U.PORTO

MESTRADO INTEGRADO EM MEDICINA

Association Between Exposure to Interpersonal Violence and Cardiac, Metabolic, and Renal Diseases – A Cohort Study in a Local Health Unit in Portugal

Joana Gaspar Nunes Silva

M

2024

U.PORTO
FMUP FACULDADE DE MEDICINA
UNIVERSIDADE DO PORTO

UC Dissertação - DECLARAÇÃO DE INTEGRIDADE

Eu, Joana Gaspar Nunes Silva, abaixo assinado, nº mecanográfico 201905210, estudante do 6º ano do Ciclo de Estudos Integrado em Medicina, na Faculdade de Medicina da Universidade do Porto, declaro ter actuado com absoluta integridade na elaboração do meu trabalho de Dissertação ou Monografia.

Neste sentido, confirmo que **NÃO** incorri em plágio (acto pelo qual um indivíduo, mesmo por omissão, assume a autoria de um determinado trabalho intelectual, ou partes dele). Mais declaro que todas as frases que retirei de trabalhos anteriores pertencentes a outros autores, foram referenciadas, ou redigidas com novas palavras, tendo colocado, neste caso, a citação da fonte bibliográfica.

Faculdade de Medicina da Universidade do Porto, 29/06/2025

Assinatura conforme cartão de identificação:

Joana Gaspar Nunes Silva

U.PORTO
FMUP FACULDADE DE MEDICINA UNIVERSIDADE DO PORTO

UC Dissertação – DECLARAÇÃO DE REPRODUÇÃO

NOME

Joana Gaspar Nunes Silva

NÚMERO DE ESTUDANTE

201905210

E-MAIL

joana.gasparnunessilva@gmail.com

DESIGNAÇÃO DA ÁREA DO PROJECTO

Medicina Clínica

TÍTULO DISSERTAÇÃO/~~MONOGRAFIA~~ (riscar o que não interessa)

Association between exposure to interpersonal violence and cardiac, metabolic, and renal diseases - A cohort study in a Local Health Unit in Portugal

ORIENTADOR

Teresa Maria Salgado de Magalhães

COORIENTADOR (se aplicável)

Rita Azevedo Lopes

ASSINALE APENAS UMA DAS OPÇÕES:

É AUTORIZADA A REPRODUÇÃO INTEGRAL DESTE TRABALHO APENAS PARA EFEITOS DE INVESTIGAÇÃO, MEDIANTE DECLARAÇÃO ESCRITA DO INTERESSADO, QUE A TAL SE COMPROMETE.	☐
É AUTORIZADA A REPRODUÇÃO PARCIAL DESTE TRABALHO (INDICAR, CASO TAL SEJA NECESSÁRIO, Nº MÁXIMO DE PÁGINAS, ILUSTRAÇÕES, GRÁFICOS, ETC.) APENAS PARA EFEITOS DE INVESTIGAÇÃO, MEDIANTE DECLARAÇÃO ESCRITA DO INTERESSADO, QUE A TAL SE COMPROMETE.	☐
DE ACORDO COM A LEGISLAÇÃO EM VIGOR, (INDICAR, CASO TAL SEJA NECESSÁRIO, Nº MÁXIMO DE PÁGINAS, ILUSTRAÇÕES, GRÁFICOS, ETC.) NÃO É PERMITIDA A REPRODUÇÃO DE QUALQUER PARTE DESTE TRABALHO.	☒

Faculdade de Medicina da Universidade do Porto, 29/06/2025

Assinatura conforme cartão de identificação: Joana Gaspar Nunes Silva

U.PORTO
FMUP FACULDADE DE MEDICINA UNIVERSIDADE DO PORTO

UC Dissertação - DECLARAÇÃO DE TRANSPARÊNCIA RELATIVAMENTE À UTILIZAÇÃO DE FERRAMENTAS DE CHATBOT GENERATIVO BASEADAS EM LARGE LANGUAGE MODELS

Eu, Joana Gonçalo Nunes Silva, abaixo assinado, nº mecanográfico 201905210, estudante do 6º ano do Ciclo de Estudos Integrado em Medicina, na Faculdade de Medicina da Universidade do Porto, declaro que:

☒ Não procedi à utilização de ferramentas de *chatbox* generativo baseadas em *large language models* para nenhuma das tarefas no contexto do meu trabalho de Dissertação ou Monografia

☐ Procedi à utilização de ferramentas de *chatbox* generativo baseadas em *large language models* no contexto do meu trabalho de Dissertação ou Monografia, encontrando-se todas as interacções (*prompts* e respostas) transcritas em anexo bem como a indicação das aplicações utilizadas.

Neste sentido, confirmo que a eventual utilização de ferramentas de *chatbox* generativo baseadas em *large language models* no contexto do meu trabalho de Dissertação ou Monografia foi exclusivamente descrita na sequência de *prompts* e respostas transcritos em anexo e nas aplicações indicadas.

Faculdade de Medicina da Universidade do Porto, 29/06/2025

Assinatura conforme cartão de identificação:

Joana Gonçalo Nunes Silva

Agradecimentos

Venho de longe e, por fim, alcanço o término desta etapa marcante do meu percurso académico.

Em primeiro lugar, não posso deixar de expressar a minha mais profunda gratidão àqueles que sempre estiveram ao meu lado desde o primeiro momento da minha vida: os meus pais, Carla e Miguel. A vossa presença constante, o vosso esforço incansável e o vosso amor incondicional foram essenciais para que pudesse realizar o sonho de me tornar médica. Obrigada por trabalharem tanto para que nunca me faltasse conforto e estabilidade, especialmente nos momentos de maior exigência. Fizeram de mim uma mulher resiliente e determinada. Apesar das minhas dificuldades naturais com a investigação, o vosso incentivo nunca esmoreceu e ajudou-me a não desistir, mesmo que esta tese tenha sido concluída com algum atraso. Afinal, tendo feito grande parte do curso em época de recurso, não seria a tese a exceção.

Ao meu irmão Dinis, que, apesar de por vezes ser ausente, fez sempre o seu melhor para me apoiar neste período mais desafiante, deixo também um agradecimento especial.

À minha avó Guida, é com enorme orgulho que sigo os passos de uma mulher forte e independente, e procuro honrar essa herança.

Aos meus amigos – Marta, Clara, Aleixo, Bruna, Joaninha, Neca, Jojó, Mapota, Duda, Simão, Chico, Lucas e Bia – o meu mais sincero agradecimento pela vossa amizade incondicional. Obrigada por me acompanharem, acalmarem, ajudarem nos momentos de maior insegurança e, sobretudo, por me prendarem de sanidade mental ao longo deste processo exigente. Sem vocês, provavelmente teria sucumbido ao peso desta jornada.

À Mariana, minha parceira de tese, agradeço profundamente pela colaboração, apoio e partilha dos desafios que enfrentámos em conjunto.

Agradeço à minha orientadora, Doutora Teresa Magalhães, pela paciência, orientação e confiança depositada em mim ao longo deste trabalho. Apesar dos atrasos, consegui concluir esta etapa. Um agradecimento igualmente sentido à coorientadora, Dr.ª Rita Lopes, pelo seu incentivo contínuo, conselhos valiosos e disponibilidade.

Agradeço ainda à Doutora Cristina Gavina, à Unidade de Saúde Local de Matosinhos e a todos os envolvidos por todo o apoio concedido para a realização deste estudo.

Por último, e mais importante, agradeço a mim mesma. Por toda a resiliência que mostrei não só neste processo, mas ao longo destes 6 anos. Superei-me de muitas formas e feitios, mas de facto fazer um trabalho de investigação, sem grandes bases por trás, foi dos maiores, sem dúvida.

Joana, estás longe do mundo, mas perto de ser médica, nunca duvides de ti.

Work in line with the journal's "BMC Primary Care" guidelines.

Association Between Exposure to Interpersonal Violence and Cardiac, Metabolic, and Renal Diseases – A Cohort Study in a Local Health Unit in Portugal

Original research article

Joana Gaspar-Silva [a T].

a - Faculty of Medicine, University of Porto, 4200-319 Porto, Portugal.

[T] - equally contributed to this work as first author.

Corresponding author: Cristina Gavina

Email: cristina.gavina@ulsm.min-saude.pt

Phone: +351 914 013 385

Alameda Professor Hernâni Monteiro, 4200-319 Porto Portugal

E-mail:

joana.gasparnunessilva@gmail.com

Word count: 4 614

Abstract

Introduction: Interpersonal violence (IV) is a major public health issue with significant sociocultural, economic, and health impacts. It increases the risk of physical, psychological, and behavioral repercussions, including premature mortality. Despite evidence linking IV to systemic diseases, research on its association with cardiorenal-metabolic diseases remains limited. This study aimed to characterize patients with suspected exposure to IV. Secondary objectives included comparing the incidence of cardiorenal-metabolic diseases between suspected victims and the general population over 5- and 10-year periods.

Methods: A real-world, retrospective, and observational study was conducted using electronic health registers (EHR) from a Local Health Unit in Portugal, between 2003 and 2023. All patients aged 18 years or older with at least one entry in the EHR within 365 days before the index date and at least one primary healthcare appointment in the preceding 3 years were included. The exposed cohort included patients with documented suspicion of IV in the EHR, according to codes or text expressions. Variables studied included sociodemographics, risk behaviors, psychiatric disorders, and cardiorenal-metabolic diseases. Statistical analysis employed both descriptive and inferential methods to assess the associations.

Results: The suspected IV cohort comprised 232 398 patients, while the non-suspected IV cohort included 60 465 patients, with a slight predominance of females in both. Median ages were 55.96 and 58.83 years, respectively. IV suspected patients demonstrated higher incidence of health risk factors, such as smoking (21.8% vs 6.3%), excessive alcohol consumption (11.2% vs 2.3%), drug abuse (18.9% vs 5.4%), and psychiatric disorders (76.4% vs 30.8%). Notably, in the 5-year follow-up, suspected IV was strongly associated with: acute kidney disease (HR=2.20, 95% CI= [1.84-2.63]), non-alcoholic fatty liver disease

(HR=2.04, 95% CI= [1.70-2.46]), and ischemic stroke disease (HR=2.01, 95% CI= [1.78-2.27]).

Discussion and Conclusions: This study found that individuals with suspected IV exhibited a higher incidence of health risk behaviours and most cardio-renal-metabolic diseases. These findings highlight the importance of incorporating IV screening and integrating preventive strategies into routine healthcare. Enhancing the detection and documentation of IV within EHRs is essential to support effective clinical responses and public health planning. Further research is warranted to evaluate interventions targeting the long-term health effects of IV.

Keywords: interpersonal violence, health impact, cardiac diseases, metabolic diseases, renal diseases.

Introduction

The World Health Organization (WHO) declared violence a major public health problem in 1996 and, in 2002, defined it as the "intentional use of physical force or power, threatened or actual, against oneself, another person, or a group or community, which either results in or has a high likelihood of resulting in injury, death, psychological harm, maldevelopment, or deprivation" [1].

Experiencing interpersonal violence (IV) significantly impacts victims' lives at sociocultural and economic levels, but primarily affects their health. It increases the risk of physical, psychological, and behavioral outcomes and contributes to premature mortality (due to natural diseases or violent causes such as homicide, suicide, or accidents). [2].

Victims often experience changes such as disruption of the hypothalamic-pituitary-adrenal axis and autonomic nervous system dysfunction – mechanisms that regulate stress responses and are implicated in many systemic diseases. However, research on the risk of

metabolic diseases (e.g., metabolic syndrome, dyslipidemia, type 2 diabetes mellitus - T2DM), cardiovascular diseases - CVD (e.g., hypertension, acute myocardial infarction, stroke), and renal diseases (e.g., chronic kidney disease - CKD) in this population remains limited [3].

Strong clinical and epidemiological evidence supports the interrelationship between T2DM, CVD, and CKD – a cluster referred to as cardiorenal-metabolic disease. This condition currently represents one of the most pressing public health challenges. [4].

Cardiorenal-metabolic diseases exhibit sex-based differences in risk and manifestation: men tend to develop CVD earlier (e.g., myocardial infarction and hypertension), whereas postmenopausal women and those with a higher prevalence of autoimmune diseases are more prone to cardiovascular complications [5].

In Portugal, the most common metabolic disorders and their respective prevalence include: (a) metabolic syndrome (33.4% among individuals aged 25-74 years [6]); (b) hypercholesterolemia (total cholesterol >240mg/dl, which affects 31.3% of the population in Continental Portugal [7]); (c) diabetes (13%, according to the *International Diabetes Federation*, among individuals aged 20-79 years [8]); (d) non-alcoholic fatty liver disease (NAFLD), of 17% [9].

