Alla ricerca della verità:
subire o controllare i bias?

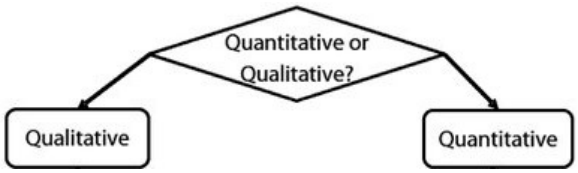
Non si può parlare
di conoscenza scientifica
senza considerare
il metodo
che l'ha generata

Diversi gli obiettivi…

Diversi i disegni di ricerca…

Diverso il rigore metodologico…

Diversa la fiducia attribuibile ai risultati



Quale dei seguenti argomenti associ alla ricerca qualitativa?

- La qualità delle vita negli anziani diabetici
- I ricordi dei pazienti dimessi dalla terapia intensiva
- La qualità delle cure percepita dai degenti in un reparto medico
- La qualità della formazione ricevuta dagli studenti del CdL in infermieristica
- I determinanti di salute nelle popolazioni rurali del Pakistan
- L'impatto del COVID-19 su salute mentale e benessere negli infermieri di TI

Ricerca: Qualitativa o Quantitativa?

Ricerca quantitativa

- Mira a compiere generalizzazioni sulla popolazione partendo da osservazioni obiettive effettuate su un campione.
- Si avvale di metodi di indagine basati sulla misurazione quantitativa dei fenomeni di interesse e la convalida/confutazione dell'ipotesi sulla base di inferenze statistiche effettuate sui dati misurati.

Ricerca qualitativa

- Studia problemi di ricerca associati a fenomeni ed esperienze umane.
- Si avvale di metodi di indagine che documentano le storie e cercano i significati soggettivi nelle esperienze delle persone (es. osservazione partecipata, narrazioni verbali o scritte, interviste, focus group).

Metodo misto

- Associa metodi quantitativi e qualitativi per avere una visione complementare e più approfondita di un certo fenomeno.

La direzione del tempo

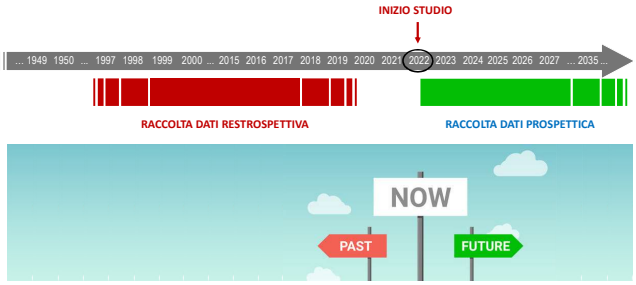
Studio retrospettivo

- Prende in esame eventi già accaduti e conclusi
- Utilizza informazioni esistenti, da raccogliere (es. analisi di cartelle cliniche) o già raccolte per ragioni diverse dallo studio (es. dataset clinici o amministrativi)
- Gli eventi di interesse si sono già verificati nel momento in cui inizia lo studio
- Può essere trasversale o longitudinale

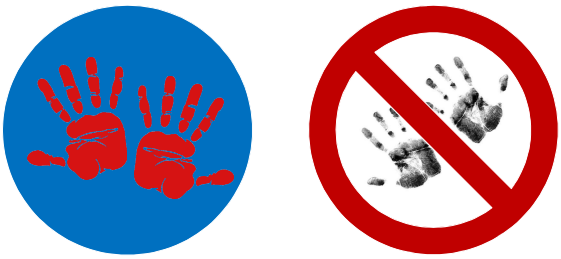
Studio prospettico

- Raccoglie dati iniziando nel presente e terminando nel futuro
- Gli eventi di interesse devono ancora accadere nel momento in cui inizia lo studio
- Viene progettato prima di raccogliere qualsiasi dato
- Può essere trasversale o longitudinale

La direzione del tempo



L'interferenza dei ricercatori



SPERIMENTALE **OSSERVAZIONALE**

L'interferenza dei ricercatori

STUDI OSSERVAZIONALI (o non sperimentali)

- Caratterizzati dall'assenza di intervento attivo da parte dei ricercatori, che si limitano a osservare un fenomeno
- **Descrittivi**: serie di casi, studi ecologici, distribuzione spaziale, andamento temporale
- **Analitici**:
  - studi longitudinali (studi di coorte, studi caso-controllo)
  - studi trasversali

STUDI SPERIMENTALI (e quasi-sperimentali)

- Caratterizzati dalla presenza di un trattamento/intervento stabilito dai ricercatori su di un gruppo di soggetti
- Consentono di verificare se l'associazione sia di tipo causale

Studi Osservazionali (non sperimentali)
Descrittivi

Studi Osservazionali Descrittivi

- Rivelano la frequenza e distribuzione spaziale di eventi sanitari in popolazioni o gruppi di individui (mortalità, morbosità, natalità, ecc.)
- Rispondono a tre importanti esigenze di conoscenza
  - Chi è interessato dal fenomeno
  - Quando si manifesta il fenomeno?
  - Dove si produce il fenomeno?
- Identificano quindi le caratteristiche degli individui (**chi**) esposti a un certo rischio e **dove** e **quando** tale rischio potrebbe manifestarsi
- Forniscono informazioni essenziali per la programmazione sanitaria
- Premessa per la formulazione di ipotesi eziologiche da verificare attraverso studi analitici

Maternal, Perinatal and Neonatal Outcomes With COVID-19: A Multicenter Study of 242 Pregnancies and Their 248 Infant Newborns During Their First Month of Life

Miguel A Marín Gabriel, MD, PhD,† Mar Reyne Vergeli, MD,‡ Sonia Caserío Carbonero, MD, PhD,§ Laia Sole, MD,¶ Tamara Carrizosa Molina, MD,‖ Irene Rivero Calle, MD, PhD,** Irene Cuadrado Pérez, MD,†† Blanca Álvarez Fernández, MD,‡‡ Azul Forti Buratti, MD, PhD,§§ and Aurora Fernández-Cañadas Morillo, RM, PhD,¶¶ on behalf of the Neo-COVID-19 Research Group*

Background: Our aim was to describe the clinical features of mothers with coronavirus disease 2019 (COVID-19) infection during gestation or delivery, and the potential vertical transmission. We also wish to evaluate the possible horizontal transmission after hospital discharge, by means of a follow-up of all the newborns included at 1 month of age.
Methods: This multicenter descriptive study involved 16 Spanish hospitals. We reviewed the medical records of 242 pregnant women diagnosed with COVID-19 from March 13 to May 31, 2020, when they were in their third trimester of pregnancy. They and their 248 newborn infants were monitored until the infant was 1 month old.
Results: Caesarean sections (C-sections) were performed on 63 (26%) women. The initial clinical symptoms were coughing (33%) and fever (29.7%). Mothers hospitalized due to COVID-19 pathology had a higher risk of ending their pregnancy via C-section ($P = 0.027$). Newborns whose mothers had been admitted due to their COVID-19 infection had a higher risk of premature delivery ($P = 0.006$). We admitted 115 (46.3%) newborn

