

Supplemental Tables for:

Association of polypharmacy with colorectal cancer survival among older patients

Ben Schöttker et al.

Table S1. List of ATC codes or ATC code groups of combination drugs containing 2 or 3 active substances for the modified polypharmacy definition

Combination drugs	ATC codes
Containing 2 active substances	<p>A03C, A03D, A03E, A05C, A07C, A11A, A11J, C02N, C03E, C04B, C07B, C07C, C07E, C07G, D06C, D07B, D07C, D07X, G03E, G03F, H02B, J01R, M01B, N06C, R05F, R05G, S02C, S03C,</p> <p>A02AD, A02AF, A02AG, A02AX, A05AC, A09AC, A10BD, A11CB, A11EB, A11EC, A11ED, A11EX, A11GB, A12AX, B03AD, C01EX, C02LB, C02LE, C02LF, C02LK, C02LL, C02LN, C02LX, C03AB, C03AH, C03AX, C03BB, C03BK, C03CB, C07FA, C09BA, C09BB, C09DA, C09DB, C10BA, C10BB, C10BE, C10BP, D10AA, G01BA, G01BC, G01BD, G01BF, G02AC, G03AA, G03AB, G03CC, G03HB, J01CR, J01EE, L01XY, N01AG, N02AG, N05CB, N05CX, R01AB, R03AH, R03AK, R03AL, R03DB, R06AK, S01BB, S01BX, S01CB, S01CC, V06DA, V06DB, V06DD, V06DE, V06DX,</p> <p>A01AA30, A01AA51, A01AB50, A01AB53, A01AB57, A01AB62, A01AB75, A01AB76, A01AB78, A01AB84, A01AB85, A01AB88, A01AB90, A01AC54, A01AD50, A01AD65, A01AD69, A01AD71, A01AE51, A01AE52, A01AE53, A01AE54, A01AE55, A01AH20, A01AP30, A01AP50, A01AP52, A02AA10, A02AB10, A02AC10, A02AD01, A02AD10, A02AH20, A02BA51, A02BA53, A02BX50, A02BX51, A02BX62, A02BX63, A02BX70, A02BX71, A02BX77, A02XA52, A02XA53, A02XH20, A02XH50, A02XP30, A03AB53, A03AH20, A03AP30, A03AX20, A03AX50, A03AX58, A03AX63, A03BA20, A03FA51, A03FA54, A03FP30, A03HH20, A04AB52, A04AB54, A04AB55, A04AB56, A04AB57, A04AB58, A04AD50, A04AD51, A04AD54, A04AH20, A05AA20, A05AA54, A05AA55, A05AB20, A05AH20, A05AP30, A05AX50, A05BA09, A05BA50, A05BA60, A05BA61, A05BA63, A05BA66, A05BA67, A05BA71, A05BH20, A05BP51, A06AA51, A06AB20, A06AB30, A06AB52, A06AB53, A06AB56, A06AB57, A06AB58, A06AB59, A06AB60, A06AB63, A06AC51, A06AC53, A06AC55, A06AC59, A06AD10, A06AD61, A06AD65, A06AG03, A06AG10, A06AG11, A06AG20, A07AA51, A07AA54, A07AA54, A07AB50, A07AX51, A07AX55, A07BA51, A07BB51, A07BC30, A07BC51, A07BC54, A07BC55, A07BP51, A07DA51, A07DA52, A07DA53, A07DA54, A07EA51, A07FA20, A07FA50, A07FA51, A07FA52, A07XA50, A07XA51, A07XH20, A07XP30, A08AA53, A08AA53, A08AA56, A08AA57, A08AA63, A08AB20, A08AH20, A09AA50, A09AA52, A09AA57, A09AB50, A09AH20, A09AX50, A10AB30, A10AC30, A10AD06, A10AD30, A10AE30, A10AE56, A10BH51, A10XH20, A10XP30, A11CC20, A11CC80, A11DB01, A12AA20, A12AH20, A12BA30, A12BA51, A12BA52, A12BA54, A12CC30, A12CC50, A12CD51, A12CD52, A12CH20, A12CX50, A13AH20, A13AP30, A14AA50, A15AA50, A15AA51, A16AA50, B01AB51, B01AB63, B01AC30, B01AC34, B01AC36, B01AC56, B01AD51, B02BC30, B02BC51, B02BC57, B02BD01, B02BD06, B02BP50, B03AA20, B03AA50, B03AE03, B03AE10, B03BA51, B03BA53, B03BB51, B03XH20, B05AA51, B05AA55, B05AA56, B05AA57, B05BA10, B05BB04, B05BB10, B05BB53, B05BC51, B05BC53, B05CA10, B05CB10, B05CX10, B05DB50, B05XA06, B05XA30, B05XA31, B05XC30, B05XX03, B05ZA50, B05ZB50, B06AA02, B06AA55, C01AA20, C01AA52, C01AA54, C01AA55, C01AA56, C01AA58, C01AB51, C01AC51, C01AC54, C01AC55, C01AC71, C01AH20, C01AH50, C01AP30, C01AP50, C01AP51, C01AP52, C01AP53, C01BA50, C01BA51, C01BA70, C01BA71, C01CA30, C01CA50, C01CA51, C01CA55, C01CA58, C01CA68, C01CA81, C01CB51, C01CB54, C01CH20, C01DA20, C01DA52, C01DA54, C01DA55, C01DA57, C01DA58, C01DA59, C01DA63, C01DA70, C01DX51, C01DX52, C01DX53, C01DX54, C01DX55, C01DX72, C01EH20, C01EH50, C01EP30, C01EP51, C02AA03, C02AA52, C02AA53, C02AA57, C02AP51, C02KH20, C02KP30, C02KP52, C02LA01, C02LA02, C02LA03, C02LA04, C02LA07, C02LA08, C02LA09, C02LA50, C02LC01, C02LC05, C02LG01, C02LG02, C02LG03, C03BA82, C03XH20, C03XP30, C04AA52, C04AA81, C04AC20, C04AC51, C04AC52, C04AC53, C04AC58, C04AD50, C04AD54, C04AD56, C04AE51, C04AE54, C04AF51, C04AH20, C05AA51, C05AA54, C05AA55, C05AA56, C05AA58, C05AA60, C05AA61, C05AA62, C05AA64, C05AA65, C05AD20, C05AD51, C05AD53, C05AD54, C05AD55, C05AD58, C05AD59, C05AD60, C05AD61, C05AD62, C05AF51, C05AH20, C05AP30, C05AP52, C05AX02, C05AX03,</p>

