A call for standardized reporting of early-onset colorectal peritoneal metastases

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Background **The incidence of colorectal cancer (CRC) in patients under 50 years of age, i.e., early-onset CRC, has increased in the past two decades. Colorectal peritoneal metastases (CPM) will develop in 10–30% of CRC patients. CPM traditionally had a dismal prognosis, but surgery and novel systemic treatments appear to increase survival. Determining potential age-associated risk and prognostic factors is optimized when analyses use standardized age groupings.**

Methods **We performed a review of early-onset CPM studies and compared variables used, e.g., age stratification and definitions of synchronous and metachronous CPM. We included studies published in PubMed up to November 2022 if results were stratified by age.**

Results **Of 114 screened publications in English, only 10 retrospective studies met inclusion criteria. Incidence of CPM was higher in younger CRC patients (e.g. 23% vs. 2% for <25 vs. ≥25 years, $P < 0.0001$; and 57% vs. 39% vs. 4% for <20 vs. 20–25 vs. >25 years, $P < 0.001$); two studies reported higher proportion of younger African American CPM patients (e.g. 16% vs. 6% for <50 vs. ≥50 years). Studies used seven different age-stratification methods, presenting comparison challenges.**

Conclusion **Studies showed a higher proportion of CPM in younger patients, but directly comparing results was not possible due to inconsistent reporting. To better address this issue, CRC and CPM studies stratified by standard age groups (e.g. <50 vs. ≥50) are needed.**

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Introduction

The peritoneum is the third most common site of metastasis from colorectal cancer (CRC) after the liver and lung (Mohamed *et al.*, 2020). Colorectal peritoneal metastases (CPM) can be fatal as there are limited treatment options (Kerscher *et al.*, 2013; Adachi *et al.*, 2015). Widespread peritoneal metastasis is sometimes called peritoneal carcinomatosis (NICE, 2020) and should be considered distinct from resectable CPM. Of those patients who die from CRC, 40–80% have CPM (Koppe *et al.*, 2006). CPM is the second most common cause of death in CRC patients, after liver metastases (Macrì *et al.*, 2020). The incidence of those diagnosed when under 50, that is, those who have early-onset CRC, is increasing globally (Perea and Winter, 2023). Early-onset CRC patients are more likely to have metastatic CRC at diagnosis (liver metastasis, or peritoneal metastasis, or both) compared to those age 50 and over (24.4% vs. 18.8%, $P < 0.001$) (Kneuertz *et al.*, 2015; Yeo *et al.*, 2017; Himbert *et al.*, 2021). Presentation of CRC often differs depending on age at diagnosis – which appears to influence demographics, tumor site, pathogenic genetic variants, pathology, and metastatic profile of CRC (Yeo *et al.*, 2017; Riihimäki *et al.*, 2018; Segev *et al.*, 2018; Stoffel and Murphy, 2020). Treatment guidelines for CPM are not currently age specific as there is

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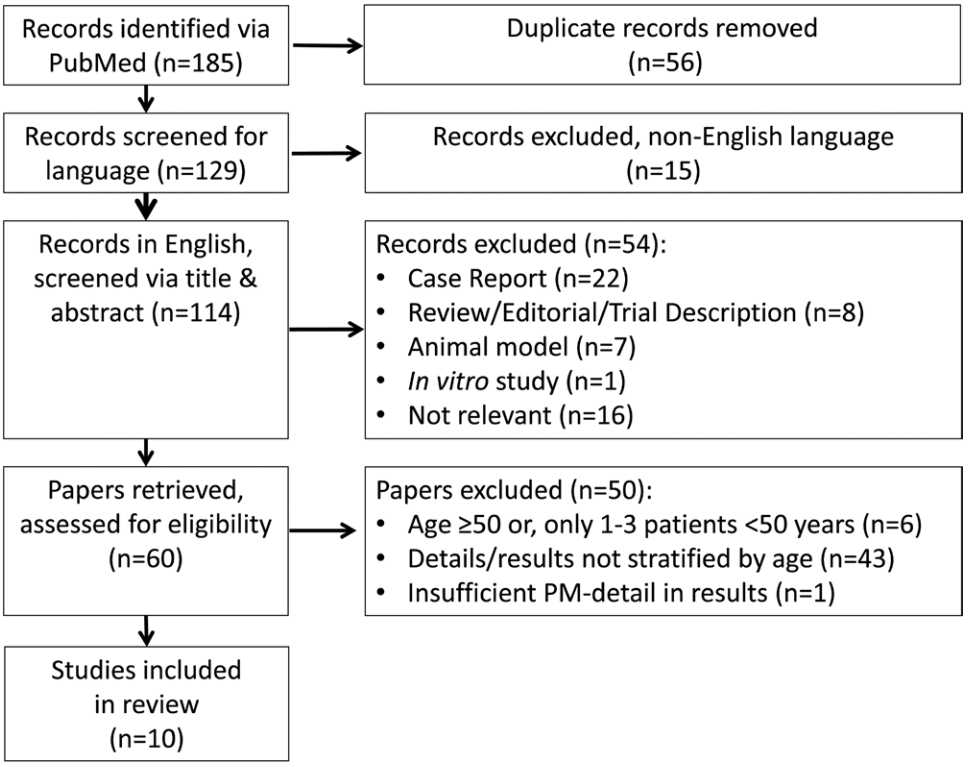
Fig. 1



