
Sali.2016 <sup>141</sup>	NR	Italy	general population	CTC	1286	53.55	54-65(mean=59)
				colonoscopy	496	54.2	54-65(mean=59)
Schoen.2012 <sup>142</sup>		United States	general population	FS	67071		55-74
		United States		colonoscopy	17672		55-74
Segnan.2002 <sup>143</sup>	30d	Italy	general population	FS	9911		55-64
				colonoscopy	775		55-64
Segnan.2005 <sup>144</sup>		Italy	general population	colonoscopy	332		55-64
		Italy	general population	FS	4466		55-64
Steele.2020 <sup>145</sup>	NR	United Kingdom	general population	FS	4597		59-61
				colonoscopy	440		59-61
Stoop.2012 <sup>146</sup>	4w	Netherland	general population	colonoscopy	1276	50	50-75(mean=60.8)

				CTC	982	51	50-75(mean=60.9)
Verne.1998 <sup>147</sup>	NR	United Kingdom	general population	FS	1116		50-75
				FOBT	1245		50-75
Zalis.2012 <sup>148</sup>	NR	United States	general population	CTC	618	47	mean=60.4
				colonoscopy	605	47	mean=60.4
Lindholm.2008 <sup>149</sup>	9y	Sweden	general population	FOBT	34144		60-64
				Usual care	34164		60-64
Atkin W. 2017 <sup>150</sup>	17y	United Kingdom	general population	FS	57098	51	
				Usual care	112936	51	
Holme.2018 <sup>151+</sup> Holme.2014 <sup>152</sup>	14.8y	Norway	general population	FS/FS+FOBT	20552	50.1	50-64
				Usual care	78126	50.2	50-64
Miller E A. 2019 <sup>153</sup>	5y	United States	general population	FS	77433	49.5	55-74
				Usual care	77444	49.5	55-74
Pitk niemi J.2015 <sup>154</sup>	4.5y	Finland	general population	FOBT	180210	50.2	60-69
				Usual care	180282	50.2	60-69
Kronborg. 2004 <sup>155</sup>	17y	Denmark	general population	FOBT	30967	52	45-75
				Usual care	30966	52	45-75
Scholefield.2012 <sup>156</sup>	19.5y	United Kingdom	general population	FOBT	76466	51.98	45-74
				Usual care	76384	51.94	45-74
Zheng.2003 <sup>157</sup>	5y	China	general population	FIT	94423	48.97	≥30
				Usual care	97838	43.87	≥30
ThiisEvensen.1999 <sup>158</sup>	13y	Norway	general population	FS	400		
				Usual care	399		
Hardcastle.1986 <sup>159</sup>	2y	United Kingdom	general population	FOBT	10253		45-74
				Usual care	10272		45-74
				FOBT	25918		59-61
Malila N.2008 <sup>160</sup>	NR	Finland	general population	FOBT	52998	55.68	60-69
				Usual care	53002	50.47	60-69
Shaukat A.2013 <sup>161</sup>	30y	United States	general population	FOBT	31157	52.1	50-80
				Usual care	15394	51.7	50-80
Mandel.2000 <sup>162</sup>	18y	United States	general population	gFOBT	31082		
				usual care	15363		
Segnan.2011 <sup>163</sup>	11.4y	Italy	general population	FS	17136	55-64	50
				usual care	17136	55-64	49.5

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## Supplementary File 5: Risk of bias assessment

### RCTs

Study	①	②	③	④	⑤	⑥	⑦	Total	Risk of bias
Chrissidis.2004.	NA	NA	NA	1	1	NA	1	3	moderate
Atkin.2017.	NA	NA	NA	NA	1	1	1	3	moderate
Holme.2018.	1	1	NA	NA	NA	1	1	4	moderate
Sali.2016.	1	1	NA	1	1	NA	NA	4	moderate
Steele. 2020.	1	1	1	1	0	NA	1	5	low
Miller.2019.	NA	NA	NA	1	NA	1	NA	2	high
Pitk niemi.2015.	NA	NA	NA	NA	NA	NA	NA	0	high
Schoen.2012.	1	1	NA	1	1	NA	1	5	low
Kronborg. 2004.	1	1	NA	1	NA	NA	NA	3	moderate
Lindholm.2008.	1	1	1	1	1	1	1	7	low
Malila.2008.	1	1	NA	1	1	1	1	6	low
Scholefield.2012.	1	1	1	1	1	NA	1	6	low
Shaukat.2013.	1	1	NA	1	0	1	1	5	low
Quintero.2012.	NA	1	1	1	1	1	1	6	low
This-Evensen.1999.	NA	1	1	1	1	1	1	6	low
Stoop.2012.	1	1	NA	NA	1	1	1	5	low
Brevinge.1997.	1	1	NA	NA	1	NA	NA	3	moderate
Hardcastle.1986.	1	NA	NA	NA	1	NA	NA	2	high
Gondal.2003.	1	NA	NA	NA	1	NA	1	3	moderate
Rasmussen. 1999.	1	1	NA	NA	1	NA	NA	3	moderate
Kobiela.2019.	NA	1	1	1	1	1	1	6	low
Zheng.2003.	1	NA	NA	1	1	1	1	5	low
Faivre.2004.	0	NA	NA	1	1	1	1	4	moderate
Segnan.2002.	1	1	NA	NA	0	1	1	4	moderate
Gupta.2013.	NA	NA	1	1	1	1	1	5	low
Atkin. 2002	1	1	NA	1	1	1	1	6	low
Brethauer, M.2016	1	1	1	NA	1	1	0	5	low
Holme 2014	1	1	NA	NA	NA	1	0	3	moderate
Mandel.1993	1	1	NA	NA	1	1	NA	4	moderate
Mandel.2000	NA	NA	NA	1	1	1	NA	3	moderate

Segnan.2005	1	1	1	1	1	1	NA	6	low
Segnan. 2011	1	1	1	1	NA	1	NA	5	low
Verne.1998	1	1	NA	NA	1	1	0	4	moderate
Michael.2012	1	1	NA	NA	1	NA	1	3	moderate

Note: Risk of bias evaluation criteria for RCT studies (Cochrane Reviewer's Handbook 5.0.1)

- ① Generation of randomized series; (1=low risk, 0=high risk, NA=unclear)
- ② allocation concealment; (1=low risk, 0=high risk, NA=unclear)
- ③ Study subjects and study personnel blinded; (1=low risk, 0=high risk, NA=unclear)
- ④ Outcome assessment blinded; (1=low risk, 0=high risk, NA=unclear)
- ⑤ Completeness of outcome data; (1=low risk, 0=high risk, NA=unclear)
- ⑥ Selective reporting; (1=low risk, 0=high risk, NA=unclear)
- ⑦ Other sources of bias; (1=low risk, 0=high risk, NA=unclear)

## Cohorts

Study	Cohort selection				Compa rability	Outcome			Total	Risk of bias
	①	②	③	④		⑤	⑥	⑦		
Kubisch.2016.	1	1	1	1	2	1	1	1	9	low
Lee.2007.	1	1	1	1	1	1	1	1	8	low
J rvinen H J.2000.	0	1	1	1	1	1	1	1	7	low
Eldridge.2013.	1	1	1	0	1	1	0	1	6	moderate
Gatto.2003.	1	1	1	1	1	1	0	0	6	moderate
Chiu.2015.	1	1	1	1	1	1	0	0	6	moderate
Bjerrum.2016.	1	0	1	1	2	1	1	1	8	low
Lee.2019.	1	1	1	0	1	1	1	1	7	low
Kavanagh.1998.	1	1	1	0	1	1	1	0	6	moderate
Manser.2012.	1	1	1	0	2	1	1	0	7	low
Nishihara.2013	0	0	0	0	1	1	1	1	4	moderate
Niv.2002	1	0	1	1	2	1	1	1	8	low
Shen.2015	1	1	1	1	1	1	1	1	8	low
Lashner.1990	1	1	1	1	1	1	1	1	8	low
Tam.2013	1	1	1	1	1	1	0	1	7	low
Ferlitsch.2011	1	1	1	0	1	1	1	0	6	moderate
Viiala.2007	1	1	1	0	0	1	1	0	5	moderate
Kim.2007	0	1	1	1	2	1	1	0	7	low
Libby.2012	1	1	1	1	2	1	1	1	9	low
Hatfield.2018.	1	1	1	1	2	1	1	1	9	low
Johnson.2008.	1	1	1	1	0	1	1	1	7	low