Combination drugs ATC codes

Containing 2 active substances

C05AX13, C05BA51, C05BA53, C05BA54, C05BA55, C05BB56, C05BP30, C05BP51, C05BP52, C05BX51, C05BZ20, C05BZ59, C05CA20, C05CA51, C05CA53, C05CA54, C05CA57, C05CA59, C05CH20, C05CH50, C05CP30, C05CP50, C05CP51, C05CP52, C05CP53, C05CP54, C05CX54, C06AA50, C06AH20, C07AA57, C07AB52, C07AB57, C07FB02, C07FB03, C07FB07, C07FB22, C07FB23, C07FB24, C07FB26, C08CA55, C08DA51, C08DA81, C08GA01, C08GA02, C08GA23, C09DX02, C09XA52, C09XA53, C10AD52, C10BX01, C10BX02, C10BX03, C10BX05, D01AA20, D01AA51, D01AA91, D01AC20, D01AC51, D01AC52, D01AC53, D01AC60, D01AE20, D01AE51, D01AE54, D01AE62, D01AE68, D01AE74, D01AE75, D02AA20, D02AB51, D02AB52, D02AC52, D02AC54, D02AE51, D02AP53, D02AX20, D02BA20, D02BB51, D03AA51, D03AC50, D03AH20, D03AP30, D03AP51, D03AP52, D03AP54, D03AP57, D03AX50, D03AX53, D03AX69, D03AX70, D03AX71, D03AX77, D03AX79, D03BA20, D03BA50, D03BA52, D03BA53, D03BA54, D03BA55, D04AA82, D04AA91, D04AB51, D04AB54, D04AB61, D04AH20, D04AX51, D04AX54, D04AX55, D05AA50, D05AA51, D05AA52, D05AC51, D05AX51, D05AX52, D05AX56, D05BH20, D05BX51, D06AA20, D06AX20, D06AX52, D06AX54, D06AX58, D06AX64, D06BA50, D06BA51, D06BA55, D06BA62, D06BA63, D06BA64, D06BB20, D06BB53, D06BB65, D07AB30, D08AB52, D08AC52, D08AC54, D08AC55, D08AE50, D08AE51, D08AE53, D08AE56, D08AE57, D08AG52, D08AH51, D08AH53, D08AH60, D08AJ51, D08AJ53, D08AJ57, D08AJ58, D08AJ59, D08AJ60, D08AK52, D08AK60, D08AL50, D08AX30, D08AX51, D08AX53, D08AX55, D08AX69, D09AA30, D09AA51, D09AA65, D09AC50, D10AD51, D10AD52, D10AD53, D10AD54, D10AE51, D10AF51, D10AF52, D10AF53, D10AF54, D10AX30, D10AX52, D10AX59, D10AX60, D10AX61, D10AX62, D10BH20, D10BX50, D11AA50, D11AA51, D11AA52, D11AA53, D11AB30, D11AB50, D11AB51, D11AB55, D11AB56, D11AB58, D11AB61, D11AB62, D11AB63, D11AC50, D11AC52, D11AC58, D11AC61, D11AF51, D11AF52, D11AF55, D11AG50, D11AX50, D11AX52, D11AX57, D11BH20, D11BH51, G01AA20, G01AA51, G01AA64, G01AE10, G01AF20, G01AX20, G01AX66, G01AX67, G01AX75, G01AX77, G02BB01, G02CD20, G02CH20, G02CH30, G02CP53, G02CP54, G02CP55, G02CX55, G02CX56, G03CA53, G03CD51, G03CD53, G03GA21, G04BA51, G04BC50, G04BD59, G04BD63, G04BD65, G04BD66, G04BE30, G04BE52, G04BE54, G04BE70, G04BH20, G04BH30, G04BP30, G04BP50, G04BP51, G04BX50, G04CA51, G04CA52, G04CA53, G04CH20, G04CP30, G04CP50, G04CP52, G04CP55, G04CP56, G04CX54, H