CVD remains the leading cause of death in Portugal, accounting for 27.9% of female deaths and 36.3% of male deaths according to the *World Heart Federation's 2024 Scorecard* [10]. Coronary artery disease, acute myocardial infarction, and stroke are the primary contributors to this mortality rate. Standardized mortality rates per sex are reported as 51.1, 30.3, and 19.3 per 100 000 inhabitants for these conditions, respectively, according to the *Portuguese General Health Direction* (DGS) [11]. Other prevalent CVDs in Portugal include: (a) pulmonary thromboembolism, 35 per 100 000 adult inhabitants aged ≥18 years [12]; (b) hypertension, 43.1%, particularly among older men [7]; (c) chronic heart failure, 4.4% in

adults, rising to 12.7% among those aged 70-79 years and 16.1% among individuals aged ≥80 years [13]; (d) peripheral arterial disease, 3-10% in the overall population and 15-20% in those aged ≥70 years [14]; (e) atrial fibrillation, 2.5% among individuals aged ≥40 years, being higher from age 70 onwards [15].

Regarding renal diseases, the RENA study reported an overall CKD prevalence of 20.9% in primary healthcare in Portugal, with rates significantly increasing with age [16].

The relationship between IV and the development of cardiorenal-metabolic diseases has been explored in a generalist approach through a retrospective cohort study conducted in the United Kingdom (from 1995 to 2017). This study concluded that among women exposed to intimate partner violence (n=18 547), 181 experienced a cardiovascular event compared to 644 women from the non-exposed control group (n=72 231), which was conveyed into an adjusted IRR (incidence rate ratio) of composite CVD (1.31; 95% CI, 1.11-1.55; p=0.001). Additionally, there was an increased risk of subsequent T2DM, ischemic heart disease, stroke, and mortality. However, there were no statistically significant differences in developing heart failure, peripheral vascular disease, or hypertension [17]. No Portuguese study has specifically addressed this issue, which prompted the investigators to undertake the present research.

This study aimed to characterize patients with suspected victims of IV regarding the presence of cardiorenal-metabolic diseases. Secondary objectives included comparing the incidence of cardiac, metabolic, and renal diseases between suspected victims and the general population over 5- and 10-year periods.

Materials and methods

Study Design and Setting

The present study is based on electronic health registers (EHR). It is a real-world, retrospective, and observational study, involving a cohort of participants registered at the Local Health Unit of Matosinhos (ULSM) between 2003 and 2023.

ULSM is a major healthcare organisation comprising 14 primary care units supported by a central hospital, *Pedro Hispano Hospital*. It provides healthcare services to 177 445 individuals (according to the *National Database of the National User Registry* – RNU 202505) and serves as an initial point of contact for many victims of IV.

This study relies on subparagraphs (i) and (j) of Article 9 of the *European Union's General Data Protection Regulation* (RGPD) 2016/679 as legal grounds for processing sensitive personal data. These provisions allow data processing for reasons of public interest in public health and scientific research purposes, respectively.

Ethical approval was obtained from the ULSM Health Ethics Committee and the Local Information Protection and Security Committee. Approval codes were issued as follows: No. 91/CES/JAS on October 14, 2022, and No. 71/CLPSI/2022 on December 21, 2022. Researchers did not have access to identifiable data. No data was extracted outside the ULSM infrastructure.

Participants

Participants were included if they met all the following criteria: (a) age ≥18 years old; (b) had at least one entry in the EHR within the 365 days prior to the index date; (c) had at least one primary healthcare appointment in the preceding 3 years preceding any event of interest (this interval was defined based on national indicators for primary healthcare usage in Portugal). The exclusion criteria were applied to individuals who had any of the following circumstances: (a) lacked information on sex; (b) had an age that could not be calculated.

The index date was defined as the time between 1 January 2003 and 31 December 2023 during which the population met all the criteria above.

The analysed group included participants registered at the ULSM who met all the criteria before and had been coded or had textual expressions for suspected IV. Suspicion of IV experience was identified using ICD (*International Classification of Diseases*)-9, ICD-10, and ICPC (*International Classification of Primary Care*)-2 classification codes, as well as textual expressions. All the used codes and textual expressions can be found in Supplementary Material 1.

The control group included participants registered at the ULSM who met all the criteria before and had not been coded or did not have textual expressions for suspected IV.

Variables

All variables were defined using ICD-9, ICD-10, ICPC-2, and ATC (Anatomical Therapeutic Chemical) classification codes, as well as laboratory, clinical, and demographic data available at the institution, accessible in Supplementary Material 1. All variables are detailed in the Results section.

Age was treated both as a continuous quantitative variable and stratified into categorical groups (18-39, 40-64, 65-84, and ≥85 years).

Categorical quantitative variables included: sex (female and male), risk factors (acute stress reaction, adjustment reaction, alcohol abuse, any psychiatric disorder excluding childhood and adolescent onset, current smoker, drug abuse, exposure to radiation, post-traumatic stress disorder, pregnancy history, use of psychotropic medication – antidepressants, antipsychotics, anxiolytics, and hypnotics/sedatives –, and use of oral contraceptives) and cardiorenal-metabolic outcomes (acute kidney disease, atrial fibrillation, CKD, heart failure, hypercholesterolemia, hypertension, hypertriglyceridemia,

ischemic stroke, myocardial infarction, NAFLD, obesity, peripheral arterial disease, pulmonary embolism, and T2DM).

Data sources/measurements

All data processing and analyses were performed using custom analytic programs developed specifically for this study. These programs were executed within the secure ULSM data center, with no external data extraction or direct researcher access to the raw data. The study packages - designed to run on ULSM's local infrastructure (*Apache Spark Framework v3.2.1*) - implemented the full data pipeline, including harmonization of source data (aligned with OMOP CDM v5.4), variable derivation, statistical analysis, and generation of aggregated results reports.

Patient demographic and clinical characteristics were described for each cohort. Continuous variables were summarised using the median (P50) and interquartile range (IQR), while categorical variables were expressed as absolute and relative frequencies. When a variable included five or fewer individuals, the count was reported as ≤5 to protect patients' privacy.

To evaluate the development of cardiorenal-metabolic outcomes at 5 and 10 years of follow-up, adjusting for confounders (age, sex, smoking status, alcohol abuse, drug abuse, and prior psychiatric disorders), Cox proportional hazards models were fitted to estimate hazard ratios (HRs) with corresponding 95% confidence intervals (CIs). This was possibly due to the application of the cluster method available in the R Survival package, version 4.3.2. [18]

The propensity score (PS) was estimated using multivariable logistic regression, incorporating seven covariates selected a priori. Standardised mean difference (SMD) was calculated before and after matching to assess covariate balance, with an absolute

SMD<0.1 considered indicative of acceptable balance. All incidence analyses were conducted on the matched cohorts.

The population in the cohort suspected of being victims of IV was matched to those in the non-suspected IV group using a nearest neighbour matching method, based on female sex, age, current smoker, alcohol abuse, drug abuse, any psychiatric disorder, and the violence-exposed population. The matching procedure was implemented using the MatchIt package (version 4.5.5) within R software (version 4.1.3).

Bias

The population served by ULSM is predominantly urban and has access to a comprehensive range of healthcare services, which may not be representative of other regions in Portugal; consequently, selection bias may be present. This analysis was based on retrospective data obtained from EHR, which are susceptible to bias and residual confounding, thereby inherently limiting causal inference. To mitigate these effects, minimal exclusion criteria were applied, and data from both primary and secondary care sources were used.

Underreporting of suspected IV cases may also occur due to missing EHR entries, absence of appropriate medical coding, or victims' difficulty in recognizing or disclosing their circumstances, particularly in cases involving psychological violence or neglect, where physical indicators are less apparent. This could result in an underestimation of IV incidence.

Furthermore, primary care settings, which comprise the majority of ULSM, provide detailed records, owing to patients' easy access to general practitioners and active surveillance protocols. These differences should be considered when comparing findings with studies conducted in secondary care facilities or in prospective cohorts of pre-selected patients, who may present with more advanced disease and consequently higher associated risks.

Study Size

Formal sample size estimation was deemed unnecessary, given that the study aimed to include the entire population that fulfilled inclusion criteria.

Results

The suspected IV (SIV) cohort comprised 60 465 patients (Table 1). The median age was 55.96 years for the SIV cohort and 58.83 for the non-suspected IV (NSIV) cohort. The most affected age group was between 40 and 64 years (41.6% in the SIV cohort). With increasing age beyond this range, the number of suspected cases decreased, as demonstrated in the group aged >84 years, where the advanced age contributed to a smaller population size and correspondingly fewer cases of SIV (2.7%) – Table 1.

Regarding the sex of the cohorts, most patients with SIV were female (57.9%), as were the NSIV patients (59.1%) - Table 2.

Table 1. Age groups distribution (years) - n (%).

Groups	**NSIV** (n=232 398)		**SIV** (n=60 465)	
18-40	69 990 (30.1)		20 307 (33.6)	
40-64	88 405 (38.0)		25 141 (41.6)	
64-84	63 805 (27.5)		13 373 (22.1)	
>84	10 198 (4.4)		1 644 (2.7)	
Median age	**P50**	**IQR***	**P50**	**IQR**
	52.83	31.72	55.96	27.40

*IQR – interquartile range.

Table 2. Sex distribution – n (%).

	NSIV (n=232 398)	**SIV** (n=60 465)
Female	137 298 (59.1)	35 016 (57.9)
Male	95 100 (40.9)	25 449 (42.1)

228

229 Risk health factors were markedly more incident in individuals with SIV compared to those
230 in the NSIV group (Table 3). The most common comorbidity among the SIV group was any
231 psychiatric disorder (76.4%), much higher than in the NSIV group (30.8%). Radiation
232 exposure was recorded in ≤5 cases, rendering statistical analysis infeasible. Consequently,
233 this variable was not included in further analysis due to its limited significance and
234 representation.

235 **Table 3.** Pre-index health risk factors - n (%).

		NSIV (n=232 398)	**SIV** (n=60 465)
Acute stress reaction		2 769 (1.2)	2 953 (4.9)
Adjustment reaction		845 (0.4)	1 318 (2.2)
Alcohol abuse		5 350 (2.3)	6 750 (11.2)
Any psychiatric disorder*		71 637 (30.8)	46 163 (76.4)
Any stress-related disorder		3 777 (1.6)	4 443 (7.4)
Current smoker		14 711 (6.3)	13 208 (21.8)
Drug abuse		12 651 (5.4)	11 410 (18.9)
Exposure to radiation		16 (0.0)	≤5
Oral contraceptives		11 685 (5.0)	6 625 (11.00)
Post-traumatic stress disorder		238 (0.1)	465 (0.8)
Pregnancy history		16 569 (7.1)	8 581 (14.2)
Medication	Antidepressants	32 500 (14.00)	25 376 (42.00)

	Antipsychotics	7 345 (3.2)	9 939 (16.4)
	Anxiolytics	52 486 (22.9)	32 000 (52.9)
	Hypnotics/sedatives	12 697 (5.5)	8 222 (13.6)

*Excluding childhood and adolescent onset

Cardio-renal-metabolic conditions were markedly more common among SIV individuals when compared to those with NSIV (Table 4). Conditions with particularly high incidence in the SIV group included hypercholesterolaemia (65.3%), CKD (42.2%), and hypertriglyceridaemia (32.7%).

Table 4. Pre-index cardio-renal-metabolic diseases – n (%).

	NSIV (n=232 398)	**SIV** (n=60 465)
Acute kidney disease	2 632 (1.1)	2 061 (3.4)
Atrial fibrillation	13 813 (5.9)	4 822 (8.00)
CKD	45 202 (19.5)	25 507 (42.2)
Heart failure	11 402 (4.9)	5 472 (9.1)
Hypercholesterolemia	95 298 (41.0)	39 487 (65.3)
Hypertension	71 622 (30.8)	29 784 (49.3)
Hypertriglyceridemia	40 178 (17.3)	19 779 (32.7)
Ischemic stroke	8 501 (3.7)	5 600 (9.3)
Myocardial infarction	6 802 (2.9)	3 727 (6.2)
NAFLD	3 038 (1.3)	2 552 (4.2)
Obesity	38 898 (16.7)	18 857 (372)
Peripheral arterial disease	6 340 (2.7)	3 822 (6.3)
Pulmonary embolism	1 212 (0.5)	388 (0.6)
T2DM	28 649 (12.3)	11 881 (19.7)

The matched cohorts consisted of 31 043 individuals NSIV and 27 606 with SIV (Table 5). Overall, the matching process achieved adequate covariate balance for most variables, although age remained slightly imbalanced. The proportion of females was similar and predominant across groups. There are significantly higher rates of current smoking status, alcohol, and drug abuse in the SIV group. A history of psychiatric disorders was the most incident comorbidity.

