Socioeconomic and demographic inequalities in stage at diagnosis and survival among colorectal cancer patients: evidence from a Swiss population-based study

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Abstract: Socioeconomic inequalities in cancer stage at diagnosis and survival are important public health issues. This study investigates the association between socioeconomic position (SEP) and colorectal cancer (CRC) stage at diagnosis and survival in Switzerland, a European country with highest level of medical facilities and life expectancy. We used population-based CRC data from seven Swiss cantonal cancer registries 2001-2008 (N = 10,088) linked to the Swiss National Cohort (SNC). Follow-up information was available until the end of 2013. SEP was estimated based on education. The association between cancer stage and SEP was assessed using logistic regression models including cancer localization (colon/rectum), sex, age, civil status, urbanity of residence, language region, and nationality (Swiss/non-Swiss). Survival was analyzed using competing risk regressions reporting subhazard ratios (SHRs) for the risk of dying due to CRC. We observed a social gradient for later stage CRC with adjusted odds ratios (ORs) of 1.11 (95% CI: 0.97-1.19) and 1.28 (95% CI: 1.08-1.50) for middle and low SEP compared to high SEP. Further, single compared to married people had elevated odds of being diagnosed at later stages. Survival was lower in patients with CRC with low SEP in the unadjusted model (SHR: 1.18, 95% CI: 1.07-1.30). After adjustment for stage at diagnosis and further sociodemographic characteristics, significant survival inequalities by SEP disappeared but remained for non-Swiss compared to Swiss citizens and for patients living in nonurban areas compared to their urban counterparts. Swiss public health strategies should facilitate equal access to CRC screening and optimal CRC care for all social groups and in all regions of Switzerland.

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### Suppl. Table 1: Distribution of socioeconomic and demographic characteristics of the cantons participating in the study and all Switzerland (population aged 30-84 years), Census 2000

| Socioeconomic and demographic characteristics | Cantons participating in the study | Whole of Switzerland |
|-----------------------------------------------|-----------------------------------|----------------------|
|                                               | N      | column % | N      | column % |
| **Socioeconomic position (SEP)**              |        |          |        |          |
| low SEP                                      | 489,870| 23.8     | 1,078,424| 23.7   |
| middle SEP                                   | 999,265| 48.5     | 2,331,895| 51.3   |
| high SEP                                     | 507,472| 24.6     | 1,010,800| 22.2   |
| unknown                                      | 64,338 | 3.1      | 124,213 | 2.7    |
| **Sex**                                      |        |          |        |          |
| male                                         | 991,467| 48.1     | 2,202,279| 48.5   |
| female                                       | 1,069,478| 51.9   | 2,343,053| 51.6   |
| **Age at diagnosis**                         |        |          |        |          |
| 30-49 years                                  | 1,039,029| 50.4   | 2,287,496| 50.3   |
| 50-64 years                                  | 590,850 | 28.7     | 1,288,317| 28.3   |
| 65-74 years                                  | 284,981 | 13.8     | 637,993 | 14.0   |
| 75-84 years                                  | 146,085 | 7.1      | 331,526 | 7.3    |
| **Civil status**                             |        |          |        |          |
| single                                       | 321,193| 15.6     | 683,058 | 15.0   |
| married                                      | 1,393,206| 67.6   | 3,134,345| 69.0   |
| widowed                                      | 143,630 | 7.0      | 323,982 | 7.1    |
| divorced                                     | 202,916 | 9.9      | 403,947 | 8.9    |
| **Urbanity of residence**                    |        |          |        |          |
| urban                                        | 712,110 | 34.6     | 1,309,476| 28.8   |
| peri-urban                                   | 1,021,000| 49.5   | 2,059,108| 45.3   |
| rural                                        | 327,835 | 15.9     | 1,176,748| 25.9   |
| **Language-region**                          |        |          |        |          |
| German-speaking region                       | 877,042| 42.6     | 3,278,361| 72.1   |
| French-speaking region                       | 980,809| 47.6     | 1,054,883| 23.2   |
| Nationality          | N     | row % | N     | row % |
|----------------------|-------|-------|-------|-------|
| Italian-speaking     | 203,094 | 9.9  | 212,088 | 4.7  |
| Nationality          |       |      |       |       |
| Swiss                | 1,585,929 | 77.0 | 3,700,941 | 81.4 |
| non-Swiss            | 475,016 | 23.1 | 844,391 | 18.6 |
| **Total**            | 2,060,945 | 45.3 | 4,545,332 | 100.0 |