Kim.2013	1	1	1	1	1	1	1	1	8	low
Pabby.2005	1	1	1	1	0	1	1	1	7	low
B. Strum W.2006	1	1	1	0	1	1	0	1	6	moderate
Britton.2015	1	0	1	1	2	1	1	1	8	low
Morois.2014	1	1	1	0	0	1	1	0	5	moderate
Larsen.2018.	1	1	1	1	1	1	0	0	6	moderate
Tran.2014	1	0	1	1	2	1	1	1	8	low
Lallemmand.1984	0	0	1	1	1	1	1	1	6	moderate
Senore.2011	1	1	1	1	1	1	1	1	8	low
Warren.2009	1	1	1	1	2	1	1	1	9	low
Zafar.2014	1	1	1	1	2	1	1	0	8	low
Stock.2013	1	1	1	0	2	1	1	0	7	low
Johannes.2008	1	1	1	1	2	1	1	0	8	Low
Giorgi.2015	1	1	1	1	1	1	1	1	8	Low
Hamza.2014	1	1	1	1	2	1	1	1	8	Low
Kahi.2009	0	0	1	1	1	1	1	1	6	Low
Kistler.2011	0	1	1	1	1	1	1	1	7	Low
Ventura.2014	1	1	1	1	0	1	1	0	6	Low

Note: Cohort study research risk of bias evaluation (NOS scale)

(1) Cohort selection

1) Representativeness of the exposure cohort

a. Good representation\* (1 point)

b. Good representation\* (1 point)

c. Poor representation, such as selection of nurses, volunteers, etc. (score 0)

d. No description of the source of the cohort (0 points)

2) Selection of non-exposure cohort

a. From the same population as the exposed cohort, such as the same community\* (1 point)

b. From a different population than the exposed cohort (0 points)

c. No source described (0 points)

3) Determination of exposure

a. Rigorous, accurate records (e.g., surgical records) (score 1)

b. Structured interview (score 1)

c. Self-report (score 0)

d. Not described (score 0)

4) No study subject already had the disease under study at the beginning of the study a. Yes (score 1)

b. No (score 0)

(2) Comparability evaluation (multiple choice, maximum 2 points) Comparability of exposed and non-exposed cohorts (design and analysis phase)

a. Selection and analysis of controls based on the most important factors (score 1)

b. Select and analyze controls based on other important factors (e.g., second most important factor) (score 1)

### (3) Outcome

#### 1) Outcome measurement methods

a. Independent, blinded measurement or assessment (score 1)

b. Based on reliable records (score 1)

c. Self-reported (score 0)

d. Not described (score 0)

#### 2) Is the follow-up period sufficiently long for the disease under study?

a. Yes (score 1)

b. No (too short, most did not occur for the disease under study) (score 0)

#### 3) Completeness of follow-up

a. Follow-up is complete, all study subjects were followed up (score 1)

b. Follow-up rate >80%, a few missed visits, little bias, and descriptive analysis of missed visits (score 1)

c. Follow-up rate  $\leq$  80%, no descriptive analysis of the missing respondents (score 0)

d. Not described (scored 0)

## Case series

Study	①	②	③	④	⑤	⑥	⑦	⑧	Total	Risk of bias
Khalid-de.2011	0	1	1	0	1	1	1	1	6	low
Nagata. 2017	1	1	1	0	1	1	1	1	7	low
Portillo.2018.	1	1	1	0	1	1	1	1	7	low
Waldmann.2016	1	1	1	1	1	0	1	1	7	low
Arana-Arri.2018	1	1	1	1	1	0	1	1	7	low
Strul.2006	1	1	1	1	1	0	1	1	7	low
Sawatzki.2015	0	1	1	1	1	0	1	1	6	low
Forsberg.2017	1	1	1	1	1	0	1	1	7	low
McClellan.2015	0	1	0	1	1	0	1	1	5	moderate
Mikkelsen.2018	1	1	1	1	1	0	1	1	7	low
Saraste.2016	1	1	1	1	1	0	1	1	7	low
Wan.2002	0	1	1	0	0	0	1	1	4	moderate
Lee.2012	1	1	1	1	1	0	1	1	7	low
Hoff.2006	1	1	1	1	1	1	1	1	8	low
Hayman.2013	1	1	1	1	1	0	1	1	6	low
Mansmann.2008	1	1	0	1	1	0	1	1	6	low
De Jonge.2012	1	1	0	1	1	0	1	1	6	low
Pickhardt.2003	1	1	1	1	1	0	1	1	7	low
Wong.2019	1	1	1	1	1	1	1	1	8	low
Ko.2010	1	1	0	1	1	0	1	1	6	low
Kang.2009	0	1	1	1	1	0	1	1	6	low

Quallick.2009	1	1	1	1	1	0	1	1	7	low
Singh.2009	0	1	1	1	1	0	1	1	6	low
Hamdani.2013	1	1	1	1	1	0	1	1	7	low
Blotière.2014	1	1	1	1	1	0	1	1	7	low
Bokemeyer.2009	1	1	1	1	1	0	1	1	7	low
Iafrate.2013	1	1	1	1	1	0	1	1	7	low
Nelson.2002	0	1	1	1	1	0	1	1	6	low
Edwards.2004	1	1	1	1	1	0	1	1	7	low
Sosna.2006	1	1	1	1	1	0	1	1	7	low
Chukmaitov.2013	1	1	1	1	1	0	1	1	7	low
Cooper.2013	1	1	1	1	1	0	1	1	7	low
Korman.2003	1	1	1	1	1	0	1	1	7	low
Cheng.2002	0	1	1	0	1	0	1	1	5	moderate
Loffeld.2011	0	1	0	0	1	1	1	1	5	moderate
Lorenzo.2010	1	1	0	1	1	0	1	0	5	moderate
Rabeneck.2008	1	1	1	1	1	0	1	1	7	low
Xirasagar.2010	1	1	1	1	1	0	1	0	6	low
Ib ez J.2018	0	1	0	1	1	0	1	1	5	moderate
Sewitch.2018	0	1	1	1	1	0	1	1	6	low
Yamauchi.2017	0	1	0	0	1	0	1	1	4	moderate
Telford.2016	1	1	1	1	1	0	1	1	7	low
Quyn.2018	1	1	1	1	1	0	1	1	7	low
Derbyshire.2018	1	1	1	1	1	0	1	1	7	low
Castro.2013	1	1	1	1	1	0	1	0	6	low
Hilsden.2015	0	1	1	1	1	0	1	1	6	low
Zwink.2017	1	1	1	1	1	0	1	1	7	low
Wang.2018	1	1	1	1	1	0	1	1	7	low
Laanani.2019	1	1	1	1	1	0	1	1	7	low
Denis.2013	1	1	1	1	1	0	1	1	7	low
Meagher.1994	0	1	1	1	1	0	1	0	5	moderate
Bowles.2004	1	1	1	0	1	0	1	1	6	low
Pace.2016	0	1	0	1	1	0	1	1	5	moderate
Bair.2009	0	1	1	1	1	1	1	1	7	low
Ho.2012	1	1	1	1	1	0	1	0	6	low
Hsieh.2009	0	1	1	0	1	0	1	0	4	moderate
Levin.2002	0	1	1	1	1	0	1	1	6	low
Exbrayat.2010	0	1	1	0	1	0	1	1	5	moderate
Kozbial.2014	1	1	1	1	1	0	1	1	7	low
Rutter.2012	1	1	1	1	1	1	1	0	7	low
Sagawa.2012	1	1	0	0	1	0	1	0	4	moderate
Parente.2013	1	1	1	1	1	0	1	1	7	low
Suissa.2012	1	1	0	0	1	0	1	0	4	moderate

Pox.2012	1	1	1	1	1	0	1	1	7	low
Sieg.2001	1	1	0	1	1	0	1	0	5	moderate
Randall.2013	0	1	1	0	1	0	1	0	4	moderate
Kim.2010	1	1	1	1	1	0	1	1	7	low
Levin.2006	0	1	1	1	1	0	1	1	6	low
Binefa.2013	1	1	1	1	1	0	1	1	7	low
Cao.2011	0	1	1	1	1	0	1	1	6	low
Horiuchi.2013	0	1	1	1	1	0	1	1	6	low
Adeyemo.2014	0	1	1	1	1	0	1	1	6	low
Ankur.2002	0	1	1	0	0	0	1	0	3	moderate
Berhane.2009	0	1	1	1	0	1	1	1	6	low
Bielawska.2014	1	1	1	1	0	0	1	0	5	moderate
Cotterill.200	0	1	1	1	1	0	1	0	5	moderate
Crispin.2009	1	1	1	1	0	0	1	0	5	moderate
Ko.2007	0	1	1	1	1	0	1	1	6	low
Denters.2013	1	1	1	0	1	0	1	0	5	moderate
Ellul.2010	1	1	1	0	1	0	1	1	6	low
Garcia.2012	0	1	1	0	1	0	1	0	4	moderate
Johnson.2012	1	1	1	0	1	0	1	0	5	moderate
Kewenter.1996	1	1	1	0	1	0	1	0	5	moderate
Lieberman.2000	1	1	1	0	1	0	1	0	5	moderate
Marbet.2008	1	1	1	0	1	0	1	0	5	moderate
Rutter.2014	1	1	1	1	0	0	1	1	6	low
Samalavicius.2013	1	1	1	1	0	0	1	1	6	low
Steele.2009	1	1	1	1	0	0	1	1	6	low
Sung.2003	1	1	1	1	1	0	1	1	7	low
Tepes.2017	1	1	1	1	0	0	1	1	6	low
Vanaclochai.2019	1	1	1	1	1	0	1	1	7	low

