eAppendix 1. ICD Codes for Analytic Variables

Diagnosis	ICD Codes
Posttraumatic Stress Disorder (PTSD)	ICD-10: F43.1
Depression Diagnoses	ICD-8: 296.09, 296.29, 296.99, 298.09, 300.4, 300.19 ICD-10: F32, F33
Alcohol Abuse Diagnoses	ICD-8: 303.x ICD-10: F10.x
Drug Abuse Diagnoses	ICD-8: 304.x ICD-10: F11.x-F19.x
Generalized Anxiety Disorder	ICD-8: 300.0 ICD-10: F41.1
Panic Disorder	ICD-10: F41.0
Phobias	ICD-8: 300.2 ICD-10: F40.9
Charlson Comorbidity Index Diagnoses	
Myocardial Infarction	ICD-8: 410 ICD-10: I21-I23
Congestive Heart Failure	ICD-8: 427.09 – 427.11, 427.19, 428.99, 782.49 ICD-10: I50, I1 1.0, I1 3.0, I13.2
Peripheral Vascular Disease	ICD-8: 440-445 ICD-10: I70-I74, I77
Cerebrovascular Disease	ICD-8: 430-438 ICD-10:I60-I69, G45, G46
Dementia	ICD-8: 290.09-290.19, 293.09 ICD-10: F00-F03, F05.1, G30
Chronic Pulmonary Disease	ICD-8: 490-493, 515-518 ICD-10: J40-J47, J60-J67, J68.4, J70.1, J70.3, J84.1, J92.0, J96.1, J98.2, J98.3
Connective Tissue Diseases	ICD-8: 712, 716, 734, 446, I35.99 ICD-10: M05, 6, M08, M09, M30-M36, D86

Mild Liver Disease	ICD-8: 571, 573.01, 573.04 ICD-10: B18, K70.0-K70.3, K70.9, K71, K73, K74, K76.0
Diabetes Mellitus Without Organ Damage	ICD-8: 249.00, 249.06, 249.07, 249.09 ICD-10: E10.0, E10.1, E10.9, E11.0, E11.1, E11.9
Diabetes Mellitus With Organ Damage	ICD-8: 249.01-249.05, 249.08 ICD-10: E10.2-E10.8, E11.2, E11.8
Hemiplegia	ICD-8: 344 ICD-10: G81, G82
Moderate to Severe Renal Disease	ICD-8: 403, 404, 580-584, 590.09, 593.19, 753.10, 753.19, 792 ICD-10: I12, I13, N00-N05, N07, N11, N14, N17-N19, Q61
Non-Metastatic Solid Tumor	ICD-8: I40-I49 ICD-10: C00-C75
Leukemia	ICD-8: 204-207 ICD-10: C91-C95
Lymphoma	ICD-8: 200-203, 275.59 ICD-10: C81-C85, C88, C90, C96
Moderate to Severe Liver Disease	ICD-8: O70.00, O70.02, O70.04, O70.06, O70.08, 573.00, 456.00-456.09 ICD-10: B15.0, B16.0, B16.2, B19.0, K70.4, K72, K76.6, I85
Metastatic Cancer	ICD-8:I95-I99 ICD-10: C76-C80
AIDS	ICD-8: O79.83 ICD-10: B21-B24
GI Disorders	
Esophagitis	ICD-8: 530.90, 530.91 ICD-10: K20, K21
Stomach ulcer	ICD-8: 531 ICD-10: K25
Duodenal ulcer	ICD-8: 532 ICD-10: K26
Peptic ulcer, site unspecified	ICD-8: 533 ICD-10: K27
Gastritis and duodenitis	ICD-8: 535 ICD-10: K29
Acute appendicitis	ICD-8: 540 ICD-10: K35
Diverticula of the intestines	ICD-8: 562

	ICD-10: K57
Chronic enteritis and ulcerative colitis	ICD-8: 563 ICD-10: K50, K51
Irritable bowel syndrome	ICD-8: 564.19 ICD-10: K58
Acute and subacute necrosis of the liver	ICD-8: 570 ICD-10: K70, K71, K72, K73
Cirrhosis of the liver	ICD-8: 571 ICD-10: K74
Cholelithiasis	ICD-8: 574 ICD-10: K80
Cholecystitis and cholangitis	ICD-8: 575 ICD-10: K81