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**Suppl. Table 2**: Contribution of colorectal cancer cases and person-years by cancer registry: incidence period 05/12/2000 - 31/12/2008, patients aged 30-84 years at diagnosis

| CR     | all stages | with stage information |
|--------|------------|------------------------|
|        | Cases (N)  | Person-years (PY) of follow-up | % of pooled PY | Cases (N)  | Person-years (PY) of follow-up | % of pooled PY |
| Fribourg | 294        | 1,344                   | 2.4          | 277        | 1,273                   | 2.4          |
| Geneva   | 1,214      | 7,250                   | 12.8         | 1,147      | 7,016                   | 13.4         |
| Neuchâtel | 601        | 3,284                   | 5.8          | 540        | 3,125                   | 6.0          |
| Ticino   | 1,276      | 7,216                   | 12.7         | 1,224      | 6,967                   | 13.3         |
| Valais   | 910        | 5,043                   | 8.9          | 855        | 4,771                   | 9.1          |
| Vaud     | 2,021      | 11,754                  | 20.7         | 1,704      | 10,064                  | 19.2         |
| Zurich   | 3,772      | 20,766                  | 36.7         | 3,400      | 19,298                  | 36.7         |

Note: 82 cases (0.8%) out of originally 10,170 cases aged 30-84 years have been excluded due to missing SEP information. From the remaining dataset (N=10,088), 140 (1.4%) additional cases were excluded for survival analyses due to zero survival time (death certificate only cases or cases first diagnosed at autopsy).
**Suppl. Table 3**: Odds ratios (OR) of later colorectal cancer stage at diagnosis (Stage I-II versus Stage III-IV)

|                     | Model 1         | Model 2         | Model 3         | Model 4         | Model 5*        |
|---------------------|-----------------|-----------------|-----------------|-----------------|-----------------|
|                     | OR  [95%CI]     | OR  [95%CI]     | OR  [95%CI]     | OR  [95%CI]     | OR  [95%CI]     |
| **SEP**             |                 |                 |                 |                 |                 |
| High SEP (ref.)     |                 |                 |                 |                 |                 |
| Middle SEP          | 1.00 [0.90-1.12]| 1.00 [0.90-1.11]| 1.00 [0.90-1.12]| 1.00 [0.90-1.12]| 0.99 [0.90-1.11]|
| Low SEP             | 1.05 [0.94-1.19]| 1.05 [0.93-1.19]| 1.05 [0.92-1.19]| 1.05 [0.92-1.19]| 1.04 [0.92-1.19]|
| **Sex**             |                 |                 |                 |                 |                 |
| male (ref.)         |                 |                 |                 |                 |                 |
| female              | 1.12 [1.03-1.23]| 1.12 [1.03-1.23]| 1.12 [1.03-1.23]| 1.12 [1.03-1.23]| 1.12 [1.03-1.23]|
| **Age at diagnosis**|                 |                 |                 |                 |                 |
| 50-64 years (ref.)  |                 |                 |                 |                 |                 |
| < 50 years          | 1.36 [1.14-1.63]| 1.37 [1.14-1.64]| 1.36 [1.14-1.64]| 1.37 [1.14-1.64]|                 |
| 65-74 years         | 0.95 [0.85-1.06]| 0.95 [0.86-1.06]| 0.95 [0.86-1.06]| 0.95 [0.86-1.06]|                 |
| 75-84 years         | 0.89 [0.80-1.00]| 0.89 [0.80-1.00]| 0.89 [0.80-1.00]| 0.89 [0.80-1.00]| 0.89 [0.80-1.00]|
| **Civil status**    |                 |                 |                 |                 |                 |
| married (ref.)      |                 |                 |                 |                 |                 |
| single              | 1.32 [1.13-1.53]| 1.31 [1.13-1.53]| 1.31 [1.13-1.53]| 1.31 [1.13-1.53]| 1.31 [1.13-1.53]|
| widowed             | 0.94 [0.82-1.07]| 0.94 [0.82-1.06]| 0.94 [0.82-1.07]| 0.94 [0.82-1.07]| 0.94 [0.82-1.07]|
| divorced            | 1.09 [0.95-1.25]| 1.08 [0.94-1.25]| 1.08 [0.94-1.25]| 1.08 [0.94-1.25]| 1.09 [0.95-1.25]|
| **Nationality**     |                 |                 |                 |                 |                 |
| Swiss (ref.)        |                 |                 |                 |                 |                 |
| Non-Swiss           | 1.07 [0.96-1.20]| 1.07 [0.96-1.20]| 1.07 [0.96-1.20]| 1.07 [0.96-1.20]| 1.07 [0.96-1.21]|
| **Urbanity**        |                 |                 |                 |                 |                 |
| urban (ref.)        |                 |                 |                 |                 |                 |
| peri-urban          | 0.98 [0.89-1.07]| 0.98 [0.89-1.07]| 0.98 [0.89-1.07]| 0.98 [0.89-1.07]|                 |
| rural               | 1.01 [0.88-1.15]| 1.00 [0.88-1.15]| 1.00 [0.88-1.15]| 1.00 [0.87-1.15]|                 |
| **Language region** |                 |                 |                 |                 |                 |
| German (ref.)       |                 |                 |                 |                 |                 |
| French              | 1.03 [0.94-1.12]| 1.03 [0.94-1.12]| 0.99 [0.76-1.31]|                 |
### Localisation

