Thirty-Year Incidence and Mortality Trends in Upper and Lower Gastrointestinal Bleeding in Finland

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Abstract

IMPORTANCE Epidemiological data on lower gastrointestinal bleeding (GIB) in the general population are sparse.

OBJECTIVE To describe the incidence, recurrence, mortality, and case fatality rates of major upper GIB and lower GIB in the general population of Finland between 1987 and 2016.

DESIGN, SETTING, AND PARTICIPANTS This prospective cohort study used data from the 1987 to the 2012 cycles of the National FINRISK Study, a health examination survey that was conducted every 5 years in Finland. Survey participants were adults aged 25 to 74 years who were recruited from a population register by random sampling; those with a history of hospitalization for GIB were excluded. Participants were followed up from survey enrollment to onset of GIB that led to hospitalization, death from any cause, or study end (December 31, 2016). Follow-up was performed through linkage with national electronic health registers. Data were analyzed from February 1, 2019, to January 31, 2020.

MAIN OUTCOMES AND MEASURES Incidence, recurrence, mortality, and case fatality rates for all, upper, lower, and unspecified GIB. Outcome measures were stratified by sex and age group.

RESULTS Among the 39 054 participants included in the study, 494 (1.3%) experienced upper GIB (321 men [65.0%]; mean [SD] age, 52.8 [12.1] years) and 645 (1.7%) had lower GIB (371 men [57.5%]; mean [SD] age, 54.0 [11.7] years). The age-standardized incidence rate was 0.94 per 1000 person-years (95% CI, 0.85-1.04) for upper GIB and 1.26 per 1000 person-years (95% CI, 1.15-1.38) for lower GIB; the incidence was higher in men than in women. Between 1987 and 2016 the incidence rate of upper GIB remained mostly stable, ranging from 0.40 to 0.66 per 1000 person-years, whereas constant increases occurred in the incidence of lower GIB until the rate stabilized. The proportion of recurrent GIB events showed an increasing trend from 1987 to 2016. The upper GIB-specific mortality was higher (0.07 per 1000 person-years; 95% CI, 0.04-0.09) than the lower GIB-specific mortality (0.01 per 1000 person-years; 95% CI, 0.001-0.03). Case fatality was high for those with upper GIB (7.0%; 95% CI, 4.7-10.1) compared with those with lower GIB (0.4%; 95% CI, 0.1-1.3). Case fatality remained stable over the years but was higher in men (between 5% and 10%) than women (<2%) with GIB.

CONCLUSIONS AND RELEVANCE This study found that the overall incidence rate of upper GIB was lower than the incidence of lower GIB, but the recurrence, mortality, and 28-day case fatality were higher in participants with upper GIB. These data can serve as a reference when putting into context the rates of drug-associated GIB and can inform efforts to improve GIB care and outcome and to prevent rebleeding or death for patients with major GIB.
Introduction

Gastrointestinal bleeding (GIB) is an acute and potentially life-threatening event. Although GIB can usually be treated successfully, it represents a substantial socioeconomic burden and has a huge impact at the patient level, including hemodynamic instability, vomiting, abdominal pain, or discomfort, all of which affect daily functioning. In 2006 in the United States, the hospitalization rate associated with GIB was 375 per 100,000 people and the in-hospital mortality was 5 per 100,000 people. In the United Kingdom, the total annual cost of hospitalizations associated with acute upper GIB and its treatment was estimated to be approximately £155.5 million (approximately US $207.6 million). Individuals at high risk of GIB include those with peptic ulcers, inflammation in the gastrointestinal tract, liver cirrhosis, or polyps or tumors in the digestive tract as well as those who use blood-thinning medications or nonsteroidal anti-inflammatory drugs. Although many studies have reported the occurrence of GIB in cohorts of patients with certain prescribed medications, most studies have focused on upper GIB. Lower GIB is common, but data on lower GIB are sparse. Few studies have examined the temporal trends of GIB in the general population, and most of the available data are limited to North America and Southern Europe. Data from the general population in the Nordic region are lacking. In conducting the present cohort study, we aimed to describe the incidence, recurrence, mortality, and case fatality rates of major upper and lower GIB in the general population of Finland between 1987 and 2016.