Pancreatitis	ICD-8: 577.00, 577.01, 577.02, 557.03, 577.09, 577.10, 577.11, 577.19 ICD-10: K85

eAppendix 2. SIRs for PTSD and incident gastrointestinal disorders, stratified by psychiatric diagnosis comorbidities

	Depression Diagnosis SIR (95% CI)		Alcohol Abuse Diagnoses SIR (95% CI)		Drug Abuse Diagnoses SIR (95% CI)		Generalized Anxiety Disorder SIR (95% CI)		Panic Disorder SIR (95% CI)		Phobias SIR (95% CI)	
	No	Yes	No	Yes	No	Yes	No	Yes	No	Yes	No	Yes
All gastrointestinal disorders	1.8 (1.6, 1.9)	2.6 (1.8, 3.6)	1.7 (1.5, 1.8)	3.7 (2.9, 4.7)	1.8 (1.6. 1.9)	4.3 (2.2, 7.5)	1.8 (1.7, 2.0)	--	1.8 (1.7, 2.0)	--	1.8 (1.7, 2.0)	--
Esophagitis	2.2 (1.8, 2.6)	4.2 (2.1, 7.6)	2.1 (1.7, 2.5)	4.6 (2.6, 7.5)	2.2 (1.9, 2.7)	--	2.2 (1.9, 2.7)	--	2.2 (1.8, 2.7)	--	2.3 (1.9, 2.7)	--
Stomach ulcer	2.5 (1.8, 3.3)	--	2.4 (1.8, 3.2)	4.7 (1.5, 11)	2.5 (1.9, 3.3)	--	2.6 (1.9, 3.4)	--	2.5 (1.8, 3.3)	--	2.5 (1.9, 3.4)	--
Duodenal ulcer	1.4 (0.79, 2.3)	--	1.4 (0.79, 2.2)	--	1.4 (0.81, 2.2)	--	1.4 (0.81, 2.2)	--	1.4 (0.81, 2.2)	--	1.4 (0.80, 2.2)	--
Peptic ulcer, site unspecified	3.0 (1.6, 5.3)	--	3.2 (1.7, 5.5)	--	3.1 (1.6, 5.3)	--	3.3 (1.8, 5.6)	--	3.3 (1.8, 5.5)	--	3.3 (1.8, 5.5)	--
Gastritis and duodenitis	2.6 (2.2, 3.2)	--	2.2 (1.7, 2.7)	8.6 (5.3, 13)	2.5 (2.0, 3.1)	--	2.6 (2.1, 3.2)	--	2.6 (2.1, 3.1)	--	2.6 (2.1, 3.1)	--
Acute appendicitis	1.5 (1.2, 2.0)	--	1.6 (1.2, 2.1)	1.9 (0.60, 4.3)	1.6 (1.2, 2.0)	--	1.6 (1.2, 2.1)	--	1.6 (1.2, 2.0)	--	1.6 (1.2, 2.1)	--
Diverticula of the intestines	1.1 (0.82, 1.5)	--	1.1 (0.76, 1.5)	2.4 (0.77, 5.5)	1.2 (0.84, 1.6)	--	1.2 (0.84, 1.6)	--	1.2 (0.83, 1.5)	--	1.1 (0.83, 1.5)	--
Chronic enteritis and ulcerative colitis	1.6 (1.1, 2.3)	--	1.6 (1.1, 2.2)	--	1.6 (1.1, 2.2)	--	1.7 (1.2, 2.3)	--	1.7 (1.2, 2.3)	--	1.7 (1.2, 2.3)	--
Irritable bowel syndrome	1.8 (1.3, 2.3)	--	1.8 (1.3, 2.3)	--	1.8 (1.3, 2.3)	--	1.8 (1.4, 2.3)	--	1.8 (1.4, 2.3)	--	1.8 (1.4, 2.3)	--

Acute and subacute necrosis of the liver	2.9 (2.2, 3.9)	8.5 (3.7, 17)	2.2 (1.5, 3.0)	18 (11, 27)	3.2 (2.4, 4.1)	--	3.2 (2.4, 4.1)	--	3.3 (2.5, 4.2)	--	3.2 (2.5, 4.2)	--
Cholelithiasis	1.5 (1.2, 1.8)	--	1.5 (1.2, 1.8)	1.3 (0.53, 2.7)	1.5 (1.2, 1.7)	--	1.5 (1.2, 1.8)	--	1.5 (1.2, 1.7)	--	1.5 (1.2, 1.7)	--
Cholecystitis and cholangitis	1.8 (1.1, 2.8)	--	1.8 (1.1, 2.9)	--	1.9 (1.2, 2.9)	--	1.9 (1.2, 2.9)	--	1.9 (1.2, 2.9)	--	1.9 (1.2, 2.9)	--
Pancreatitis	2.9 (2.0, 4.1)	--	2.4 (1.6, 3.5)	10 (4.3, 20)	2.9 (2.0, 4.0)	--	2.9 (2.0, 4.0)	--	2.9 (2.0, 4.0)	--	2.9 (2.1, 4.1)	--

Note: Results not presented when fewer than 5 incident gastrointestinal disorder cases were identified in a stratification subgroup.