Table 5. Pre- and post-matching characterization and their baseline characteristics.

	Unmatched (n=292 863)				**Matched** (n=58 649)				
	NSIV (n=232 398)		*SIV (n=60 465)*		*NSIV (n=31 043)*		*SIV (n=27 606)*		SAMD
Median age	*P50*	*IQR*	P50	IQR	P50	IQR	PT50	*IQR*	
(years)	*52.83*	*31.72*	60.99	24.63	60.99	24.63	56.23	26.08	**0.19**
Female	*137 298*	*59.1*	18 423	59.4	18 423	59.4	16 204	58.7	<0.1
Current smoker	*14 711*	*6.3*	5 316	17.1	5 316	17.1	5 723	20.7	<0.1
Alcohol abuse	*5 350*	*2.3*	2 991	9.6	2 991	9.6	3 260	11.8	<0.1
Drug abuse	*12 651*	*5.4*	5 459	17.6	5 459	17.6	5 828	21.1	<0.1
*APD**	*71 637*	*30.8*	23 440	75.5	23 440	75.5	21 382	77.5	<0.1

All lines are displayed using n and %, except as otherwise specified.

**Any psychiatric disorder (*excluding childhood and adolescent onset)*

Addressing the 5th-year follow-up, there were statistical differences in most of the analysed outcomes. The highlights include acute kidney disease, NAFLD, and ischemic stroke. There were no statistical differences in atrial fibrillation and obesity – Table 6.

In the 10th-year follow-up, there were also statistical differences in most of the analysed outcomes. The highlights were equal to the 5th-year follow-up, but without statistical differences in hypertension at the 10th-year follow-up - Table 6.

Table 6. Hazard ratios for the 5th and 10th-year follow-up.

	5-year follow-up		10-year follow-up	
	HR	[95%CI]	HR	[95%CI]
Acute kidney disease	**2.20**	**[1.84-2.63]**	**1.99**	**[1.70-2.33]**
Atrial fibrillation	1.00	[0.89-1.11]	0.99	[0.88-1.10]
CKD	**1.32**	**[1.26-1.39]**	**1.31**	**[1.24-1.37]**
Heart Failure	**1.38**	**[1.25-1.53]**	**1.37**	**[1.23-1.51]**
Hypercholesterolemia	**1.11**	**[1.06-1.16]**	**1.09**	**[1.05-1.14]**
Hypertension	**1.05**	**[1.01-2.00]**	1.03	[0.99-1.08]
Hypertriglyceridemia	**1.16**	**[1.08-1.24]**	**1.15**	**[1.08-1.23]**
Ischemic stroke	**2.01**	**[1.78-2.27]**	**1.80**	**[1.60-2.02]**
Myocardial infarction	**1.74**	**[1.51-2.02]**	**1.67**	**[1.45-1.93]**
NAFLD	**2.04**	**[1.70-2.46]**	**1.86**	**[1.58-2.20]**
Obesity	1.07	[1.01-1.14]	1.05	[0.99-1.11]
Peripheral arterial disease	**1.39**	**[1.20-1.60]**	**1.32**	**[1.16-1.51]**
Pulmonary embolism	**1.79**	**[1.18-2.69]**	**1.54**	**[1.07-2.23]**
T2DM	**1.16**	**[1.09-1.24]**	**1.18**	**[1.11-1.26]**

Legend: HR – Hazard Ratio; CI – confidence interval.

Discussion

This research demonstrated that, within the two studied cohorts, individuals in the SIV group exhibited a higher incidence of health risk factors (Table 3) and adverse outcomes for certain cardiac, metabolic, and renal diseases (Table 4). Statistically significant differences were observed for most cardiorenal-metabolic diseases analysed (Table 6).

Demographics

In both cohorts, most of the studied population belonged to the 40-64-year age group, with females being the most affected sex (Tables 1 and 2). This finding is consistent with the general victim profile reported in the 2024 statistics of the *Portuguese Association for Victim Support* (APAV), which indicates a median age of 37 years and a predominance of female victims, accounting for 76.3% of cases. [18] There was also a slightly higher proportion of younger individuals observed in the SIV group (Table 1), highlighting the heightened vulnerability of this age group. This underscores the importance of investigating dating violence within this demographic. Research indicates that young individuals at higher risk are those who have previously experienced IV and lack skills to manage conflict or respond to coercion, with peer influence often reinforcing abusive behaviors [19]. To be noted also, that a substantial proportion of men were identified as possible victims of IV (Table 2). This group is underrepresented and more likely to experience severe consequences due to their lower likelihood of seeking help or recognizing IV. This results in limited knowledge about the health outcomes for male victims and more severe consequences [20].

Health Risk Factors

An association was observed between the SIV cohort and a higher incidence of most of the health risk factors examined (Table 3).

These findings are consistent with existing evidence indicating that IV experience may influence the consumption of addictive substances (e.g., alcohol, tobacco, and drugs) through direct mechanisms, such as partner coercion, or indirect pathways, including psychological trauma and self-medication to cope with distress [21-23]. Conversely, some studies suggest that individuals diagnosed with substance or alcohol abuse are more likely to suffer IV in the future [24, 25]. Irrespective of the direction of causality, the presence of a

diagnosis related to alcohol, tobacco, or drug abuse should prompt screening for IV, and vice versa.

Moreover, significant associations were found between the SIV group and various psychiatric disorders and stress-related reactions (Table 3), as previously described in the literature [23, 26]. This study also demonstrated that suspected victims are more likely to use psychiatric medication, including antidepressants and anxiolytics (Table 3), which aligns with current evidence [27].

The study further highlighted an increased incidence of pregnancy history in the SIV group (Table 3), consistent with previous research, linking IV to higher rates of unintended pregnancies, sexually transmitted diseases, and induced abortions [28, 29]. However, in contrast to some earlier studies, our findings indicate a higher use of contraceptives within the SIV cohort (Table 3) [27].

Cardiorenal-metabolic diseases

An association was observed between the SIV cohort and an increased incidence of most of the cardiorenal-metabolic diseases investigated (Table 4).

These findings are somewhat in line with the existent study, where, in the United Kingdom, 181 IV-exposed women experienced a CVD event compared with 644 of the IV-unexposed group, yielding an increased adjusted IRR of 1.31 (95% CI, 1.11–1.55; p=0.001), with a significantly higher risk of developing ischemic heart disease (1.40; 95% CI, 1.09–1.79; p=0.007) and stroke or transient ischemic attack (1.29; 95% CI, 1.02–1.63; p=0.035). There was also an elevated risk of T2DM (adjusted IRR: 1.51; 95% CI, 1.30–1.76; p<0.001) and all-cause mortality (adjusted IRR: 1.44; 95% CI, 1.24–1.67; p<0.001). No statistically significant differences were identified for heart failure (IRR: 1.15; 95% CI, 0.69–1.63; p=0.520),

peripheral vascular disease (IRR: 1.27; 95% CI, 0.75–1.86; p=0.304), or hypertension (IRR: 0.99; 95% CI, 0.88–1.12; p=0.873) [17].

In contrast to the study above, the present analysis identified statistically significant differences in the incidence of both heart failure and peripheral vascular disease (Table 6). Additionally, this study examined a greater number of diseases.

Regarding metabolic diseases, NAFLD was notably associated with the SIV group (Tables 4 and 6). NAFLD is indirectly linked with IV, with psychiatric comorbidities and elevated stress levels potentially mediating this relationship [30] [31]. A strong association between the SIV group and T2DM was likewise observed in this study (Tables 4 and 6), corroborating previous findings. This may be attributable to the impact of stress and depression in triggering pro-inflammatory responses and neuroendocrine activation, which disrupt glucose metabolism and promote insulin resistance [32, 33]. The SIV group also demonstrated a higher incidence of hypertriglyceridemia and hypercholesterolemia (Tables 4 and 6), consistent with studies indicating that physical and/or sexual violence is associated with reduced high-density lipoprotein cholesterol and elevated triglyceride levels [34, 35]. In contrast, obesity did not show a significant association with IV in this study (Table 6). Existing literature on this topic links IV to obesity or anorexia, depending on the victim's sex, the type of violence experienced, and the mediating effect of depression with persistent dysregulation of the hypothalamic-pituitary-adrenal axis and hypercortisolemia [36-39]. Such immune dysregulation and chronic inflammation may contribute to an increased risk of metabolic syndrome [40].

Regarding CVD, positive associations with the SIV group were observed in most conditions studied, including heart failure, ischemic stroke, myocardial infarction, peripheral arterial disease, and pulmonary embolism (Tables 4 and 6), which is consistent with prior research demonstrating an elevated cardiovascular risk among victims of IV [41-43]. Depression

alone is known to increase the risk of coronary heart and arterial disease, and changes the variability of the cardiac frequency, through both biological factors (e.g., systemic inflammation and elevated cortisol levels) and behavioral factors (e.g., physical inactivity, smoking, poor medication adherence, and social isolation). Victimisation by IV may exacerbate these effects, further contributing to poor cardiovascular outcomes [44]. However, no significant associations were identified between the SIV group and atrial fibrillation or hypertension (Table 6). Regarding atrial fibrillation, only one study has reported an association with traumatic life events [45]. The literature is aligned with the lack of association of hypertension and IV, where links were only observed in cases of severe abuse [46, 47].

The significant association of acute kidney disease and CKD in SIV individuals is an important finding (Tables 4 and 6), suggesting that the effects of IV extend beyond the cardiovascular and metabolic systems. There is a known association between CKD and adverse life events, including experiencing IV from childhood to adulthood, including sexual abuse. This relationship appears to differ based on genetic polymorphisms, potentially mediated through interleukin-1 receptor activity [48]. However, no literature was found supporting an association between acute kidney disease and IV.

These elevated associations between metabolic, cardiac, and renal diseases support the hypothesis of a unified cluster of cardiorenal-metabolic diseases [4].

Study limitations and future research

The following limitations were identified in this study: (a) selection bias, as the representativeness of the sample may have been affected as the recruited individuals might not fully reflect the target population, despite efforts to minimize this bias through minimal exclusion criteria and the use of comprehensive data, causal inference remains limited due to the retrospective observational nature of the study; (b) underreporting bias, as cases of

violence may be underreported due to the absence of medical coding or victims' difficulty in recognizing or communicating their situation; (c) medical coding limitations, as errors in the classification of diagnostic codes by healthcare professionals could lead to an underestimation of the observed effect size; (d) methodological differences between comparative studies, as other studies conducted in secondary care centers or prospective cohorts often include patients with more advanced disease stages, which may affect comparability; (e) lack of in-depth research in specific areas, as certain associations, such as between suspicion of IV and NAFLD or acute kidney injury, remain underexplored and require more robust and conclusive investigation.

Future research should focus on conducting prospective longitudinal studies to overcome these limitations, addressing underreporting by employing advanced natural language processing tools and qualitative analysis of EHR, investigating specific types of violence and their associations with different pathologies, examining sociocultural impacts on the incidence and effects of IV across diverse populations and expanding research to other national local health units and European research groups for broader and more definitive conclusions.

Conclusion

This study allows us to conclude that SIV group: (a) presented a higher incidence of risk behaviours for cardiorenal-metabolic diseases, such as smoking, alcohol and drug abuse, any psychiatric disorders, stress reactions, oral contraceptives use, and the use of psychotropic medication; (b) was significantly associated with the development of NAFLD, T2DM, hypercholesterolemia, hypertriglyceridemia, ischemic stroke, myocardial infarction, pulmonary embolism, heart failure, peripheral arterial disease, acute kidney disease, and CKD.

Such results underscore the need to integrate assessments for IV into general healthcare settings due to its significant impact on the incidence of cardiorenal-metabolic diseases. Furthermore, it suggests that targeted interventions aimed at mitigating the effects of IV could benefit not only victims' mental health but also reduce systemic disease risks. It is crucial to implement screening strategies and early interventions for victims within the healthcare system, focusing on preventing and managing cardiorenal-metabolic diseases. Additionally, prevention programs addressing violence and providing victim support should be integrated into strategies promoting cardiovascular, metabolic, and renal health.

Developing strategies to improve the detection and recording of IV within EHR systems is also essential. This presents an opportunity to enhance advocacy for victims within healthcare settings by promoting more effective preventive and therapeutic interventions.

Future research should evaluate specific interventions aimed at mitigating the impact of IV on cardiorenal-metabolic health.