03AA03, H03AA51, H03AA53, H03BB52, H03BH20, H03BP51, H03CA51, J01AA20, J01AA56, J01AA57, J01BA51, J01BA52, J01CA20, J01CA51, J01CE30, J01CE52, J01DD54, J01DD62, J01DH51, J01DH55, J01EB20, J01EB59, J01EB70, J01EC20, J01EC52, J01ED20, J01GB53, J01GB55, J01GB64, J01XE51, J01XX55, J04AC51, J04AM01, J04AM02, J04AM03, J04AM04, J04AM07, J05AR01, J05AR02, J05AR03, J05AR10, J05AX51, J06BB30, J07AE51, J07AG51, J07AG52, J07AG53, J07AJ51, J07AJ52, J07AM51, J07AM52, J07AP10, J07AX52, J07AX53, J07BC20, J07BD51, J07BD52, J07BD53, J07BD54, J07BJ51, L01BC52, L01BC53, L01BC63, L01CP50, L03AB60, L03AB61, L03AG50, L03AG51, L03AH20, L03AH50, L03AP50, L03AP51, L03AP52, L03AP53, L03AX50, L03AX71, M01AA51, M01AA52, M01AA53, M01AB51, M01AB55, M01AB69, M01AC56, M01AE51, M01AE52, M01AE53, M01AE56, M01AX55, M01AX68, M02AA54, M02AA56, M02AA73, M02AA78, M02AA79, M02AB51, M02AB53, M02AC50, M02AC51, M02AC52, M02AC53, M02AC54, M02AC55, M02AC56, M02AC57, M02AD50, M02AD51, M02AD52, M02AD53, M02AH20, M02AH50, M02AP30, M02AP51, M02AP52, M02AP56, M02AP57, M02AP58, M02AP59, M02AX20, M02AX30, M02AX53, M02AX54, M02AX56, M02AX69, M02AX76, M02BA54, M02BA55, M02BB51, M02BB52, M02BB53, M02BB56, M02BB59, M02BP50, M02BP51, M02BP52, M02BP53, M02BX51, M02BX55, M03BA51, M03BA52, M03BA53, M03BA57, M03BA71, M03BA72, M03BA73, M03BB52, M03BB53, M03BB72, M03BB73, M03BC51, M03BC51, M03BX54, M03BX54, M04AA51, M04AA51, M04AH20, M05BB01, M05BB02, M05BB03, M05BB06, M05BB07, M05BB08, M05BB09, M05BX53, M09AA52, M09AA72, M09AB52, M09AH20, M09AH50, M09AP30, M09AX03, M09AX55, N01AH51, N01AX63, N01BA52, N01BA53, N01BB20, N01BB51, N01BB52, N01BB53, N01BB54, N01BB57, N01BB58, N01BH20, N01BX50, N02AA51, N02AA55, N02AA57, N02AA58, N02AA59, N02AA64, N02AA65, N02AA66, N02AA69, N02AA79, N02AB52, N02AB72, N02AC52, N02AC54, N02AC74, N02AX51, N02AX52, N02AX62, N02BA20, N02BA51, N02BA55, N02BA57, N02BA59, N02BA65, N02BA71, N02BA75, N02BA77, N02BA79, N02BB51, N02BB52, N02BB53, N02BB54, N02BB56, N02BB71, N02BB72, N02BB73, N02BB74, N02BB76, N02BE51, N02BE53, N02BE54, N02BE61, N02BE71, N02BE73, N02BE74, N02BH20, N02CA51, N02CA52, N02CA71, N02CA72, N02CH20, N02CP52, N02CX57, N02CX58, N02CX59, N03AB52, N03AB54, N03AD51, N04AH20, N04BA05, N04BA06, N04BA10, N04BA11, N05BA56, N05BB51, N05BC51, N05CP30, N05CP50, N05CP51, N05CP52, N05HH20, N05HH50, N06AP51, N06BX54, N06BX64, N06DA52, N06DX10, N06DX57, N06DX66,