eAppendix 3. Analytic code used for analyses

```
%date;
libname data 'S:\Dora Farkas\PYRS_analyses\stress_GI_diseases\datasets\';

*PYRS macro - to divide persons follow-up into periods according to age and calendar period groups;
%macro pyrs(nv,varin,varlist,yrin,yrout,olist,width,pyrs,py);
 %Global pyrsn;
 %if &pyrsn= %then %let pyrsn=1;
  %else %let pyrsn=%eval(&pyrsn+1);
 array _di&pyrsn(&nv) &varin;
 array _du&pyrsn(&nv) _temporary_;
 array _dr&pyrsn(&nv) _temporary_;
 array _v&pyrsn(&nv) &varlist;
 array _o&pyrsn(&nv) _temporary_ (&olist);
 do _i=1 to &nv ;
  if _di&pyrsn(_i)<= .z then do;
   put /'Error in macro pyrs' _di&pyrsn(*)=;
   abort;
  end;
 end;
 if &yrout<= .z then do;
  put /'Error in macro Pyrs' &yrout=;
  Abort;
 end;
 _yr=&yrin;
 do _i=1 to &nv;
  _du&pyrsn(_i)=_di&pyrsn(_i);
 End;
 do until (_yr >= &yrout);
  do _i=1 to &nv;
   _v&pyrsn(_i)=
    (&width*floor((_du&pyrsn(_i)-_o&pyrsn(_i))/&width))+_o&pyrsn(_i);
   _dr&pyrsn(_i)=_v&pyrsn(_i)+&width-_du&pyrsn(_i);
  end;
  &pyrs=min(of %do _i=1 %to &nv; _dr&pyrsn(&_i) %end; );
  if (&yrout - _yr) < &pyrs then &pyrs=&yrout-_yr;
  output &py;
  do _i=1 to &nv;
    _du&pyrsn(_i)=_du&pyrsn(_i)+&pyrs;
   end;
   _yr=_yr+&pyrs;
  end;
%mend pyrs;

*macro to calculate the 95% confidence interval for SIR estimates;
%macro ci(inddata,uddata);
 data &uddata;
  set &inddata;
  format ratio 6.2;
  ratio = O/E;
  if O = 1 then do;
   Low95_sir = round(0.0253*O/E,.01);
```

```
    Upper95_sir = round(5.57*O/E,.01);
   end;
   if O = 2 then do;
    Low95_sir = round(0.121*O/E,.01);
    Upper95_sir = round(3.61*O/E,.01);
   end;
   if O = 3 then do;
    Low95_sir = round(0.206*O/E,.01);
    Upper95_sir = round(2.92*O/E,.01);
   end;
   if O = 4 then do;
    Low95_sir = round(0.272*O/E,.01);
    Upper95_sir = round(2.56*O/E,.01);
   end;
   if O = 5 then do;
    Low95_sir = round(0.324*O/E,.01);
    Upper95_sir = round(2.33*O/E,.01);
   end;
   if O = 6 then do;
    Low95_sir = round(0.367*O/E,.01);
    Upper95_sir = round(2.18*O/E,.01);
   end;
   if O = 7 then do;
    Low95_sir = round(0.401*O/E,.01);
    Upper95_sir = round(2.06*O/E,.01);
   end;
   if O = 8 then do;
    Low95_sir = round(0.431*O/E,.01);
    Upper95_sir = round(1.97*O/E,.01);
   end;
   if O = 9 then do;
    Low95_sir = round(0.458*O/E,.01);
    Upper95_sir = round(1.90*O/E,.01);
   end;
   if O > 9 then do;
    Low95_sir = round(((1-1/(9*O)-1.96/(3*sqrt(O)))**3)*O/E,.01);
    Upper95_sir = round(((1-1/(9*(O+1))+1.96/(3*sqrt(O+1)))**3)*(O+1)/E,.01);;
   end;
  run;
%mend ci;

proc format;
        value age_diag_gr
                1 = '16 - 39 years'
                2 = '40 - 59 years'
                3 = '60+ years';
        value sex
                0 = 'Female'
                1 = 'Male';
        value yn
                1 = 'Yes'
                0 = 'No';
        value com_gr
```

```
                0 = 'Low (CCI = 0)'
                1 = 'Medium or high (CCI = 1+)';
        value marital_gr
                1 = 'Married/Registered patnership'
                2 = 'Single'
                3 = 'Divorced'
                4 = 'Widow'