Since the beginning of the pandemic caused by severe acute respiratory syndrome coronavirus 2 (SARS coronavirus 2) declared March 11, 2020, by the World Health Organization (WHO),[1] million have been infected worldwide, and hundreds of thousands have died. The infection caused by this virus appears to have a milder impact on children,[2] and more so in neonates, in whom, to date, vertical transmission has not been proven.[3–5] Sporadic severe cases have been reported in this group of neonatal patients.[5,6]

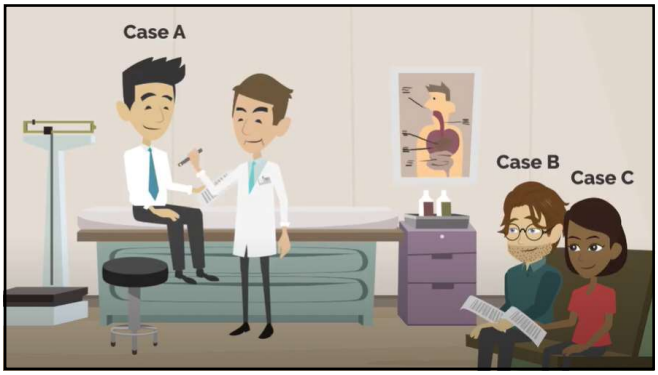
Currently, there is insufficient evidence regarding a possible SARS coronavirus 2 transmission via breastmilk.[4,5] The WHO, United Nations International Children's Emergency Fund, and the Centers for Disease Control and Prevention continue to recommend breast-feeding in this scenario, applying basic hygienic measures.[10–12].

Protocols regarding how to best manage both mother and newborn have evolved day by day as the pandemic progressed and our knowledge on the matter improved. At first, recommendations

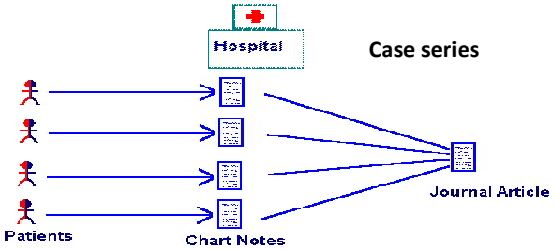
Studi Osservazionali Descrittivi

Case(s) report

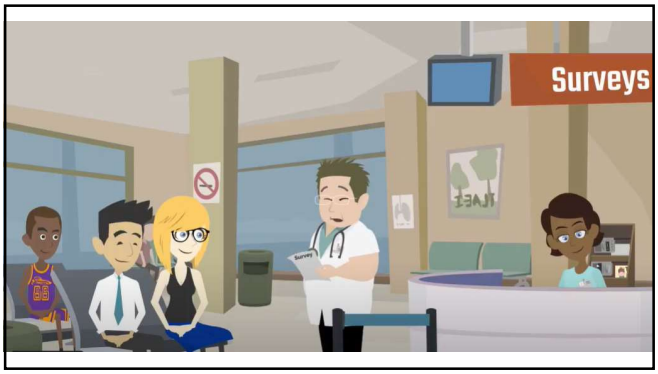
- Descrive la storia clinica di un singolo paziente
- È una segnalazione di un evento singolare, raro o particolare
- Si parla di case series se l'articolo riporta più casi simili
- Spesso spunto per effettuare una revisione della letteratura sul tema



Case(s) report



Case series



The Open Nursing Journal, 2018, 12, 67-75 67

BENTHAM OPEN

The Open Nursing Journal

Content list available at: www.benthamopen.com/TONURSJ/

DOI: 10.2174/1874434601812010067

RESEARCH ARTICLE

ICU Nurses' Perceived Barriers to Effective Enteral Nutrition Practices: A Multicenter Survey Study

Muhammad W. Darawad[1,*], Nedal Alfasfos[2], Ismael Zaki[3], Malek Alnajar [1], Sawsan Hammad[1] and Osama A. Samarkandi[3]

[1]School of Nursing, the University of Jordan, Amman, 11942 Jordan
[2]Faculty of Nursing, Alahliya Amman University, Amman, Jordan
[3]Prince Sultan bin Abdulaziz College for Emergency Medical Services, King Saud University, Riyadh, Saudi Arabia

Aims:

To explore Jordanian ICU nurses' perceived barriers for enteral nutrition that hinders them from utilizing the recommended EN guidelines.

Methods:

A descriptive cross-sectional design was utilized using self-administered questionnaire. A total of 131 nurses participated from different hospitals representing different healthcare sectors in Jordan.

Results:

The five barriers subscales' means were almost equal ranging from 4.04 (Delivery of EN to the Patient) to 4.33 (ICU Resources) (out of 7). The most important barrier was "Not enough nursing staff to deliver adequate nutrition" (M=4.80, SD=1.81, 60%), followed by "Fear of adverse events due to aggressively feeding patients" (M= 4.59, SD=1.50, 56%). Although no significant differences in the mean barrier score were revealed, minimal significant differences were revealed that were distributed among different barrier subscales.

International investigation on temporary anchorage device use: A survey of orthodontists

Kelsea Y. Ashton[a], Shuying S. Jiang[b], Mary Anne Melo[c], Jose A. Bosio[d,*]

[a] Private Practice, Carbondale, Illinois
[b] Research Associate I, Department of Institutional Assessment and Quality Improvement, Rutgers School of Dental Medicine, Newark, New Jersey
[c] Clinical Professor, Chair of the Department of Advance General Dentistry, University of Maryland School of Dentistry, Baltimore, Maryland
[d] Endowed Clinical Associate Professor, Division Chief and Orthodontic Program Director, Division of Orthodontics, Department of Orthodontics and Pediatric Dentistry, University of Maryland School of Dentistry, Baltimore, Maryland

ARTICLE INFO

Article history:
Received 12 February 2023
Revised 21 March 2023
Accepted 11 April 2023
Available online xxx

Keywords:
International sample
Orthodontists
Survey
Temporary anchorage device (TAD)

ABSTRACT

Background: This study investigates characteristics of temporary anchorage devices (TADs) use by surveying a sample of international orthodontists. Furthermore, the survey investigates the stability, insertion technique, and failure rate of TADs and professionals' experience in residency, and it also attempts to establish guidelines for its use in everyday practice.

Methods: A 18-question survey was sent to orthodontists worldwide asking opinion-based, case-specific, and placement technique questions regarding TADs. Results were collected from 251 survey respondents. The country/regions of practice and length of time practicing orthodontics were the independent variables.

Results: Survey respondents indicated that most orthodontists rarely or sporadically use TADs. Significant differences were also found for TAD utilization purposes, sizes, and placement techniques among different countries/regions and for failure rates (1 or more of the last 6 TADs placed failed--61.6%). A significant difference was found in how many TADs orthodontists placed in residency versus private practice (56% vs. 15%) in relation to how long they have been practicing, but it did not greatly affect the frequency of use, mechanics, or placement technique.