List of abbreviations

APAV - Portuguese Association for Victim Support

ATC – Anatomical Therapeutic Chemical (classification system)

CKD – Chronic kidney disease

CVD – Cardiovascular Disease

DGS – Portuguese General Health Direction

EHR – Electronic Health Record

ICD – International Classification of Diseases

ICPC – International Classification of Primary Care

IRR – Incidence Rate Ratio

IV – Interpersonal Violence

NAFLD – Non-Alcoholic Fatty Liver Disease

NSIV – Non-suspected Interpersonal Violence

RGPD – General Data Protection Regulation

SIV – Suspected Interpersonal Violence

T2DM – Type 2 Diabetes Mellitus

ULSM – Local Health Unit of Matosinhos

WHO – World Health Organization

Declarations

Ethics approval and consent to participate

Data access and ethical approval were obtained from the ULSM Health Ethics Committee and the Local Information Protection and Security Committee. Approval codes were issued as follows: No. 91/CES/JAS on October 14, 2022, and No. 71/CLPSI/2022 on December 21, 2022. To ensure data security, the ULSM Information Technology Department conducted and performed the data collection process on ULSM servers. Researchers did not have direct access to identifiable data, or any information extracted outside the ULSM infrastructure. The ULSM Information Technology Department de-identified all data before processing. This de-identification adhered to the Health Insurance Portability and Accountability Act (HIPAA) safe harbor criteria, ensuring compliance with international standards for data protection.

Consent for publication

This study relies on subparagraphs (i) and (j) of Article 9 of the European Union's General Data Protection Regulation (RGPD) 2016/679 as legal grounds for processing sensitive personal data. These provisions allow data processing for reasons of public interest in public health and scientific research purposes, respectively.

Availability of data and materials

The original contributions presented in this study are included in the article/supplementary material. Further inquiries can be directed to the corresponding author.

Competing interests

The authors affirm that all research was conducted without financial or commercial relationships that could be construed as potential competing interests.

Funding

The authors declare that no financial support was received for conducting this research or preparing/publishing this article.

Author contributions

JGS: Formal analysis, investigation, writing – original draft preparation; RL: Data curation, investigation, methodology, resources, supervision, writing – review & editing; TM: Data curation, methodology, resources, supervision, writing – review & editing; CG: Data curation, investigation, methodology, resources.

Acknowledgments

449 The authors would like to acknowledge the Local Health Unit of Matosinhos, Portugal, for
450 granting permission to design this study and supporting its execution.

451 Supplementary material

452 The supplementary material used in this article is available below.

453 **Supplementary material 1:** ULSM Violence, health risk factors, and cardio-renal-
454 metabolic diseases variable definition – codes and textual expressions.

Variable	Definition	
Violence codes	- ICD-9 code 99580	- ICD-10 code t74
	- ICD-9 code 99581	- ICD-10 code t75
	- ICD-9 code 99582	- ICD-10 code t76
	- ICD-9 code 99583	- ICD-10 code x8[5-9]
	- ICD-9 code 99584	- ICD-10 code y9[0-9]
	- ICD-9 code 99585	- ICPC-2 code z12
	- ICD-9 code e96	- ICPC-2 code z13
	- ICD-10 code t71	- ICPC-2 code z25
	- ICD-10 code t73	

Violence expressions	text	- (A|a)mea(c|ç)	- (P|p)edrad
		- (I|i)nsult	- (F|f)acad
		- (H|h)umilh	- (E|s)sfaquead
		- (G|g)rit	- (D|d)ispar
		- (B|b)err	- (B|b)alead
		- (D|d)estrui	- (P|p)ontap
		- (P|p)ersegui	- (P|p)aulad
		- (P|p)roibi	- (E|e)mpurr
		- (O|o)brigad(o|a) a	- (E|e)stalad
		- (P|p)r(a|á)ticas sex	- (A|a)pert(ã|a)o
		- (P|p)r(a|á)tica sex	- (A|a)pert(õ|o)es
		- (F|f)or(c|ç)ad(o|a)	- (B|b)at(e|i)
		- (L|l)atada	- (A|a)gress
		- (B|b)ofet	- (A|a)gred
		- (S|s)apatad	- (E|e)sgana
		- (C|c)hapad	- (S|s)ufoc
		- (M|m)urr	- (E|e)strang
		- (S|s)oco	- (A|a)bandon
		- (P|p)ancad	- (M|m)ordid

Age	Ad-hoc vocabulary	
Sex	Ad-hoc vocabulary	
Smoking	Ad-hoc vocabulary and/or ICPC-2 code p17.	
Alcohol abuse	- ICD-9 code 291	- ICD-10 code f10
	- ICD-9 code 303	- ICPC-2 code p15
Drug abuse	- ICD-9 code 292	- ICD-10 code f15
	- ICD-9 code 304	- ICD-10 code f16
	- ICD-9 code 305	- ICD-10 code f18
	- ICD-10 code f11	- ICD-10 code f19
	- ICD-10 code f12	- ICPC-2 code p18
	- ICD-10 code f13	- ICPC-2 code p19
	- ICD-10 code f14	
Suicidal ideation	- ICD-9 code v6284	- ICD-10 code x6[0-9]
	- ICD-9 code e95[0-8]	- ICD-10 code x7[0-9]
	- ICD-10 code r45851	- ICD-10 code x8[0-3/4]
	- ICD-10 code t1491	- ICPC-2 code p77
	- ICD-10 code z9151	

Social deprivation	- ICD-10 code z604	
Memory disorder	- ICD-9 code 78093	- ICD-10 code r413
	- ICD-10 code r411	- ICPC-2 code p20
	- ICD-10 code r412	- ICPC-2 code p70
Sleep disorder	- ICD-9 code 327	- ICD-9 code 78056
	- ICD-9 code 29182	- ICD-9 code 78059
	- ICD-9 code 29285	- ICD-10 code g47
	- ICD-9 code 3074	- ICD-10 code f51
	- ICD-9 code 78050	- ICPC-2 code p06
Chronic pain	- ICD-9 code 3382	- ICD-10 code r521
	- ICD-9 code 33829	- ICD-10 code r522
Psychosocial stress	- ICD-9 code v62	- ICD-10 code z62
	- ICD-10 code z59	- ICD-10 code z63
	- ICD-10 code z60	- ICD-10 code z64
	- ICD-10 code z61	- ICD-10 code z65

Major disorder	psychiatric	- ICD-9 code 290	- ICD-10 code f6
		- ICD-9 code 291	- ICD-10 code f7
		- ICD-9 code 292	- ICD-10 code f8
		- ICD-9 code 293	- ICD-10 code f9
		- ICD-9 code 294	- ICPC-2 code p70
		- ICD-9 code 295	- ICPC-2 code p71
		- ICD-9 code 296	- ICPC-2 code p72
		- ICD-9 code 297	- ICPC-2 code p73
		- ICD-9 code 298	- ICPC-2 code p74
		- ICD-9 code 299	- ICPC-2 code p75
		- ICD-9 code 30	- ICPC-2 code p76
		- ICD-9 code 31	- ICPC-2 code p77
		- ICD-10 code f0	- ICPC-2 code p78
		- ICD-10 code f1	- ICPC-2 code p79
		- ICD-10 code f2	- ICPC-2 code p80
		- ICD-10 code f3	- ICPC-2 code p81
		- ICD-10 code f4	- ICPC-2 code p98
		- ICD-10 code f5	- ICPC-2 code p99

Headache	- ICD-9 code 7840 - ICD-10 code r51 - ICD-10 code g442	- ICPC-2 code n01 - ICPC-2 code n90 - ICPC-2 code n95
Eating disorder	- ICD-9 code 3075 - ICD-10 code f50	- ICPC-2 code p86
Post-traumatic stress	- ICD-9 code 30981 - ICD-10 code f4310 - ICD-10 code f4311	- ICD-10 code f4312 - ICPC-2 code p82
Antipsychotics	- ATC code n05a	
Hypnotics and sedatives	- ATC code n05c	
Antidepressants	- ATC code n06a	
Anxiolytics	- ATC code n05b	
Obesity (BMI of 30 or higher)	Ad-hoc vocabulary and/or ICPC2 code t82	

Hypertension	Fulfilling at least one of the following conditions: ▪ ICD-10 code i10 ▪ ICD-9 code 401 ▪ ICPC2 codes K86, K87 ▪ Having 2 Systolic Blood Pressure observations equal or above 140mmHg registered at least 7 days apart ▪ Having 2 Diastolic Blood Pressure observations equal or above 90mmHg registered at least 7 days apart	
Unstable angina	- ICD-9 code 411 - ICD-10 code i200	- ICPC-2 code k74
Myocardial infarction	- ICD-9 code 410 - ICD-9 code 412 - ICD-10 code i21 - ICD-10 code i22	- ICD-10 code i252 - ICD-10 code i256 - ICPC-2 code k75
Ischemic stroke	- ICD-9 code 433 - ICD-9 code 434 - ICD-9 code 435 - ICD-9 code 436 - ICD-9 code 437	- ICD-9 code 438 - ICD-10 code i63 - ICD-10 code i65 - ICD-10 code i66

Pulmonary Embolism	- ICD-9 code 4151	- ICD-9 code v1255
	- ICD-9 code 673	- ICD-10 code i26
Heart failure	- ICD-9 code 40403	- ICD-10 code i130
	- ICD-9 code 40413	- ICD-10 code i132
	- ICD-9 code 40493	- ICD-10 code i50
	- ICD-9 code 428	- ICPC-2 code k77
	- ICD-10 code i110	
Peripheral arterial disease	- ICD-9 code 440	- ICD-10 code i742
	- ICD-9 code 44(3-4)	- ICD-10 code i743
	- ICD-9 code 441	- ICD-10 code i744
	- ICD-9 code 444	- ICD-10 code i745
	- ICD-9 code 4442	- ICD-10 code i748
	- ICD-10 code i702	- ICD-10 code i749
	- ICD-10 code i739	- ICPC-2 code k92
Atrial fibrillation	- ICD-9 code 4273	- ICPC-2 code k78
	- ICD-10 code i48	
Acute kidney disease	- ICD-9 code 584	- ICD-10 code n17

Chronic kidney disease	Fulfilling at least one of the following criteria: a) having biochemical confirmation defined as either of the following: ▪ At least 2 UACR measures of ≥30 mg/g ≥90 days apart; ▪ At least 2 eGFR measures of < 60 ml/min/1.73^2 ≥90 days apart; b) having at least one relevant diagnosis code: ▪ ICD9 codes: 585, 250.4 ▪ ICD10 codes: E10.2, E11.2, E12.2, E13.2, E14.2, I12.0, I12.9, I13.1, I13.2, N18, Z99.2
Hypertriglyceridemia (Triglycerides > 175)	Laboratory vocabulary
Hypercholesterolemia (Cholesterol > 190)	Laboratory vocabulary

Type 2 diabetes mellitus	Not having an ICD9 or ICD10 (ICD-10 code e11) code for Type 1 Diabetes Mellitus and meeting at least one of the following criteria: ▪ At least one measurement of blood glucose ≥ 200 mg/dL; ▪ At least one measurement of HbA1c ≥ 6.5% ▪ Having had a prescription of glucose lowering drugs excluding biguanides. Or having an ICD-10 code e11.	
Non-alcoholic steatohepatitis	- ICD-9 code 5718 - ICD-9 code 5719	- ICD-10 code k76

455

456 # References

457 1. Krug EG, Mercy JA, Dahlberg LL, Zwi AB: **The world report on violence and health**.
458 *Lancet* 2002, **360**(9339):1083-1088.10.1016/S0140-6736(02)11133-0
459 2. Saúde DGd: **Violência Interpessoal - Abordagem, Diagnóstico e Intervenção nos**
460 **Serviços de Saúde**. In., 2 edn; 2016: 268.
461 3. Clemente-Teixeira M, Magalhaes T, Barrocas J, Dinis-Oliveira RJ, Taveira-Gomes T:
462 **Health Outcomes in Women Victims of Intimate Partner Violence: A 20-Year**
463 **Real-World Study**. *Int J Environ Res Public Health* 2022,
464 **19**(24).10.3390/ijerph192417035
465 4. Marassi M, Fadini GP: **The cardio-renal-metabolic connection: a review of the**
466 **evidence**. *Cardiovasc Diabetol* 2023, **22**(1):195.10.1186/s12933-023-01937-x

5. Regitz-Zagrosek V, Kararigas G: **Mechanistic Pathways of Sex Differences in Cardiovascular Disease**. *Physiol Rev* 2017, **97**(1):1-37.10.1152/physrev.00021.2015

6. Alves R, Santos AJ, Kislaya I, Nunes B, Freire AC: **[Metabolic Syndrome in Portugal: Prevalence and Associated Factors]**. *Acta Med Port* 2022, **35**(9):633-643.10.20344/amp.15051

7. Bourbon MA, A.C.; Rato, Q.: **Prevalência de Fatores de Risco Cardiovasculares na População Portuguesa**. In.

8. Saúde. PMdSD-Gd: **PROGRAMA NACIONAL PARA A DIABETES DESAFIOS E ESTRATÉGIAS**. In. Lisboa: Direção-Geral da Saúde; 2021: 108.