                5 = 'Unknown';
run;


proc format;
        value $outcome
                "outcome_overall" = "GI diseases overall              "
                "outcome_1" =  "Esophagitis"
                "outcome_2" =  "Stomach ulcer"
                "outcome_3" =  "Duodenal ulcer"
                "outcome_4" =  "Peptic ulcer, site unspecified"
                "outcome_5" =  "Gastrojejunal ulcer"
                "outcome_6" =  "Gastritis & duodenitis"
                "outcome_7" =  "Acute appendicitis"
                "outcome_8" =  "Diverticula of the intestines"
                "outcome_9" =  "Chronic enteritis & ulcerative colitis"
                "outcome_10" =  "Irritable colon"
                "outcome_11" =  "Acute & subacute necrosis of the liver"
                "outcome_12" =  "Cirrhosis of the liver"
                "outcome_13" =  "Cholelithiasis"
                "outcome_14" =  "Cholecystitis & cholangitis"
                "outcome_15" =  "Pancreatitis";
        value gr
                1 = "At 1 year of follow-up"
                2 = "At 5 years of follow-up "
                3 = "At 10 years of follow-up"
                4 = "At end of follow-up     ";
run;

data grundkohorte;
        set data.grundkohorte_20160603;
run;

*create the PTSD cohort;
data PTSD_cohort;
        set grundkohorte;
        if . < d_uddto;

        if RSS_type = 2;
run; *4.076 obs;

data OBSrater;
        set PTSD_cohort;

        exact_age = round((d_uddto - birth)/365.25,.01);
```

```
        if 16 <= exact_age < 40 then age_diag_gr = 1;
        if 40 <= exact_age < 60 then age_diag_gr = 2;
        if 60 <= exact_age then age_diag_gr = 3;

        if comorbiditet = 0 then com_gr = 0;
        if comorbiditet >= 1 then com_gr = 1;

        ft_overall = (enddate_overall - d_uddto)/365.25;

run;


*****************************************************************;
*****************************************************************;

*macro to calculate the SIR estimates for a given outcome;
%macro outcome(outcome);

        data baggrundsrater_&outcome;
                set grundkohorte;

                aarind=max(year(indrejse_dato)+(indrejse_dato-mdy(1,1,year(indrejse_dato)))/365.25,1995);
                ageind=(max(indrejse_dato,mdy(1,1,1995)) - birth)/365.25;
                aarud=year(enddate_&outcome)+((enddate_&outcome)-mdy(1,1,year(enddate_&outcome)))/365.25;

        run;

        data PYRSbaggrund_&outcome;
                set baggrundsrater_&outcome;
                %pyrs(2,ageind aarind, agegr periode, aarind, aarud, 0 1995, 5, rtid,  PYRSbaggrund_&outcome);
           keep cpr agegr periode sex rtid GI_dis_date_&outcome;
        run;

        data PYRSbaggrund_&outcome;
                set PYRSbaggrund_&outcome;
                if agegr>99 then agegr=99;
        run;

        proc summary nway data = PYRSbaggrund_&outcome;
                class agegr periode sex;
                var rtid;
                output out = TID_baggrund_&outcome  sum(rtid)=TID_Baggrund ;
        run;

        data PYRSbaggrund1_&outcome;
                set PYRSbaggrund_&outcome;