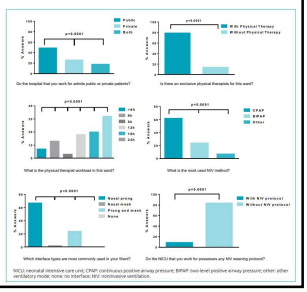
Conclusions: The frequency of TAD use is similar in many different countries and among different age groups. Although the collected responses suggested significant differences among respondents from different countries, the variability of results for TAD use worldwide prevent the establishment of clear guidelines.

Tuttavia...

Use of noninvasive mechanical ventilation weaning protocol in neonatal intensive care units in Brazil: a descriptive study

Uso de protocolo de desmame de ventilação mecânica não invasiva em unidades de terapia intensiva neonatal no Brasil: estudo descritivo

Jéssica Delamuta Vitti[a], Antonio Adolfo Mattos de Castro[b], Nelson Francisco Serrão Júnior[b]



Studi Osservazionali (non sperimentali) *Analitici*

Studi Osservazionali Analitici

Studi analitici (o investigativi)

- Obiettivo: definire e quantificare relazioni fra uno o più fattori di esposizione e uno o più esiti
- Si distinguono studi **trasversali** e studi **longitudinali**

Studi Osservazionali Trasversali

Singola osservazione

Studi Osservazionali Trasversali

Detti anche «studio di prevalenza», «cross-sectional study» («survey»)

- Indagine nelle quali un campione di soggetti viene intervistato o esaminato per avere risposte rispetto a un quesito in un certo momento
- Equivale a una istantanea in cui tutti i dati vengono ottenuti in un momento preciso (lo studio "taglia trasversalmente"): **osservazione singola**
- Mira a misurare in una popolazione la presenza di una o più condizioni (malattia, condizione clinica, fattore di rischio) in quel certo momento: **esposizione ed esito rilevati nello stesso tempo**
- Può essere prospettico (nuova raccolta dati) o retrospettivo (analisi dati esistenti)

Studi Osservazionali Trasversali

Impact of satisfaction with physician–patient communication on self-care and adherence in patients with hypertension: cross-sectional study

Natalia Świątoniowska-Lonc[1], Jacek Polański[2], Wojciech Tański[3] and Beata Jankowska-Polańska[1*]

Abstract

Background: Hypertension (HT) requires patients to continuously monitor their blood pressure, strictly adhere to therapeutic recommendations, and self-manage their illness. A few studies indicate that physician–patient communication and the patient's satisfaction with the therapeutic relationship may affect the course and outcomes of the treatment process. Research is still lacking on the association between satisfaction with physician–patient communication and adherence to treatment or self-care in chronically ill patients. The aim of the study was to evaluate the relationship between satisfaction with physician–patient communication and self-care and adherence in patients with HT undergoing chronic treatment.

Methods: The following instruments were used: the Adherence to Refills and Medication Scale (ARMS) for evaluating adherence (12–48 points), the Self-Care of Hypertension Inventory (SCHI) for self-care level (0–100 points), and the Communication Assessment Tool (CAT) for evaluating satisfaction with physician–patient communication. Socio-demographic and clinical data were obtained from patients' medical records. The research

Methods

Aim

The aim of the study was to evaluate the relationship between satisfaction with physician–patient communication and self-care and adherence in patients with HT undergoing chronic treatment.

The primary outcome of our study was the perceived quality of the physician–patient communication. The secondary outcome was the relationship between physician–patient communication on the one hand, and pharmaceutical adherence and self-care on the other.

Design

The present research has a cross-sectional and observational study design. Data were collected between January 2019 and August 2019 from patients who reported for follow-up appointments at the clinical division of internal medicine with specialization in hypertension. The study used a closed-ended standardized survey.

Statistical analysis

Patients were broken down into two groups: group 1 — poor communication ($n = 34$), group 2 — good communication ($n = 216$).

Correlations between quantitative variables were analyzed using Pearson's correlation coefficient (if distributions for both were normal) or Spearman's correlation coefficient (otherwise) [27]. Multivariate analysis of the independent impact of the selected variables on the quantitative variable was performed using linear regression. The results are shown as regression model parameter values with a 95% confidence interval (CI). Variable distribution normality was verified using the Shapiro-Wilk test. All analyses used a significance threshold of 0.05. i.e. all p values of less than 0.05 were interpreted as showing significant associations. The analyses were performed using the R software, version 3.6.0 [28].

Table 1 Socio-demographic and clinical characteristics of the study group

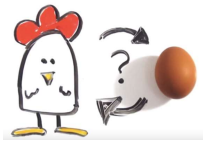
Variable		Poor communication ($n = 34$)	Good communication ($n = 216$)	p
Age	mean ± SD	65.68 ± 10.69	60.53 ± 14.73	0.049 NP
Duration of HT in years	mean ± SD	10.24 ± 10.77	12.4 ± 10.34	0.124 NP
Appointment duration [min]	mean ± SD	16.21 ± 9.52	20.08 ± 10.13	0.008 NP
Time spent discussing the patient's problems [min]	mean ± SD	7.38 ± 7.22	10.43 ± 9.39	0.037 NP
Sex	Female	18 (52.94%)	122 (56.48%)	0.841
	Male	16 (47.06%)	94 (43.52%)	chi2
Place of residence	Rural	6 (17.65%)	51 (23.61%)	0.582
	Urban	28 (82.35%)	165 (76.39%)	chi2
Relationship status	Single	9 (26.47%)	65 (30.09%)	0.82
	In a relationship	25 (73.53%)	151 (69.91%)	chi2
Education	Primary or none	3 (8.82%)	20 (9.26%)	0.762
	High school	20 (58.82%)	112 (51.85%)	F
	College/university	11 (32.35%)	84 (38.89%)	
Professional status	Professionally active	9 (26.47%)	77 (35.65%)	0.338
	Retirement pensioner	20 (58.82%)	96 (44.44%)	F
	Disability pensioner	3 (8.82%)	34 (15.74%)	
	Unemployed	2 (5.88%)	9 (4.17%)	
Financial standing	Wealthy	0 (0.00%)	12 (5.56%)	0.723
	Able to afford all that is needed and save some money	14 (41.18%)	83 (38.43%)	F

Table 3 Comparison of self-care and adherence levels between groups broken down by satisfaction with patient-provider communication

SC-HI	All patients $N = 250$		Poor communication (CAT 0–42) $N = 34$		Good communication (CAT 43–70) $N = 216$		p
	Mean	SD	Mean	SD	Mean	SD	
Self-care maintenance	56.73	18.57	53.12	16.67	57.3	18.82	0.224*
Self-care management	64.17	21.18	56.62	22.54	65.36	20.77	0.059**
Self-care confidence	62.47	24.39	51.47	26.03	64.2	23.72	0.005**
ARMS [points]	16.63	4.6	18.88	5.76	16.28	4.3	0.104**

* Normal distribution in groups, Student's t-test; ** lack of normal distribution in groups, *Mann* Whitney test, *SD* standard deviation, *SC-HI* The Self-Care of Hypertension Inventory, *ARMS* The Adherence to Refills and Medication Scale, *CAT* The Communication Assessment

Studi Osservazionali Trasversali



Qual è la causa e quale è l'effetto?