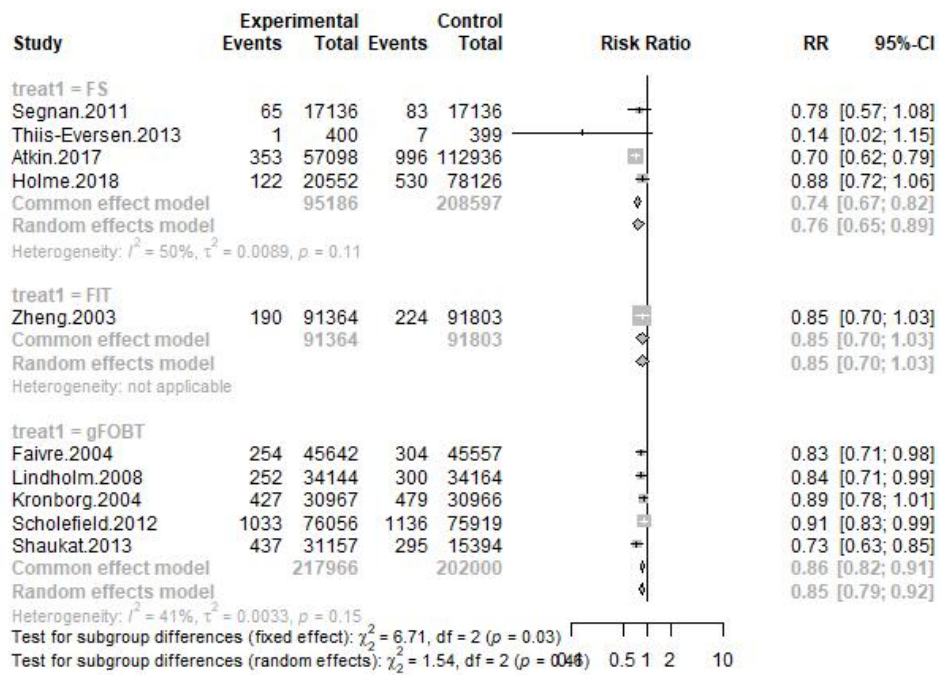
Note: Risk of bias evaluation criteria for case series studies (NICE)

- ① To improve the representativeness of the study results, cases in the case series should preferably be from different levels of healthcare institutions in a multicenter study; (1=yes, 0=no or not reported)
- ② Clear and unambiguous description of the hypothesis or purpose and objectives of the study; (1=yes, 0=no or not reported)
- ③ Clear reporting of inclusion and exclusion criteria; (1=yes, 0=no or not reported)
- ④ Clear definition of the measured outcome; (1=yes, 0=no or not reported)
- ⑤ The data collected should meet the intended objectives; (1=yes, 0=no or not reported)
- ⑥ Patients are accurately described as being recruited consecutively; (1=yes, 0=no or not reported)
- (vii) Clearly and unambiguously describe the main findings of the study; (1=yes, 0=no or not reported)
- (8) Stratified analysis and reporting of outcomes, such as by disease stage, abnormal laboratory

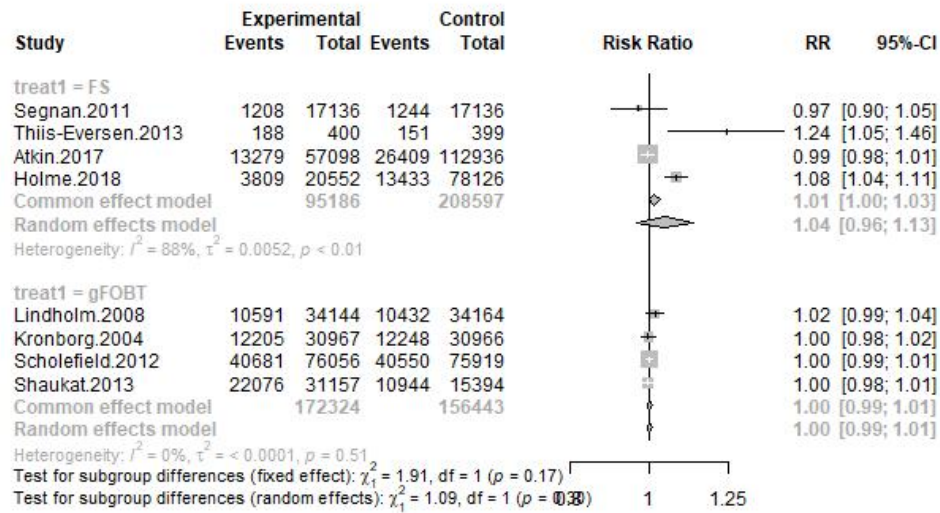
results, and patient characteristics; (1=Yes, 0=No or not reported)

## Supplementary File 6: Sensitive analysis for effectiveness (RCTs)

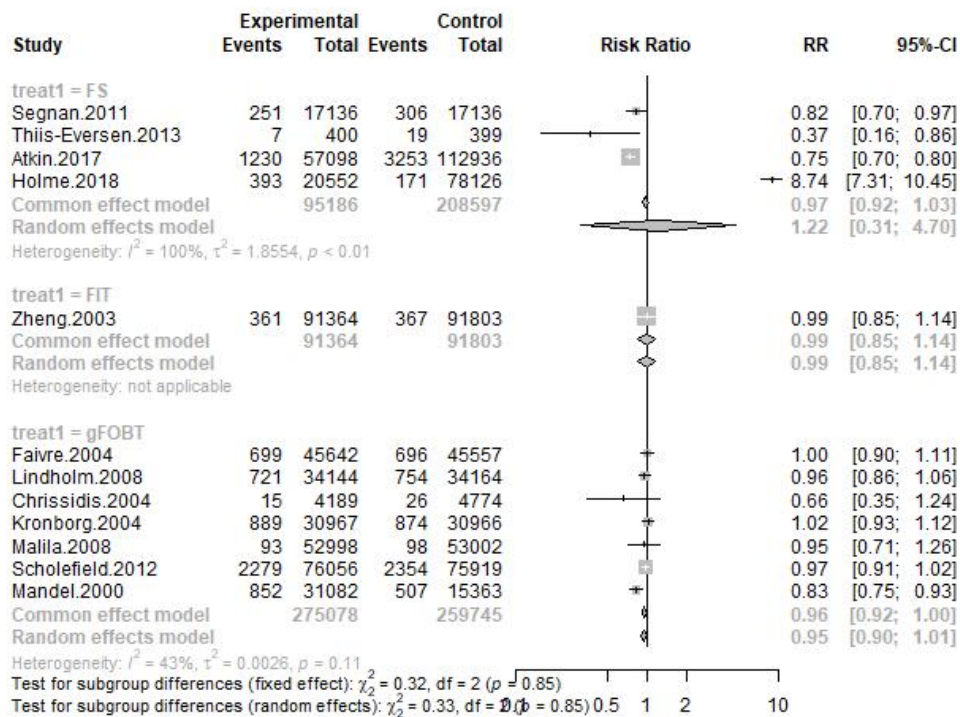
### CRC Mortality



## All-cause Mortality



## CRC Incidence



## Supplementary File 7: GRADE of effectiveness (RCTs & cohorts)

### CRC Incidence

Treat VS Control	Study Number	Study Design	Decrease quality of evidence					Increase quality of evidence			Quality of evidence
			Limitations	Inconsistency	Indirections	Imprecision	Reporting bias	Large effect	Plausible confounding	Dose response	
colonoscopy VS usual care	5	cohort	no serious	very serious	no serious	no serious	NA	large	no	no	very low
colonoscopy VS usual care	3	cohort	no serious	serious	no serious	no serious	NA	no	no	no	very low
FS VS usual care	5	RCT	no serious	serious	no serious	no serious	NA				low
FS VS usual care	2	cohort	no serious	serious	no serious	very serious	NA	no	no	no	very low
gFOBT VS usual care	9	RCT	serious	serious	no serious	no serious	NA				very low
gFOBT VS usual care	4	cohort	no serious	serious	no serious	no serious	NA	no	no	no	very low
FIT VS usual care	1	RCT	no serious	no serious	no serious	no serious	NA				moderate
FIT VS usual care	6	cohort	no serious	very serious	no serious	very serious	NA	no	no	no	very low