Methods

The National FINRISK Study surveys were approved by the ethical committee of the Finnish Institute of Health and Welfare and the Coordinating Ethical Committee of Helsinki and Uusimaa Hospital District in Finland. Informed consent for all participants was obtained at the beginning of the FINRISK surveys. Study participants were pseudonymized, and the secondary use of the survey data in the present observational prospective cohort study was approved by the Finnish Institute of Health and Welfare in 2017. We followed the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) reporting guideline.

Study Design and Study Population

This cohort study used data from participants in the FINRISK health examination surveys in Finland. Briefly, FINRISK, which followed the EHES (European Health Examination Survey) and the MONICA (Monitoring of Trends and Determinants in Cardiovascular Disease) project protocols, was a large population-based, cross-sectional study on risk factors of chronic, noncommunicable diseases. In each survey, a random and representative sample of the population was invited from several geographic regions of Finland, and those who responded to the invitation were enrolled. Initiated in 1972, the FINRISK surveys were carried out every 5 years, with a cohort size of 6000 to 8800 per survey. Participants were stratified into cohorts that contained at least 250 people of each sex and each 10-year age group from each geographical area. The participation rate in the 1972 survey was approximately 90% but gradually decreased over time to approximately 50% in 2012.

We included data from the 1987 to 2012 FINRISK survey cohorts. A total of 39,438 unique participants aged 25 to 74 years were enrolled in the surveys during these periods. Of these participants, 384 were excluded because they had a history of hospitalization for GIB at baseline, resulting in a cohort size of 39,054 individuals. Baseline characteristics, including age, sex, marital status, educational level, occupation, and geographical area, were ascertained at enrollment. To identify incident cases of GIB, we followed up the participants using record linkage to the nationwide electronic health registers, which included the hospital discharge register and causes of death register. These national registers cover virtually all persons living in Finland. The follow-up period was from the date of enrollment in the survey (when the health examination was conducted) to the onset
of GIB that led to hospitalization, death from any cause, or end of the follow-up period (December 31, 2016), whichever occurred first.

We further subdivided the cohort into participants with incident GIB and those without incident GIB. Cases of GIB were stratified into upper, lower, or unspecified GIB using International Classification of Diseases, Ninth Revision (ICD-9) or International Statistical Classification of Diseases and Related Health Problems, Tenth Revision (ICD-10) codes. The list of ICD-9 and ICD-10 codes for upper, lower, and unspecified GIB is available in eTable 1 in the Supplement. A participant could have experienced GIB at more than 1 site, and a separate follow-up was conducted for each type of GIB (upper, lower, and unspecified). Incidents of major GIB were defined as GIB that led to hospitalization or GIB-specific death and were identified from the hospital discharge register and causes of death register using ICD-9 and ICD-10 codes. These events were either the main or the top 3 contributing factors in hospitalization or the underlying, direct, or contributing causes of death. Gastrointestinal bleeding was considered unspecified when the location of the bleeding was not recorded or could not be identified, and therefore the ICD-9 or ICD-10 code used was unspecified GIB. Recurrent GIB was identified from incident GIB until death or the end of the follow-up period, and the diagnoses had to be more than 30 days apart. The recurring GIB had to be of the same type as the incident GIB; that is, the event was considered recurrent if an individual with incident upper GIB experienced another upper GIB, if an individual with incident lower GIB experienced another lower GIB, or if an individual with incident unspecified GIB experienced any other type of GIB at any site.

Statistical Analysis
We calculated incidence rates, recurrence rates, and GIB-specific mortality rates of all GIB, upper GIB, lower GIB, and unspecified GIB as the number of events divided by the person-time at risk. Case fatality was calculated as the number of deaths from GIB within 28 days of experiencing a GIB event divided by the number of individuals with incident GIB during the follow-up. Baseline age was used to calculate the person-time at risk and to stratify participants into different age groups (eg, 24-29, 30-39, 40-49 years and so on) to ascertain the age-specific rates. Age standardization was conducted using the European standard population weights. Incidence and mortality rates were reported per 1000 person-years, and case fatality was reported as a percentage. These outcome measures were further stratified by participant sex, age group (when possible), and GIB type (upper, lower, or unspecified).