PRISMA flow diagram describing the study selection process. PRISMA, Preferred Reporting Items for Systematic Reviews and Meta-Analyses.

little evidence to show age-related differences in treatment response (Yeo *et al.*, 2017; The Chicago Consensus on peritoneal surface malignancies, 2020; Kelly *et al.*, 2022; Morris *et al.*, 2022), and age of CPM patients does not appear to be a significant predictor of either total or severe complications (Macrì *et al.*, 2020). This may be a true reflection of the situation or may be due to a lack of accurate age stratification reporting in the literature.

Methods

This review followed guidelines from the Preferred Reporting Items for Systematic Reviews and Meta-Analyses extension for Scoping Reviews (Tricco *et al.*, 2018). PubMed was searched for publications that focused on CPM, where the population explicitly included younger- or early-onset CRC patients, with no other restrictions (e.g. date, study format). Searches were run in August 2022 and repeated in November 2022. The search terms and other details are available in Supplementary Materials, Supplemental digital content 1, *http://links.lww.com/EJCP/A390*.

Results

PubMed searches yielded 185 papers, of which 114 were unique papers published in the English language (Fig. 1). These 114 papers were screened by reading the title and abstract.

Fifty-four papers were excluded because they were case reports, reviews, editorials, trial descriptions, animal models, in-vitro studies, or not relevant for other reasons. Sixty papers were retrieved, read, and assessed for eligibility. One paper was ineligible because while the abstract mentioned the age distribution of CPM, the authors did not expand further in the main body of the paper. Forty-nine papers were excluded from the review for age-related reasons: six studies had 0–3 patients under age 50. Forty-three studies included patients under age 50 but did not present results stratified by age or did not stratify using an age ≤50 years old for stratification; one study provided above/below-age data but failed to include symbols (≥ or ≤) or descriptive text to indicate which group included the cutoff age (Sternberg *et al.*, 1994; Nakae *et al.*, 1995; Nakamura *et al.*, 1999; Akasu *et al.*, 2000; el-Ghazawy *et al.*, 2001; Luna-Pérez *et al.*, 2002; Al-Shamsi *et al.*, 2003; Kanemitsu *et al.*, 2003; Carmignani *et al.*, 2004; Lloyd *et al.*, 2006; Nervi *et al.*, 2006; Lawson *et al.*, 2008; Sobhani *et al.*, 2008; Song *et al.*, 2009; Aghili *et al.*, 2010; Lemmens *et al.*, 2011; Sjo *et al.*, 2011; Lieu *et al.*, 2014; Park *et al.*, 2014; Saluja *et al.*, 2014; Adachi *et al.*, 2015; Lam *et al.*, 2015; Sica *et al.*, 2015; Simkens *et al.*, 2015; 2016; Maillet *et al.*, 2016; Wang *et al.*, 2016; Cicero *et al.*, 2017; Hojo *et al.*, 2017; Patil *et al.*, 2017; Cigdem Arslan *et al.*, 2018; Kondo *et al.*, 2021; Melli *et al.*, 2021; Rieser *et al.*, 2021a, 2021b;