### CRC Mortality

Treat VS Control	Study Number	Study Design	Decrease quality of evidence					Increase quality of evidence			Quality of evidence
			Limitations	Inconsistency	Indirections	Imprecision	Reporting bias	Large effect	Plausible confounding	Dose response	
colonoscopy VS usual care	4	cohort	no serious	no serious	no serious	no serious	NA	large	no	no	low

colonoscopy VS usual care	3	cohort	no serious	no serious	no serious	no serious	NA	large	no	no	low
FS VS usual care	5	RCT	no serious	no serious	no serious	no serious	NA				moderate
gFOBT VS usual care	6	RCT	no serious	no serious	no serious	no serious	NA				moderate
gFOBT VS usual care	3	cohort	no serious	serious	no serious	serious	NA	no	no	no	very low
FIT VS usual care	1	RCT	no serious	no serious	no serious	serious	NA				low
FIT VS usual care	5	cohort	no serious	very serious	no serious	serious	NA	large	no	no	very low

## All-cause Mortality

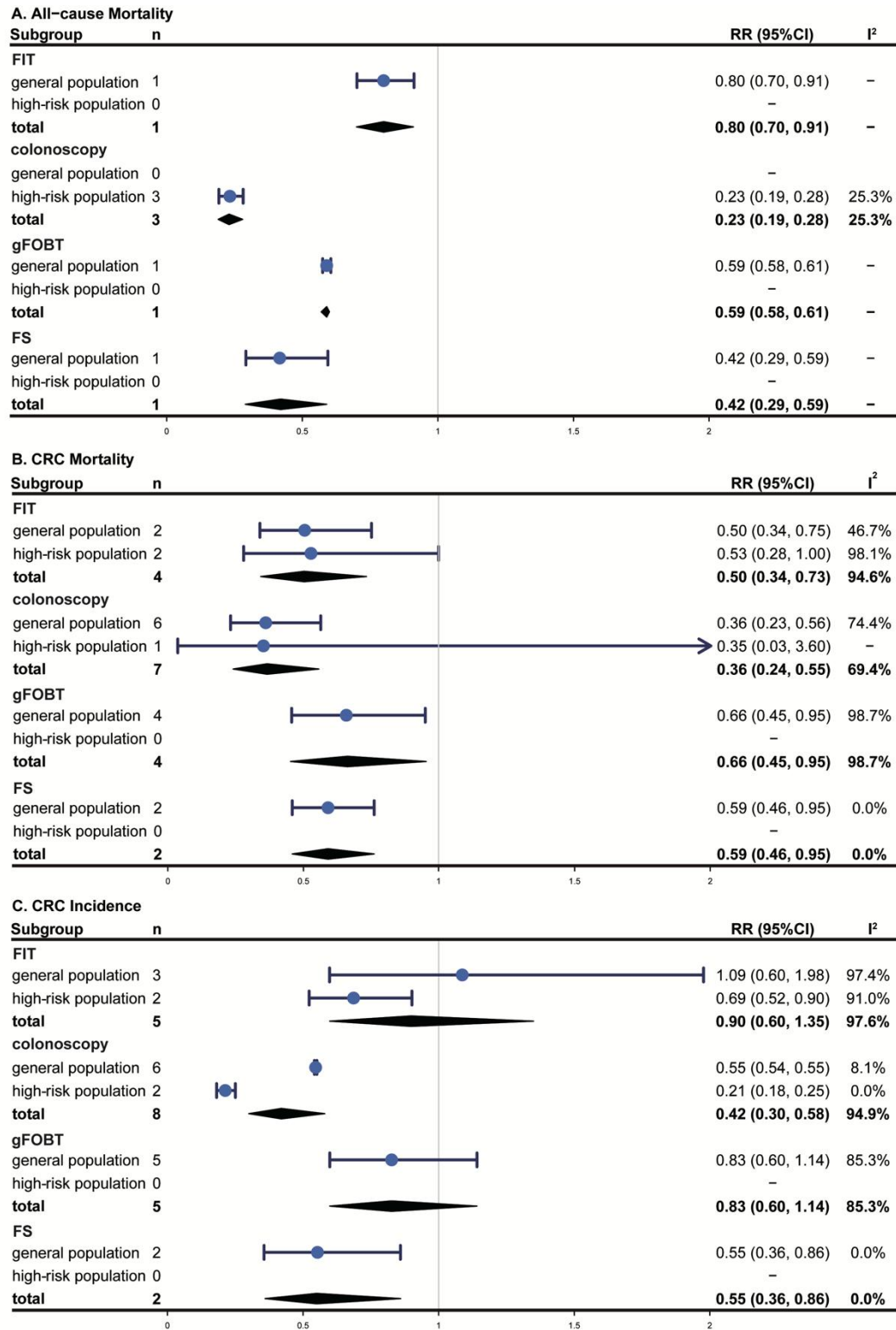
Treat VS Control	Study Number	Study Design	Decrease quality of evidence					Increase quality of evidence			Quality of evidence
			Limitations	Inconsistency	Indirections	Imprecision	Reporting bias	Large effect	Plausible confounding	Dose response	
FS VS usual care	4	RCT	no serious	serious	no serious	no serious	NA				low
FS VS usual care	1	cohort	no serious	no serious	no serious	no serious	NA	large	no	no	low
gFOBT VS usual care	5	RCT	no serious	serious	no serious	no serious	NA				low
gFOBT VS usual care	1	cohort	no serious	no serious	no serious	no serious	NA	no	no	no	very low

FIT VS

usual care	2	cohort	no serious	very serious	no serious	serious	NA	no	no	no	very low
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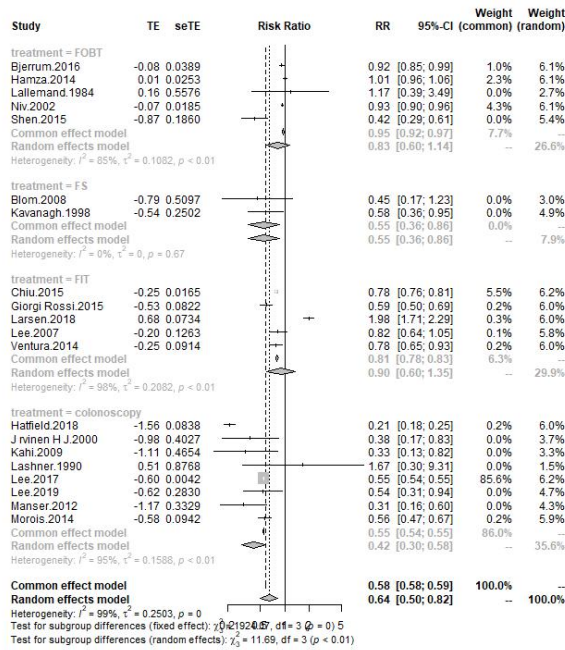
## Supplementary File 8: Results of meta-analysis for effectiveness outcomes in cohort studies



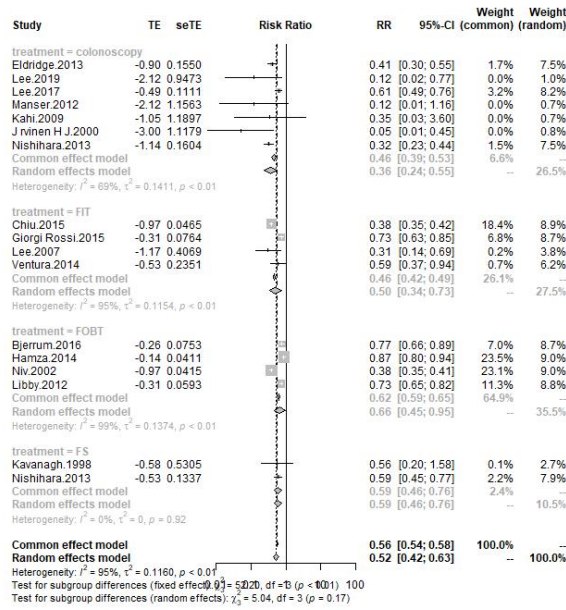
CRC: colorectal cancer; FS: flexible sigmoidoscopy; gFOBT: guaiac-based fecal occult blood test; FIT: fecal immunochemical test; n: number of included studies; RR: risk ratio; CI: confidence interval.