Combination drugs	ATC codes
Containing 2 active substances	N07AA51, N07BC51, N07CA52, N07CH20, N07XB52, N07XB54, N07XB56, N07XH20, N07XX59, P01AA52, P01AR53, P01AX52, P01BB51, P01BD51, P01BF01, P01BF02, P01BF03, P01BF05, P01BF06, P02CA51, P02CX50, P03AA54, P03AB51, P03AC52, P03AC53, P03AC54, P03AP51, R01AC51, R01AD52, R01AD53, R01AD57, R01AD58, R01AD60, R01AD61, R01AD64, R01AH20, R01AH50, R01AP56, R01AX30, R01BA51, R01BA52, R01BA53, R01BA54, R01BA56, R01BA57, R01BH20, R01BP30, R02AA50, R02AA51, R02AA52, R02AA55, R02AA56, R02AA59, R02AA71, R02AA72, R02AA73, R02AA74, R02AA82, R02AA84, R02AB20, R02AB52, R02AB54, R02AB80, R02AD50, R02AD51, R02AD52, R02AH20, R02AP30, R02AP52, R02AX50, R02AX52, R03AA51, R03AA52, R03AB52, R03AB53, R03CA51, R03CA52, R03CA53, R03CB51, R03CB53, R03CC53, R03CC54, R03CC63, R03DA20, R03DA50, R03DA51, R03DA52, R03DA53, R03DA54, R03DA55, R03DA57, R03DA63, R03DA73, R03DA74, R03DA82, R03DA90, R03DH20, R03DX50, R04AH20, R04AH50, R04AP30, R04AP50, R04AX53, R05CA10, R05CA50, R05CA51, R05CB10, R05CB50, R05CB52, R05CH20, R05CH50, R05CP30, R05CP51, R05CP59, R05DA20, R05DA50, R05DA54, R05DA56, R05DA59, R05DA64, R05DB20, R05DB53, R05DB54, R05DB55, R05DB68, R05DB80, R05XA01, R05XA02, R05XA03, R05XA04, R05XA05, R05XA06, R05XA07, R05XA08, R05XA09, R05XA10, R05XA12, R05XC01, R05XC02, R05XH20, R05XH51, R05XH52, R06AA52, R06AA54, R06AA56, R06AA57, R06AA59, R06AB51, R06AB52, R06AB54, R06AB56, R06AC52, R06AC53, R06AD52, R06AD55, R06AE51, R06AE53, R06AE55, R06AE57, R06AX51, R06AX53, R06AX57, R06AX58, R06AX80, R07AA30, R07AB50, R07AB52, R07AB53, R07AH20, S01AA20, S01AA30, S01AB20, S01AX20, S01CA01, S01CA02, S01CA03, S01CA04, S01CA05, S01CA06, S01CA07, S01CA08, S01CA09, S01CA10, S01CA11, S01CA12, S01CA13, S01CA21, S01CA22, S01CA52, S01CA53, S01CA54, S01CA56, S01CA57, S01EA51, S01EA52, S01EB51, S01EB58, S01ED51, S01ED52, S01ED54, S01ED55, S01ED61, S01ED62, S01ED63, S01ED66, S01ED67, S01ED68, S01ED69, S01FA51, S01FA56, S01GA50, S01GA51, S01GA52, S01GA53, S01GA55, S01GA56, S01GX51, S01HA30, S01JA51, S01KA51, S01XA30, S01XA50, S01XA52, S01XA76, S01XA85, S01XA86, S01XA87, S01XA89, S01XB50, S01XB52, S01XB53, S01XB54, S01XC20, S01XC51, S01XC55, S01XC56, S01XC57, S01XC58, S01XH20, S01XH51, S02AA30, S02BA56, S02DA30, S02DA51, S02DA55, S02DA57, S02DC30, S02DH20, S02DH50, S03AA30, V03AB05, V03AE04, V03AK50, V03AX50, V04BA20, V04CM20, V04CN20, V04CO20, V04CX50, V04CX51, V04CZ02, V04CZ04, V04CZ05, V04CZ10, V06BA50, V06CA50, V06CX50, V06DC20, V06DC51, V07AN50, V07LH04, V08AA20
Containing 3 active substances	C07D, A02BD, A11DB03, A11DB04, A12AX51, B03AE01, B03AE02, B03AE04, C02LA51, C02LA52, C02LA58, C02LA71, C02LC51, C02LG51, C02LG73, C07FB25, C08GA53, C09BX01, C09DX01, C09DX03, C09XA54, C10BX04, G01BE50, J04AM05, J04AM06, J05AR04, J05AR05, J05AR06, J05AR07, J05AR08, J05AR09, J05AR11, L01BC73, M05BB04, M05BB05, M05BB10, N04BA03, P01BF04, S01CA55

Table S2. List of ATC codes or ATC code groups excluded from the count of drugs for the modified polypharmacy definition