Table 1 Characteristics of included study in the current review

Author (year)	Country	Data period	Setting	Participants, total *n*	Younger age *n* (% total)	Age cutoff
Haleshappa *et al.* (2017)	India	2010–2014	Hospital	320	89 (28)	40
Hayes-Jordan *et al.* (2020)	USA	1991–2017	Hospital	859	94 (11)	25
Kaplan *et al.* (2019)	Turkey	2003–2015	Multiple hospitals	410	173 (17)	25
Kelly *et al.* (2022)	UK & Republic of Ireland	2000–2021	CPM Registry	1138	202 (18)	45
Lurvink *et al.* (2021)	Netherlands	January–June 2015	Cancer Registry	7233	~300 (4)*	50
Okuno *et al.* (1987)	Japan	1972–1984	Hospital	570	57 (10)	40
Rao *et al.* (1985)	USA	1964–1984	Hospital	30	30 (100)	25
Solomon *et al.* (2019)	USA	2007–2017	Hospital	98	43 (44)	50
van der Heide *et al.* (2021)	USA	2010–2016	National Database	124 587	1123 (1)	30
Zhou *et al.* (2022)	China	2017–2019	Hospital	140	46 (33)	50

CPM, colorectal peritoneal metastases.
*See Supplementary Table S3, Supplemental digital content 1, *http://links.lww.com/EJCP/A390*

Sharma *et al.*, 2021; Tabchouri *et al.*, 2021; Yang *et al.*, 2021; Zhou *et al.*, 2021; Flood *et al.*, 2022; Iwasaki *et al.*, 2022; McCleary *et al.*, 2022; Meyer *et al.*, 2022; Nagao *et al.*, 2022).

Ten studies with relevant age-stratified information on CPM were included in the review (Table 1). All 10 studies were retrospective in nature, albeit with additional follow-up in some studies (Rao *et al.*, 1985; Okuno *et al.*, 1987; Haleshappa *et al.*, 2017; Kaplan *et al.*, 2019; Solomon *et al.*, 2019; Hayes-Jordan *et al.*, 2020; Lurvink *et al.*, 2021; van der Heide *et al.*, 2021; Kelly *et al.*, 2022; Zhou *et al.*, 2022). Six studies analyzed single-hospital records (Rao *et al.*, 1985; Okuno *et al.*, 1987Haleshappa *et al.*, 2017; ; Solomon *et al.*, 2019Hayes-Jordan *et al.*, 2020; ; Zhou *et al.*, 2022), one study analyzed data from multiple hospitals combined (Kaplan *et al.*, 2019), two studies analyzed a single-country cancer database/registry (Lurvink *et al.*, 2021; van der Heide *et al.*, 2021) and one study analyzed data from a two-country dedicated CPM registry (Kelly *et al.*, 2022) (Table 1). Study publication dates ranged from 1985 through 2022. Four studies were based in the USA, while the six other studies were based in China, India, Japan, Netherlands, Turkey, and UK/Republic of Ireland (Table 1).

Nine studies compared younger/older age groups of patients with CPM, while one study described differences for age divisions within a younger cohort (age ≤ 25 years old, Fig. 2) (Kaplan *et al.*, 2019). There was limited consensus regarding the appropriate age division for young/early versus older ages; three studies used age 25, another three used age 50, two chose age 40, and two studies used age 30 or age 45 years old (Table 1, Fig. 2). There was also no consistent definition of age group even among studies choosing the same stratifying age: Lurvink *et al.* (2021) and Solomon *et al.* (2019) both used <50 versus ≥50, while Zhou *et al.* (2022) used ≤50 versus >50 (Fig. 2, Supplementary Table S1, Supplemental digital content 1, http://links.lww.csom/EJCP/A390). An additional challenge to comparing age ranges among studies was the lack of standardization. Studies reported ages using a mixture of mean, or median, with either true age range or interquartile range (IQR) or SD (Supplementary Table S1, Supplemental digital content 1, *http://links.lww.com/EJCP/A390*.).