The 95% CIs for rates were calculated using the Byar method for 10 or more events and the exact method for fewer than 10 events, and for proportions were calculated using the Wilson Score method. Time trends in incidence rates were calculated for every 5-year period of the FINRISK surveys from 1987 to 2012 (ie, 1987-1991, 1992-1996, 1997-2001, 2002-2006, 2007-2011, and 2012-2016), and these survey cohorts were followed up from enrollment to the fifth year of the study period. Time trends in recurrence rate were calculated as the number of recurrent GIB events divided by the total number of GIB events within each of the 5-year periods from 1987 to 2016. Time trends in case fatality were calculated as the proportions for each of the 5-year periods from 1987 to 2016. The difference in the absolute numbers between upper GIB and lower GIB was calculated for each of the 5-year periods from 1987 to 2016.

All statistical calculations and plots were done with R, version 3.6.1 (R Foundation for Statistical Computing). Data were analyzed from February 1, 2019, to January 31, 2020.

Results
Study Population and Characteristics
The study included 39,054 participants, who contributed 627,516 person-years of follow-up for a median duration of 14.9 years. Of these participants, 1081 (2.8%) experienced a major GIB event, with 494 (1.3%) having upper GIB, 645 (1.7%) having lower GIB, and 135 (0.3%) having unspecified GIB, whereas 37,973 individuals (97.2%) did not experience GIB. The mean (SD) baseline age was
53.4 (11.9) years for all participants with incident GIB cases and 47.2 (13.2) years for those with no GIB. The participants with lower GIB and unspecified GIB were slightly older (mean [SD] age, 54.0 [11.7] years and 54.9 [11.0] years) than those experiencing upper GIB (52.8 [12.1] years), but all GIB groups were composed predominantly of male participants (upper: 65.0% men [n = 321]; lower: 57.5% [n = 371]; unspecified: 61.5% [n = 83]). The proportion of men among the participants experiencing GIB was 59.9% (n = 648) and among those without GIB was 47.5% (n = 18 026), whereas the proportions of women were 40.1% (n = 433) and 52.5% (n = 19 947), respectively. The baseline characteristics of participants are presented in eTable 2 in the Supplement.

### Incidence of Major GIB

During the entire study period (1987-2016), the overall crude incidence rate of GIB was 1.74 per 1000 person-years (95% CI, 1.64-1.85) and the overall age-standardized rate was 2.10 per 1000 person-years (95% CI, 1.96-2.25). When stratified by sex, the overall age-standardized rate was higher in men than in women (2.62 per 1000 person-years [95% CI, 2.40-2.86] vs 1.62 per 1000 person-years [95% CI, 1.45-1.81]). Furthermore, when stratified by the site of GIB, the incidence rate was highest for participants with lower GIB (1.26 per 1000 person-years; 95% CI, 1.15-1.38), followed by those with upper GIB (0.94 per 1000 person-years; 95% CI, 0.85-1.04) and those with unspecified GIB (0.26 per 1000 person-years; 95% CI, 0.22-0.32). The age-standardized rates for upper GIB and lower GIB were higher in men (upper: 1.27 per 1000 person-years [95% CI, 1.12-1.44]; lower: 1.50 per 1000 person-years [95% CI, 1.34-1.68]) than in women (upper: 0.64 per 1000 person-years [95% CI, 0.54-0.76]; lower: 1.04 per 1000 person-years [95% CI, 0.90-1.20]). For unspecified GIB, no difference was observed between the sexes (men: 0.33 per 1000 person-years [95% CI, 0.26-0.41] vs women: 0.21 per 1000 person-years [95% CI, 0.15-0.28]) (Table 1).