# Supplementary File 9: Results of pairwise meta-analysis for cohort studies

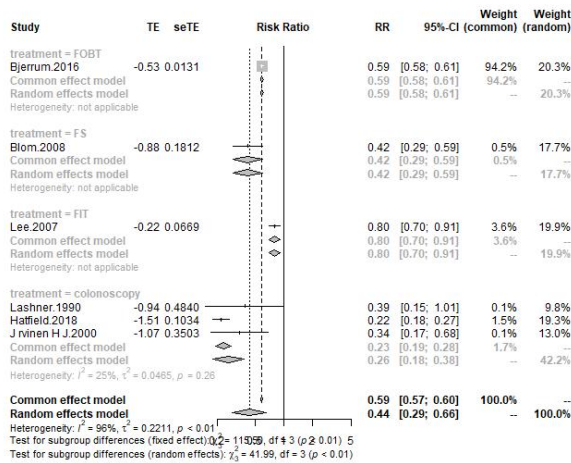
## CRC Incidence



# CRC Mortality



# All-cause Mortality



studyid	adjusted confounders	treatment	regression	indicator
Bjerrum.2016	sex and age	gFOBT	cox	HR
Blom.2008	sex	FS		IRR
Chiu.2015		FIT		RR
Giorgi		FIT		IRR
Rossi.2015	sex and age			IRR
Hamza.2014		gFOBT		SMR
Hatfield.2018		colonoscopy		RR
Jrvinen H J.2000		colonoscopy		RR

Kahi.2009		colonoscopy		SIR
Kavanagh.1998	age, family history of colon cancer, body mass index (wt/ht <sup>2</sup> )(in quintiles), pack years of smoking before age 30, physical activity (in quintiles), and intake of dietary fiber (in quintiles),	FS		RR
Lallemand.1984	folate (in quintiles), red meat, methionine (in quintiles), alcohol (in quintiles), total fat (in quintiles) and aspirin (2+/week).	gFOBT		RR
Larsen.2018		FIT		RR
Lashner.1990	age, sex, duration of disease	colonoscopy	cox	HR
Lee.2007		FIT		RR
Lee.2017		colonoscopy		RR
Lee.2019	age, sex, race/ethnicity, Charlson comorbidity score, and body mass index.	colonoscopy	cox	HR
Manser.2012	lifestyle, smoking, and body mass index as well as family history	colonoscopy	logistic	OR
Morois.2014		colonoscopy	cox	HR
Niv.2002		gFOBT		RR
Shen.2015		gFOBT		RR
Ventura.2014	sex and age	FIT	cox	HR
	Age, Body-mass index, History of colorectal cancer in firstdegree relative, Smoking status, Weekly physical activity level (METs), Red-meat intake (servings/day) Folate intake (µg/day), Calcium intake (mg/day), Total caloric intake (kcal/day) Alcohol intake (g/day), Current multivitamin use (%) Regular use of aspirin (%), Nonsteroidal antiinflammatory drug use (%), Cholesterol-lowering drug use (%), History of postmenopausal hormone use (%)			
		colonoscopy		RR
Libby.2012		gFOBT		RR
Eldridge.2013	HLS (physical activity, body mass index, waist-to-hip ratio, alcohol consumption, and intakes of red meat, processed meat, fibre, milk, and calcium)	colonoscopy	cox	RR

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# Supplementary File 10: Results of meta-analysis for safety outcomes

## Severe bleeding

Study	Events	Total	Events per 10000 observations	Events	95%-CI
treat = colonoscopy					
Lee 2012	49	38119	12.85	[9.51; 16.99]	
Hoff 2006	2	5450	3.67	[0.44; 13.25]	
Hayman 2013	0	311	0.00	[0.00; 117.91]	
Mansmann 2008	520	22567	22.07	[20.22; 24.05]	
Khalid-de Bakker 2011	0	214	0.00	[0.00; 170.90]	
Sawatki 2015	0	104	0.00	[0.00; 348.48]	
Mikkelsen 2018	60	14611	41.06	[31.35; 52.83]	
Sarasie 2016	18	2966	60.69	[36.01; 95.74]	
Quyn 2018	213	50754	41.97	[38.53; 47.98]	
Singh 2009	21	24488	8.58	[5.31; 13.11]	
Biolàre 2014	933	946128	9.86	[9.24; 10.51]	
Bokemeier 2009	19	259125	0.71	[0.43; 1.10]	
Chukmatov 2013	3822	2311304	16.54	[16.02; 17.07]	
Cheng 2002	0	7411	0.00	[0.00; 4.98]	
Lorenzo-Zúñiga 2010	59	25155	23.45	[17.86; 30.24]	
Xirasagar 2010	1	9814	1.02	[0.03; 5.68]	
Hilsden 2015	54	18402	29.34	[22.05; 38.27]	
Vanadocha-Espi 2019	63	48667	12.95	[9.95; 16.56]	
Zwink 2017	35	5217	67.09	[46.77; 93.18]	
Bowles 2004	6	9217	6.51	[2.39; 14.16]	
Bair 2009	2	3739	5.35	[0.65; 19.31]	
Exbrayat 2010	5	2553	19.58	[6.36; 45.64]	
Kozbial 2014	71	59830	11.87	[9.27; 14.97]	
Rutler 2012	122	43334	28.15	[23.39; 33.61]	
Poz 2012	573	2820819	2.03	[1.87; 2.20]	
Horiuchi 2013	0	2301	0.00	[0.00; 16.02]	
De Jonge 2012	4	1140	35.09	[9.57; 89.59]	
Portillo 2018	330	48429	68.14	[61.01; 75.87]	
Waldmann 2016	165	159081	10.37	[8.85; 12.08]	
Araña-Art 2018	245	39008	62.81	[55.21; 71.15]	
Forstberg 2017	846	592469	14.28	[13.33; 15.27]	
McClellan 2015	0	1155	0.00	[0.00; 31.89]	
Wan 2002	2	8296	2.41	[0.29; 8.71]	
Castro 2013	1	3354	2.98	[0.08; 16.60]	
Nelson 2002	7	3189	21.95	[8.83; 45.17]	
Strul 2006	0	1177	0.00	[0.00; 31.29]	
Wong 2019	2	321	62.31	[7.55; 223.24]	
Ko 2010	34	21541	15.93	[11.04; 22.26]	
Rabeneck 2008	137	99354	14.13	[11.89; 16.70]	
Ib ez J 2018	10	8821	11.34	[5.44; 20.84]	
Sewitch 2018	1	419	23.87	[0.60; 132.25]	
Telford 2016	6	1591	37.71	[13.85; 81.90]	
Wang 2018	8164	2794224	29.22	[20.59; 39.86]	
Laanani 2019	9459	4079340	23.19	[22.72; 23.66]	
Denis 2013	31	10246	30.26	[20.57; 42.92]	
Pace 2016	6	3229	18.58	[6.82; 40.40]	
Parente 2013	5	4366	11.45	[3.72; 26.69]	
Suissa 2012	3	6581	4.56	[0.94; 13.32]	
Sieg 2001	7	96658	0.72	[0.29; 1.49]	
Randall 2013	4	3978	10.06	[2.74; 25.73]	
Levin 2006	15	16303	9.20	[5.15; 15.17]	
Binefs 2013	15	1731	83.75	[46.95; 137.76]	
Segnan 2002	1	774	12.92	[0.33; 71.77]	
Faire 2004	0	1298	0.00	[0.00; 28.38]	
Quintero 2012	20	27270	7.33	[4.48; 11.32]	
Chrisidis 2004	0	156	0.00	[0.00; 233.69]	
Atkin 2002	9	2042	44.07	[20.17; 83.50]	
Stoop 2012	2	1274	15.70	[1.90; 56.59]	
Gondal 2003	4	2520	15.87	[4.33; 40.59]	
Rasmussen 1999	0	502	0.00	[0.00; 73.21]	
Steele 2020	0	440	0.00	[0.00; 83.49]	
Segnan 2005	1	331	30.21	[0.76; 167.17]	
Brethauer 2016	18	12556	14.34	[8.50; 22.65]	
Senore 2011	15	1183	126.80	[71.14; 208.27]	
Tran 2014	68	27395	24.55	[19.07; 31.12]	
Warren 2009	11	5338	20.61	[10.29; 36.84]	
Ferlitsch 2011	54	44296	12.19	[9.16; 15.90]	
Zafar 2014	371	53668	69.13	[62.29; 76.51]	
Stock 2013	4	8654	4.62	[1.25; 11.83]	
Johnson 2008	1	2530	3.95	[0.10; 22.00]	
Kubisch 2016	966	523988	18.44	[17.29; 19.63]	
Costenli 2005	0	152	0.00	[0.00; 239.77]	
Crispin 2009	10	23077	0.42	[0.20; 0.78]	
Denters 2013	1	272	36.76	[0.83; 203.13]	
Marbet 2008	3	2041	14.70	[3.03; 42.90]	
Garcia 2012	6	983	61.04	[22.43; 132.38]	
Lieberman 2000	0	3116	19.26	[7.07; 41.88]	
Kewenter 1996	1	189	52.91	[1.34; 291.26]	
Ellul 2010	3	1036	28.96	[5.98; 84.39]	
Gupta 2012	1	1056	9.47	[0.24; 52.65]	
Berhane 2009	5	11803	4.24	[1.38; 8.88]	
Kistler 2011	3	115	260.87	[54.12; 743.46]	
Mandel 1993	11	12235	8.99	[4.49; 16.08]	
Tepes 2017	4	13915	2.87	[0.78; 7.36]	
Rutler 2014	52	130779	3.98	[2.97; 5.21]	
SUING 2003	1	504	19.84	[0.50; 110.05]	
Zalis 2012	0	605	0.00	[0.00; 60.79]	
Common effect model		16080456	14.88	[14.69; 15.07]	
Random effects model			14.48	[10.91; 18.55]	
Heterogeneity: $I^2 = 99\%$ , $\tau^2 = 0.0005$ , $p = 0$					
treat = CTC					
Piochard 2003	1	1232	8.12	[0.21; 45.14]	
Kim 2010	0	577	0.00	[0.00; 63.73]	
Stoop 2012	3	979	30.54	[6.32; 89.29]	
Zafar 2014	4	1380	28.99	[7.90; 74.05]	
Johnson 2008	0	2531	0.00	[0.00; 14.56]	
Johnson 2012	1	2530	3.95	[0.10; 22.00]	
Zalis 2012	0	605	0.00	[0.00; 60.79]	
Common effect model		9834	4.73	[1.41; 10.81]	
Random effects model			5.43	[0.30; 16.90]	
Heterogeneity: $I^2 = 66\%$ , $\tau^2 = 0.0004$ , $p < 0.01$					
treat = FS					
Levin 2002	2	109532	0.18	[0.02; 0.66]	
Segnan 2002	0	9911	0.00	[0.00; 3.72]	
Abin 2002	12	40320	2.98	[1.54; 5.20]	
Brevigne 1997	1	1430	6.99	[0.16; 39.90]	
Gondal 2003	0	12960	0.00	[0.00; 2.85]	
Rasmussen 1999	0	2235	0.00	[0.00; 16.49]	
Steele 2020	0	4597	0.00	[0.00; 8.02]	
Segnan 2005	0	4466	0.00	[0.00; 8.29]	
Verna 1998	0	1116	0.00	[0.00; 33.00]	
Senore 2011	8	1494	53.55	[23.15; 105.24]	
Viala 2007	0	3402	0.00	[0.00; 10.84]	
Pabby 2005	4	7384	5.42	[1.48; 13.86]	
Antur 2002	0	5017	0.00	[0.00; 7.35]	
Kewenter 1996	0	2108	0.00	[0.00; 17.48]	
Common effect model		205972	0.52	[0.25; 0.88]	
Random effects model			0.82	[0.00; 3.12]	
Heterogeneity: $I^2 = 53\%$ , $\tau^2 = 0.0003$ , $p < 0.01$					
Test for subgroup differences (fixed effect): $\chi^2 = 612.54$ , $df = 2$ ( $p < 0.01$ )					
Test for subgroup differences (random effects): $I^2 = 408.28$ , $df = 2$ ( $p < 0.01$ )					