9. Leitao J, Carvalhana S, Cochicho J, Silva AP, Velasco F, Medeiros I, Alves AC, Bourbon M, Oliveiros B, Rodrigues V *et al*: **Prevalence and risk factors of fatty liver in Portuguese adults**. *Eur J Clin Invest* 2020, **50**(6):e13235.10.1111/eci.13235

10. Federation WH: **Portugal: Cardiovascular Disease Scorecard 2024**. In.; 2024.

11. Cérebro-Cardiovasculares PNpaD: **PROGRAMA NACIONAL PARA AS DOENÇAS CÉREBRO-CARDIOVASCULARES**. In.: Direção-Geral da Saúde; 2017: 21.

12. Gouveia M, Pinheiro L, Costa J, Borges M: **[Pulmonary Embolism in Portugal: Epidemiology and In-Hospital Mortality]**. *Acta Med Port* 2016, **29**(7-8):432-440.10.20344/amp.6367

13. Ceia F, Fonseca C, Mota T, Morais H, Matias F, de Sousa A, Oliveira A, Investigators E: **Prevalence of chronic heart failure in Southwestern Europe: the EPICA study**. *Eur J Heart Fail* 2002, **4**(4):531-539.10.1016/s1388-9842(02)00034-x

14. Simões MIO: **Caracterização da carga da doença arterial periférica dos membros inferiores: Contributos para um melhor conhecimento do peso desta doença no internamento hospitalar**. In.; 2016: 87.

15. Bonhorst D, Mendes M, Adragao P, De Sousa J, Primo J, Leiria E, Rocha P: **Prevalence of atrial fibrillation in the Portuguese population aged 40 and over: the FAMA study**. *Rev Port Cardiol* 2010, **29**(3):331-350

16. Vinhas J, Aires I, Batista C, Branco P, Brandao J, Nogueira R, Raposo JF, Rodrigues E: **RENA Study: Cross-Sectional Study to Evaluate CKD Prevalence in Portugal**. *Nephron* 2020, **144**(10):479-487.10.1159/000508678

17. Chandan JS, Thomas T, Bradbury-Jones C, Taylor J, Bandyopadhyay S, Nirantharakumar K: **Risk of Cardiometabolic Disease and All-Cause Mortality in Female Survivors of Domestic Abuse**. *J Am Heart Assoc* 2020, **9**(4):e014580.10.1161/JAHA.119.014580

18. Vítima) AAPdAà: **Estatísticas APAV Totais Nacionais 2024**. In.; 2025: 5.

19. Tapp J, Moore E: **Risk assessments for dating violence in mid to late adolescence and early adulthood**. *Crim Behav Ment Health* 2016, **26**(4):278-292.10.1002/cbm.2013

20. Machado A, Santos A, Matos M: **(Un)Acknowledgment of Men as Victims of Intimate Partner Violence**. *Violence Vict* 2023, **38**(2):250-266.10.1891/VV-2022-0022

21. Ogden SN, Dichter ME, Bazzi AR: **Intimate partner violence as a predictor of substance use outcomes among women: A systematic review**. *Addict Behav* 2022, **127**:107214.10.1016/j.addbeh.2021.107214

22. Coker AL, Davis KE, Arias I, Desai S, Sanderson M, Brandt HM, Smith PH: **Physical and mental health effects of intimate partner violence for men and women**. *Am J Prev Med* 2002, **23**(4):260-268.10.1016/s0749-3797(02)00514-7

23. Bonomi AE, Anderson ML, Reid RJ, Rivara FP, Carrell D, Thompson RS: **Medical and psychosocial diagnoses in women with a history of intimate partner violence**. *Arch Intern Med* 2009, **169**(18):1692-1697.10.1001/archinternmed.2009.292

24. Waller MW, Iritani BJ, Christ SL, Clark HK, Moracco KE, Halpern CT, Flewelling RL: **Relationships among alcohol outlet density, alcohol use, and intimate partner violence victimization among young women in the United States**. *J Interpers Violence* 2012, **27**(10):2062-2086.10.1177/0886260511431435

25. Devries KM, Child JC, Bacchus LJ, Mak J, Falder G, Graham K, Watts C, Heise L: **Intimate partner violence victimization and alcohol consumption in women: a systematic review and meta-analysis**. *Addiction* 2014, **109**(3):379-391.10.1111/add.12393

26. White SJ, Sin J, Sweeney A, Salisbury T, Wahlich C, Montesinos Guevara CM, Gillard S, Brett E, Allwright L, Iqbal N *et al*: **Global Prevalence and Mental Health Outcomes of Intimate Partner Violence Among Women: A Systematic Review and Meta-Analysis**. *Trauma Violence Abuse* 2024, **25**(1):494-511.10.1177/15248380231155529

27. Wuest J, Merritt-Gray M, Lent B, Varcoe C, Connors AJ, Ford-Gilboe M: **Patterns of medication use among women survivors of intimate partner violence**. *Can J Public Health* 2007, **98**(6):460-464.10.1007/BF03405439

28. Chisholm CA, Bullock L, Ferguson JEJ, 2nd: **Intimate partner violence and pregnancy: epidemiology and impact**. *Am J Obstet Gynecol* 2017, **217**(2):141-144.10.1016/j.ajog.2017.05.042

29. Pallitto CC, Campbell JC, O'Campo P: **Is intimate partner violence associated with unintended pregnancy? A review of the literature**. *Trauma Violence Abuse* 2005, **6**(3):217-235.10.1177/1524838005277441

30. Soto-Angona O, Anmella G, Valdes-Florido MJ, De Uribe-Viloria N, Carvalho AF, Penninx B, Berk M: **Non-alcoholic fatty liver disease (NAFLD) as a neglected metabolic companion of psychiatric disorders: common pathways and future approaches**. *BMC Med* 2020, **18**(1):261.10.1186/s12916-020-01713-8

31. Kang D, Zhao D, Ryu S, Guallar E, Cho J, Lazo M, Shin H, Chang Y, Sung E: **Author Correction: Perceived stress and non-alcoholic fatty liver disease in apparently healthy men and women**. *Sci Rep* 2020, **10**(1):21978.10.1038/s41598-020-78911-0

32. Joseph JJ, Golden SH: **Cortisol dysregulation: the bidirectional link between stress, depression, and type 2 diabetes mellitus**. *Ann N Y Acad Sci* 2017, **1391**(1):20-34.10.1111/nyas.13217

33. Mason SM, Wright RJ, Hibert EN, Spiegelman D, Jun HJ, Hu FB, Rich-Edwards JW: **Intimate partner violence and incidence of type 2 diabetes in women**. *Diabetes Care* 2013, **36**(5):1159-1165.10.2337/dc12-1082

34. Stene LE, Jacobsen GW, Dyb G, Tverdal A, Schei B: **Intimate partner violence and cardiovascular risk in women: a population-based cohort study**. *J Womens Health (Larchmt)* 2013, **22**(3):250-258.10.1089/jwh.2012.3920

35. Bosch J, Weaver TL, Arnold LD, Clark EM: **The Impact of Intimate Partner Violence on Women's Physical Health: Findings From the Missouri Behavioral Risk Factor Surveillance System**. *J Interpers Violence* 2017, **32**(22):3402-3419.10.1177/0886260515599162

36. Ferdos J, Rahman M: **Exposure to intimate partner violence and malnutrition among young adult Bangladeshi women: cross-sectional study of a nationally representative sample**. *Cad Saude Publica* 2018, **34**(7):e00113916.10.1590/0102-311X00113916

37. Alhalal E: **Obesity in women who have experienced intimate partner violence**. *J Adv Nurs* 2018, **74**(12):2785-2797.10.1111/jan.13797

38. Bornstein SR, Schuppenies A, Wong ML, Licinio J: **Approaching the shared biology of obesity and depression: the stress axis as the locus of gene-environment interactions**. *Mol Psychiatry* 2006, **11**(10):892-902.10.1038/sj.mp.4001873

570 39. Dockray S, Susman EJ, Dorn LD: **Depression, cortisol reactivity, and obesity in**
571 **childhood and adolescence**. *J Adolesc Health* 2009, **45**(4):344-
572 350.10.1016/j.jadohealth.2009.06.014
573 40. Kendall-Tackett KA: **Inflammation, cardiovascular disease, and metabolic**
574 **syndrome as sequelae of violence against women: the role of depression,**
575 **hostility, and sleep disturbance**. *Trauma Violence Abuse* 2007, **8**(2):117-
576 126.10.1177/1524838007301161
577 41. Jakubowski KP, Murray V, Stokes N, Thurston RC: **Sexual violence and**
578 **cardiovascular disease risk: A systematic review and meta-analysis**. *Maturitas*
579 2021, **153**:48-60.10.1016/j.maturitas.2021.07.014
580 42. Halpern LR, Shealer ML, Cho R, McMichael EB, Rogers J, Ferguson-Young D, Mouton
581 CP, Tabatabai M, Southerland J, Gangula P: **Influence of Intimate Partner Violence**
582 **(IPV) Exposure on Cardiovascular and Salivary Biosensors: Is There a**
583 **Relationship?** *J Natl Med Assoc* 2017, **109**(4):252-261.10.1016/j.jnma.2017.08.001
584 43. Liu X, Logan J, Alhusen J: **Cardiovascular Risk and Outcomes in Women Who**
585 **Have Experienced Intimate Partner Violence: An Integrative Review**. *J*
586 *Cardiovasc Nurs* 2020, **35**(4):400-414.10.1097/JCN.0000000000000654
587 44. Wright EN, Hanlon A, Lozano A, Teitelman AM: **The impact of intimate partner**
588 **violence, depressive symptoms, alcohol dependence, and perceived stress on**
589 **30-year cardiovascular disease risk among young adult women: A multiple**
590 **mediation analysis**. *Prev Med* 2019, **121**:47-54.10.1016/j.ypmed.2019.01.016
591 45. Westcott SK, Beach LY, Matsushita F, Albert CM, Chatterjee N, Wong J, Williams DR,
592 Vinayagamoorthy M, Buring JE, Albert MA: **Relationship Between Psychosocial**
593 **Stressors and Atrial Fibrillation in Women >45 Years of Age**. *Am J Cardiol* 2018,
594 **122**(10):1684-1687.10.1016/j.amjcard.2018.07.044

46. Mason SM, Wright RJ, Hibert EN, Spiegelman D, Forman JP, Rich-Edwards JW: **Intimate partner violence and incidence of hypertension in women**. *Ann Epidemiol* 2012, **22**(8):562-567.10.1016/j.annepidem.2012.05.003

47. Clark CJ, Everson-Rose SA, Alonso A, Spencer RA, Brady SS, Resnick MD, Borowsky IW, Connett JE, Krueger RF, Suglia SF: **Effect of partner violence in adolescence and young adulthood on blood pressure and incident hypertension**. *PLoS One* 2014, **9**(3):e92204.10.1371/journal.pone.0092204

48. Li C, Chen J, Chen Y, Zhang C, Yang H, Yu S, Song H, Fu P, Zeng X: **The association between patterns of exposure to adverse life events and the risk of chronic kidney disease: a prospective cohort study of 140,997 individuals**. *Transl Psychiatry* 2024, **14**(1):424.10.1038/s41398-024-03114-4

STROBE Statement—checklist of items that should be included in reports of observational studies

	Item No.	Recommendation	Page No.
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract "Association Between Exposure to Interpersonal Violence and Cardiac, Metabolic, and Renal Diseases – A Cohort Study in a Local Health Unit in Portugal "	Page 1
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found "Introduction: Interpersonal violence (IV) is a major public health issue with significant sociocultural, economic, and health impacts. It increases the risk of physical, psychological, and behavioral repercussions, including premature mortality. Despite evidence linking IV to systemic diseases, research on its association with cardiorenal-metabolic diseases remains limited. This study aimed to characterize patients with suspected exposure to IV. Secondary objectives included comparing the incidence of cardiorenal-metabolic diseases between suspected victims and the general population over 5- and 10-year periods. Methods: A real-world, retrospective, and observational study was conducted using electronic health registers (EHR) from a Local Health Unit in Portugal, between 2003 and 2023. All patients aged 18 years or older with at least one entry in the EHR within 365 days before the index date and at least one primary healthcare appointment in the preceding 3 years were included. The exposed cohort included patients with documented suspicion of IV in the EHR, according to codes or text expressions. Variables studied included sociodemographics, risk behaviors, psychiatric disorders, and cardiorenal-metabolic diseases. Statistical analysis employed both descriptive and inferential methods to assess the associations. Results: The suspected IV cohort comprised 232 398 patients, while the non-suspected IV cohort included 60 465 patients, with a slight predominance of females in both. Median ages were 55.96 and 58.83 years, respectively. IV suspected patients demonstrated higher incidence of health risk factors, such as smoking (21.8% vs 6.3%), excessive alcohol consumption (11.2% vs 2.3%), drug abuse (18.9% vs 5.4%), and psychiatric disorders (76.4% vs 30.8%). Notably, in the 5-year follow-up, suspected IV was strongly associated with: acute kidney disease (HR=2.20, 95% CI= [1.84-2.63]), non-alcoholic fatty liver disease (HR=2.04, 95% CI= [1.70-2.46]), and ischemic stroke disease (HR=2.01, 95% CI= [1.78- 2.27]). Discussion and Conclusions: This study found that individuals with suspected IV exhibited a higher incidence of health risk behaviours and most cardio-renal-metabolic diseases. These findings highlight the importance of incorporating IV screening and integrating preventive strategies into routine healthcare. Enhancing the detection and documentation of IV within EHRs is essential to support effective clinical responses and public health planning. Further research is warranted to evaluate interventions targeting the long-term health effects of IV."	Page 2-3
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported "The World Health Organization (WHO) declared violence a major public health problem in 1996 and, in 2002, defined it as the "intentional use of physical force or	Pages 3-5

power, threatened or actual, against oneself, another person, or a group or community, which either results in or has a high likelihood of resulting in injury, death, psychological harm, maldevelopment, or deprivation" [1].