### Table 1. Incidence Rates of Gastrointestinal Bleeding per 1000 Person-Years Between 1987 and 2016

<table>
<thead>
<tr>
<th>Variable</th>
<th>Upper GIB</th>
<th>Lower GIB</th>
<th>Unspecified GIB</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>No. of cases</td>
<td>Person-years</td>
<td>Incidence rate (95% CI)</td>
</tr>
<tr>
<td>Men</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Overall crude rate</td>
<td>321</td>
<td>290 385.05</td>
<td>1.11 (0.99-1.23)</td>
</tr>
<tr>
<td>Age-standardized rate</td>
<td>NA</td>
<td>NA</td>
<td>1.27 (1.12-1.44)</td>
</tr>
<tr>
<td>Age-specific rate</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>24-29 y</td>
<td>18</td>
<td>36 649.38</td>
<td>0.49 (0.29-0.78)</td>
</tr>
<tr>
<td>30-39 y</td>
<td>40</td>
<td>69 205.99</td>
<td>0.58 (0.41-0.79)</td>
</tr>
<tr>
<td>40-49 y</td>
<td>68</td>
<td>72 365.87</td>
<td>0.94 (0.73-1.19)</td>
</tr>
<tr>
<td>50-59 y</td>
<td>97</td>
<td>65 343.17</td>
<td>1.48 (1.20-1.81)</td>
</tr>
<tr>
<td>60-69 y</td>
<td>75</td>
<td>39 129.32</td>
<td>1.92 (1.51-2.40)</td>
</tr>
<tr>
<td>70-74 y</td>
<td>23</td>
<td>7691.90</td>
<td>2.99 (1.89-4.49)</td>
</tr>
<tr>
<td>Women</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Overall crude rate</td>
<td>173</td>
<td>334 257.16</td>
<td>0.52 (0.44-0.60)</td>
</tr>
<tr>
<td>Age-standardized rate</td>
<td>NA</td>
<td>NA</td>
<td>0.64 (0.54-0.76)</td>
</tr>
<tr>
<td>Age-specific rate</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>24-29 y</td>
<td>9</td>
<td>46 464.70</td>
<td>0.19 (0.09-0.37)</td>
</tr>
<tr>
<td>30-39 y</td>
<td>19</td>
<td>81 689.35</td>
<td>0.23 (0.14-0.36)</td>
</tr>
<tr>
<td>40-49 y</td>
<td>35</td>
<td>81 552.84</td>
<td>0.43 (0.30-0.60)</td>
</tr>
<tr>
<td>50-59 y</td>
<td>52</td>
<td>75 957.69</td>
<td>0.68 (0.51-0.90)</td>
</tr>
<tr>
<td>60-69 y</td>
<td>46</td>
<td>41 490.36</td>
<td>1.11 (0.81-1.48)</td>
</tr>
<tr>
<td>70-74 y</td>
<td>12</td>
<td>7102.26</td>
<td>1.69 (0.87-2.95)</td>
</tr>
<tr>
<td>Total</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Crude rate</td>
<td>494</td>
<td>624 642.87</td>
<td>0.79 (0.72-0.86)</td>
</tr>
<tr>
<td>Age-standardized rate</td>
<td>NA</td>
<td>NA</td>
<td>0.94 (0.85-1.04)</td>
</tr>
</tbody>
</table>

Abbreviations: GIB, gastrointestinal bleeding; NA, not applicable.

* Recruitment of FINRISK survey participants aged 70 to 74 years mainly started in 1997.
We found that a total of 102 upper GIB events and 108 lower GIB events occurred in the study participants after restricting each FINRISK cohort (1987-2012) from enrollment to 5 years of follow-up to obtain incidence rates for each of the 5-year periods from 1987 to 2016. Trends over the years showed that the incidence of upper GIB remained stable over the past 30 years between 0.40 and 0.66 per 1000 person-years, except for a slight increase to 0.95 per 1000 person-years that occurred in the 1997 to 2001 period (Figure 1). For lower GIB, the incidence constantly increased from 0.06 per 1000 person-years in the 1987 to 1991 period to 1.12 per 1000 person-years in the 2002 to 2006 period. Since then, the incidence rate of lower GIB has decreased by almost half (0.54 per 1000 person-years), has become stable in the past decade, and is similar to the upper GIB incidence rate (0.45 per 1000 person years; 95% CI, 0.24-0.77) (Figure 1). The difference in the absolute number of events between upper GIB and lower GIB was that the number of upper GIB events was higher than lower GIB (118 vs 92) until the 1997 to 2001 period. Since then, the number of lower GIB events has increased substantially and remained high until the end of follow-up on December 31, 2016 (eFigure in the Supplement).