Exclusion Criteria	ATC codes
Food supplements	A11, V06, A12, A13, A02X, C10AX06
Homeopathic or anthroposophical drugs	V60, N05H, A01AH, A03AH, A04AH, A05AH, A05BH, A07XH, A08AH, A09AH, A10XH, B03XH, C01AH, C01CH, C01EH, C02KH, C03XH, C04AH, C05AH, C05CH, C06AH, D05BH, D10BH, G02CH, G04BH, G04CH, H03BH, H05AH, L01CH, L03AH, M02AH, M04AH, M09AH, N01BH, N02BH, N02CH, N04AH, N06AH, N07CH, N07XH, R01AH, R01BH, R03DH, R05CH, R05FH, R05XH, R07AH, S02DH, R05CP, R05DP02, R05DP04, R05DP07
Herbal drugs (Selection)	A03AP, C05AP, R05DP
Non-systemic acting drugs	D02, D03, D04, D08, D09, D11, R01A, R02, R04, S01, V04, V07, V08, V09, V20, D01A, D06A, M02A, M02B, P03A, P03B, A01AA, A01AP, D07AA, D07BA, D07CA, D07XA, G02CD, M09AX, S02DC, C10AX13
Antithrombotic agents for short term use ^a	B01A
NSAIDs for short term use ^a	M01A, B01AC06, N02BA01, N02BA51, N02BA71, M01BA01, M01BA03
Drugs against peptic ulcer disease for short term use ^a	A02B

^a Short-term use was assumed if the drug was only reported in the hospital discharge letter but not in the interview with the patient.

Table S3. Associations of the baseline characteristics of older colorectal cancer patients with polypharmacy (traditional definition).

Variables	N _{total}	Polypharmacy		
		N (%) ^a	Age and sex adjusted OR [95% CI]	Multivariable ^b OR [95% CI]
Sex				
Female	1334	926 (69.4)	Ref	Ref
Male	1905	1222 (64.2)	0.84 [0.72-0.97]	0.65 [0.51-0.83]
Age at CRC diagnosis				
Per 1-year increase	-	-	1.05 [1.04-1.06]	1.01 [0.99-1.02]
Years of schooling				
≤9	2318	1576 (68.0)	Ref	Ref
10-11	486	307 (63.2)	0.80 [0.65-0.98]	0.97 [0.75-1.25]
≥12	435	265 (60.9)	0.79 [0.64-0.98]	0.95 [0.73-1.24]
Year of CRC diagnosis				
2003-2007	1098	646 (58.8)	Ref	Ref
2008-2012	1223	834 (68.2)	1.50 [1.26-1.78]	1.84 [1.48-2.29]
2013-2016	918	668 (72.8)	1.83 [1.51-2.22]	2.44 [1.90-3.12]
Tumor location				
Colon	2088	1404 (67.2)	Ref	Ref
Rectum	1151	744 (64.6)	0.96 [0.83-1.12]	1.17 [0.97-1.42]
Tumor stage				
I	769	524 (68.1)	Ref	Ref
II	1082	733 (67.7)	0.94 [0.77-1.15]	1.00 [0.79-1.28]
III	985	638 (64.8)	0.84 [0.68-1.02]	1.17 [0.86-1.60]
IV	403	253 (62.8)	0.82 [0.63-1.06]	1.17 [0.81-1.69]
(Neo-) adjuvant chemotherapy				
Yes	1211	723 (59.7)	0.72 [0.61-0.83]	0.76 [0.59-0.99]
No	2028	1425 (70.3)	Ref	Ref
BMI (kg/m ²)				
< 25	1197	721 (60.2)	Ref	Ref
25-29.9	1417	950 (67.0)	1.45 [1.23-1.71]	1.04 [0.85-1.27]
≥30	625	477 (76.3)	2.47 [1.98-3.09]	1.33 [1.01-1.73]
Lifetime physical activity (MET-h/week)				
T1	1079	715 (66.3)	Ref	Ref
T2	1080	738 (68.3)	1.09 [0.91-1.31]	1.01 [0.81-1.26]
T3	1080	695 (64.4)	1.00 [0.83-1.20]	1.01 [0.80-1.27]
Smoking status				
Never smoker	1466	956 (65.2)	Ref	Ref
Former smoker	1473	1011 (68.6)	1.42 [1.20-1.69]	1.30 [1.06-1.61]
Current smoker	300	181 (60.3)	1.06 [0.82-1.39]	1.19 [0.87-1.64]
Lifetime alcohol consumption				
None	603	420 (69.7)	Ref	Ref
T1	873	597 (68.4)	1.04 [0.82-1.31]	1.14 [0.86-1.50]
T2	883	544 (61.6)	0.85 [0.66-1.09]	0.95 [0.71-1.28]
T3	880	587 (66.7)	1.16 [0.90-1.51]	1.20 [0.87-1.66]
Red meat consumption				
<1 time/week	259	179 (69.1)	Ref	Ref
1 time/week	735	480 (65.3)	0.86 [0.63-1.17]	0.93 [0.63-1.36]
Multiple times per week	2245	1489 (66.3)	0.96 [0.72-1.28]	0.92 [0.64-1.32]
Processed meat consumption				
<1 time/week	406	272 (67.0)	Ref	Ref
1 time/week	426	268 (62.9)	0.85 [0.64-1.14]	0.88 [0.62-1.25]
Multiple times per week	2407	1608 (66.8)	1.07 [0.85-1.34]	1.06 [0.79-1.42]
Functional status				
Excellent	629	377 (59.9)	Ref	Ref
Fair	1214	739 (60.9)	1.05 [0.83-1.31]	1.08 [0.84-1.40]
Poor	1396	1032 (73.9)	1.73 [1.34-2.23]	1.40 [1.03-1.89]
Comorbidity				
Hypertension				
No	984	377 (38.3)	Ref	Ref
Yes	2255	1771 (78.5)	5.64 [4.79-6.65]	4.15 [3.44-5.00]