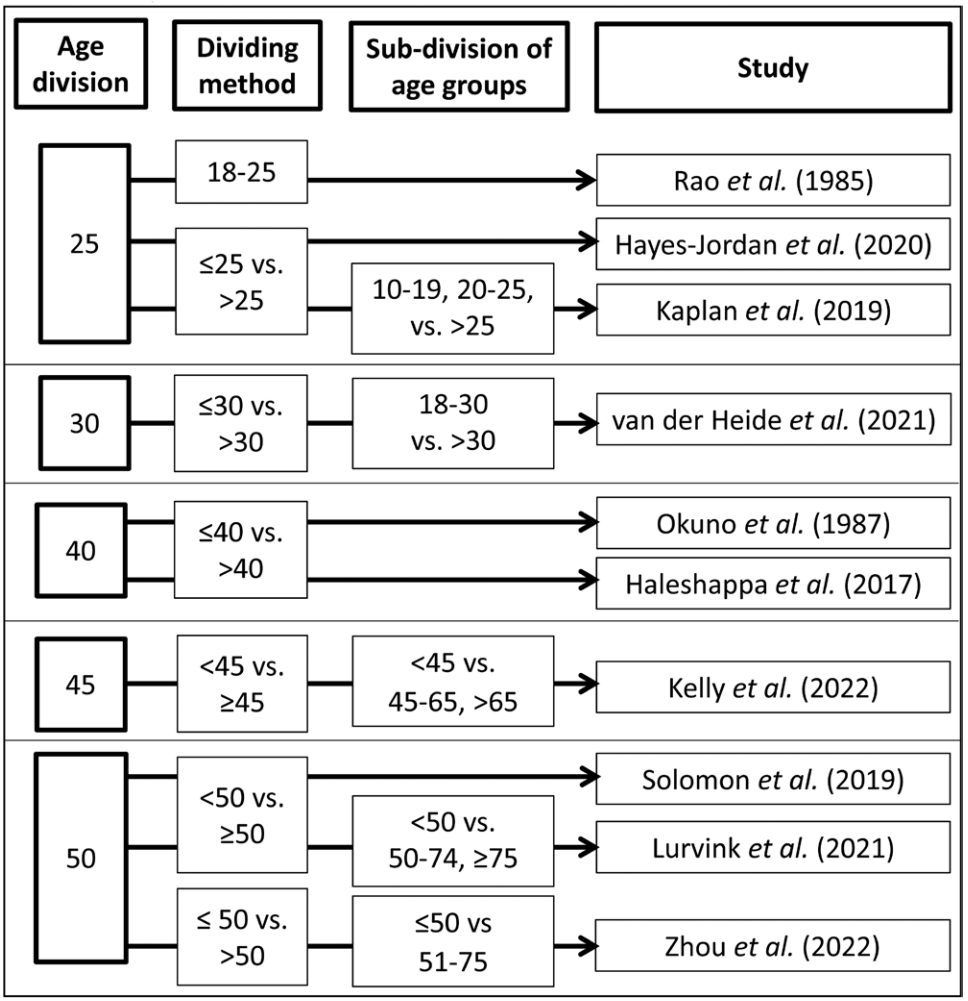
In all studies which divided their CRC cohorts at age 25 or 30, the younger age groups had a greater proportion of males with CPM. (Fig. 2, Supplementary Table S1, Supplemental digital content 1, *http://links.lww.com/EJCP/A390*) (Rao *et al.*, 1985; Kaplan *et al.*, 2019; Hayes-Jordan *et al.*, 2020; van der Heide *et al.*, 2021). Distribution of race/ethnicity was discussed in three of the four US-based studies (Rao *et al.*, 1985; Solomon *et al.*, 2019; van der Heide *et al.*, 2021) but none of the non-US-based studies discussed race/ethnicity. A greater proportion of younger African American patients developed CPM in two studies (20 and 16% of patients with CRC age ≤30 and <50 years, compared with 15 and 6% of CRC patients age >30 and ≥50 years, Supplementary Table S2, Supplemental digital content 1, *http://links.lww.com/EJCP/A390*.) (Solomon *et al.*, 2019; van der Heide *et al.*, 2021).

