**Supplementary Table 1: Database searched from PubMed (until April 2022)**

|  |  |
| --- | --- |
| **#** | **Searches** |
| 1 | "Colonic Neoplasms"[Mesh] |
| 2 | "colonic neoplasm"[Title/Abstract] OR "neoplasm colonic"[Title/Abstract] OR "neoplasms colonic"[Title/Abstract] OR "colon neoplasms"[Title/Abstract] OR "colon neoplasm"[Title/Abstract] OR "neoplasm colon"[Title/Abstract] OR "neoplasms colon"[Title/Abstract] OR "cancer of colon"[Title/Abstract] OR "colon cancers"[Title/Abstract] OR "colon cancer"[Title/Abstract] OR "cancer colon"[Title/Abstract] OR "cancers colon"[Title/Abstract] OR "cancer of the colon"[Title/Abstract] OR "colonic cancer"[Title/Abstract] OR "cancer colonic"[Title/Abstract] OR "cancers colonic"[Title/Abstract] OR "colonic cancers"[Title/Abstract] OR "colon adenocarcinoma"[Title/Abstract] OR "adenocarcinoma colon"[Title/Abstract] OR "adenocarcinomas colon"[Title/Abstract] OR "colon adenocarcinomas"[Title/Abstract] |
| 3 | 1 OR 2 |
| 4 | "Neoadjuvant Therapy"[Mesh] |
| 5 | preoperative chemotherapy[Title/Abstract] |
| 6 | (((((((((((((((((((Neoadjuvant Therapies[Title/Abstract]) OR (Therapy, Neoadjuvant[Title/Abstract])) OR (Neoadjuvant Treatment[Title/Abstract])) OR (Neoadjuvant Treatments[Title/Abstract])) OR (Treatment, Neoadjuvant[Title/Abstract])) OR (Neoadjuvant Systemic Therapy[Title/Abstract])) OR (Neoadjuvant Systemic Therapies[Title/Abstract])) OR (Systemic Therapy, Neoadjuvant[Title/Abstract])) OR (Therapy, Neoadjuvant Systemic[Title/Abstract])) OR (Neoadjuvant Systemic Treatment[Title/Abstract])) OR (Neoadjuvant Systemic Treatments[Title/Abstract])) OR (Systemic Treatment, Neoadjuvant[Title/Abstract])) OR (Treatment, Neoadjuvant Systemic[Title/Abstract])) OR (Neoadjuvant Chemotherapy[Title/Abstract])) OR (Chemotherapy, Neoadjuvant[Title/Abstract])) OR (Neoadjuvant Chemotherapies[Title/Abstract])) OR (Neoadjuvant Chemotherapy Treatment[Title/Abstract])) OR (Chemotherapy Treatment, Neoadjuvant[Title/Abstract])) OR (Neoadjuvant Chemotherapy Treatments[Title/Abstract])) OR (Treatment, Neoadjuvant Chemotherapy[Title/Abstract]) |
| 7 | 4 OR 5 OR 6 |
| 8 | 3 AND 7 |
| **Total hits** | **624** |