Recurrence of Major GIB
We found a total of 60 recurrent upper GIB events in patients with an incident upper GIB, 49 recurrent lower GIB events in patients with an incident lower GIB, and 26 recurrent GIB events in patients with an incident unspecified GIB. The estimated recurrence rate of unspecified GIB was the highest (71.5 per 1000 person-years; 95% CI, 40.2-113.5), but the absolute number of cases was low (n = 26). The recurrence rate for upper GIB was higher (22.4 per 1000 person-years; 95% CI, 20.0-24.8).

Table 2. Recurrence Rates of Gastrointestinal Bleeding per 1000 Person-Years Between 1987 and 2016

<table>
<thead>
<tr>
<th>Variable</th>
<th>Incident upper GIB</th>
<th>Incident lower GIB</th>
<th>Incident unspecified GIB</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>No. of cases</td>
<td>Person-years</td>
<td>Recurrence rate (95% CI)</td>
</tr>
<tr>
<td>Men</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Overall crude rate</td>
<td>39</td>
<td>1460.0</td>
<td>26.7 (19.0-36.5)</td>
</tr>
<tr>
<td>Age-standardized rate</td>
<td>NA</td>
<td>NA</td>
<td>26.0 (18.4-35.7)</td>
</tr>
<tr>
<td>Women</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Overall crude rate</td>
<td>21</td>
<td>1125.8</td>
<td>18.7 (11.5-28.5)</td>
</tr>
<tr>
<td>Age-standardized rate</td>
<td>NA</td>
<td>NA</td>
<td>18.6 (11.0-29.2)</td>
</tr>
<tr>
<td>Total</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Crude rate</td>
<td>60</td>
<td>2585.7</td>
<td>23.2 (17.7-29.9)</td>
</tr>
<tr>
<td>Age-standardized rate</td>
<td>NA</td>
<td>NA</td>
<td>22.4 (16.9-29.0)</td>
</tr>
</tbody>
</table>

Abbreviations: GIB, gastrointestinal bleeding; NA, not applicable.
than the recurrence rate for lower GIB (12.3 per 1000 person-years; 95% CI, 8.9-16.6).

When stratified by sex, the recurrence rate for upper GIB was higher in men than in women, and no difference in recurrence rate was observed for lower GIB (Table 2). The proportions of recurrent events calculated over the 5-year survey cohorts from 1987 to 2012 tended to increase over time (Figure 2). After an incident upper GIB, 73.3% of recurrent upper GIB events (n = 44 of 60) occurred within 1 year and 88.3% of recurrent upper GIB events (n = 53 of 60) took place within 3 years, with a median (interquartile range [IQR]) follow-up of 3 (1-16) months. After an incident lower GIB event, 79.6% of recurrent lower GIB events (n = 39 of 49) occurred within 1 year and 91.8% of recurrent lower GIB events (n = 45 of 49) occurred within 3 years, with a median (IQR) follow-up of 2.5 (1-6) months.

**GIB-Specific Mortality and 28-Day Case Fatality**

We observed 57 deaths associated with GIB during the entire study period, of which 38 (66.7%) were attributed to upper GIB, 4 (7.0%) attributed to lower GIB, and 15 (26.3%) attributed to unspecified GIB. The overall age-standardized GIB-specific mortality rate was 0.11 per 1000 person-years (95% CI, 0.08-0.14), 0.18 per 1000 person-years (95% CI, 0.13-0.24) in men, and 0.04 per 1000 person-years (95% CI, 0.02-0.08) in women. The upper GIB-specific mortality rate was 0.07 per 1000 person-years (95% CI, 0.04-0.09), the lower GIB-specific mortality rate was 0.01 per 1000 person-years (95% CI, 0.001-0.03), and the unspecified GIB-specific mortality rate was 0.03 per 1000 person-years (95% CI, 0.02-0.05). Upper GIB-specific mortality rates were higher in men than in women (0.11 per 1000 person-years [95% CI, 0.07-0.16] vs 0.03 per 1000 person-years [95% CI, 0.04-0.09]) (eTable 3 in the Supplement).