Experiencing interpersonal violence (IV) significantly impacts victims' lives at sociocultural and economic levels, but primarily affects their health. It increases the risk of physical, psychological, and behavioral outcomes and contributes to premature mortality (due to natural diseases or violent causes such as homicide, suicide, or accidents). [2].

Victims often experience changes such as disruption of the hypothalamic-pituitary-adrenal axis and autonomic nervous system dysfunction – mechanisms that regulate stress responses and are implicated in many systemic diseases. However, research on the risk of metabolic diseases (e.g., metabolic syndrome, dyslipidemia, type 2 diabetes mellitus - T2DM), cardiovascular diseases - CVD (e.g., hypertension, acute myocardial infarction, stroke), and renal diseases (e.g., chronic kidney disease - CKD) in this population remains limited [3].

Strong clinical and epidemiological evidence supports the interrelationship between T2DM, CVD, and CKD – a cluster referred to as cardiorenal-metabolic disease. This condition currently represents one of the most pressing public health challenges. [4].

Cardiorenal-metabolic diseases exhibit sex-based differences in risk and manifestation: men tend to develop CVD earlier (e.g., myocardial infarction and hypertension), whereas postmenopausal women and those with a higher prevalence of autoimmune diseases are more prone to cardiovascular complications [5].

In Portugal, the most common metabolic disorders and their respective prevalence include: (a) metabolic syndrome (33.4% among individuals aged 25-74 years [6]); (b) hypercholesterolemia (total cholesterol >240mg/dl, which affects 31.3% of the population in Continental Portugal [7]); (c) diabetes (13%, according to the International Diabetes Federation, among individuals aged 20-79 years [8]); (d) non-alcoholic fatty liver disease (NAFLD), of 17% [9].

CVD remains the leading cause of death in Portugal, accounting for 27.9% of female deaths and 36.3% of male deaths according to the World Heart Federation's 2024 Scorecard [10]. Coronary artery disease, acute myocardial infarction, and stroke are the primary contributors to this mortality rate. Standardized mortality rates per sex are reported as 51.1, 30.3, and 19.3 per 100 000 inhabitants for these conditions, respectively, according to the Portuguese General Health Direction (DGS) [11]. Other prevalent CVDs in Portugal include: (a) pulmonary thromboembolism, 35 per 100 000 adult inhabitants aged ≥18 years [12]; (b) hypertension, 43.1%, particularly among older men [7]; (c) chronic heart failure, 4.4% in adults, rising to 12.7% among those aged 70-79 years and 16.1% among individuals aged ≥80 years [13]; (d) peripheral arterial disease, 3-10% in the overall population and 15-20% in those aged ≥70 years [14]; (e) atrial fibrillation, 2.5% among individuals aged ≥40 years, being higher from age 70 onwards [15].

Regarding renal diseases, the RENA study reported an overall CKD prevalence of 20.9% in primary healthcare in Portugal, with rates significantly increasing with age [16].

The relationship between IV and the development of cardiorenal-metabolic diseases has been explored in a generalist approach through a retrospective cohort study conducted in the United Kingdom (from 1995 to 2017). This study concluded that among women exposed to intimate partner violence (n=18 547), 181 experienced a cardiovascular event

		compared to 644 women from the non-exposed control group (n=72 231), which was conveyed into an adjusted IRR (incidence rate ratio) of composite CVD (1.31; 95% CI, 1.11-1.55; p=0.001). Additionally, there was an increased risk of subsequent T2DM, ischemic heart disease, stroke, and mortality. However, there were no statistically significant differences in developing heart failure, peripheral vascular disease, or hypertension [17]. No Portuguese study has specifically addressed this issue, which prompted the investigators to undertake the present research."	
Objectives	3	State specific objectives, including any prespecified hypotheses "This study aimed to characterize patients with suspected victims of IV regarding the presence of cardiorenal-metabolic diseases. Secondary objectives included comparing the incidence of cardiac, metabolic, and renal diseases between suspected victims and the general population over 5- and 10-year periods."	Page 5
Methods			
Study design	4	Present key elements of study design early in the paper "The present study is based on electronic health registers (EHR). It is a real-world, retrospective, and observational study, involving a cohort of participants registered at the Local Health Unit of Matosinhos (ULSM) between 2003 and 2023."	Page 6
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection "ULSM is a major healthcare organisation comprising 14 primary care units supported by a central hospital, Pedro Hispano Hospital. It provides healthcare services to 177 445 individuals (according to the National Database of the National User Registry – RNU 202505) and serves as an initial point of contact for many victims of IV. This study relies on subparagraphs (i) and (j) of Article 9 of the European Union's General Data Protection Regulation (RGPD) 2016/679 as legal grounds for processing sensitive personal data. These provisions allow data processing for reasons of public interest in public health and scientific research purposes, respectively. Ethical approval was obtained from the ULSM Health Ethics Committee and the Local Information Protection and Security Committee. Approval codes were issued as follows: No. 91/CES/JAS on October 14, 2022, and No. 71/CLPSI/2022 on December 21, 2022. Researchers did not have access to identifiable data. No data was extracted outside the ULSM infrastructure."	Page 6
Participants	6	(*a*) *Cohort study*—Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up "Participants were included if they met all the following criteria: (a) age ≥18 years old; (b) had at least one entry in the EHR within the 365 days prior to the index date; (c) had at least one primary healthcare appointment in the preceding 3 years preceding any event of interest (this interval was defined based on national indicators for primary healthcare usage in Portugal). The exclusion criteria were applied to individuals who had any of the following circumstances: (a) lacked information on sex; (b) had an age that could not be calculated. The index date was defined as the time between 1 January 2003 and 31 December 2023 during which the population met all the criteria above. The analysed group included participants registered at the ULSM who met all the criteria before and had been coded or had textual expressions for suspected IV. Suspicion of IV experience was identified using ICD (International Classification of Diseases)-9, ICD-10, and ICPC (International Classification of Primary Care)-2	Pages 6-8

		classification codes, as well as textual expressions. All the used codes and textual expressions can be found in Supplementary Material 1. The control group included participants registered at the ULSM who met all the criteria before and had not been coded or did not have textual expressions for suspected IV. To evaluate the development of cardiorenal-metabolic outcomes at 5 and 10 years of follow-up, adjusting for confounders (age, sex, smoking status, alcohol abuse, drug abuse, and prior psychiatric disorders), Cox proportional hazards models were fitted to estimate hazard ratios (HRs) with corresponding 95% confidence intervals (CIs). This was possibly due to the application of the cluster method available in the R Survival package, version 4.3.2. [18]"	
		(*b*) *Cohort study*—For matched studies, give matching criteria and number of exposed and unexposed	Page 9 and 13
		"The population in the cohort suspected of being victims of IV was matched to those in the non-suspected IV group using a nearest neighbour matching method, based on female sex, age, current smoker, alcohol abuse, drug abuse, any psychiatric disorder, and the violence-exposed population. The matching procedure was implemented using the MatchIt package (version 4.5.5) within R software (version 4.1.3). The matched cohorts consisted of 31 043 individuals NSIV and 27 606 with SIV (Table 5). Overall, the matching process achieved adequate covariate balance for most variables, although age remained slightly imbalanced. The proportion of females was similar and predominant across groups. There are significantly higher rates of current smoking status, alcohol, and drug abuse in the SIV group. A history of psychiatric disorders was the most incident comorbidity. "	
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	Pages 7-8
		"All variables were defined using ICD-9, ICD-10, ICPC-2, and ATC (Anatomical Therapeutic Chemical) classification codes, as well as laboratory, clinical, and demographic data available at the institution, accessible in Supplementary Material 1. All variables are detailed in the Results section. Age was treated both as a continuous quantitative variable and stratified into categorical groups (18-39, 40-64, 65-84, and ≥85 years). Categorical quantitative variables included: sex (female and male), risk factors (acute stress reaction, adjustment reaction, alcohol abuse, any psychiatric disorder excluding childhood and adolescent onset, current smoker, drug abuse, exposure to radiation, post-traumatic stress disorder, pregnancy history, use of psychotropic medication – antidepressants, antipsychotics, anxiolytics, and hypnotics/sedatives –, and use of oral contraceptives) and cardiorenal-metabolic outcomes (acute kidney disease, atrial fibrillation, CKD, heart failure, hypercholesterolemia, hypertension, hypertriglyceridemia, ischemic stroke, myocardial infarction, NAFLD, obesity, peripheral arterial disease, pulmonary embolism, and T2DM)."	
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	Pages 8-9
		"All data processing and analyses were performed using custom analytic programs developed specifically for this study. These programs were executed within the secure ULSM data center, with no external data extraction or direct researcher access to the raw data. The study packages - designed to run on ULSM's local infrastructure (Apache Spark Framework v3.2.1) - implemented the full data pipeline, including harmonization	

		of source data (aligned with OMOP CDM v5.4), variable derivation, statistical analysis, and generation of aggregated results reports. Patient demographic and clinical characteristics were described for each cohort. Continuous variables were summarised using the median (P50) and interquartile range (IQR), while categorical variables were expressed as absolute and relative frequencies. When a variable included five or fewer individuals, the count was reported as ≤5 to protect patients' privacy."	
Bias	9	Describe any efforts to address potential sources of bias "The population served by ULSM is predominantly urban and has access to a comprehensive range of healthcare services, which may not be representative of other regions in Portugal; consequently, selection bias may be present. This analysis was based on retrospective data obtained from EHR, which are susceptible to bias and residual confounding, thereby inherently limiting causal inference. To mitigate these effects, minimal exclusion criteria were applied, and data from both primary and secondary care sources were used. Underreporting of suspected IV cases may also occur due to missing EHR entries, absence of appropriate medical coding, or victims' difficulty in recognizing or disclosing their circumstances, particularly in cases involving psychological violence or neglect, where physical indicators are less apparent. This could result in an underestimation of IV incidence. Furthermore, primary care settings, which comprise the majority of ULSM, provide detailed records, owing to patients' easy access to general practitioners and active surveillance protocols. These differences should be considered when comparing findings with studies conducted in secondary care facilities or in prospective cohorts of pre-selected patients, who may present with more advanced disease and consequently higher associated risks."	Page 9
Study size	10	Explain how the study size was arrived at "Formal sample size estimation was deemed unnecessary, given that the study aimed to include the entire population that fulfilled inclusion criteria."	Page 10