Studies with age-stratified proportions of CPM in general CRC populations showed a higher incidence of CPM in younger patients (Table 2): 25% versus 11% [10–19 vs. 20–25 years, (Kaplan *et al.*, 2019)]; 23% versus 2% [≤25 vs. >25 years, (Hayes-Jordan *et al.*, 2020)]; 14%, versus 1% [≤25 vs. >25 years, (Kaplan *et al.*, 2019)]; 28% versus 19% [18–30 vs. >30 years, (van der Heide *et al.*, 2021)]; 12% versus 4% [<40 vs. ≥40 years (Okuno *et al.*, 1987)].

A study of patients from a specialized CPM registry reported that extent of CPM was highest in the <45-year age group [median peritoneal cancer index (PCI) score = 8, IQR 11], and lowest for those age >65 years (median PCI score = 6, IQR 9) [Table 2, (Kelly *et al.*, 2022)]. This was in contrast with a hospital-based study which reported a lower burden of CPM in those under 50 (median PCI score = 9, IQR 4–17, <50 years; median PCI score = 10, IQR 6–21, ≥50 years) [Table 2, (Solomon *et al.*, 2019)].

Younger patients with CRC were more likely to develop metachronous CPM [hazard ratio (HR) = 1.63, 95% confidence interval (CI): 1.10–2.42, <50 vs. 50–74 years, Table 2, (Lurvink *et al.*, 2021)]. Younger high-risk

Fig. 2



Age division methods used in the included age-stratified studies.

patients (T4 tumors and/or lymph node involvement) were also more likely to develop metachronous CPM than older patients [HR = 1.91, 95% CI: 1.24–9.94, <50 vs. 50–74 years, Table 2, (Lurvink *et al.*, 2021)].

Discussion

Epidemiology of colorectal peritoneal metastases

CPM develops in around 10–30% of those with CRC (Kerscher *et al.*, 2013; Desai and Moustarah, 2022). There are limitations in parsing out epidemiological trends by age as prior studies do not represent contemporary treatment and do not use standardized age groupings. In a study of 16 962 males (median age, 69.7 years) who were diagnosed with metastases from their colorectal primary during 1987–2012, liver metastases were most common (72%), followed by lung (32%) and peritoneum (13%) (Riihimäki *et al.*, 2018). Similar proportions were reported in 14 429 females (median age, 71.3 years) (Riihimäki *et al.*, 2018). Smaller studies reporting metastases in younger patients show an increasing incidence of CPM as age decreases. Okuno *et al.* (1987) reported CPM in 12.5% of those under 40, compared with 4.3% in those ≥40. Hayes-Jordan *et al.* (2020) reported a 23% incidence of CPM in 41 patients with colon cancer aged 10–25 while lung and liver metastases occurred in 4 and 3% respectively. Kaplan *et al.* (2019) reported different metastatic profiles for patients aged 20–25 and 10–19: of 141 patients aged 20–25 (median age 23), 13% had liver metastases, 11% CPM, and 3% lung metastases; while in those aged 10–19 (median age 18) metastasis to the peritoneum was most common (25% CPM, 22% liver metastases, 6% lung metastases).

A French study of 9134 patients from 1976 to 2011 found incidence of synchronous and metachronous CPM of 6 and 7% respectively, with no difference by age (Quere *et al.*, 2015). More recent data from the USA (2000–2011) determined for those under 50, the incidence of distant (metastatic) disease is increasing at a faster rate than

Table 2 Findings related to colorectal peritoneal metastases of included studies in the current review