After restricting the follow-up to 5 years, we found a total of 13 GIB-specific deaths of participants. A maximum of 1 to 3 deaths occurred in each of the 5-year periods from 1987 to 2016. The numbers were too low to enable us to calculate reliable estimates for trends over time.

Forty-nine of the 57 total deaths (86.0%) occurred within 28 days of GIB diagnosis; of these 49 deaths, 34 were from upper GIB, 3 were from lower GIB, and 12 were from unspecified GIB. The overall age-standardized case fatality during the study period was 4.7% (95% CI, 3.3-6.3). When stratified by sex, the case fatality was 6.5% (95% CI, 4.5-9.0) in men and 1.8% (95% CI, 0.7-3.6) in women. The age-standardized case fatality was 7.0% (95% CI, 4.7-10.1) in participants with upper GIB, 0.4% (95% CI, 0.1-1.3) in participants with lower GIB, and 8.8% (95% CI, 3.9-16.2) in participants with unspecified GIB (eTable 3 in the Supplement).

![Figure 2. Recurrent Major Upper and Lower Gastrointestinal Bleeding (GIB) for 5-Year Cohorts](https://jamanetwork.com/)

Error bars indicate 95% CIs.
Trends in case fatality for overall GIB among men showed an initial decrease but have remained constant between 5% and 10%. For women, this case fatality trend was less than 2% in the past 2 decades (Figure 3). The limited number of events did not permit us to perform meaningful analyses of case fatality stratified by type of GIB.

Discussion

This population-based cohort study from Finland found that the incidence rate of lower GIB was substantially higher than that of upper GIB, and incidence of upper GIB has remained stable over the past 30 years. With eradication of Helicobacter pylori, the rate of peptic ulcer bleeding has decreased. However, upper GIB associated with H pylori composes approximately 15% to 20% of all upper GIB events; therefore, eradication of H pylori would not substantially alter the trends of overall upper GIB, which might have been counterbalanced by non-H pylori-associated upper GIB and other risk factors over the study period.22 We observed a substantial increase in the incidence of lower GIB until 2006, which decreased by almost half and then stabilized in the past decade. This trend coincided with a slight increase in the incidence of colorectal cancer between 1987 and 2016, which was higher in men than women.23 Overall, the recurrence rate of upper GIB was twice as high as the recurrence rate of lower GIB and slightly increased over the years. Further research into the potential factors associated with the increasing trends is required. Case fatality from GIB remained stable during most of the follow-up period, with higher case fatality in men than in women. Overall, the incidence and fatality associated with GIB improved from the earlier FINRISK survey periods that we analyzed. In the later surveys, however, these rates became stable, and no further improvement was observed.

A recent study in New Zealand that analyzed data from 2002 to 2015 of a population with predominantly European ancestry reported that the incidence rate of nonfatal GIB was 2.19 per 1000 person-years, which was similar to findings in the present study.24 A review of studies from Europe on acute upper GIB that used data from the 1990s reported that the incidence rate of acute upper GIB ranged from 0.36 to 1.72 per 1000 person-years,13 which was within or higher than the range shown in the present study. Compared with the present study, the incidence rates of upper GIB in the United States (from 1998 to 2006) were higher at between 1.46 and 1.70 per 1000 person-years and were comparable to those of Spain (from 1996 to 2005), which ranged from 0.47 to 0.87 per 1000 person-years.2,12 Furthermore, similar to the present study, these studies showed decreased or stable incidence of upper GIB over the years, a higher incidence in men than in women, and increased...
incidence with age. Few studies that reported the incidence of lower GIB in the general population showed that the rates in the United States (1998-2006), Spain (1996-2005), and Italy (2001-2010) were about half of the rate reported in our study. Similar to this study, previous studies reported a slight increasing trend in the incidence of lower GIB or complications. Unlike other studies, the present study showed that the incidence of lower GIB was significantly higher in men than in women.