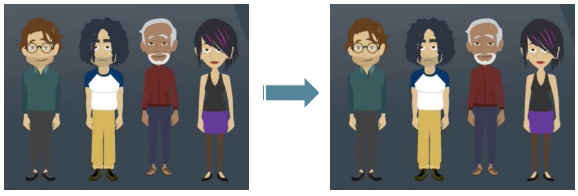
- Esposizione ed esito vengono osservati simultaneamente
- Si descrivono «associazioni» o «correlazioni» (ecc.) statistiche
- **Impossibile** stabilire un nesso di causa-effetto fra evento in studio e fattore determinante

È stato più volte dimostrato che la prevalenza di disordini mentali è maggiore nei soggetti di bassa classe sociale.
Quindi i disturbi mentali (evento) si sviluppano con maggior frequenza nei soggetti di bassa classe sociale (determinante)
oppure...
Quindi i soggetti con disturbi mentali (determinante) tendono a scendere nella scala sociale (evento) dove vengono individuati al momento dell'indagine?

Studi Osservazionali Longitudinali

- Seguono nel tempo (*follow up*) uno o più gruppi di persone per valutare l'insorgenza di una nuova condizione o l'evoluzione di una condizione nota (es. studi di incidenza): **osservazioni ripetute**
- Si realizzano con dati ottenuti nel susseguirsi del tempo, possono dunque essere sia retrospettivi, sia prospettici
- Studio longitudinale retrospettivo: è uno studio longitudinale effettuato con dati del passato.
- Studio longitudinale prospettico: è uno studio longitudinale all'inizio del quale si raccolgono i dati riferiti al momento corrente, per poi seguirne l'evoluzione nel tempo
- **Studi di coorte** (prospettici o retrospettivi)
- **Studi caso-controllo** (sempre retrospettivi)

Studi Osservazionali Longitudinali

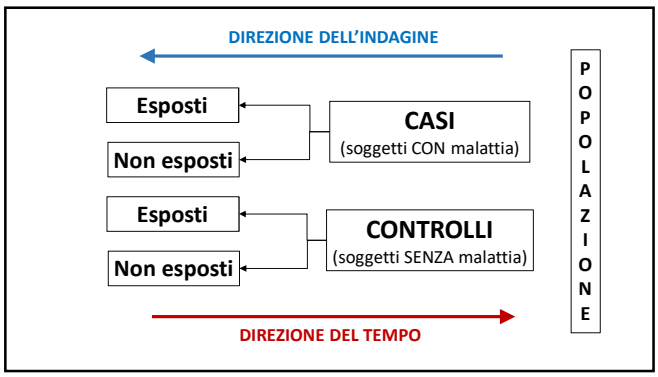


T0 **T1**

Studi Osservazionali Longitudinali

Studi caso-controllo

- Sempre retrospettivi
- I soggetti con una data malattia o condizione ("casi) vengono confrontati con altri soggetti ("controlli, il più possibile simili tranne che per l'assenza di malattia) esplorando nel passato le abitudini e i comportamenti



Case-Control Study Examining the Association between Selective Serotonin Reuptake Inhibitors Use and Hepatocellular Carcinoma

Shih-Wei Lai[1,2], Kuan-Fu Liao[3,4], Cheng-Li Lin[1,5] and Hsien-Feng Lin[2,6]**

[1] Department of Medicine, China Medical University, Taichung, Taiwan, [2] Department of Family Medicine, China Medical University Hospital, Taichung, Taiwan, [3] Department of Medicine, Tzu Chi University, Hualien, Taiwan, [4] Department of Internal Medicine, Taichung Tzu Chi General Hospital, Taichung, Taiwan, [5] Management Office for Health Data, China Medical University Hospital, Taichung, Taiwan, [6] Department of Chinese Medicine, China Medical University, Taichung, Taiwan

Objectives: The purpose of the study was to assess the relationship between selective serotonin reuptake inhibitors use and hepatocellular carcinoma in Taiwan.
Methods: Using the database of the Taiwan National Health Insurance Program, we conducted a case-control study to identify 4901 subjects aged 20 years and more with newly diagnosed hepatocellular carcinoma in 2000–2013 as the cases. We randomly selected 19604 subjects aged 20 years and more without hepatocellular carcinoma as the controls. Both cases and controls were matched with sex and age. Ever use of selective serotonin reuptake inhibitors was defined as a subject who had at least a prescription for selective serotonin reuptake inhibitors before index date. Never use was defined as a subject who never had a prescription for selective serotonin reuptake inhibitors before index date. The odds ratio (OR) and 95% confidence interval (CI) for hepatocellular carcinoma associated with selective serotonin reuptake inhibitors use was estimated by the multivariable logistic regression model.

Selection of Subjects

We identified subjects aged 20 years and more with newly diagnosed hepatocellular carcinoma (International Classification of Diseases, Ninth Revision, Clinical Modification, ICD-9 codes 155, 155.0, and 155.2) from 2000 to 2013 as the cases. The date of subjects being diagnosed with hepatocellular carcinoma was defined as the index date. Subjects without the diagnosis of hepatocellular carcinoma were randomly selected as the controls.

Casi

Controlli

Both cases and controls were matched with sex, age (5-year interval), and the year of index date. Subjects who had any other cancer (ICD-9 codes 140-208) before the index date were excluded from the study. The definition of subject selection was adapted from previous studies (Lai et al., 2013a,b).

TABLE 1 | Characteristics between cases with hepatocellular carcinoma and controls.

	Cases *N* = 4901		Controls *N* = 19604		
Variable	***n***	**(%)**	***n***	**(%)**	***P*-value***
Sex					0.99
Female	1351	(27.6)	5404	(27.6)	
Male	3550	(72.4)	14200	(72.4)	
Age group (years)					0.99
20–39	828	(16.9)	3312	(16.9)	
40–64	1820	(37.1)	7280	(37.1)	
65–84	2253	(46.0)	9012	(46.0)	
Age (years), mean ± standard deviation†	62.5 ± 12.3		62.3 ± 12.4		0.44
Ever use of selective serotonin reuptake inhibitors	371	(7.57)	1187	(6.05)	0.001
Other medications					
Ever use of metformin	1173	(23.9)	2827	(14.4)	<0.001
Ever use of statin	581	(11.9)	3646	(18.6)	<0.001
Comorbidities before index date					
Alcohol-related disease	799	(16.3)	998	(5.09)	<0.001
Cardiovascular disease	1653	(33.7)	6647	(33.9)	0.81
Chronic kidney disease	511	(10.4)	1295	(6.61)	<0.001
Chronic liver disease	4110	(83.9)	3029	(15.5)	<0.001
Chronic obstructive pulmonary disease	911	(18.6)	3233	(16.5)	<0.001
Diabetes mellitus	990	(20.2)	1898	(9.68)	<0.001
Hyperlipidemia	1137	(23.2)	5905	(30.1)	<0.001
Hypertension	2454	(50.1)	9316	(47.5)	<0.001

TABLE 2 | Odds ratio and 95% confidence interval of hepatocellular carcinoma associated with selective serotonin reuptake inhibitors use by logistical regression model.