Author (year)	Findings related to CPM
Haleshappa *et al.* (2017)	Younger patients had shorter survival than older patients (< 40 vs. > 40 years, 23 vs. 35 months, $P = 0.0029$). Younger patients were prone to aggressive CRC; 36% had Stage IV cancer. The liver was the most common site of metastasis ($n = 15$, 17%). Eleven patients <40 had CPM (12%). There was no significant difference in survival with respect to the site of metastases.
Hayes-Jordan *et al.* (2020)	Forty-nine (52%) patients aged ≤25 years had Stage IV CRC; the peritoneum was their most common metastatic site. There were highly significant differences between CPM incidence in younger and older patients: 23% of patients ≤25 years versus 2% patients >25 years.
Kaplan *et al.* (2019)	CPM was more common in younger patients: (14%, $n = 24$ vs. 1% $n = 2$; ≤25 vs. >25 years, $P < 0.001$). Adolescents showed the highest rate of CPM: 25% of adolescents (8/32, age 10–19) versus 11% of young adults (16/141, age 20–25). Presence of metastases was the only significant factor affecting survival (OR = 4.97, 95% CI: 3.00–8.22, $P < 0.001$).
Kelly *et al.* (2022)	The extent of CPM was highest for patients in the <45-year age group (median PCI 8, IQR 11), and lowest for those aged>65 years (median PCI 6, IQR 9). Survival was shortest in the <45-year age group. Patients with complete cytoreduction (CC) CC0 status after surgery and HIPEC treatment (i.e. no visible CPM remaining) had a median survival of 33, 40, and 39 months for age groups <45, 45–65, and >65 years respectively.
Lurvink *et al.* (2021)	More young patients developed metachronous CPM (HR = 1.63, 95% CI: 1.10–2.42, $P = 0.015$, <50 vs. 50–74 years). High-risk younger patients (i.e. T4 tumor stage and/or lymph node involvement) were more likely to develop metachronous CPM after primary tumor resection (HR = 1.91, 95% CI: 1.24–2.94, $P = 0.003$, <50 vs. 50–74 years).
Okuno *et al.* (1987)	CPM was three times more common in younger patients (12% vs. 4%, <40 vs. ≥40 years). Overall survival rate was lower for younger CPM patients, but survival rate among those who underwent curative resection rate was similar for both age groups.
Rao *et al.* (1985)	Twenty younger patients (67%, ages 18–25 years, median age 15 years) had peritoneal metastases, and only three patients had no metastases (10%). Authors attribute advanced metastatic) disease at diagnosis in 26 patients (87%) to delayed diagnosis due to 'vague abdominal pain symptoms' combined with aggressive mucinous CRC variants ($n = 25$, 83%).
Solomon *et al.* (2019)	Among patients of African American origin, synchronous CPM was present in all younger CRC patients (7/7100%, <50 years); and 67% of older CRC patients (2/3, 67%, ≥50 years). For all races combined, rate of synchronous CPM was 63% (27/43, <50 years) and 42% (23/55, ≥50 years). Median PCI score was 9 (IQR 4–17) for younger CPM patients, and 10 (IQR 6–21) for older CPM patients, that is, lesser burden of CPM in younger age group. There was longer median survival for <50 versus ≥50-year age groups whether CRS/HIPEC treatment was considered or not. In multivariate analysis, the strongest predictor of survival was PCI score (HR = 1.12, 95% CI: 1.07–1.17, $P < 0.001$) followed by younger age group (HR = 0.43, 95% CI: 0.21–0.91, $P = 0.026$).
van der Heide *et al.* (2021)	CPM was found in 28% of younger patients (320/1123, ≤30 years) and 19% of older patients (22 897/123 464, >30 years).
Zhou *et al.* (2022)	Almost all younger patients (44/46, 96%, ≤50 years) had synchronous CPM, whereas 51% of older patients had synchronous CPM (48/94, >50 years). Despite differences in CPM incidence, age groups had equivalent survival rates following CRS/HIPEC treatments.

CC, complete cytoreduction score; CI, confidence interval; CPM, colorectal peritoneal metastases; CRC, colorectal cancer; CRS, cytoreductive surgery; HIPEC, hyperthermic intraperitoneal chemotherapy; HR, hazard ratio; IQR, interquartile range; PCI, peritoneal cancer index; OR, odds ratio.

the incidence of localized or regional cancer (3% vs. 1% increase per year) (Yeo *et al.*, 2017).