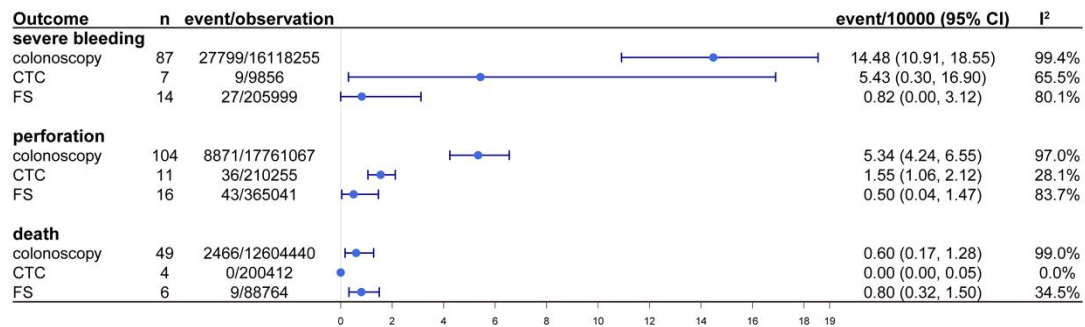
# Perforation

Study	Events	Total	Events per 1000 observations	Events	95%-CI
treat = colonoscopy					
Lee 2012	35	38133	0.918	9.18	[6.39; 12.76]
Hoff 2006	1	5451	0.183	1.83	[0.05; 10.22]
Hayman 2013	0	311	0.000	0.00	[0.00; 117.91]
Mansmann 2009	69	236018	0.292	2.92	[2.27; 3.70]
Khalid-de Bakker 2011	0	214	0.000	0.00	[0.00; 170.90]
Sawatvki 2015	0	104	0.000	0.00	[0.00; 348.48]
Mikkelsen 2018	15	14656	1.023	10.23	[5.73; 16.87]
Saratz 2016	3	2981	1.006	10.06	[2.08; 29.38]
Ouy 2018	45	50922	0.884	8.84	[6.45; 11.82]
Kang 2009	53	44481	1.192	11.92	[8.93; 15.58]
Singh 2009	29	24480	1.185	11.85	[7.94; 17.01]
Blotère 2014	424	946637	0.448	4.48	[4.06; 4.93]
Bokemeyer 2009	55	269089	2.04	20.4	[15.4; 26.6]
Chumakov 2013	773	214353	3.34	33.4	[3.11; 3.56]
Korman 2003	37	115963	3.19	31.9	[2.25; 4.40]
Cheng 2002	2	7409	2.70	27.0	[0.33; 9.75]
Lorenzo-Zuhiga 2010	13	25201	5.16	51.6	[2.75; 8.82]
Yarasagar 2010	2	9813	2.04	20.4	[0.25; 7.36]
Hilsden 2015	4	18452	2.17	21.7	[0.59; 5.55]
Vanadocha-Espi 2019	98	48632	20.15	201.5	[16.36; 24.55]
Zwint 2017	8	5244	15.26	152.6	[4.59; 30.04]
Bowles 2004	12	9211	13.03	130.3	[6.73; 22.75]
Bair 2009	1	3740	2.67	26.7	[0.07; 14.89]
Esbayak 2010	1	2557	3.91	39.1	[0.10; 21.77]
Rutter 2012	21	43435	4.83	48.3	[2.99; 7.39]
Pox 2012	439	2820953	1.56	15.6	[1.41; 1.71]
Honouchi 2013	0	2301	0.000	0.00	[0.00; 16.02]
De Jonge 2012	1	1143	0.75	7.5	[0.22; 49.65]
Portillo 2018	148	48611	30.45	304.5	[25.74; 35.76]
Waldmann 2016	20	159226	1.26	12.6	[0.77; 1.94]
Aranz-kn 2018	196	39148	27.08	270.8	[22.17; 32.74]
Forsberg 2017	637	592678	10.75	107.5	[9.93; 11.62]
McChellan 2015	7	1154	8.67	86.7	[0.22; 48.19]
Dierckx 2018	147	262962	5.59	55.9	[4.72; 6.57]
Castro 2013	3	3352	8.95	89.5	[1.85; 26.13]
Qualick 2009	4	39605	1.02	10.2	[0.28; 2.62]
Hämäläinen 2013	50	80668	6.24	62.4	[4.54; 8.23]
Nelson 2002	0	3195	0.000	0.00	[0.00; 11.54]
Strul 2006	0	1177	0.000	0.00	[0.00; 31.29]
Wong 2019	1	322	31.06	310.6	[0.79; 171.81]
Ko 2010	4	21371	1.87	18.7	[0.51; 4.78]
Loffeld 2011	26	19109	13.61	136.1	[8.89; 19.93]
Rabeneck 2008	54	97037	5.56	55.6	[4.18; 7.26]
Ip et al 2018	13	8816	14.74	147.4	[7.85; 25.20]
Telford 2016	3	1594	18.82	188.2	[3.88; 54.90]
Wang 2018	1650	2800738	5.89	58.9	[5.61; 6.18]
Laaran 2019	2996	4089001	7.34	73.4	[7.08; 7.60]
Denis 2013	10	10267	9.74	97.4	[4.67; 17.90]
Meagher 1994	0	645	0.000	0.00	[0.00; 57.03]
Pace 2016	6	3229	18.58	185.8	[6.82; 40.40]
Heien 2009	3	8486	3.16	31.6	[0.65; 9.23]
Sagawa 2012	8	10818	7.40	74.0	[3.19; 14.57]
Parente 2013	2	4371	4.58	45.8	[0.55; 16.52]
Siuissa 2012	3	6581	4.56	45.6	[0.94; 13.32]
Sieg 2001	13	96652	1.35	13.5	[0.72; 2.30]
Ransall 2013	3	3979	7.54	75.4	[1.56; 22.02]
Levin 2006	15	16303	9.20	92.0	[5.15; 15.17]
Binefa 2013	3	803	16.64	166.4	[3.43; 48.55]
Cao 2011	1	2199	4.55	45.5	[0.12; 25.31]
Sagnan 2002	1	774	12.92	129.2	[0.33; 71.77]
Falva 2004	0	1286	0.000	0.00	[0.00; 29.38]
Quintero 2012	1	26702	0.37	3.7	[0.01; 2.09]
Quintero 2012	0	587	0.000	0.00	[0.00; 62.85]
Christidis 2004	0	156	0.000	0.00	[0.00; 233.69]
Atkin 2002	4	2047	19.54	195.4	[5.33; 49.96]
Stoop 2012	0	1276	0.000	0.00	[0.00; 29.87]
Gonzal 2003	6	2516	23.83	238.3	[8.75; 51.79]
Rasmussen 1999	0	502	0.000	0.00	[0.00; 73.21]
Steele 2020	0	440	0.000	0.00	[0.00; 83.49]
Schoen 2012	19	17653	10.76	107.6	[6.48; 16.80]
Sall 2016	0	495	0.000	0.00	[0.00; 74.10]