	Crude		Adjusted†	
Variable	**OR**	**(95% CI)**	**OR**	**(95% CI)**
Ever use of selective serotonin reuptake inhibitors (never use as a reference)	1.27	(1.13, 1.43)	0.92	(0.79, 1.08)

†*Initially, all variables were included in the univariable logistic regression model. Only those significantly associated with hepatocellular carcinoma in the univariable logistic regression model could be further included in the multivariable logistic regression model. Therefore, only metformin use, statin use, alcohol-related disease, chronic kidney disease, chronic liver disease, chronic obstructive pulmonary disease, diabetes mellitus, hyperlipidemia, and hypertension could be further included for adjustment.*

TABLE 3 | Association between selective serotonin reuptake inhibitors use and hepatocellular carcinoma among high risk subjects.

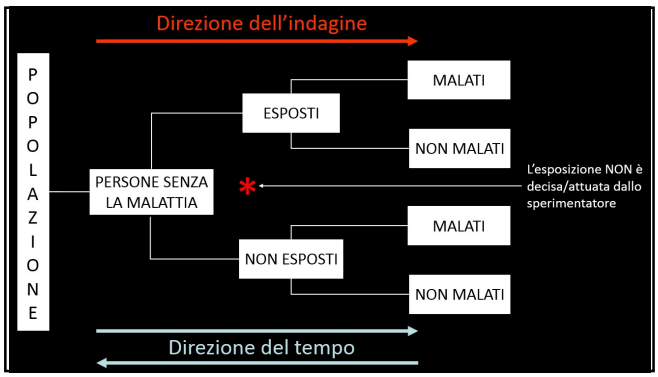
Selective serotonin reuptake inhibitors	**Any comorbidity***	**Case number/control number**	**Adjusted OR†**	**(95% CI)**
Never use	Yes	3922/4479	1.00	(Reference)
Ever use	Yes	339/490	0.89	(0.75, 1.06)

**Comorbidities including alcohol-related disease, chronic liver disease, and diabetes mellitus. †Adjustment for metformin use, statin use, chronic kidney disease, chronic obstructive pulmonary disease, hyperlipidemia, and hypertension.*

Studi Osservazionali Longitudinali

Studi di coorte

- Verificano nel tempo il verificarsi di un certo esito in due o più sottogruppi (coorti) di persone selezionate in base alla loro differente esposizione a un particolare agente
- L'esposizione NON è decisa/attuata dallo sperimentatore, ed è indipendente dalla partecipazione allo studio
- Può essere necessario considerare tempi molto lunghi



Active smoking and risk of breast cancer in a Danish nurse cohort study

Zorana Jovanovic Andersen[1*], Jeanette Therming Jørgensen[1], Randi Grøn[1], Elvira Vaclavik Brauner[2,3] and Elsebeth Lynge[1]

Abstract

Background: No scientific consensus has been reached on whether active tobacco smoking causes breast cancer. We examine the association between active smoking and breast cancer risk in Denmark, which has some of the highest smoking and breast cancer rates in women worldwide.

Methods: We used the data from a nationwide Danish Nurse Cohort on 21,867 female nurses (age > 44 years) who at recruitment in 1993 or 1999 reported information on smoking status, onset, duration, and intensity, as well as breast cancer risk factors. We obtained data on incidence of breast cancer from Danish Cancer Registry until 2013, and used Cox regression models to analyze the association between smoking and breast cancer.

Results: Of 21,831 women (mean age 53.2 years) 1162 developed breast cancer during 15.7 years of follow-up. 33.7% of nurses were current and 30.0% former smokers at cohort baseline. Compared to never smokers, we found increased risk of breast cancer of 18% in ever (hazard ratio and 95% confidence interval: 1.18; 1.04–1.34) and 27% in current (1.27; 1.11–1.46) smokers. We detected a dose-response relationship with smoking intensity with the highest breast cancer risk in women smoking >15 g/day (1.31; 1.11–1.56) or >20 pack-years (1.32; 1.12–1.55). Parous women who smoked heavily (>10 pack-years) before first childbirth had the highest risk of breast cancer (1.58; 1.20–2.10). Association between smoking and breast cancer was not modified by menopausal status, obesity, alcohol or hormone therapy use, and seemed to be limited to the estrogen receptor positive breast cancer subtype.

Conclusions: Active smoking increases risk of breast cancer, with smoking before first birth being the most relevant exposure window.

The Danish nurse cohort

The Danish Nurse Cohort [18] was inspired by the American Nurses' Health Study to initially investigate the health effects of hormone therapy (HT) in a European population. The cohort was initiated in 1993 by sending a questionnaire to 23,170 female Danish nurses (> 44 years), members of the Danish Nursing Organization, which included 95% of all nurses in Denmark. In total, 19,898 (86%) nurses replied, and the cohort was reinvestigated in 1999, including an additional 10,534 nurses (who turned 44 years in the period 1993–99), of whom 8833 (84%) replied. Nurses filled out the questionnaire at recruitment on working conditions, weight and height, lifestyle (diet, active smoking, alcohol consumption, and leisure time physical activity), parity, age at first birth, age of menarche and menopause, and use of oral contraceptives (OC) and HT. We utilized baseline information from 1993 (19,898) or 1999 (8833) for 28,731 female nurses. Using a unique identification number we linked the cohort participants to Civil Registration System [19] to obtain vital status information at 31st December 2012 (active, date of death or emigration).

Popolazione arruolata

Active tobacco smoking

Data on active tobacco smoking were obtained from the baseline questionnaire in 1993 or 1999, and included questions on smoking status (never/former/current), smoking duration (years), age at smoking onset (years), average number of cigarettes, cheerots, and cigars smoked per day, and on smoking a pipe (yes/no) in ever smokers. Based on this information we calculated smoking intensity in g/day by equating a cigarette to 1 g, a cheroot to 3 g, and a cigar to 4.5 g of tobacco, and pack-years of smoking by multiplying the number of packs per day (1 pack = 20 g) and the number of years smoked. We defined onset of smoking before and after 1st birth in parous women and age of 21 years (mean age of smoking initiation in the cohort) in nulliparous women. Pack-years of smoking before 1st childbirth, between 1st childbirth and menopause, and after menopause was calculated from information on age of smoking onset, age at 1st birth, and age at menopause in parous postmenopausal women. No information was collected on passive smoking in the Danish Nurse Cohort.