In a study of cancer registry data (1976–2011), factors associated with the incidence of synchronous CPM included being female, having a right-sided tumor, mucinous colorectal adenocarcinoma, and acute presentation as an emergency due to obstruction or perforation (Quere *et al.*, 2015). In a hospital-based study of data from the period 1986–2009, Kerscher *et al.* (2013) found that being less than 62 years of age, having a left-sided tumor, and having N2- and/or T4-status, were risk factors for developing metachronous CPM. Kanemitsu *et al.* (2003) (1965–1994 data) reported that Japanese patients with mucinous adenocarcinoma were more likely to have CPM (19.6%) than those with non-mucinous adenocarcinoma (5.6%). Mucinous adenocarcinomas may be more common in patients with Lynch syndrome (hereditary nonpolyposis CRC) (Kanemitsu *et al.*, 2003).

Barriuso *et al.* (2021) analyzed 30 matched samples of CPM and primary colorectal tumor tissue from patients aged 34–75 years (mean age 59.5 years) and found a suite of 20 genes where five genes were downregulated and 15 were upregulated when CPM was present. Nerve growth factor receptor, IL6, and cluster of differentiation 36 were upregulated in synchronous CPM (Barriuso *et al.*, 2021). After adjusting for cancer stage, age, and sex, the 20-gene regulation pattern was associated with an adjusted HR (aHR) for overall survival [aHR high-risk group (vs. low-risk) = 2.32, 95% CI: 1.69–3.19] and disease-free survival (aHR = 2.08, 95% CI: 1.50–2.91) (Barriuso *et al.*, 2021). While these genes appear to be associated with CPM incidence, causality cannot be determined. A high positivity rate of Ki67 in primary colorectal tumor tissue may also be related to cancer recurrence including metachronous CPM (Tsubomoto *et al.*, 2023).

Three possible reasons to explain the higher incidence of CPM in younger patients are firstly some cancers tend to be more biologically aggressive in the young, secondly, there is little organized CRC screening below age 45 and so tumors may be more advanced at presentation, and thirdly CPM may be under-diagnosed in older patients due to less intensive investigation in those whose treatment options may be regarded as limited.

Epidemiology of colorectal peritoneal metastases sub-types

Signet ring cell cancer (SRCC) tends to be detected at a late stage, resulting in a poor prognosis (Tung *et al.*, 1996). SRCC cells are shaped like a signet ring; the 'signet' portion of the

ring is formed by the nucleus pushing into the cell wall due to internal pressure from excess intracytoplasmic mucin (Benesch and Mathieson, 2020). About 20% of 80 000 SRCC cases reported in the US during 1975–2016 were located in the colon (15.3%) and rectum (4.3%); gastric cancer had the highest burden of SRCC (56.8%) (Benesch and Mathieson, 2020).

SRCC-CRC is rare in the general population, occurring in less than 3% of those with CRC. SRCC-CRC is more common in early-onset CRC (diagnosed before age 50) than in later-onset CRC. An analysis of 1077 patients in Taiwan from 1985 to 1990 showed that SRCC arising from a colorectal primary was present in 16% of patients aged <40 years but only 2% of patients aged 40–69 years (Tung *et al.*, 1996).

SRCC tumors are highly aggressive with rapid proliferation, frequently present with bowel perforation, and exhibit significant perineural and lymphovascular invasion making them more likely to metastasize. The incidence of CPM is higher in those with SRCC than those without SRCC (Tung *et al.*, 1996; Hugen *et al.*, 2014; Lurvink *et al.*, 2021).

Inconsistent reporting in colorectal peritoneal metastases studies

Inconsistent definitions for synchronous and metachronous colorectal peritoneal metastases

Data from the 10 studies which met inclusion criteria showed a trend of younger age being associated with the incidence of CPM (Table 2); however, differences in reporting patient/tumor characteristics and between the presentation of study results prevented most direct comparisons. For example, there was no consensus on the timeframe to differentiate synchronous and metachronous CPM (Okuno *et al.*, 1987; Solomon *et al.*, 2019; Hayes-Jordan *et al.*, 2020; Lurvink *et al.*, 2021; Kelly *et al.*, 2022; Zhou *et al.*, 2022).