| Colon (ref.) | rectum |
|-------------|--------|
| 0.99 [0.90-1.08] | 0.99 [0.90-1.08] |

* Additionally adjusted for canton of residence to account for unmeasured canton characteristics associated with SEP and stage.

** German-speaking region: eastern parts of the canton of Fribourg, eastern parts of the canton of Valais (upper Valais), canton of Zurich; French-speaking region: western parts of the canton of Fribourg, canton of Geneva, canton of Neuchâtel, western parts of the canton of Valais (Central and Lower Valais), canton of Vaud; Italian-speaking region: canton of Ticino.
### Suppl. Table 4: Odds ratios (OR) of later colorectal cancer stage at diagnosis (Stage I-III versus Stage IV)

|                           | Model 1       | Model 2       | Model 3       | Model 4       | Model 5*       |
|---------------------------|---------------|---------------|---------------|---------------|---------------|
|                           | OR [95%CI]    | OR [95%CI]    | OR [95%CI]    | OR [95%CI]    | OR [95%CI]    |
| **SEP**                   |               |               |               |               |               |
| High SEP (ref.)           |               |               |               |               |               |
| Middle SEP                | 1.03 [0.91-1.18] | 1.05 [0.92-1.20] | 1.05 [0.92-1.20] | 1.06 [0.92-1.21] | 1.05 [0.92-1.20] |
| Low SEP                   | 1.00 [0.86-1.15] | 1.02 [0.88-1.19] | 1.00 [0.86-1.17] | 1.01 [0.87-1.18] | 0.98 [0.84-1.15] |
| **Sex**                   |               |               |               |               |               |
| male (ref.)               |               |               |               |               |               |
| female                    | 1.02 [0.92-1.14] | 1.03 [0.92-1.15] | 1.01 [0.90-1.12] | 1.02 [0.91-1.14] |               |
| **Age at diagnosis**      |               |               |               |               |               |
| 50-64 years (ref.)        |               |               |               |               |               |
| < 50 years                | 1.20 [0.98-1.48] | 1.21 [0.99-1.49] | 1.21 [0.98-1.48] | 1.21 [0.99-1.49] |               |
| 65-74 years               | 0.93 [0.82-1.06] | 0.94 [0.82-1.06] | 0.92 [0.81-1.05] | 0.93 [0.81-1.05] |               |
| 75-84 years               | 0.92 [0.80-1.05] | 0.92 [0.80-1.05] | 0.89 [0.77-1.02] | 0.90 [0.78-1.03] |               |
| **Civil status**          |               |               |               |               |               |
| married (ref.)            |               |               |               |               |               |
| single                    | 1.25 [1.05-1.48] | 1.24 [1.04-1.47] | 1.24 [1.04-1.48] | 1.25 [1.05-1.49] |               |
| widowed                   | 0.90 [0.76-1.07] | 0.89 [0.76-1.06] | 0.90 [0.76-1.06] | 0.90 [0.76-1.07] |               |
| divorced                  | 1.21 [1.03-1.42] | 1.20 [1.03-1.42] | 1.21 [1.02-1.42] | 1.23 [1.04-1.45] |               |
| **Nationality**           |               |               |               |               |               |
| Swiss (ref.)              |               |               |               |               |               |
| Non-Swiss                 | 1.09 [0.95-1.24] | 1.07 [0.94-1.23] | 1.07 [0.93-1.23] | 1.09 [0.95-1.25] |               |
| **Urbanity**              |               |               |               |               |               |
| urban (ref.)              |               |               |               |               |               |
| peri-urban                | 0.95 [0.85-1.07] | 0.95 [0.85-1.07] | 0.96 [0.86-1.08] |               |               |
| rural                     | 0.99 [0.85-1.16] | 0.98 [0.83-1.15] | 0.92 [0.78-1.09] |               |               |
| **Language region****     |               |               |               |               |               |
| German (ref.)             |               |               |               |               |               |
| French                    | 1.15 [1.03-1.28] | 1.14 [1.02-1.28] | 1.03 [0.76-1.41] |               |               |
Localisation