Esposizione

Breast cancer definition

We linked the records of 28,731 nurses using unique identification number to the Danish Cancer Register [20] to extract all cancer diagnoses until 2013. First, we extracted data for nurses with diagnoses for any (other than non-melanoma skin cancer) cancer before baseline (1st April 1993 or 1st April 1999), these nurses were excluded from the analyses. Secondly, among nurses without prior cancer, we extracted primary invasive breast cancer diagnoses (ICD-10 codes C50), as the main outcome, and any other cancer (other than non-melanoma skin cancer) between cohort baseline (1st April 1993 or 1st April 1999) and 31st December 2012. Furthermore, we extracted data on breast cancer subtype by estrogen receptor (ER) and progesterone receptor (PR) status from the clinical database of the Danish Breast Cancer Cooperative Group. [21]

Esito (outcome)

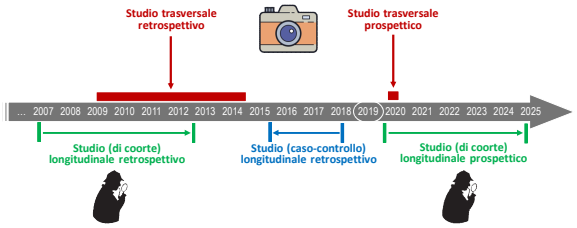
Table 1 Description of the Danish Nurse Cohort (n = 21,831) at the time of recruitment in 1993 or 1999 and by breast cancer status during follow-up until 2013

	Total N = 21,831	Breast Cancer N = 1162	No Breast Cancer N = 20,669
Age			
Mean (SD) age at baseline (years)	53.2 (8.0)	53.7 (7.6)	53.2 (8.1)
Birth Cohort			
Born 1900–1934, n (%)	5179 (23.7)	295 (25.4)	4884 (23.6)
Born 1935–1944, n (%)	6707 (30.7)	428 (36.8)	6279 (30.4)
Born 1945–1949, n (%)	4564 (20.9)	244 (21.0)	4320 (20.9)
Born 1950–1955, n (%)	5381 (24.6)	195 (16.8)	5186 (25.1)
Reproductive Factors			
Mean (SD) age at menarche	13.5 (1.5)	13.5 (1.5)	13.5 (1.5)
Nulliparous, n (%)	3170 (14.5)	189 (16.3)	2981 (14.4)
Mean (SD) number of children in parous women	2.3 (0.9)	2.3 (0.9)	2.3 (0.9)
Mean (SD) age at first birth in parous women	25.9 (4.0)	25.9 (4.0)	26.3 (4.1)
Postmenopausal, n (%)	12,376 (56.7)	696 (59.9)	11,680 (56.5)
Body Mass Index (BMI)			
Mean (SD) BMI (kg/m^2)	23.7 (3.5)	23.8 (3.5)	23.7 (3.5)
BMI < 18.5 kg/m^2, n (%)	529 (2.4)	22 (1.9)	507 (2.5)

Table 3 Association between active smoking and breast cancer in 21,831 women in the Danish Nurse Cohort

	N	Person-years	No. of cases	Age adjusted HR (95% CI)	Fully[a] adjusted HR (95% CI)
Never smoked (ref.)	7923	126,950	379	1.00	1.00
Former smoker	6557	102,190	338	1.11 (0.96–1.29)	1.08 (0.94–1.26)
Current smoker	7351	113,400	445	1.32 (1.15–1.51)	1.27 (1.11–1.46)
Ever smokers	13,908	215,589	783	1.22 (1.08–1.38)	1.18 (1.04–1.34)
Smoking duration among ever smokers					
≤ 10 years	2925	47,335	156	1.10 (0.92–1.33)	1.10 (0.91–1.33)
11–20 years	3175	50,151	175	1.17 (0.98–1.40)	1.15 (0.96–1.38)
21–30 years	4456	68,818	259	1.26 (1.08–1.48)	1.24 (1.06–1.46)
> 30 years	3295	49,285	193	1.32 (1.11–1.57)	1.21 (1.01–1.46)
p-value for trend					*0.004*
Every increase of 10 years				1.08 (1.04–1.12)	1.06 (1.02–1-11)
Smoking (Tobacco) Intensity among ever smokers					
> 6 g/day	3098	49,245	161	1.10 (0.91–1.32)	1.07 (0.89–1.29)
6–10 g/day	4317	67,410	235	1.17 (0.99–1.38)	1.14 (0.97–1.34)
11–15 g/day	3050	46,962	175	1.25 (1.05–1.50)	1.22 (1.02–1.46)
> 15 g/day	3443	51,973	212	1.37 (1.16–1.62)	1.31 (1.11–1.56)
p-value for trend					*0.001*
Every increase of 10 g/day				1.05 (0.97–1.14)	1.04 (0.95–1.13)

Studi Osservazionali



equator network

Enhancing the QUAlity and Transparency Of health Research

Reporting guidelines for main study types

Randomised trials	CONSORT	Extensions
Observational studies	STROBE	Extensions
Systematic reviews	PRISMA	Extensions
Study protocols	SPIRIT	PRISMA-P
Diagnostic/prognostic studies	STARD	TRIPOD
Case reports	CARE	Extensions
Clinical practice guidelines	AGREE	RIGHT
Qualitative research	SRQR	COREQ
Animal pre-clinical studies	ARRIVE	
Quality improvement studies	SQUIRE	
Economic evaluations	CHEERS	

- Arabic
- Chinese
- Dutch
- French
- German
- Greek
- Italian
- Japanese
- Korean
- Persian
- Polish
- Portuguese
- Russian
- Spanish
- Turkish
- Vietnamese

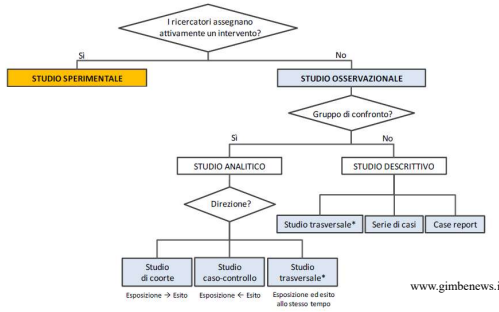
STROBE Statement—checklist of items that should be included in reports of observational studies

	Item No	Recommendation
Title and abstract	1	(a) Indicate the study's design with a commonly used term in the title or the abstract (b) Provide in the abstract an informative and balanced summary of what was done and what was found
Introduction		
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported
Objectives	3	State specific objectives, including any prespecified hypotheses
Methods		
Study design	4	Present key elements of study design early in the paper
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection
Participants	6	(a) *Cohort study*—Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up *Case-control study*—Give the eligibility criteria, and the sources and methods of case ascertainment and control selection. Give the rationale for the choice of cases and controls *Cross-sectional study*—Give the eligibility criteria, and the sources and methods of selection of participants (b) *Cohort study*—For matched studies, give matching criteria and number of exposed and unexposed *Case-control study*—For matched studies, give matching criteria and the number of controls per case
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable
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
Bias	9	Describe any efforts to address potential sources of bias
Study size	10	Explain how the study size was arrived at
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why
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 *Case-control study*—If applicable, explain how matching of cases and controls was addressed *Cross-sectional study*—If applicable, describe analytical methods taking account of sampling strategy (e) Describe any sensitivity analyses
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
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)
Outcome data	15*	*Cohort study*—Report numbers of outcome events or summary measures over time *Case-control study*—Report numbers in each exposure category, or summary measures of exposure *Cross-sectional study*—Report numbers of outcome events or summary measures
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
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses
Discussion		
Key results	18	Summarise key results with reference to study objectives
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
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence
Generalisability	21	Discuss the generalisability (external validity) of the study results
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

*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.