                by cpr agegr periode;
                if last.cpr;
        run;



        *****************************************************************;
```

```
*****************************************************************;


data time1_&outcome;
   set OBSrater;

   if 365 < enddate_&outcome - d_uddto then do;
         enddate_&outcome = d_uddto + 365;
         GI_dis_date_&outcome = .;
   end;
   format ageind 6.2 aarind 8.2 aarud 8.2;
   ageind = (d_uddto - birth)/365.25;
   aarind = year(d_uddto) + (d_uddto - mdy(1,1,year(d_uddto)))/365.25;
   aarud = year(enddate_&outcome) + (enddate_&outcome - mdy(1,1,year(enddate_&outcome)))/365.25;
   latens = 1;
   %pyrs(2,ageind aarind , agegr periode, aarind, aarud, 0 1995, 5, rtid,  time1_&outcome);
run;

data time1__&outcome;
   set OBSrater;

   if enddate_&outcome - d_uddto <= 365 then delete;
   d_uddto = d_uddto + 365;
   format ageind 6.2 aarind 8.2 aarud 8.2;
   ageind = (d_uddto - birth)/365.25;
   aarind = year(d_uddto) + (d_uddto - mdy(1,1,year(d_uddto)))/365.25;
   aarud = year(enddate_&outcome) + (enddate_&outcome - mdy(1,1,year(enddate_&outcome)))/365.25;
   latens = 2;
   %pyrs(2,ageind aarind , agegr periode, aarind, aarud, 0 1995, 5, rtid,  time1__&outcome);
run;

data PYRSobs_&outcome;
  set time1_&outcome time1__&outcome;
  if agegr>99 then agegr=99;
run;


proc means data=PYRSobs_&outcome n min max sum median;
         var rtid agegr periode;
run;

data PYRSbaggrund2_&outcome;
         set PYRSbaggrund1_&outcome;
         if . < GI_dis_date_&outcome then event_baggrund=1; else event_baggrund=0;
run;


proc sort data=PYRSobs_&outcome;
         by cpr agegr periode;
run;

data PYRSobs1_&outcome;
         set PYRSobs_&outcome;
```

```
		by cpr agegr periode;
		if last.cpr and . < GI_dis_date_&outcome then event_obs=1; else event_obs=0;
	run;

	proc summary nway data = PYRSbaggrund2_&outcome;
		class agegr periode sex;
		var event_baggrund;
		output out = p1_&outcome  sum(event_baggrund)=event_baggrund ;
	run;

	proc summary nway data = PYRSobs1_&outcome;
		class agegr periode sex latens age_diag diag_year substance_abuse_before com_gr
				marital_gr depression_before gen_anx_dis_before panic_dis_before phobias_before
alcohol_before drug_dep_before;
		var rtid event_obs;
		output out = p0_&outcome  sum(rtid)=TID_obs sum(event_obs)=event_obs;
	run;

	data PYRS_&outcome;
		merge p1_&outcome(in=q1 drop = _TYPE_ _FREQ_ ) p0_&outcome(in=q2 drop = _TYPE_ _FREQ_ )
TID_Baggrund_&outcome(in=q3 drop = _TYPE_ _FREQ_ );
		by agegr periode sex;
		if q1 and q2 and q3 ;
		E_i=tid_obs*(event_baggrund/tid_baggrund);
	run;

	data PYRS_&outcome;
		set PYRS_&outcome;
		V1 = 'TOTAL                                          ';
		if sex = 0 then V2 = 'FEMALE  ';
		if sex = 1 then V2 = 'MALE    ';
		if 16 <= age_diag < 40      then V3 = 'AGE AT PTSD DIAGNOSIS: 16-39 ';
		if 40 <= age_diag < 60 then V3 = 'AGE AT PTSD DIAGNOSIS: 40-59';
		if 60 <= age_diag then V3 = 'AGE AT PTSD DIAGNOSIS: 60+   ';
		if substance_abuse_before = 0 then V4 = 'SUBSTANCE ABUSE: NO ';