Colon (ref.)
rectum

| Language | Hazard Ratio | 95% CI   |
|----------|--------------|----------|
| Italian  | 1.18         | [1.01-1.38] |
|          | 1.16         | [0.99-1.36] |
|          | 1.21         | [1.03-1.42] |

* Additionally adjusted for canton of residence to account for unmeasured canton characteristics associated with SEP and stage.

**German-speaking region: eastern parts of the canton of Fribourg, eastern parts of the canton of Valais (upper Valais), canton of Zurich; French-speaking region: western parts of the canton of Fribourg, canton of Geneva, canton of Neuchâtel, western parts of the canton of Valais (Central and Lower Valais), canton of Vaud; Italian-speaking region: canton of Ticino.
Suppl. Table 5. Cause-specific hazard ratios (CHR) in patients with colorectal cancer

|                          | colorectal cancer death | death due to other causes |
|--------------------------|-------------------------|--------------------------|
|                          | CHR    | [95%CI]       | CHR    | [95%CI]       |
| **SEP**                  |         |               |         |               |
| High SEP (ref.)          |         |               |         |               |
| Middle SEP               | 1.01   | [0.92-1.12]   | 1.16   | [1.00-1.34]   |
| Low SEP                  | 1.12   | [1.00-1.25]   | 1.24   | [1.02-1.71]   |
| **Sex**                  |         |               |         |               |
| male (ref.)              |         |               |         |               |
| female                   | 0.93   | [0.86-1.01]   | 0.65   | [0.58-0.73]   |
| **Age at diagnosis**     |         |               |         |               |
| 50-64 years (ref.)       |         |               |         |               |
| < 50 years               | 0.68   | [0.57-0.81]   | 0.47   | [0.30-0.72]   |
| 65-74 years              | 1.25   | [1.13-1.37]   | 2.29   | [1.94-1.21]   |
| 75-84 years              | 2.00   | [1.81-2.20]   | 15.48  | [1.35-1.62]   |
| **Civil status**         |         |               |         |               |
| married (ref.)           |         |               |         |               |
| single                   | 1.04   | [0.92-1.19]   | 1.14   | [1.00-1.29]   |
| widowed                  | 0.99   | [0.88-1.11]   | 0.89   | [0.79-1.00]   |
| divorced                 | 1.00   | [0.88-1.13]   | 1.10   | [0.98-1.24]   |
| **Nationality**          |         |               |         |               |
| Swiss (ref.)             |         |               |         |               |
| Non-Swiss                | 1.23   | [1.10-1.36]   | 1.15   | [1.04-1.27]   |
| **Urbanity**             |         |               |         |               |
| urban (ref.)             |         |               |         |               |
| peri-urban               | 1.16   | [1.07-1.26]   | 1.04   | [0.93-1.16]   |
| rural                    | 1.15   | [1.02-1.30]   | 1.01   | [0.85-1.19]   |
| Language region* |                |                |                |
|-----------------|----------------|----------------|----------------|
| German (ref.)   |                |                |                |
| French          | 0.96 [0.77-1.20] | 1.00 [0.70-1.43] |
| Italian         | 0.93 [0.82-1.04] | 1.02 [0.88-1.19] |
| Localisation    |                |                |                |
| Colon (ref.)    |                |                |                |
| rectum          | 1.11 [1.02-1.19] | 1.01 [0.91-1.13] |
| Stage at diagnosis |            |                |                |
| Stage I (ref.)  |                |                |                |
| Stage II        | 3.24 [2.57-4.08] | 1.08 [0.95-1.24] |
| Stage III       | 8.34 [6.70-10.39] | 1.03 [0.89-1.19] |
| Stage IV        | 35.50 [28.54-44.16] | 2.12 [1.77-2.53] |