Variables	N _{total}	Polypharmacy		
		N (%) ^a	Age and sex adjusted OR [95% CI]	Multivariable ^b OR [95% CI]
Cardiac insufficiency				
No	2560	1565 (61.1)	Ref	Ref
Yes	679	583 (85.9)	3.41 [2.70-4.31]	1.58 [1.20-2.08]
Acute coronary syndrome				
No	2845	1797 (63.2)	Ref	Ref
Yes	394	351 (89.1)	4.64 [3.34-6.44]	1.94 [1.32-2.84]
History of myocardial infarction				
No	2640	1607 (60.9)	Ref	Ref
Yes	599	541 (90.3)	5.96 [4.48-7.92]	2.95 [2.13-4.10]
History of stroke				
No	2849	1821 (63.9)	Ref	Ref
Yes	390	327 (83.9)	2.71 [2.04-3.60]	1.92 [1.39-2.65]
Atrial fibrillation				
No	2816	1774 (63.0)	Ref	Ref
Yes	423	374 (88.4)	4.06 [2.98-5.54]	2.85 [2.01-4.03]
COPD				
No	2933	1901 (64.8)	Ref	Ref
Yes	306	247 (80.7)	2.27 [1.69-3.06]	1.97 [1.40-2.78]
Type II diabetes mellitus				
No	2403	1434 (59.7)	Ref	Ref
Yes	836	714 (85.4)	3.94 [3.20-4.87]	2.63 [2.07-3.33]
Depression				
No	2985	1945 (65.2)	Ref	Ref
Yes	254	203 (79.9)	2.19 [1.59-3.02]	2.14 [1.48-3.10]
Chronic pain				
No	1274	752 (59.0)	Ref	Ref
Yes	1965	1396 (71.0)	1.63 [1.41-1.90]	1.37 [1.14-1.64]
Gastrointestinal illness				
No	2531	1652 (65.3)	Ref	Ref
Yes	708	496 (70.1)	1.24 [1.03-1.49]	1.22 [0.98-1.52]
Anemia				
No	2896	1902 (65.7)	Ref	Ref
Yes	343	246 (71.7)	1.19 [0.92-1.53]	1.08 [0.79-1.47]
Hypothyroidism				
No	3072	2005 (65.3)	Ref	Ref
Yes	167	143 (85.6)	3.12 [2.00-4.86]	2.57 [1.57-4.21]

Values in bold are statistically significant ($p < 0.05$)

Abbreviations: BMI, body mass index; CI, confidence interval; COPD, chronic obstructive pulmonary disease; MET, metabolic equivalent of task; OR, odds ratio; Ref, reference.

^a The column N(%) was calculated using the imputation dataset 1.

^b Effect estimates of a multivariable model comprising all variables shown in this table.

Table S4. The associations of polypharmacy (traditional definition) with up to 5-year overall, colorectal cancer specific, and non-cancer specific survival in older CRC patients

	N _{total}	N _{cases} (%)	Model 1 ^a HR [95% CI]	Model 2 ^b HR [95% CI]	Model 3 ^c HR [95% CI]
Overall Survival					
0-4 drugs	1091	316 (29.0)	Ref	Ref	Ref
5-7 drugs	1123	358 (31.9)	1.06 [0.91-1.23]	1.10 [0.95-1.29]	1.04 [0.88-1.22]
≥8 drugs	1025	396 (38.6)	1.25 [1.08-1.46]	1.36 [1.17-1.59]	1.16 [0.96-1.39]
Colorectal Cancer Specific Survival					
0-4 drugs	1069	211 (19.7)	Ref	Ref	Ref
5-7 drugs	1092	208 (19.1)	0.96 [0.79-1.16]	1.02 [0.84-1.24]	1.05 [0.85-1.29]
≥8 drugs	984	196 (19.9)	1.00 [0.82-1.22]	1.17 [0.95-1.44]	1.23 [0.96-1.57]
Non-Cancer Specific Survival					
0-4 drugs	1069	57 (5.3)	Ref	Ref	Ref
5-7 drugs	1092	97 (8.9)	1.46 [1.05-2.03]	1.46 [1.05-2.04]	1.18 [0.83-1.67]
≥8 drugs	984	142 (14.4)	2.23 [1.63-3.04]	2.22 [1.61-3.06]	1.27 [0.88-1.84]

Values in bold are statistically significant (p<0.05)

Abbreviations: CI, confidence interval; HR, hazard ratio.

^a Adjusted for age and sex.