Ricerca Quantitativa



www.gimbenews.it

*descrittivo o analitico a seconda del metodo di analisi dei dati

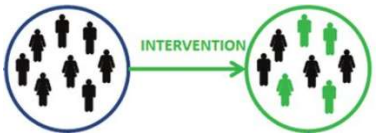
Studi Sperimentali (clinical trials)

Studi Sperimentali (clinical trials)

- Sono sempre prospettici
- Il ricercatore **interviene attivamente e direttamente** nella sperimentazione applicando attivamente un fattore modificante (**intervento**)
- Viene valutata l'efficacia dell'intervento rispetto a uno o più **esiti**
- Le modalità di selezione dei soggetti da studiare vengono stabilite dallo sperimentatore in base all'ambito di interesse della ricerca (es. affetti da una certa malattia o a rischio per un certo esito)

Studi Sperimentali (clinical trials)

- Idealmente, in uno studio sperimentale «ben disegnato», l'**unico** elemento a indurre una modifica dell'esito dovrebbe essere l'intervento.
- Questo presuppone di analizzare **soggetti identici** fra di loro
- Ambizione poco realistico a causa
  - della "variabilità biologica"
  - dei fattori di confondimento



Studi Sperimentali (clinical trials)

1) GRAVITA' DELLO STATO MORBOSO: influenza la risposta del paziente al trattamento. L'introduzione di pazienti di ogni gravità rischia di rendere meno sensibile l'esperimento

2) ETA' DEL PAZIENTE: pazienti più giovani possono apparentemente rispondere meglio solo perché le difese organiche sono più efficienti rispetto a quelle degli anziani

3) SESSO DEL PAZIENTE: fattori ormonali possono in[illegible] sull'esito di un trattamento. Il dosaggio del farmaco non è d[illegible] in base al sesso, quindi il genere femminile medicamente ric[illegible]ggia più alto superiore

4) TERAPIE CONCOMITANTI: pos[illegible] sul risultato perché la loro efficacia può oscurare quello della nuo[illegible]pia o per il verificarsi di interazioni

5) OSSERVATORE: N[illegible]rmità dei criteri di diagnosi, di valutazione, di e[illegible]t (descritti opportunamente nel protocollo sperimentale), rin[illegible]e una quota di variabilità nella risposta attribuibile alla diversità tra oss[illegible]tori. Il fenomeno è particolarmente evidente nello studio di patologie di natura psichiatrica.

6) CONDIZIONI AMBIENTALI: Una buona assistenza infermieristica, un ambiente ospedaliero confortevole possono contribuire ad una favorevole evoluzione del quadro morboso

7) ABITUDINI ALIMENTARI E DI VITA: Marcate differenze nel tipo di dieta, nel consumo di tabacco ed alcool influenzano la farmacocinetica (con conseguente effetto farmacodinamico) e l'andamento della patologia.

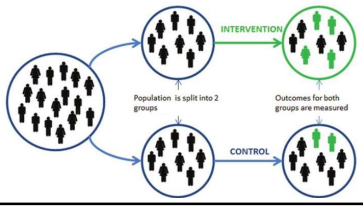
ecc, ecc...

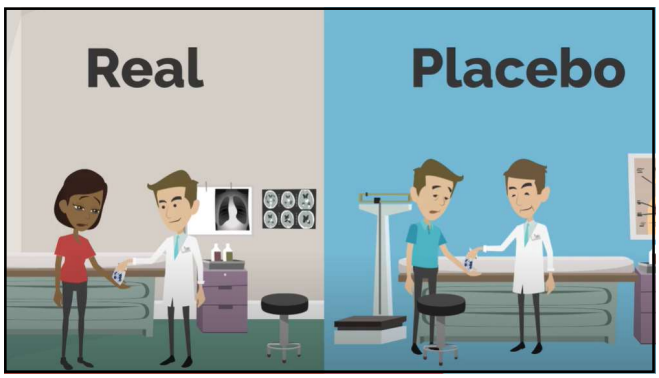
~~Assenza~~
di fattori confondenti

Selezione
di partecipanti <u>omogenei</u>
per ALCUNI
fattori confondenti

Studi Sperimentali (clinical trials)

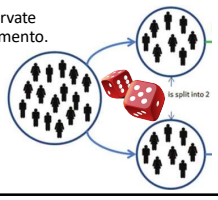
- Possono essere **controllati (controlled)**: i soggetti coinvolti nello studio sono suddivisi in due gruppi (o bracci)
  - braccio sperimentale, che riceve il trattamento
  - braccio di controllo che riceve un trattamento diverso o nessun trattamento.
- I gruppi devono risultare il più possibile **omogenei**, e quindi **comparabili**





Studi Sperimentali

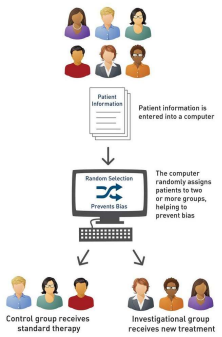
- Possono essere **randomizzati**:
  partecipanti assegnati in maniera casuale ai gruppi che ricevono il trattamento o al confronto (es. placebo o altro trattamento)
- La randomizzazione aumenta la probabilità che altre variabili, non considerate nel disegno dello studio, si distribuiscano in maniera uniforme nel gruppo sperimentale e in quello di controllo.
- In questo modo, le differenze eventualmente osservate tra i due gruppi possono essere attribuite al trattamento.
- La randomizzazione non garantisce che i gruppi così generati siano perfettamente identici: l'analisi statistica considera questa possibilità e la quantifica.



Bias di assegnazione (allocation bias)

Randomizzazione

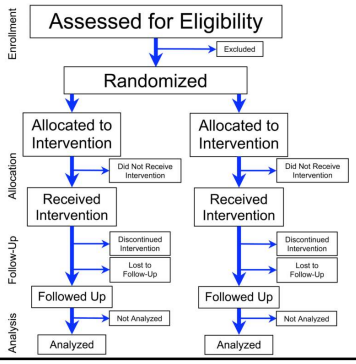
- Attribuzione casuale di ogni paziente al gruppo sottoposto a un trattamento oppure al gruppo di controllo
- Assicura che tutti i fattori prognostici - sia noti che sconosciuti - si distribuiscano omogeneamente nel due gruppi
- Se è affettutata correttamente (es. generatori numeri random, moneta, dado, sorteggio) ogni soggetto ha la stessa probabilità di essere assegnato al gruppo sperimentale o al gruppo di controllo
- Se la randomizzazione non è eseguita in maniera corretta (giorno di ammissione in ospedale, giudizio del medico, preferenze del paziente, alternanza) è possibile introdurre un bias di selezione anche negli studi randomizzati



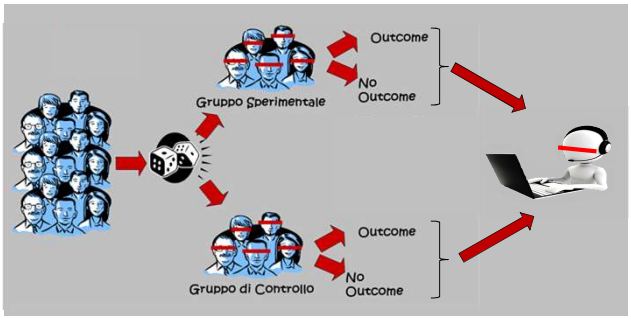
Bias di esecuzione (Performance bias)

Eligible participants will be randomised to either the nilvadipine or placebo treatment group. The nilvadipine capsules and placebo capsules will be packaged and labelled identically. Randomisation will be at the level of the individual patient, using block randomisation with randomly varying block sizes and stratified by country site. Once the patient has been randomised, the online system will automatically recognise which treatment packs are located in each study pharmacy at the recruiting study site and will randomly select a pack in the appropriate trial arm to be dispensed to the patient. All study staff at all sites will be blinded to treatment allocation and will remain blind until the end of the trial.