		if substance_abuse_before = 1 then V4 = 'SUBSTANCE ABUSE: YES';
		if com_gr = 0 then V5 = 'CCI = 0  ';
		if com_gr >= 1 then V5 = 'CCI = 1+';

		if marital_gr = 1 then V6 = '  MARRIED/REGISTERED PARTNERSHIP';
		if marital_gr = 2 then V6 = '  SINGLE';
		if marital_gr = 3 then V6 = ' DIVORCED';
		if marital_gr = 4 then V6 = ' WIDOW';
		if marital_gr = 5 then V6 = 'UNKNOWN';
		if depression_before = 0 then V7 = 'DEPRESSION: NO ';
		if depression_before = 1 then V7 = 'DEPRESSION: YES';
		if alcohol_before = 0 then V8 = 'ALCOHOL USE DISORDER: NO ';
		if alcohol_before = 1 then V8 = 'ALCOHOL USE DISORDER: YES';
		if drug_dep_before = 0 then V9 = 'DRUG DEPENDENCE: NO ';
		if drug_dep_before = 1 then V9 = 'DRUG DEPENDENCE: YES';
		if gen_anx_dis_before = 0 then V10 = 'GENERALIZED ANXIETY DISORDER: NO ';
		if gen_anx_dis_before = 1 then V10 = 'GENERALIZED ANXIETY DISORDER: YES';
		if panic_dis_before = 0 then V11 = 'PANIC DISORDER: NO ';
```

```
		if panic_dis_before = 1 then V11 = 'PANIC DISORDER: YES';
		if phobias_before = 0 then V12 = 'PHOBIAS: NO ';
		if phobias_before = 1 then V12 = 'PHOBIAS: YES';

		if Latens = 1 then V13 = 'FOLLOW-UP 0-1 YEAR';
		if Latens = 2 then V13 = 'FOLLOW-UP 1+ YEAR ';
	run;


	%macro strata;
		data all;
			d=1;
			output;
		run;
		%do j = 1 %to 13;
			proc summary nway data = PYRS_&outcome;
				class V&j;
				var E_i event_obs TID_obs;
				format TID_obs 10.2;
				output out = strata (drop = _TYPE_ _FREQ_) sum(E_i) = E sum(event_obs) = O
sum(tid_obs) = tid_obs;
			run;

			data all;
				set all strata(in = b);
				if b then text = V&j;
				output;
				drop V&j;
			run;
		%end;

		data outcome_&outcome;
			set all;
			if d = 1 then delete;
			drop d;
		run;

		%ci(outcome_&outcome,outcome_&outcome);

	%mend strata;

	%strata;

	data final_SIR_results;
		set final_SIR_results(in = q1) outcome_&outcome(in = q2);
		if q2 then outcome = "outcome_&outcome";
	run;

	proc datasets nolist nodetails;
		delete p0_&outcome p1_&outcome PYRSobs1_&outcome PYRSbaggrund2_&outcome
			baggrundsrater_&outcome PYRSbaggrund_&outcome TID_baggrund_&outcome
PYRSbaggrund1_&outcome time15_&outcome time510_&outcome time10__&outcome PYRSobs_&outcome;
	run;
```

```
	quit;

%mend outcome;

*macro to collect SIR estimates for all outcomes;
%macro collect_SIR_results;

	data final_SIR_results;
		d = 1;
	run;
	%outcome(overall);

	%do i = 1 %to 15;
		%outcome(&i);
	%end;

	data final_SIR_results;
		set final_SIR_results;

		ci=" ("||put(Low95_sir,6.2)||"-"||put(Upper95_sir,6.2)||")";
		ci=compress(ci,' ');
		SIR_CI=" "||put(ratio,6.2)||" "||put(ci,$20.)||" ";

		if Low95_sir < 1 then Low95_sir_b = put(Low95_sir,6.2); else Low95_sir_b = put(Low95_sir,6.1);
		if Upper95_sir < 1 then Upper95_sir_b = put(Upper95_sir,6.2); else Upper95_sir_b =
put(Upper95_sir,6.1);
		if ratio < 1 then ratio_b = put(ratio,6.2); else ratio_b = put(ratio,6.1);

		ci_b=" ("||Low95_sir_b||"-"||Upper95_sir_b||")";
		ci_b=compress(ci_b,' ');
		SIR_CI_b=" "||ratio_b||" "||put(ci_b,$20.)||" ";

		format outcome $outcome.;

		if d = 1 then delete;
		drop d;
	run;

%mend collect_SIR_results;

%collect_SIR_results;
```