^b Adjusted for age, sex, tumor stage, tumor location, year of CRC diagnosis, neoadjuvant/adjuvant chemotherapy, year of schooling, smoking status, BMI, lifetime physical activity, lifetime alcohol consumption, red meat consumption, and processed meat consumption.

^c Adjusted for variables of model 2, functional status, and comorbidity.

Table S5. Subgroup analyses for the associations of polypharmacy (traditional definition) with up to 5-year overall survival in older colorectal cancer patients

Age	65-74 Years			≥ 75 years					
	N _{total}	N _{cases} (%)	HR [95% CI] ^a	N _{total}	N _{cases} (%)	HR [95% CI] ^a			
0-4 drugs	651	163 (25.0)	Ref	440	153 (34.8)	Ref			
5-7 drugs	585	147 (25.1)	1.03 [0.80-1.31]	538	211 (39.2)	1.12 [0.90-1.41]			
≥8 drugs	416	127 (30.5)	1.36 [1.00-1.84]	609	269 (44.2)	1.17 [0.92-1.49]			
Sex	Female			Male					
	N _{total}	N _{cases} (%)	HR [95% CI] ^a	N _{total}	N _{cases} (%)	HR [95% CI] ^a			
0-4 drugs	408	118 (28.9)	Ref	683	198 (29.0)	Ref			
5-7 drugs	455	149 (32.8)	1.08 [0.83-1.41]	668	209 (31.3)	0.99 [0.80-1.22]			
≥8 drugs	471	186 (39.5)	1.32 [0.99-1.77]	554	210 (37.9)	1.05 [0.82-1.34]			
Tumor location	Colon			Rectum					
	N _{total}	N _{cases} (%)	HR [95% CI] ^a	N _{total}	N _{cases} (%)	HR [95% CI] ^a			
0-4 drugs	684	210 (30.7)	Ref	407	106 (26.0)	Ref			
5-7 drugs	720	229 (31.8)	0.92 [0.75-1.13]	403	129 (32.0)	1.28 [0.97-1.69]			
≥8 drugs	684	263 (38.5)	1.03 [0.82-1.30]	341	133 (39.0)	1.46 [1.05-2.03]			
Chemotherapy	No Chemotherapy			Chemotherapy					
	N _{total}	N _{cases} (%)	OR [95% CI] ^a	N _{total}	N _{cases} (%)	OR [95% CI] ^a			
0-4 drugs	603	136 (22.6)	Ref	488	180 (36.9)	Ref			
5-7 drugs	707	180 (25.5)	0.92 [0.67-1.27]	414	177 (42.8)	1.27 [0.91-1.79]			
≥8 drugs	717	256 (35.7)	1.14 [0.81-1.61]	307	139 (45.3)	1.26 [0.84-1.91]			
Tumor stage	Stage I and II			Stage III			Stage IV		
	N _{total}	N _{cases} (%)	HR [95% CI] ^a	N _{total}	N _{cases} (%)	HR [95% CI] ^a	N _{total}	N _{cases} (%)	HR [95% CI] ^a
0-4 drugs	593	101 (17.0)	Ref	341	96 (28.2)	Ref	149	117 (78.5)	Ref
5-7 drugs	646	115 (17.8)	0.87 [0.65-1.16]	335	129 (38.5)	1.32 [0.99-1.77]	137	113 (82.5)	1.03 [0.77-1.38]
≥8 drugs	606	163 (26.9)	0.99 [0.72-1.35]	297	138 (46.5)	1.33 [0.96-1.84]	115	91 (79.1)	1.12 [0.79-1.59]
Functional status	Excellent			Fair			Poor		
	N _{total}	N _{cases} (%)	HR [95% CI] ^a	N _{total}	N _{cases} (%)	HR [95% CI] ^a	N _{total}	N _{cases} (%)	HR [95% CI] ^a
0-4 drugs	205	41 (20.0)	Ref	324	87 (26.9)	Ref	198	69 (34.9)	Ref
5-7 drugs	192	42 (21.9)	1.27 [0.76-2.11]	298	83 (27.9)	1.10 [0.78-1.55]	298	133 (44.6)	1.22 [0.90-1.67]
≥8 drugs	115	35 (30.4)	1.68 [0.91-3.08]	264	89 (33.7)	1.28 [0.86-1.88]	374	159 (42.5)	0.99 [0.70-1.40]

Values in bold are statistically significant (p<0.05)

Abbreviations: CI, confidence interval; HR, hazard ratio; OR, odds ratio.

^aAdjusted for age, sex, tumor stage, tumor location, year of CRC diagnosis, neoadjuvant/adjuvant chemotherapy, year of schooling, smoking status, BMI, lifetime physical activity, lifetime alcohol consumption, red meat consumption, processed meat consumption, functional status, and comorbidity except stratifying factor.