Brethauer 2016	1	12573	0.80	8.0	[0.02; 4.43]
Senore 2011	0	1198	0.000	0.00	[0.00; 30.74]
Galfo 2003	77	39209	19.64	196.4	[15.50; 24.54]
Tran 2014	19	27744	6.85	68.5	[4.12; 10.69]
Warren 2009	3	5346	5.61	56.1	[1.16; 16.39]
Ferlicich 2011	3	44347	0.68	6.8	[0.14; 1.96]
Zafar 2014	46	53993	8.52	85.2	[6.24; 11.36]
Stock 2013	7	8851	8.09	80.9	[3.25; 16.66]
Tam 2013	25	86076	2.96	29.6	[1.88; 4.29]
Kim 2007	7	3156	22.18	221.8	[8.92; 45.62]
Johnson 2008	0	2531	0.000	0.00	[0.00; 14.56]
Kim 2013	26	94806	2.75	27.5	[1.80; 4.03]
Kubisch 2016	136	524810	2.57	25.7	[2.16; 3.04]
Cottenill 2005	0	152	0.000	0.00	[0.00; 239.77]
Crispin 2009	69	236018	2.92	29.2	[2.27; 3.70]
Diercks 2013	0	273	0.000	0.00	[0.00; 134.21]
Marbet 2008	1	2043	4.89	48.9	[0.12; 27.24]
Garza 2012	3	986	30.43	304.3	[6.28; 89.66]
Lieberman 2000	0	3121	0.000	0.00	[0.00; 11.81]
Ko 2007	0	502	0.000	0.00	[0.00; 73.21]
Bielawska 2014	62	544412	1.14	11.4	[0.87; 1.46]
Kewenter 1996	2	188	106.38	1063.8	[12.91; 378.99]
Cooper 2013	101	165426	11.11	111.1	[4.97; 17.42]
Adeyemo 2014	48	117956	4.07	40.7	[3.00; 5.39]
Elul 2010	0	1039	0.000	0.00	[0.00; 35.44]
Gupta 2012	1	1056	9.47	94.7	[0.24; 52.65]
Samalavicus 2013	40	56842	7.04	70.4	[5.03; 9.58]
Berhane 2009	2	11806	1.69	16.9	[0.21; 6.12]
Mandel 1993	4	12242	3.27	32.7	[0.89; 6.36]
Tapeš 2017	7	13912	5.03	50.3	[2.02; 10.36]
Rutter 2014	78	130753	5.97	59.7	[4.72; 7.44]
SUNG 2003	0	505	0.000	0.00	[0.00; 72.78]
Zalis 2012	0	605	0.000	0.00	[0.00; 60.79]
Common effect model		17752196	4.52	45.2	[4.42; 4.62]
Random effects model			5.34	53.4	[4.24; 6.55]
Heterogeneity: $I^2 = 97\%$ , $\tau^2 = 0.0001$ , $p = 0$					
treat = CTC					
Infante 2013	7	40114	1.75	17.5	[0.70; 3.69]
Edwards 2004	0	340	0.000	0.00	[0.00; 107.91]
Kim 2010	0	577	0.000	0.00	[0.00; 63.73]
Nagata 2017	21	147418	1.42	14.2	[0.88; 2.18]
Siena 2006	7	11863	5.90	59.0	[2.37; 12.15]
Stoop 2012	0	982	0.000	0.00	[0.00; 37.49]
Sall 2016	0	1286	0.000	0.00	[0.00; 29.84]
Zafar 2014	1	1383	7.23	72.3	[0.18; 40.22]
Kim 2007	0	3120	0.000	0.00	[0.00; 11.82]
Johnson 2008	0	2531	0.000	0.00	[0.00; 14.56]
Zalis 2012	0	605	0.000	0.00	[0.00; 60.79]
Common effect model		216219	1.55	15.5	[1.06; 2.12]
Random effects model			1.58	15.8	[1.00; 2.28]
Heterogeneity: $I^2 = 29\%$ , $\tau^2 = 0.0001$ , $p = 0.18$					
treat = FS					
Levin 2002	2	109532	0.18	1.8	[0.02; 0.66]
Sagnan 2002	1	9910	0.01	0.1	[0.03; 6.66]
Atkin 2002	1	40331	0.25	2.5	[0.01; 1.38]
Gonzal 2003	0	12960	0.000	0.00	[0.00; 2.85]
Rasmussen 1999	0	2235	0.000	0.00	[0.00; 16.49]
Steele 2020	0	4597	0.000	0.00	[0.00; 8.02]
Schoen 2012	3	67068	0.45	4.5	[0.09; 1.31]
Veine 1988	0	1116	0.000	0.00	[0.00; 33.00]
Senore 2011	0	1502	0.000	0.00	[0.00; 24.53]
B. Strum W. 2006	0	3147	0.000	0.00	[0.00; 11.72]
Galfo 2003	31	35267	8.79	87.9	[5.97; 12.47]
Viala 2007	0	3402	0.000	0.00	[0.00; 10.84]
Tam 2013	1	46157	0.22	2.2	[0.01; 1.21]
Kim 2013	1	20652	0.48	4.8	[0.01; 2.70]
Akbar 2002	0	5917	0.000	0.00	[0.00; 7.55]
Kewenter 1996	3	2105	14.25	142.5	[2.84; 41.59]
Common effect model		364998	0.55	5.5	[0.33; 0.81]
Random effects model			0.50	5.0	[0.04; 1.47]
Heterogeneity: $I^2 = 94\%$ , $\tau^2 = 0.0001$ , $p = 0.01$					
Test for subgroup differences (fixed effects): $\chi^2 = 335.76$ , $df = 2$ ( $p < 0.01$ )					
Test for subgroup differences (random effects): $I^2 = 94.16$ , $df = 2$ ( $p < 0.001$ )					