Continued on next page

Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why "Age was treated both as a continuous quantitative variable and stratified into categorical groups (18-39, 40-64, 65-84, and ≥85 years). Categorical quantitative variables included: sex (female and male), risk factors (acute stress reaction, adjustment reaction, alcohol abuse, any psychiatric disorder excluding childhood and adolescent onset, current smoker, drug abuse, exposure to radiation, post-traumatic stress disorder, pregnancy history, use of psychotropic medication – antidepressants, antipsychotics, anxiolytics, and hypnotics/sedatives –, and use of oral contraceptives) and cardiorenal-metabolic outcomes (acute kidney disease, atrial fibrillation, CKD, heart failure, hypercholesterolemia, hypertension, hypertriglyceridemia, ischemic stroke, myocardial infarction, NAFLD, obesity, peripheral arterial disease, pulmonary embolism, and T2DM)."	Pages 7-8
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding (*b*) Describe any methods used to examine subgroups and interactions (*c*) Explain how missing data were addressed (*d*) *Cohort study*—If applicable, explain how loss to follow-up was addressed (*e*) Describe any sensitivity analyses "To evaluate the development of cardiorenal-metabolic outcomes at 5 and 10 years of follow-up, adjusting for confounders (age, sex, smoking status, alcohol abuse, drug abuse, and prior psychiatric disorders), Cox proportional hazards models were fitted to estimate hazard ratios (HRs) with corresponding 95% confidence intervals (CIs). This was possibly due to the application of the cluster method available in the R Survival package, version 4.3.2. [18] The propensity score (PS) was estimated using multivariable logistic regression, incorporating seven covariates selected a priori. Standardised mean difference (SMD) was calculated before and after matching to assess covariate balance, with an absolute SMD<0.1 considered indicative of acceptable balance. All incidence analyses were conducted on the matched cohorts. The population in the cohort suspected of being victims of IV was matched to those in the non-suspected IV group using a nearest neighbour matching method, based on female sex, age, current smoker, alcohol abuse, drug abuse, any psychiatric disorder, and the violence-exposed population. The matching procedure was implemented using the MatchIt package (version 4.5.5) within R software (version 4.1.3)."	Pages 8-9
Results			
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed (b) Give reasons for non-participation at each stage (c) Consider use of a flow diagram "The suspected IV (SIV) cohort comprised 60 465 patients (Table 1). The median age was 55.96 years for the SIV cohort and 58.83 for the non-suspected IV (NSIV) cohort. The most affected age group was between 40 and 64 years (41.6% in the SIV cohort). With increasing age beyond this range, the number of suspected cases decreased, as demonstrated in the group aged >84 years, where the advanced age contributed to a smaller population size and	Page 10

		correspondingly fewer cases of SIV (2.7%) – Table 1. Regarding the sex of the cohorts, most patients with SIV were female (57.9%), as were the NSIV patients (59.1%) - Table 2."	
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders (b) Indicate number of participants with missing data for each variable of interest (c) *Cohort study*—Summarise follow-up time (eg, average and total amount) "Risk health factors were markedly more incident in individuals with SIV compared to those in the NSIV group (Table 3). The most common comorbidity among the SIV group was any psychiatric disorder (76.4%), much higher than in the NSIV group (30.8%). Radiation exposure was recorded in ≤5 cases, rendering statistical analysis infeasible. Consequently, this variable was not included in further analysis due to its limited significance and representation."	Page 11
Outcome data	15*	*Cohort study*—Report numbers of outcome events or summary measures over time "Cardio-renal-metabolic conditions were markedly more common among SIV individuals when compared to those with NSIV (Table 4). Conditions with particularly high incidence in the SIV group included hypercholesterolaemia (65.3%), CKD (42.2%), and hypertriglyceridaemia (32.7%)."	Page 12
Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included (*b*) Report category boundaries when continuous variables were categorized (*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period "Addressing the 5th-year follow-up, there were statistical differences in most of the analysed outcomes. The highlights include acute kidney disease, NAFLD, and ischemic stroke. There were no statistical differences in atrial fibrillation and obesity – Table 6. In the 10th-year follow-up, there were also statistical differences in most of the analysed outcomes. The highlights were equal to the 5th-year follow-up, but without statistical differences in hypertension at the 10th-year follow-up - Table 6."	Page 14

Continued on next page

Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	X
Discussion			
Key results	18	Summarise key results with reference to study objectives "This research demonstrated that, within the two studied cohorts, individuals in the SIV group exhibited a higher incidence of health risk factors (Table 3) and adverse outcomes for certain cardiac, metabolic, and renal diseases (Table 4). Statistically significant differences were observed for most cardiorenal-metabolic diseases analysed (Table 6)."	Page 14
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias "The following limitations were identified in this study: (a) selection bias, as the representativeness of the sample may have been affected as the recruited individuals might not fully reflect the target population, despite efforts to minimize this bias through minimal exclusion criteria and the use of comprehensive data, causal inference remains limited due to the retrospective observational nature of the study; (b) underreporting bias, as cases of violence may be underreported due to the absence of medical coding or victims' difficulty in recognizing or communicating their situation; (c) medical coding limitations, as errors in the classification of diagnostic codes by healthcare professionals could lead to an underestimation of the observed effect size; (d) methodological differences between comparative studies, as other studies conducted in secondary care centers or prospective cohorts often include patients with more advanced disease stages, which may affect comparability; (e) lack of in-depth research in specific areas, as certain associations, such as between suspicion of IV and NAFLD or acute kidney injury, remain underexplored and require more robust and conclusive investigation."	Pages 18-19
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence "Demographics In both cohorts, most of the studied population belonged to the 40-64-year age group, with females being the most affected sex (Tables 1 and 2). This finding is consistent with the general victim profile reported in the 2024 statistics of the Portuguese Association for Victim Support (APAV), which indicates a median age of 37 years and a predominance of female victims, accounting for 76.3% of cases. [18] There was also a slightly higher proportion of younger individuals observed in the SIV group (Table 1), highlighting the heightened vulnerability of this age group. This underscores the importance of investigating dating violence within this demographic. Research indicates that young individuals at higher risk are those who have previously experienced IV and lack skills to manage conflict or respond to coercion, with peer influence often reinforcing abusive behaviors [19]. To be noted also, that a substantial proportion of men were identified as possible victims of IV (Table 2). This group is underrepresented and more likely to experience severe consequences due to their lower likelihood of seeking help or recognizing IV. This results in limited knowledge about the health outcomes for male victims and more severe consequences [20]. Health Risk Factors An association was observed between the SIV cohort and a higher incidence of most of the health risk factors examined (Table 3). These findings are consistent with existing evidence indicating that IV experience may influence the consumption of addictive substances (e.g., alcohol, tobacco, and drugs) through direct mechanisms, such as partner coercion, or indirect pathways, including psychological trauma and	Pages 15-18

self-medication to cope with distress [21-23]. Conversely, some studies suggest that individuals diagnosed with substance or alcohol abuse are more likely to suffer IV in the future [24, 25]. Irrespective of the direction of causality, the presence of a diagnosis related to alcohol, tobacco, or drug abuse should prompt screening for IV, and vice versa.

Moreover, significant associations were found between the SIV group and various psychiatric disorders and stress-related reactions (Table 3), as previously described in the literature [23, 26]. This study also demonstrated that suspected victims are more likely to use psychiatric medication, including antidepressants and anxiolytics (Table 3), which aligns with current evidence [27].

The study further highlighted an increased incidence of pregnancy history in the SIV group (Table 3), consistent with previous research, linking IV to higher rates of unintended pregnancies, sexually transmitted diseases, and induced abortions [28, 29]. However, in contrast to some earlier studies, our findings indicate a higher use of contraceptives within the SIV cohort (Table 3) [27].

Cardiorenal-metabolic diseases

An association was observed between the SIV cohort and an increased incidence of most of the cardiorenal-metabolic diseases investigated (Table 4).

These findings are somewhat in line with the existent study, where, in the United Kingdom, 181 IV-exposed women experienced a CVD event compared with 644 of the IV-unexposed group, yielding an increased adjusted IRR of 1.31 (95% CI, 1.11–1.55; p=0.001), with a significantly higher risk of developing ischemic heart disease (1.40; 95% CI, 1.09–1.79; p=0.007) and stroke or transient ischemic attack (1.29; 95% CI, 1.02–1.63; p=0.035). There was also an elevated risk of T2DM (adjusted IRR: 1.51; 95% CI, 1.30–1.76; p<0.001) and all-cause mortality (adjusted IRR: 1.44; 95% CI, 1.24–1.67; p<0.001). No statistically significant differences were identified for heart failure (IRR: 1.15; 95% CI, 0.69–1.63; p=0.520), peripheral vascular disease (IRR: 1.27; 95% CI, 0.75–1.86; p=0.304), or hypertension (IRR: 0.99; 95% CI, 0.88–1.12; p=0.873) [17].

In contrast to the study above, the present analysis identified statistically significant differences in the incidence of both heart failure and peripheral vascular disease (Table 6). Additionally, this study examined a greater number of diseases.

Regarding metabolic diseases, NAFLD was notably associated with the SIV group (Tables 4 and 6). NAFLD is indirectly linked with IV, with psychiatric comorbidities and elevated stress levels potentially mediating this relationship [30] [31]. A strong association between the SIV group and T2DM was likewise observed in this study (Tables 4 and 6), corroborating previous findings. This may be attributable to the impact of stress and depression in triggering pro-inflammatory responses and neuroendocrine activation, which disrupt glucose metabolism and promote insulin resistance [32, 33]. The SIV group also demonstrated a higher incidence of hypertriglyceridemia and hypercholesterolemia (Tables 4 and 6), consistent with studies indicating that physical and/or sexual violence is associated with reduced high-density lipoprotein cholesterol and elevated triglyceride levels [34, 35]. In contrast, obesity did not show a significant association with IV in this study (Table 6). Existing literature on this topic links IV to obesity or anorexia, depending on the victim's sex, the type of violence experienced, and the mediating effect of depression with persistent dysregulation of the hypothalamic-pituitary-adrenal axis and hypercortisolemia [36-39]. Such immune dysregulation and chronic inflammation may contribute to an increased risk of metabolic syndrome [40].

Regarding CVD, positive associations with the SIV group were observed in most conditions studied, including heart failure, ischemic stroke, myocardial infarction, peripheral arterial disease, and pulmonary embolism (Tables 4 and 6), which is consistent with prior research

		demonstrating an elevated cardiovascular risk among victims of IV [41-43]. Depression alone is known to increase the risk of coronary heart and arterial disease, and changes the variability of the cardiac frequency, through both biological factors (e.g., systemic inflammation and elevated cortisol levels) and behavioral factors (e.g., physical inactivity, smoking, poor medication adherence, and social isolation). Victimisation by IV may exacerbate these effects, further contributing to poor cardiovascular outcomes [44]. However, no significant associations were identified between the SIV group and atrial fibrillation or hypertension (Table 6). Regarding atrial fibrillation, only one study has reported an association with traumatic life events [45]. The literature is aligned with the lack of association of hypertension and IV, where links were only observed in cases of severe abuse [46, 47]. The significant association of acute kidney disease and CKD in SIV individuals is an important finding (Tables 4 and 6), suggesting that the effects of IV extend beyond the cardiovascular and metabolic systems. There is a known association between CKD and adverse life events, including experiencing IV from childhood to adulthood, including sexual abuse. This relationship appears to differ based on genetic polymorphisms, potentially mediated through interleukin-1 receptor activity [48]. However, no literature was found supporting an association between acute kidney disease and IV. These elevated associations between metabolic, cardiac, and renal diseases support the hypothesis of a unified cluster of cardiorenal-metabolic diseases [4].	
Generalisability	21	Discuss the generalisability (external validity) of the study results "Future research should focus on conducting prospective longitudinal studies to overcome these limitations, addressing underreporting by employing advanced natural language processing tools and qualitative analysis of EHR, investigating specific types of violence and their associations with different pathologies, examining sociocultural impacts on the incidence and effects of IV across diverse populations and expanding research to other national local health units and European research groups for broader and more definitive conclusions."	Page 19
Other information			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based "The authors declare that no financial support was received for conducting this research or preparing/publishing this article."	Page 22

*Give information separately for cases and controls in case-control studies and, if applicable, for exposed and unexposed groups in cohort and cross-sectional studies.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at www.strobe-statement.org.

BMC Primary Care Research Article Guidelines

Research article

Criteria

Research articles should report on original primary research, but may report on systematic reviews of published research provided they adhere to the appropriate reporting guidelines which are detailed in our editorial policies. Please note that non-commissioned pooled analyses of selected published research will not be considered. Studies reporting descriptive results from a single institution or region will only be considered if analogous data have not been previously published in a peer reviewed journal and the conclusions provide distinct insights that are of relevance to a regional or international audience.

BMC Primary Care strongly encourages that all datasets on which the conclusions of the paper rely should be available to readers. We encourage authors to ensure that their datasets are either deposited in publicly available repositories (where available and appropriate) or presented in the main manuscript or additional supporting files whenever possible. Please see Springer Nature's data repository guidance. Where a widely established research community expectation for data archiving in public repositories exists, submission to a community-endorsed, public repository is mandatory. A list of data where deposition is required, with the appropriate repositories, can be found on the Editorial Policies Page.

Authors who need help depositing and curating data may wish to consider contacting our Research Data Support Helpdesk.

Professionally produced Visual Abstracts
*BMC Primary Care*will consider visual abstracts. As an author submitting to the journal, you may wish to make use of services provided at Springer Nature for high quality and affordable visual abstracts where you are entitled to a 20% discount. Click here to find out more about the service, and your discount will be automatically be applied when using this link.