Table S6. The association of polypharmacy (traditional definition) with chemotherapy-related neurological and gastrointestinal adverse drug reactions (ADRs) in older CRC patients

	N_{total}	N_{cases} (%)	Model 1^a OR [95% CI]	Model 2^b OR [95% CI]	Model 3^c OR [95% CI]
Neurological ADRs					
0-4 drugs	394	56 (14.2)	Ref	Ref	Ref
5-7 drugs	330	55 (16.7)	1.27 [0.84-1.91]	1.16 [0.89-1.51]	1.15 [0.87-1.51]
≥8 drugs	237	33 (13.9)	1.06 [0.66-1.70]	1.08 [0.80-1.47]	1.13 [0.80-1.59]
Gastrointestinal ADRs					
0-4 drugs	394	139 (35.3)	Ref	Ref	Ref
5-7 drugs	330	110 (33.3)	0.88 [0.65-1.20]	0.96 [0.79-1.18]	0.96 [0.78-1.18]
≥8 drugs	237	77 (32.5)	0.84 [0.59-1.18]	1.01 [0.80-1.26]	1.01 [0.78-1.31]

Values in bold are statistically significant (p<0.05)

Abbreviations: CI, confidence interval; OR, odds ratio.

^a Adjusted for age and sex.

^b Adjusted for age, sex, tumor stage, tumor location, year of CRC diagnosis, year of schooling, smoking status, BMI, lifetime physical activity, lifetime alcohol consumption, red meat consumption, and processed meat consumption.

^c Adjusted for variables of model 2, functional status, and comorbidity.

Table S7. The associations of polypharmacy (modified definition) with overall, colorectal cancer specific, and non-cancer specific survival in older CRC patients during up to 17 years of follow-up

	N _{total}	N _{cases} (%)	Model 1 ^a HR [95% CI]	Model 2 ^b HR [95% CI]	Model 3 ^c HR [95% CI]
Overall Survival					
0-4 drugs	1467	670 (45.7)	Ref	Ref	Ref
5-7 drugs	988	502 (50.8)	1.15 [1.02-1.29]	1.21 [1.08-1.36]	1.12 [0.98-1.27]
≥8 drugs	784	446 (56.9)	1.38 [1.22-1.56]	1.46 [1.29-1.66]	1.23 [1.06-1.43]
Colorectal Cancer Specific Survival					
0-4 drugs	1432	345 (24.1)	Ref	Ref	Ref
5-7 drugs	964	227 (23.6)	1.00 [0.85-1.18]	1.05 [0.88-1.25]	1.08 [0.89-1.30]
≥8 drugs	749	175 (23.4)	1.06 [0.88-1.27]	1.21 [0.99-1.46]	1.26 [1.00-1.58]
Non-Cancer Specific Survival					
0-4 drugs	1432	196 (13.7)	Ref	Ref	Ref
5-7 drugs	964	186 (19.3)	1.46 [1.20-1.79]	1.46 [1.19-1.79]	1.13 [0.90-1.40]
≥8 drugs	749	196 (26.2)	2.09 [1.71-2.56]	2.13 [1.73-2.62]	1.35 [1.06-1.72]

Values in bold are statistically significant (p<0.05)

Abbreviations: CI, confidence interval; HR, hazard ratio.

^a Adjusted for age and sex.

^b Adjusted for age, sex, tumor stage, tumor location, year of CRC diagnosis, neoadjuvant/adjuvant chemotherapy, year of schooling, smoking status, BMI, lifetime physical activity, lifetime alcohol consumption, red meat consumption, and processed meat consumption.

^c Adjusted for variables of model 2, functional status, and comorbidity.

Table S8. The association of polypharmacy (modified definition) with chemotherapy-related neurological and gastrointestinal adverse drug reactions (ADRs) in older CRC patients

	N_{total}	N_{cases} (%)	Model 1^a OR [95% CI]	Model 2^b OR [95% CI]	Model 3^c OR [95% CI]
Neurological ADRs					
0-4 drugs	496	70 (14.1)	Ref	Ref	Ref
5-7 drugs	290	52 (17.9)	1.38 [0.93-2.05]	1.24 [0.93-1.64]	1.24 [0.92-1.66]
≥8 drugs	175	22 (12.6)	0.94 [0.56-1.59]	0.95 [0.66-1.34]	0.95 [0.64-1.41]
Gastrointestinal ADRs					
0-4 drugs	496	172 (34.7)	Ref	Ref	Ref
5-7 drugs	290	98 (33.8)	0.93 [0.68-1.26]	0.97 [0.78-1.20]	0.95 [0.76-1.19]
≥8 drugs	175	56 (32.0)	0.85 [0.59-1.23]	1.00 [0.78-1.29]	1.00 [0.75-1.33]

Values in bold are statistically significant (p<0.05)

Abbreviations: CI, confidence interval; OR, odds ratio.

^a Adjusted for age and sex.

^b Adjusted for age, sex, tumor stage, tumor location, year of CRC diagnosis, year of schooling, smoking status, BMI, lifetime physical activity, lifetime alcohol consumption, red meat consumption, and processed meat consumption.

^c Adjusted for variables of model 2, functional status, and comorbidity.