1 German-speaking region: eastern parts of the canton of Fribourg, eastern parts of the canton of Valais (upper Valais), canton of Zurich; French-speaking region: western parts of the canton of Fribourg, canton of Geneva, canton of Neuchâtel, western parts of the canton of Valais (Central and Lower Valais), canton of Vaud; Italian-speaking region: canton of Ticino.
**Suppl. Table 6**: Odds ratios (OR) of later colorectal cancer stage at diagnosis after multiple imputation of stage

|                          | Stage I versus  | Stage I-II versus | Stage I-III versus |
|--------------------------|------------------|-------------------|--------------------|
|                          | Stage II-IV      | Stage II-IV       | Stage IV           |
|                          | OR   [95%CI]     | OR   [95%CI]      | OR   [95%CI]       |
| **SEP**                  |                  |                   |                    |
| High SEP (ref.)          |                  |                   |                    |
| Middle SEP              | 1.11  [0.97-1.28] | 1.01  [0.90-1.12] | 1.06  [0.92-1.21]  |
| Low SEP                 | 1.29  [1.10-1.52] | 1.06  [0.93-1.20] | 1.00  [0.85-1.16]  |
| **Sex**                 |                  |                   |                    |
| male (ref.)             |                  |                   |                    |
| Female                  | 1.05  [0.93-1.18] | 1.12  [1.02-1.22] | 1.01  [0.91-1.13]  |
| **Age at diagnosis**    |                  |                   |                    |
| 50-64 years (ref.)      |                  |                   |                    |
| < 50 years              | 1.16  [0.92-1.48] | 1.32  [1.11-1.58] | 1.18  [0.97-1.44]  |
| 65-74 years             | 1.02  [0.89-1.17] | 0.95  [0.86-1.06] | 0.94  [0.83-1.07]  |
| 75-84 years             | 1.18  [1.02-1.37] | 0.93  [0.83-1.04] | 0.97  [0.84-1.11]  |
| **Civil status**        |                  |                   |                    |
| married (ref.)          |                  |                   |                    |
| Single                  | 1.37  [1.11-1.68] | 1.34  [1.15-1.55] | 1.31  [1.10-1.55]  |
| Widowed                 | 1.05  [0.87-1.25] | 0.94  [0.82-1.07] | 0.89  [0.75-1.06]  |
| Divorced                | 1.17  [0.97-1.41] | 1.11  [0.97-1.27] | 1.26  [1.07-1.48]  |
| **Nationality**         |                  |                   |                    |
| Swiss (ref.)            |                  |                   |                    |
| Non-Swiss               | 1.02  [0.88-1.19] | 1.07  [0.95-1.20] | 1.08  [0.94-1.23]  |
| **Urbanity**            |                  |                   |                    |
| urban (ref.)            |                  |                   |                    |
| peri-urban              | 0.93  [0.82-1.04] | 0.97  [0.89-1.07] | 0.96  [0.86-1.07]  |
| Rural                   | 0.96  [0.80-1.15] | 1.00  [0.87-1.14] | 0.93  [0.79-1.09]  |
UICC stage was imputed with 25 imputations using the following variables as predictors: age at diagnosis and follow-up time as continuous predictors, SEP, sex, civil status, nationality, urbanity, language region, tumour localisation and follow-up status (alive, death due to CRC, other cause of death) as categorical predictors\(^1\), and an interaction term between follow-up time and follow-up status\(^3\). All models have been additionally adjusted for canton of residence.