**Supplementary Table 2: Database searched from Embase (until April 2022)**

|  |  |
| --- | --- |
| **#** | **Searches** |
| 1 | 'colon cancer'/exp |
| 2 | ‘colonic neoplasm’:ti,ab OR ‘neoplasm colonic’:ti,ab OR ‘neoplasms colonic’:ti,ab OR ‘colon neoplasms’:ti,ab OR ‘colon neoplasm’:ti,ab OR ‘neoplasm colon’:ti,ab OR ‘neoplasms colon’:ti,ab OR ‘cancer of colon’:ti,ab OR ‘colon cancers’:ti,ab OR ‘colon cancer’:ti,ab OR ‘cancer colon’:ti,ab OR ‘cancers colon’:ti,ab OR ‘cancer of the colon’:ti,ab OR ‘colonic cancer’:ti,ab OR ‘cancer colonic’:ti,ab OR ‘cancers colonic’:ti,ab OR ‘colonic cancers’:ti,ab OR ‘colon adenocarcinoma’:ti,ab OR ‘adenocarcinoma colon’:ti,ab OR ‘adenocarcinomas colon’:ti,ab OR ‘colon adenocarcinomas’:ti,ab |
| 3 | 1 OR 2 |
| 4 | 'neoadjuvant chemotherapy'/exp |
| 5 | 'preoperative chemotherapy'/exp |
| 6 | 'neoadjuvant therapies':ti,ab OR 'therapy, neoadjuvant':ti,ab OR 'neoadjuvant treatment':ti,ab OR 'neoadjuvant treatments':ti,ab OR 'treatment, neoadjuvant':ti,ab OR 'neoadjuvant systemic therapy':ti,ab OR 'neoadjuvant systemic therapies':ti,ab OR 'systemic therapy, neoadjuvant':ti,ab OR 'therapy, neoadjuvant systemic':ti,ab OR 'neoadjuvant systemic treatment':ti,ab OR 'neoadjuvant systemic treatments':ti,ab OR 'systemic treatment, neoadjuvant':ti,ab OR 'treatment, neoadjuvant systemic':ti,ab OR 'neoadjuvant chemotherapy':ti,ab OR 'chemotherapy, neoadjuvant':ti,ab OR 'neoadjuvant chemotherapies':ti,ab OR 'neoadjuvant chemotherapy treatment':ti,ab OR 'chemotherapy treatment, neoadjuvant':ti,ab OR 'neoadjuvant chemotherapy treatments':ti,ab OR 'treatment, neoadjuvant chemotherapy':ti,ab |
| 7 | 4 OR 5 OR 6 |
| 8 | 3 AND 7 |
| **Total hits** | **2368** |

**Supplementary Table 3: Database searched from Web of Science (until April 2022)**

|  |  |
| --- | --- |
| **#** | **Searches** |
| 1 | (((((((((((((((((((((TS=(Colonic Neoplasms)) OR TS=(Colonic Neoplasm)) OR TS=(Neoplasm, Colonic)) OR TS=(Neoplasms, Colonic)) OR TS=(Colon Neoplasms)) OR TS=(Colon Neoplasm)) OR TS=(Neoplasm, Colon)) OR TS=(Neoplasms, Colon)) OR TS=(Cancer of Colon)) OR TS=(Colon Cancers)) OR TS=(Colon Cancer)) OR TS=(Cancer, Colon)) OR TS=(Cancers, Colon)) OR TS=(Cancer of the Colon)) OR TS=(Colonic Cancer)) OR TS=(Cancer, Colonic)) OR TS=(Cancers, Colonic)) OR TS=(Colonic Cancers)) OR TS=(Colon Adenocarcinoma)) OR TS=(Adenocarcinoma, Colon)) OR TS=(Adenocarcinomas, Colon)) OR TS=(Colon Adenocarcinomas) |
| 2 | ((((((((((((((((((((TS=(Preoperative Chemotherapy)) OR TS=(Neoadjuvant Therapies)) OR TS=(Therapy, Neoadjuvant)) OR TS=(Neoadjuvant Treatment)) OR TS=(Neoadjuvant Treatments)) OR TS=(Treatment, Neoadjuvant)) OR TS=(Neoadjuvant Systemic Therapy)) OR TS=(Neoadjuvant Systemic Therapies)) OR TS=(Systemic Therapy, Neoadjuvant)) OR TS=(Therapy, Neoadjuvant Systemic)) OR TS=(Neoadjuvant Systemic Treatment)) OR TS=(Neoadjuvant Systemic Treatments)) OR TS=(Systemic Treatment, Neoadjuvant)) OR TS=(Treatment, Neoadjuvant Systemic)) OR TS=(Neoadjuvant Chemotherapy)) OR TS=(Chemotherapy, Neoadjuvant)) OR TS=(Neoadjuvant Chemotherapies)) OR TS=(Neoadjuvant Chemotherapy Treatment)) OR TS=(Chemotherapy Treatment, Neoadjuvant)) OR TS=(Neoadjuvant Chemotherapy Treatments)) OR TS=(Treatment, Neoadjuvant Chemotherapy) |
| 3 | 1 AND 2 |
| **Total hits** | **2057** |