## Death caused by complications

Study	Events	Total	Events per 10000 observations	Events	95%-CI
treat = colonoscopy					
Lee.2012	0	38168		0.00	[0.00; 0.97]
Hayman.2013	1	310		32.26	[0.82; 178.41]
Mansmann.2008	3	236084		0.13	[0.03; 0.37]
Saraste.2016	0	2984		0.00	[0.00; 12.35]
Quyn.2018	1	50966		0.20	[0.00; 1.09]
Singh.2009	1	24508		0.41	[0.01; 2.27]
Korman.2003	0	116000		0.00	[0.00; 0.32]
Cheng.2002	0	7411		0.00	[0.00; 4.98]
Xirasagar.2010	0	9815		0.00	[0.00; 3.76]
Hillsden.2015	0	18456		0.00	[0.00; 2.00]
Bowles.2004	6	9217		6.51	[2.39; 14.16]
Ho.2012	13	50647		2.57	[1.37; 4.39]
Rutter.2012	7	43449		1.61	[0.65; 3.32]
Pox.2012	2	2821390		0.01	[0.00; 0.03]
Portillo.2018	1	48758		0.21	[0.01; 1.14]
Waldmann.2016	0	159246		0.00	[0.00; 0.23]
Arana-Arri.2018	0	39254		0.00	[0.00; 0.94]
Forsberg.2017	80	593235		1.35	[1.07; 1.68]
Derbyshire.2018	1	263128		0.04	[0.00; 0.21]
Nelson.2002	0	3196		0.00	[0.00; 11.54]
Strul.2006	0	1177		0.00	[0.00; 31.29]
Wong.2019	0	323		0.00	[0.00; 113.56]
Ko.2010	0	21375		0.00	[0.00; 1.73]
Rabeneck.2008	5	97086		0.52	[0.17; 1.20]
Telford.2016	0	1597		0.00	[0.00; 23.07]
Wang.2018	1321	2801067		4.72	[4.47; 4.98]
Laanani.2019	194	4088605		0.47	[0.41; 0.55]
Denis.2013	0	10277		0.00	[0.00; 3.59]
Meagher.1994	0	645		0.00	[0.00; 57.03]
Sieg.2001	2	96663		0.21	[0.03; 0.75]
Levin.2006	1	16317		0.61	[0.02; 3.41]
Kobiela.2019	327	338150		9.67	[8.65; 10.78]
Atkin.2002	1	2050		4.88	[0.12; 27.15]
Stoop.2012	1	1275		7.84	[0.20; 43.62]
Rasmussen.1999	0	502		0.00	[0.00; 73.21]
Steele.2020	0	440		0.00	[0.00; 83.49]
Brethauer.2016	0	12574		0.00	[0.00; 2.93]
Gatto.2003	4	39282		1.02	[0.28; 2.61]
Ferlitsch.2011	0	44350		0.00	[0.00; 0.83]
Stock.2013	5	8653		5.78	[1.88; 13.48]
Cotterill.2005	0	152		0.00	[0.00; 239.77]
Crispin.2009	3	236084		0.13	[0.03; 0.37]
Lieberman.2000	0	3121		0.00	[0.00; 11.81]
Cooper.2013	480	165047		29.08	[26.54; 31.80]
Gupta.2012	0	1507		0.00	[0.00; 24.45]
Samalavicius.2013	6	56876		1.05	[0.39; 2.30]
Berhane.2009	0	11808		0.00	[0.00; 3.12]
Kistler.2011	0	118		0.00	[0.00; 307.78]
Steele.2009	0	8631		0.00	[0.00; 4.27]
Common effect model		12601974		0.98	[0.92; 1.03]
Random effects model				0.60	[0.17; 1.28]
Heterogeneity: $I^2 = 99\%$ , $\tau^2 = 0.0001$ , $p = 0$					
treat = CTC					
lafrate.2013	0	40121		0.00	[0.00; 0.92]
Nagata.2017	0	147439		0.00	[0.00; 0.25]
Sosna.2006	0	11870		0.00	[0.00; 3.11]
Stoop.2012	0	982		0.00	[0.00; 37.49]
Common effect model		200412		0.00	[0.00; 0.05]
Random effects model				0.00	[0.00; 0.05]
Heterogeneity: $I^2 = 0\%$ , $\tau^2 = 0$ , $p = 1.00$					
treat = FS					
Atkin.2002	6	40326		1.49	[0.55; 3.24]
Rasmussen.1999	0	2235		0.00	[0.00; 16.49]
Steele.2020	0	4597		0.00	[0.00; 8.02]
Gatto.2003	2	35296		0.57	[0.07; 2.05]
Atkin.1998	1	1284		7.79	[0.20; 43.32]
Ankur.2002	0	5017		0.00	[0.00; 7.35]
Common effect model		88755		0.80	[0.32; 1.50]
Random effects model				0.65	[0.11; 1.64]
Heterogeneity: $I^2 = 34\%$ , $\tau^2 = < 0.0001$ , $p = 0.18$					
Test for subgroup differences (fixed effect): $\chi^2 = 77.41$ , $df = 2$ ( $p < 0.01$ )					
Test for subgroup differences (random effects): $I^2 = 50.32$ , $df = 2$ ( $p < 0.01$ )					

## Supplementary File 11: Forest plot of safety outcomes



CTC: computed tomography colonography; FS: flexible sigmoidoscopy.

## Supplementary File 12: Subgroup analysis of safety outcomes

### Severe bleeding

treatment	n	event/10000(95%CI)	I-square
<b>colonoscopy</b>			
case series	65	14.08 (10.19, 18.60)	99.6%
RCT	13	9.23 (4.05, 16.51)	57.0%
cohort	9	29.96 (10.86, 58.50)	98.0%
high risk population	7	23.67 (7.31, 49.33)	81.9%
average/high risk	10	11.58 (5.60, 19.71)	97.7%
average risk population	70	14.19 (10.16, 18.89)	99.5%
Europe	51	16.64 (11.52, 22.69)	99.5%
North America&Australia	30	14.93 (9.97, 20.89)	98.1%
Asia	6	1.18 (0.01, 4.25)	54.7%
age>50	53	18.28 (12.9, 24.58)	99.1%
<b>CTC</b>			
case series	2	3.77 (0.00, 18.60)	21.6%
RCT	3	6.82 (0.00, 30.16)	62.9%
cohort	2	6.85 (0.00, 62.17)	90.4%
high risk population	1	0.00(0.00, 16.63)	-
average/high risk	0	-	-
average risk population	6	6.78 (0.46, 20.48)	69.2%
Europe	1	30.64 (5.79, 74.990)	-
North America&Australia	6	3.41 (0.01, 12.97)	60.0%
Asia	0	-	-
age>50	6	6.82 (0.47, 20.55)	69.1%
<b>FS</b>			
case series	3	0.16 (0.01, 0.47)	0.0%
RCT	8	0.29 (0.00, 1.54)	70.9%

cohort	3	9.70 (0.00, 52.17)	91.0%
high risk population	1	0.00(0.00, 0.74)	-
average/high risk	0	-	-
average risk population	13	0.99 (0.00, 3.78)	80.8%
Europe	10	1.09 (0.00, 5.39)	81.6%
North America&Australia	4	0.53 (0.00, 3.20)	72.6%
Asia	0	-	-
age>50	12	0.85 (0.00, 3.87)	75.4%

## Perforation

treatment	n	event/10000(95%CI)	I-square
<b>colonoscopy</b>			
case series	76	5.67 (4.44, 7.05)	97.60%
RCT	16	1.07(0.00,5.57)	76.10%
cohort	12	5.00 (2.22, 8.90)	94.20%
high risk population	9	11.32 (6.52, 17.44)	86.50%
average/high risk population	14	4.00 (2.37, 6.06)	82.20%
average population	80	5.06 (3.81, 6.48)	97.50%
Europe	55	6.15 (4.37, 8.24)	98.00%
North America&Australia	38	4.74 (3.35, 6.36)	94.40%
Asia	11	4.39 (2.33, 7.10)	81.40%
age>50	55	5.68 (3.91, 7.79)	95.90%
<b>CTC</b>			
case series	5	1.66 (1.14, 2.27)	45.50%
RCT	3	0.00(0.00, 3.34)	0.00%
cohort	3	0.28 (0.00, 2.88)	37.80%
high risk population	1	0.00(0.00, 16.63)	-
average/high risk population	2	3.27 (0.53, 8.33)	77.80%
average population	8	1.30 (0.80, 1.92)	0.00%
Europe	3	1.56 (0.60, 2.98)	98.00%
North America&Australia	6	0.19 (0.00, 2.23)	0.00%
Asia	2	3.00 (0.28, 8.61)	85.10%
age>50	6	0.00 (0.00, 2.85)	0.00%
<b>FS</b>			
case series	2	0.17 (0.01, 0.49)	0.00%
RCT	8	0.35 (0.11, 0.73)	43.70%
cohort	6	0.74 (0.00, 3.68)	91.70%
high risk population	2	2.26 (0.00, 19.42)	97.00%
average/high risk population	1	0.22(0.00,0.85)	-
average population	12	0.24 (0.07, 0.5)	13.30%
Europe	9	0.24 (0.02, 0.7)	36.50%
North America&Australia	6	0.70 (0.00, 3.11)	93.50%
Asia	1	0.48 (0.00, 1.90)	-
age>50	11	0.74 (0.01, 2.62)	88.50%

## Death caused by complications

<b>treatment</b>	<b>n</b>	<b>event/10000(95%CI)</b>	<b>I-square</b>
<b>colonoscopy</b>			
case series	39	0.43 (0.08, 1.08)	99.1%
RCT	6	2.74 (0.06, 9.42)	90.2%
cohort	4	1.10 (0.00, 5.40)	85.1%
high risk population	5	2.80 (0.00, 16.86)	98.5%
general/high risk population	6	0.12 (0.03, 0.28)	0.00%
general population	38	0.50 (0.15, 1.06)	99.0%
Europe	24	0.39 (0.05, 1.03)	98.3%
North America&Australia	22	0.99 (0.10, 2.78)	98.2%
Asia	3	0.80 (0.26, 1.63)	36.5%
age>50	27	0.58 (0.03, 1.80)	99.1%
<b>CTC</b>			
case series	3	0.00 (0.00, 0.05)	0.0%
RCT	1	0.00 (0.00, 9.78)	-
cohort	0	-	-
high risk population	0	-	-
general/high risk population	2	0.00 (0.00, 0.18)	0.0%
general population	2	0.00 (0.00, 0.06)	0.0%
Europe	2	0.00 (0.00, 0.23)	0.0%
North America&Australia	0	-	-
Asia	2	0.00 (0.00, 0.06)	0.0%
age>50	1	0.00 (0.00, 9.78)	-
<b>FS</b>			
case series	1	0.00 (0.00, 1.91)	-
RCT	4	1.19 (0.42, 2.36)	4.0.1%
cohort	1	0.57 (0.05, 1.62)	-
high risk population	1	0.57 (0.05, 1.62)	-
general/high risk population	0	-	-
general population	5	0.97 (0.32, 1.99)	44.2%
Europe	3	0.20 (0.00, 2.34)	40.6%
North America&Australia	3	0.88 (0.35, 1.65)	43.4%
Asia	0	-	-
age>50	3	0.4 (0.02, 1.23)	0.0%