\(^1\) German-speaking region: eastern parts of the canton of Fribourg, eastern parts of the canton of Valais (upper Valais), canton of Zurich; French-speaking region: western parts of the canton of Fribourg, canton of Geneva, canton of Neuchâtel, western parts of the canton of Valais (Central and Lower Valais), canton of Vaud; Italian-speaking region: canton of Ticino.

\(^2\) French-speaking region: 0.68 [0.61-0.76] 0.99 [0.91-1.08] 0.74 [0.67-0.83]

\(^3\) Italian-speaking region: 0.92 [0.78-1.09] 0.96 [0.84-1.10] 1.16 [0.99-1.36]

\(^4\) Colon (ref.)
Suppl. Table 7: Sub-hazard ratios and 95% confidence intervals (95%CI), risk of colorectal cancer death in colorectal cancer patients after multiple imputation of stage

|                         | Final Model |     |
|-------------------------|-------------|-----|
|                         | SHR         | 95%CI|
| SEP                     |             |     |
| High SEP (ref.)         |             |     |
| Middle SEP              | 1.00        | [0.91-1.11] |
| Low SEP                 | 1.10        | [0.99-1.24] |
| Sex                     |             |     |
| male (ref.)             |             |     |
| female                  | 0.96        | [0.88-1.04] |
| Age at diagnosis        |             |     |
| 50-64 years (ref.)      |             |     |
| < 50 years              | 0.69        | [0.58-0.81] |
| 65-74 years             | 1.19        | [1.08-1.30] |
| 75-84 years             | 1.70        | [1.54-1.87] |
| Civil status            |             |     |
| married (ref.)          |             |     |
| single                  | 1.01        | [0.88-1.15] |
| widowed                 | 0.96        | [0.85-1.08] |
| divorced                | 1.03        | [0.91-1.16] |
| Nationality             |             |     |
| Swiss (ref.)            | 1.20        | [1.09-1.34] |
| Non-Swiss               |             |     |
| Urbanity                |             |     |
| urban (ref.)            |             |     |
| peri-urban              | 1.13        | [1.04-1.23] |
| rural                   | 1.18        | [1.05-1.32] |
Language region*

|               |         |               |
|---------------|---------|---------------|
| German (ref.) | 0.96    | [0.77-1.20]   |
| French        | 0.96    | [0.77-1.20]   |
| Italian       | 0.90    | [0.80-1.02]   |

Localisation

|               |         |               |
|---------------|---------|---------------|
| Colon (ref.)  |         |               |
| rectum        | 1.11    | [1.03-1.20]   |

Stage at diagnosis

|               |         |               |
|---------------|---------|---------------|
| Stage I (ref.)|         |               |
| Stage II      | 2.88    | [2.31-3.60]   |
| Stage III     | 7.05    | [5.69-8.73]   |
| Stage IV      | 24.93   | [20.17-30.80] |

UICC stage was imputed with 25 imputations using the following variables as predictors: age at diagnosis and follow-up time as continuous predictors, SEP, sex, civil status, nationality, urbanity, language region, tumour localisation and follow-up status (alive, death due to CRC, other cause of death) as categorical predictors, and an interaction term between follow-up time and follow-up status.

Survival was analysed using competing risk regressions based on Fine and Gray's proportional hazard model. All underlying causes of death other than colorectal cancer (CRC) were classified as competing risks. The model has been adjusted for all variables listed plus canton of residence. Results are reported as sub-hazard ratios for risk of dying due to CRC (SHRs) with 95% confidence intervals (95%CI).

*German-speaking region: eastern parts of the canton of Fribourg, eastern parts of the canton of Valais (upper Valais), canton of Zurich; French-speaking region: western parts of the canton of Fribourg, canton of Geneva, canton of Neuchâtel, western parts of the canton of Valais (Central and Lower Valais), canton of Vaud; Italian-speaking region: canton of Ticino.