The primary outcome measure is the change from baseline to week 78 in cognitive function, as assessed by the ADAS-Cog 12.



Studi randomizzati, controllati e mascherati



Studi Sperimentali

- Possono essere **aperti** o **mascherati** (**blinded**)
- Il mascheramento si verifica quando il trattamento programmato è sconosciuto a uno o più dei soggetti coinvolti nello studio
  - in "singolo cieco" (il paziente non sa se ha ricevuto il trattamento sperimentale o quello di controllo, gli sperimentatori e gli analisti sì)
  - in "doppio cieco" (né paziente né sperimentatore sanno se è stato somministrato il trattamento sperimentale o il controllo, gli analisti sì)
  - in "triplo cieco" (né i pazienti né gli sperimentatori né gli analisti sanno chi ha ricevuto il trattamento e chi il controllo).

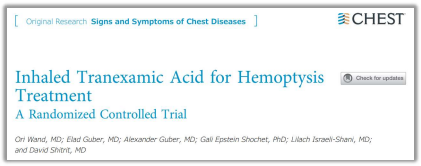
Randomized Controlled Trial

Studio
- Prospettico & specifico

Controllato
- Confronto con gruppo di controllo (placebo o attivo)
- Controllo delle procedure (solo il trattamento in esame deve variare)

Randomizzato
- ↓ bias di assegnazione
- ↓ bias di esecuzione
- ↓ effetto Hawthorne

Studi Sperimentali


[Original Research Signs and Symptoms of Chest Diseases] CHEST

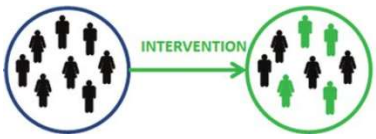
Inhaled Tranexamic Acid for Hemoptysis Treatment
A Randomized Controlled Trial

Ori Wand, MD; Elad Guber, MD; Alexander Guber, MD; Gali Epstein Shochet, PhD; Lilach Israeli-Shani, MD; and David Shitrit, MD

RESULTS: Resolution of hemoptysis within 5 days of admission was observed in more TA-treated patients than in those receiving placebo (96% vs 50%; P < .0005).

Studi Quasi-sperimentali (non controllati)

- Unico gruppo di persone esposte al trattamento/intervento sperimentale (es. confronto pre-post in uno stesso gruppo)
- Utilizzati quando non è possibile avere un gruppo di controllo (es. problemi etici: prime fasi della sperimentazione di un farmaco oncologico (fase II) su pz che non hanno risposto alla terapia standard e per i quali non esiste altra opzione terapeutica)



equator network

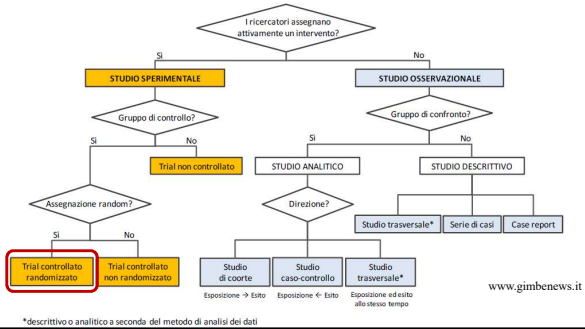
Enhancing the QUAlity and Transparency Of health Research

Reporting guidelines for main study types

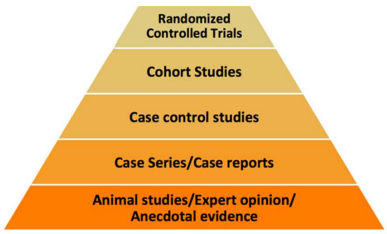
Randomised trials	CONSORT	Extensions
Observational studies	STROBE	Extensions
Systematic reviews	PRISMA	Extensions
Study protocols	SPIRIT	PRISMA-P
Diagnostic/prognostic studies	STARD	TRIPOD
Case reports	CARE	Extensions
Clinical practice guidelines	AGREE	RIGHT
Qualitative research	SRQR	COREQ
Animal pre-clinical studies	ARRIVE	
Quality improvement studies	SQUIRE	
Economic evaluations	CHEERS	

- Arabic
- Chinese
- Dutch
- French
- German
- Greek
- Italian
- Japanese
- Korean
- Persian
- Polish
- Portuguese
- Russian
- Spanish
- Turkish
- Vietnamese

Ricerca Quantitativa



The hierarchy of evidence



Valutazione critica (critical appraisal) di uno studio

Validità interna (Confidence)

- Misura quanto i risultati di uno studio siano corretti per il campione di individui che sono stati studiati.
- È detta «interna» perché si applica al campione arruolato, e non necessariamente alla popolazione «generale».
- È strettamente legata al rigore metodologico osservato nelle fasi di progettazione e conduzione dello studio e di analisi dei dati (riduzione del rischio di bias)

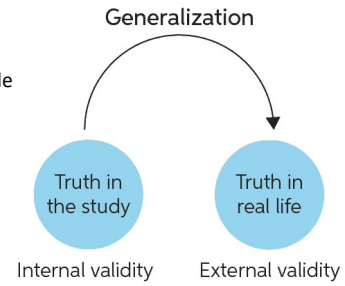
Valutazione critica (critical appraisal) di uno studio

Validità esterna (Directness)

- Rappresenta il grado di «generalizzabilità» delle conclusioni ad altre popolazioni simili di pazienti
- Misura il grado di verità dell'assunto secondo cui i pazienti studiati sono «uguali» ad altri pazienti affetti dalla stessa condizione.
- Stabilisce la «applicabilità» dei risultati della ricerca al singolo paziente.
- È strettamente dipendente dalla validità interna dello studio

Valutazione critica (critical appraisal) di uno studio

La validità interna
è il prerequisito essenziale
per la validità esterna.



Valutazione critica (critical appraisal) di uno studio

Rilevanza clinica (Relevance)

- Lo studio dev'essere scientificamente giustificato (etico)
- Fornisce una stima dell'entità e della precisione del beneficio ottenuto.
- È evidenziata da variabili metodologiche quali
  - numero adeguato di pazienti arruolati
  - ampiezza degli intervalli di confidenza (Imprecision)
  - end-point misurati (surrogati vs clinicamente rilevanti)
  - ...

Valutazione critica (critical appraisal) di uno studio

Coerenza (Consistency)

- Riproducibilità della ricerca: i risultati di uno studio devono essere confermati da altri studi
- Non può essere pertanto valutata per un singolo studio, ma deriva da revisioni sistematiche della letteratura.