**Supplementary Table 4: Database searched from Cochrane Library (until April 2022)**

|  |  |
| --- | --- |
| **#** | **Searches** |
| 1 | MeSH descriptor: [Colonic Neoplasms] explode all trees |
| 2 | (Colonic Neoplasm):ti,ab,kw OR (Neoplasm, Colonic):ti,ab,kw OR (Neoplasms, Colonic):ti,ab,kw OR (Colon Neoplasms):ti,ab,kw OR (Colon Neoplasm):ti,ab,kw OR (Neoplasm, Colon):ti,ab,kw OR (Neoplasms, Colon):ti,ab,kw OR (Cancer of Colon):ti,ab,kw OR (Colon Cancers):ti,ab,kw OR (Colon Cancer):ti,ab,kw OR (Cancer, Colon):ti,ab,kw OR (Cancers, Colon):ti,ab,kw OR (Cancer of the Colon):ti,ab,kw OR (Colonic Cancer):ti,ab,kw OR (Cancer, Colonic):ti,ab,kw OR (Cancers, Colonic):ti,ab,kw OR (Colonic Cancers):ti,ab,kw OR (Colon Adenocarcinoma):ti,ab,kw OR (Adenocarcinoma, Colon):ti,ab,kw OR (Adenocarcinomas, Colon):ti,ab,kw OR (Colon Adenocarcinomas):ti,ab,kw |
| 3 | 1 OR 2 |
| 4 | MeSH descriptor: [Neoadjuvant Therapy] explode all trees |
| 5 | (Neoadjuvant Therapies):ti,ab,kw OR (Therapy, Neoadjuvant):ti,ab,kw OR (Neoadjuvant Treatment):ti,ab,kw OR (Neoadjuvant Treatments):ti,ab,kw OR (Treatment, Neoadjuvant):ti,ab,kw OR (Neoadjuvant Systemic Therapy):ti,ab,kw OR (Neoadjuvant Systemic Therapies):ti,ab,kw OR (Systemic Therapy, Neoadjuvant):ti,ab,kw OR (Therapy, Neoadjuvant Systemic):ti,ab,kw OR (Neoadjuvant Systemic Treatment):ti,ab,kw OR (Neoadjuvant Systemic Treatments):ti,ab,kw OR (Systemic Treatment, Neoadjuvant):ti,ab,kw OR (Treatment, Neoadjuvant Systemic):ti,ab,kw OR (Neoadjuvant Chemotherapy):ti,ab,kw OR (Chemotherapy, Neoadjuvant):ti,ab,kw OR (Neoadjuvant Chemotherapies):ti,ab,kw OR (Neoadjuvant Chemotherapy Treatment):ti,ab,kw OR (Chemotherapy Treatment, Neoadjuvant):ti,ab,kw OR (Neoadjuvant Chemotherapy Treatments):ti,ab,kw OR (Treatment, Neoadjuvant Chemotherapy):ti,ab,kw |
| 6 | 4 OR 5 |
| 7 | 3 AND 6 |
| **Total hits** | **209** |

**Supplementary Table 5: Full-text articles excluded**

|  |  |  |
| --- | --- | --- |
| **Reasons** | **Number of studies** | **References** |
| Single arm | 10 | (1-10) |
| Cases with rectal cancer | 2 | (11, 12) |
| Incomplete data | 8 | (13-20) |
| Without outcomes of interest | 1 | (21) |
| Only protocol | 11 | (22-32) |

**References of excluded studies**

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15. Hussein MK, Al-Quda G, Keane CA, Marar O, Blebea J. Trends and Outcomes of Using Neoadjuvant Systemic Therapy for Clinical T4b-M0 Colon Cancer in the US: An Analysis of the National Cancer Database. Journal of the American College of Surgeons. 2021;233(5):S64-S5.

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**Supplementary Table 6: Methodological quality and risk of bias**

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| **Study** | **Modified Jadad Score** | **New Castle Ottawa (NOS)** | | | |
| **Selection**  **(0-4)** | **Comparability**  **(0-2)** | **Outcome**  **(0-3)** | **Total**  **(0-9)** |
| Foxtrot,  UK,2012 | 5 | / | / | / | / |
| Dehal,  USA,2018 | / | 2 | 2 | 3 | 7 |
| Morton,  UK,2019 | 5 | / | / | / | / |
| Gooyer,  NLD,2020 | / | 2 | 2 | 3 | 7 |
| Karoui,  France,2020 | 4 | / | / | / | / |
| Karoui,  France,2021 | 4 | / | / | / | / |
| Silva,  USA,2021 | / | 2 | 2 | 3 | 7 |
| Laursen,  Denmark,2022 | / | 2 | 2 | 3 | 7 |