Preparing your manuscript

The information below details the section headings that you should include in your manuscript and what information should be within each section.

Please note that your manuscript must include a 'Declarations' section including all of the subheadings (please see below for more information).

Title page

The title page should:

- present a title that includes, if appropriate, the study design e.g.:
  - "A versus B in the treatment of C: a randomized controlled trial", "X is a risk factor for Y: a case control study", "What is the impact of factor X on subject Y: A systematic review"
  - or for non-clinical or non-research studies a description of what the article reports
- list the full names and institutional addresses for all authors
  - if a collaboration group should be listed as an author, please list the Group name as an author. If you would like the names of the individual members of the Group to be searchable through their individual PubMed records, please include this information in the "Acknowledgements" section in accordance with the instructions below
  - Large Language Models (LLMs), such as ChatGPT, do not currently satisfy our authorship criteria. Notably an attribution of authorship carries with it accountability for the work, which cannot be effectively applied to LLMs. Use of an LLM should be properly documented in the Methods section (and if a Methods section is not available, in a suitable alternative part) of the manuscript.
- indicate the corresponding author

Abstract

The Abstract should not exceed 350 words. Please minimize the use of abbreviations and do not cite references in the abstract. Reports of randomized controlled trials should follow the CONSORT extension for abstracts. The abstract must include the following separate sections:

- **Background:** the context and purpose of the study
- **Methods:** how the study was performed and statistical tests used
- **Results:** the main findings
- **Conclusions:** brief summary and potential implications
- **Trial registration:** If your article reports the results of a health care intervention on human participants, it must be registered in an appropriate registry and the registration number and date of registration should be stated in this section. If it was not registered prospectively (before enrollment of the first participant), you should include the words 'retrospectively registered'. See our editorial policies for more information on trial registration

Keywords

Three to ten keywords representing the main content of the article.

Background

The Background section should explain the background to the study, its aims, a summary of the existing literature and why this study was necessary or its contribution to the field.

Methods

The methods section should include:

- the aim, design and setting of the study
- the characteristics of participants or description of materials
- a clear description of all processes, interventions and comparisons. Generic drug names should generally be used. When proprietary brands are used in research, include the brand names in parentheses
- the type of statistical analysis used, including a power calculation if appropriate

Results

This should include the findings of the study including, if appropriate, results of statistical analysis which must be included either in the text or as tables and figures.

Discussion

This section should discuss the implications of the findings in context of existing research and highlight limitations of the study.

Conclusions

This should state clearly the main conclusions and provide an explanation of the importance and relevance of the study reported.

List of abbreviations

If abbreviations are used in the text they should be defined in the text at first use, and a list of abbreviations should be provided.

Declarations

All manuscripts must contain the following sections under the heading 'Declarations':

- Ethics approval and consent to participate
- Consent for publication
- Availability of data and materials
- Competing interests
- Funding
- Authors' contributions
- Acknowledgements
- Authors' information (optional)

Please see below for details on the information to be included in these sections.

If any of the sections are not relevant to your manuscript, please include the heading and write 'Not applicable' for that section.

Ethics approval and consent to participate

Manuscripts reporting studies involving human participants, human data or human tissue must:

- include a statement on ethics approval and consent (even where the need for approval was waived)
- include the name of the ethics committee that approved the study and the committee's reference number if appropriate

Studies involving animals must include a statement on ethics approval and for experimental studies involving client-owned animals, authors must also include a statement on informed consent from the client or owner.

See our editorial policies for more information.

If your manuscript does not report on or involve the use of any animal or human data or tissue, please state "Not applicable" in this section.

Consent for publication

If your manuscript contains any individual person's data in any form (including any individual details, images or videos), consent for publication must be obtained from that person, or in the case of children, their parent or legal guardian. All presentations of case reports must have consent for publication.

You can use your institutional consent form or our consent form if you prefer. You should not send the form to us on submission, but we may request to see a copy at any stage (including after publication).

See our editorial policies for more information on consent for publication.

If your manuscript does not contain data from any individual person, please state "Not applicable" in this section.

Availability of data and materials

All manuscripts must include an 'Availability of data and materials' statement. Data availability statements should include information on where data supporting the results reported in the article can be found including, where applicable, hyperlinks to publicly archived datasets analysed or generated during the study. By data we mean the minimal dataset that would be necessary to interpret, replicate and build upon the findings reported in the article. We recognise it is not always possible to share research data publicly, for instance when individual privacy could be compromised, and in such instances data availability should still be stated in the manuscript along with any conditions for access.

Authors are also encouraged to preserve search strings on searchRxiv https://searchrxiv.org/, an archive to support researchers to report, store and share their searches consistently and to enable them to review and re-use existing searches. searchRxiv enables researchers to obtain a digital object identifier (DOI) for their search, allowing it to be cited.

Data availability statements can take one of the following forms (or a combination of more than one if required for multiple datasets):

- The datasets generated and/or analysed during the current study are available in the [NAME] repository, [PERSISTENT WEB LINK TO DATASETS]
- The datasets used and/or analysed during the current study are available from the corresponding author on reasonable request.
- All data generated or analysed during this study are included in this published article [and its supplementary information files].
- The datasets generated and/or analysed during the current study are not publicly available due [REASON WHY DATA ARE NOT PUBLIC] but are available from the corresponding author on reasonable request.
- Data sharing is not applicable to this article as no datasets were generated or analysed during the current study.
- The data that support the findings of this study are available from [third party name] but restrictions apply to the availability of these data, which were used under license for the current study, and so are not publicly available. Data are however available from the authors upon reasonable request and with permission of [third party name].
- Not applicable. If your manuscript does not contain any data, please state 'Not applicable' in this section.

More examples of template data availability statements, which include examples of openly available and restricted access datasets, are available here.

BioMed Central strongly encourages the citation of any publicly available data on which the conclusions of the paper rely in the manuscript. Data citations should include a persistent identifier (such as a DOI) and should ideally be included in the reference list. Citations of datasets, when they appear in the reference list, should include the minimum information recommended by DataCite and follow journal style. Dataset identifiers including DOIs should be expressed as full URLs. For example:

Hao Z, AghaKouchak A, Nakhjiri N, Farahmand A. Global integrated drought monitoring and prediction system (GIDMaPS) data sets. figshare. 2014. http://dx.doi.org/10.6084/m9.figshare.853801

With the corresponding text in the Availability of data and materials statement:

The datasets generated during and/or analysed during the current study are available in the [NAME] repository, [PERSISTENT WEB LINK TO DATASETS].[Reference number]

If you wish to co-submit a data note describing your data to be published in *BMC Research Notes*, you can do so by visiting our submission portal. Data notes support open data and help authors to comply with funder policies on data sharing. Co-published data notes will be linked to the research article the data support (example).

Competing interests

All financial and non-financial competing interests must be declared in this section.

See our editorial policies for a full explanation of competing interests. If you are unsure whether you or any of your co-authors have a competing interest please contact the editorial office.

Please use the authors initials to refer to each authors' competing interests in this section.

If you do not have any competing interests, please state "The authors declare that they have no competing interests" in this section.

Funding

All sources of funding for the research reported should be declared. If the funder has a specific role in the conceptualization, design, data collection, analysis, decision to publish, or preparation of the manuscript, this should be declared.

Authors' contributions

The individual contributions of authors to the manuscript should be specified in this section. Guidance and criteria for authorship can be found in our editorial policies.

Please use initials to refer to each author's contribution in this section, for example: "FC analyzed and interpreted the patient data regarding the hematological disease and the transplant. RH performed the histological examination of the kidney, and was a major contributor in writing the manuscript. All authors read and approved the final manuscript."

Acknowledgements

Please acknowledge anyone who contributed towards the article who does not meet the criteria for authorship including anyone who provided professional writing services or materials.

Authors should obtain permission to acknowledge from all those mentioned in the Acknowledgements section.

See our editorial policies for a full explanation of acknowledgements and authorship criteria.

If you do not have anyone to acknowledge, please write "Not applicable" in this section.

Group authorship (for manuscripts involving a collaboration group): if you would like the names of the individual members of a collaboration Group to be searchable through their individual PubMed records, please ensure that the title of the collaboration Group is included on the title page and in the submission system and also include collaborating author names as the last paragraph of the "Acknowledgements" section. Please add authors in the format First Name, Middle initial(s) (optional), Last Name. You can add institution or country information for each author if you wish, but this should be consistent across all authors.

Please note that individual names may not be present in the PubMed record at the time a published article is initially included in PubMed as it takes PubMed additional time to code this information.

Authors' information

This section is optional.

You may choose to use this section to include any relevant information about the author(s) that may aid the reader's interpretation of the article, and understand the standpoint of the author(s). This may include details about the authors' qualifications, current positions they hold at institutions or societies, or any other relevant background information. Please refer to authors using their initials. Note this section should not be used to describe any competing interests.

Footnotes

Footnotes can be used to give additional information, which may include the citation of a reference included in the reference list. They should not consist solely of a reference citation, and they should never include the bibliographic details of a reference. They should also not contain any figures or tables.

Footnotes to the text are numbered consecutively; those to tables should be indicated by superscript lower-case letters (or asterisks for significance values and other statistical data). Footnotes to the title or the authors of the article are not given reference symbols.

Always use footnotes instead of endnotes.

References

Examples of the Vancouver reference style are shown below.

See our editorial policies for author guidance on good citation practice

Web links and URLs: All web links and URLs, including links to the authors' own websites, should be given a reference number and included in the reference list rather than within the text of the manuscript. They should be provided in full, including both the title of the site and the URL, as well as the date the site was accessed, in the following format: The Mouse Tumor Biology Database. http://tumor.informatics.jax.org/mtbwi/index.do. Accessed 20 May 2013. If an author or group of authors can clearly be associated with a web link, such as for weblogs, then they should be included in the reference.

Example reference style:

Article within a journal

Smith JJ. The world of science. Am J Sci. 1999;36:234-5.

Article within a journal (no page numbers)

Rohrmann S, Overvad K, Bueno-de-Mesquita HB, Jakobsen MU, Egeberg R, Tjønneland A, et al. Meat consumption and mortality - results from the European Prospective Investigation into Cancer and Nutrition. BMC Medicine. 2013;11:63.

Article within a journal by DOI

Slifka MK, Whitton JL. Clinical implications of dysregulated cytokine production. Dig J Mol Med. 2000; doi:10.1007/s801090000086.

Article within a journal supplement

Frumin AM, Nussbaum J, Esposito M. Functional asplenia: demonstration of splenic activity by bone marrow scan. Blood 1979;59 Suppl 1:26-32.

Book chapter, or an article within a book

Wyllie AH, Kerr JFR, Currie AR. Cell death: the significance of apoptosis. In: Bourne GH, Danielli JF, Jeon KW, editors. International review of cytology. London: Academic; 1980. p. 251-306.

OnlineFirst chapter in a series (without a volume designation but with a DOI)

Saito Y, Hyuga H. Rate equation approaches to amplification of enantiomeric excess and chiral symmetry breaking. Top Curr Chem. 2007. doi:10.1007/128_2006_108.

Complete book, authored

Blenkinsopp A, Paxton P. Symptoms in the pharmacy: a guide to the management of common illness. 3rd ed. Oxford: Blackwell Science; 1998.

Online document

Doe J. Title of subordinate document. In: The dictionary of substances and their effects. Royal Society of Chemistry. 1999. http://www.rsc.org/dose/title of subordinate document. Accessed 15 Jan 1999.

Online database

Healthwise Knowledgebase. US Pharmacopeia, Rockville. 1998. http://www.healthwise.org. Accessed 21 Sept 1998.

Supplementary material/private homepage

Doe J. Title of supplementary material. 2000. http://www.privatehomepage.com. Accessed 22 Feb 2000.

University site

Doe, J: Title of preprint. http://www.uni-heidelberg.de/mydata.html (1999). Accessed 25 Dec 1999.

FTP site

Doe, J: Trivial HTTP, RFC2169. ftp://ftp.isi.edu/in-notes/rfc2169.txt (1999). Accessed 12 Nov 1999.

Organization site

ISSN International Centre: The ISSN register. http://www.issn.org (2006). Accessed 20 Feb 2007.

Dataset with persistent identifier

Zheng L-Y, Guo X-S, He B, Sun L-J, Peng Y, Dong S-S, et al. Genome data from sweet and grain sorghum (Sorghum bicolor). GigaScience Database. 2011. http://dx.doi.org/10.5524/100012.

Figures, tables and additional files

See General formatting guidelines for information on how to format figures, tables and additional files.

Submit manuscript

FACULDADE DE **MEDICINA**