Inconsistent reporting of biomarkers, gene expression, and tumor histology of colorectal peritoneal metastases

Studies reported CPM distribution for a variety of biomarkers, gene expression, and types of tumor histology, but not consistently, which prevented meaningful comparisons (Rao *et al.*, 1985; Zhou *et al.*, 2022). The status of mismatch repair proficiency/deficiency was reported infrequently (van der Heide *et al.*, 2021). Solomon *et al.* (2019) reported proportions of CPM patients with SRCC; van der Heide *et al.* (2021) and Rao *et al.* (1985) only reported proportions of patients with 'mucinous' cells, and Zhou *et al.* (2022) combined the two categories and reported proportions of patients with mucinous and/or SRCC.

Inconsistent definitions for early- and regular-onset colorectal cancer

No consensus exists on what defines early-onset CRC. The 10 studies included in this review used seven different reporting cutoff ages/methods when they reported 'early' and 'regular' onset of CRC. Details of age at CRC and/or CPM diagnosis were available for each study, however, there was no consensus on how the diagnosis age should be reported, for example, mean or median, actual range, or IQR. Some studies failed to state if the age provided was a mean or a median. These types of issues also arose for studies reporting follow-up and survival time. A final caveat faced when trying to compare results (e.g. risks, HRs) was the possibility that differences in analyzing data, for example, variations in adjustment variables, could be clouding results (Supplementary Table S4, Supplemental digital content 1, *http://links.lww.com/EJCP/A390*). Not all studies reported adjustment variables or explained how missing data was treated. These are important considerations when one tries to perform a meta-analysis (Supplementary Table S4, Supplemental digital content 1, *http://links.lww.com/EJCP/A390*).

Forty-three papers were excluded because they failed to stratify results by age, preventing us from conducting a meta-analysis comparing early-onset and regular-onset CRC. Retrospective analyses have the limitation that researchers can only report on data that was recorded: study authors may have no control/choice over the types of data available for analysis. We also acknowledge that the increasing incidence of early-onset CRC is a relatively recent development, so reporting CPM results stratified by age was not a natural priority in the past. Thus, while some studies located in PubMed searches mentioned age-related differences in CPM, the published results and data did not stratify age-associated PM differences. Results of CPM survival analyses were frequently reported in figures; without percentages or other numerical data only differences in survival trends could be inferred.

Future research

We recommend that standardized age-stratified studies are undertaken to find which factors are associated with developing synchronous and metachronous CPM. This will help guide personalized surveillance in populations at risk, target early CRC screening for those at higher risk of CPM, and potentially allow earlier treatment (Perea and Winter, 2023). Standardizing the definition of metachronous metastasis for patients with CPM would clarify survival outcomes.

Incidence of CPM stratified by race/ethnicity was given in only three of our 10 studies hence there is an opportunity to reevaluate existing data, in addition to ensuring race/ethnicity is reported in the future if this is allowed in the relevant country. Some countries do not collect data on race and/or ethnicity for historic and/or socio-cultural reasons, and instead, may collect data on country of birth (Ambrosetti and Cela, 2015; Balestra and Fleischer, 2018; Stillwell, 2022).

Conclusion

This review reported a higher proportion of CPM in young patients with CRC, compared to older CRC patients, but a direct comparison of variables was not possible due to inconsistent reporting. Concerted efforts to standardize reporting with a minimum dataset for patients with CPM would enhance the potential for comparative analyses. Standardized age-stratification of CPM should be a standard feature of future studies; we recommend <50 and ≥50 years at this time, as routine CRC screening in the US started at 50 years of age until recently. Recently, the recommended age to start CRC screening in the US was reduced to 45 years; this may eventually become the age below which CRC is defined as early onset. We recommend reporting CPM by gender within the age strata.

The Chicago Consensus on Peritoneal Surface Malignancies called for standardized approaches to the management and treatment of CPM (The Chicago Consensus on peritoneal surface malignancies, 2020). We call for standardized approaches to reporting CPM to enable the comparison and pooling of results and to accelerate the process of finding modifiable risk factors and effective treatments.

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Conflicts of interest

T.J.G. is a consultant for Tempus Labs, BillionToOne, and Pfizer Oncology. D.Q.H. is on the advisory board for Eisai and Gilead. These entities had no role in the design of the study; in the collection, analyses, or interpretation of data; in the writing of the manuscript; or in the decision to publish the results. All other authors declare they have no conflict of interest.

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