The proportion of recurrent upper GIB in the present study was within the range of a previous review (between 7% and 16%). Another review (1994-2003) on lower GIB reported that the recurrent lower GIB ranged from 10% to 40%, which was higher than observed in this study. The study from Spain reported that the mortality rates of GIB decreased over time, and several studies in the United States also reported decreasing mortality for upper GIB. However, this trend could not be calculated in this study because of the low number of cases. Overall mortality rates of lower GIB were lower in the present study than in the review of studies in 2005. Improved health care and early detection or diagnosis of bleeding are likely to be associated with the decreased mortality of GIB. Compared with the study from New Zealand, the 28-day case fatality for overall GIB was 2 times higher in our study. In addition, the trend in case fatality of GIB decreased sharply in the early years of the FINRISK surveys and remained stable in recent decades, and the case fatality range was similar to the ranges in the studies from Spain and the United States.

We believe that the findings of this study will be useful in clinical practice. Specifically, the data can inform efforts to improve the care and outcomes for patients with GIB, especially lower GIB, and to prevent recurrent bleeding or death in patients with upper GIB. Incidence, recurrence, mortality, and case fatality rates of GIB in the general population are useful to know when putting into context the rates of drug-associated GIB.

**Strengths and Limitations**

This study has some strengths. It had a population-based design, a large sample size that was representative of the general population in Finland, and minimal or no participant loss to follow-up. The long-term follow-up of 30 years enabled the analysis of temporal trends of GIB over the past 3 decades, which covered changes in both characteristics of the general population and medical practice. Studies of the trends of GIB in the general population in Europe and in Asia are needed, especially for lower GIB for which research data are sparse. Upper GIB has been extensively studied, but the data on trends in the general populations of Asia and Europe may be limited and warrant further investigation. In addition, the risk factors associated with the changes in trends need to be ascertained to identify the areas for improvement.

This study also has some limitations. The electronic health register data were originally collected for administrative purposes. Accordingly, some misclassification in recording the GIB diagnoses and causes of death may have occurred; however, the magnitude of such errors is likely to be small compared with the large number of events. The number of deaths from GIB was low, and therefore the mortality and case fatality estimates had wide CIs. Diagnostic accuracy and coding accuracy have improved over time. Therefore, the time trends, especially the early rates, must be interpreted with caution. Participation in the FINRISK surveys declined over the years, and the nonparticipants were more likely to be young, to be male, to have lower socioeconomic status, and to have more chronic illnesses, which could lead to the underrepresentation of this group, especially in later surveys. Recruitment of FINRISK survey participants aged 70 to 74 years mainly started in a few geographic areas in 1997, and hence the rates for this age group should be interpreted with caution.

**Conclusions**

This study analyzed the epidemiological data of major upper and lower GIB in a large representative sample of the general population in Finland. The incidence of upper GIB remained stable, whereas the incidence of lower GIB showed an increase over the years. Even though the overall incidence rate
of upper GIB was lower than that of lower GIB, the recurrence and mortality rates were higher in participants with upper GIB. The case fatality of all GIB remained stable in the past 2 decades. Thus, the outcomes did not seem to have improved despite more accurate diagnostic methods and likely earlier detection. The data presented here can serve as a reference for improving the care and outcome for patients with major GIB and for preventing rebleeding or death in these patients.

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REFERENCES


**SUPPLEMENT.**

eTable 1. List of ICD 9 and ICD 10 Codes for Gastrointestinal Bleedings

eTable 2. Baseline Characteristics of the Study Participants by Type of Gastrointestinal Bleeding During Follow-up

eFigure. Absolute Difference Between the Number of Upper and Lower Gastrointestinal Bleeding Events for Five-Year Period Each

eTable 3. Mortality Rates and 28-Day Case-Fatality Due to Gastrointestinal Bleedings Between 1987 and 2016