Αξιολόγηση συστηματικών σφαλμάτων

Θεόδωρος Σεργεντάνης, M.D. Ph.D., F.A.C.E.

Επίκουρος Καθηγητής Επιδημιολογίας – Μεθοδολογίας της Έρευνας

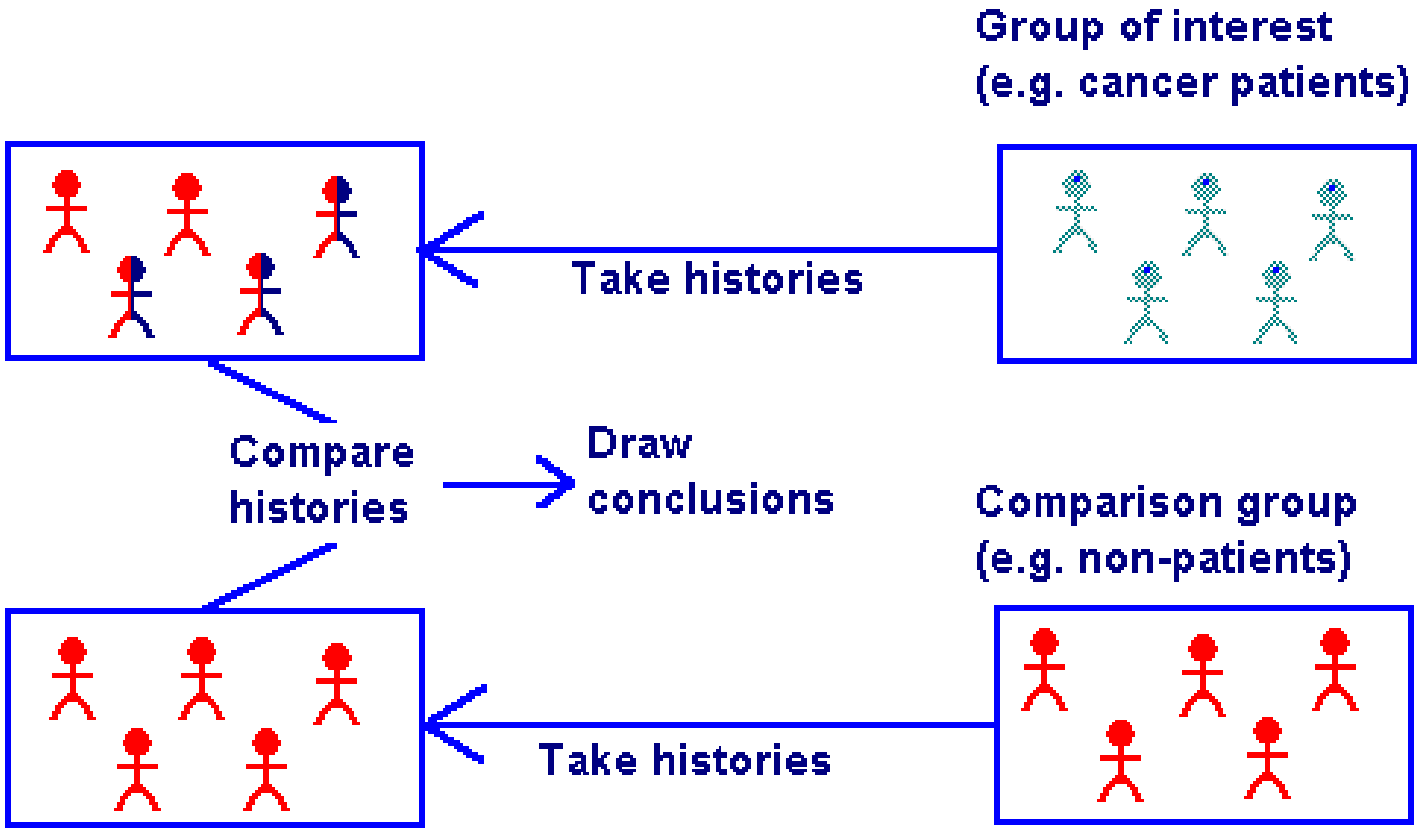
Τμήμα Πολιτικών Δημόσιας Υγείας, Σχολή Δημόσιας Υγείας, ΠΑΔΑ

Επιδιωκόμενα μαθησιακά αποτελέσματα (ILOs)

- Να *αναλύετε* την έννοια του συστηματικού σφάλματος και να την *αντιπαραβάλλετε* με την έννοια του τυχαίου σφάλματος
- Να *περιγράφετε* είδη συστηματικών σφαλμάτων
- Να *κρίνετε* την ποιότητα μιας μελέτης ασθενών-μαρτύρων, μιας προοπτικής μελέτης και μιας συγχρονικής μελέτης, βάσει της κλίμακας Newcastle-Ottawa

*στις συγχρονικές μελέτες, θα δείτε να εφαρμόζονται μέθοδοι επαγωγικής στατιστικής, ωστόσο θα τις ερμηνεύετε με περίσκεψη, δεδομένου του σχεδιασμού τους

Αναλυτική Επιδημιολογία: έρευνες ασθενών-μαρτύρων (case-control studies)



«Αναδρομική» θεώρηση

Αυθεντικότητα (accuracy)
Η τιμή που μετράται εκφράζει το πραγματικό αντικείμενο της με μικρό σφάλμα
(«η απόσταση από την πραγματικότητα»)

Ακρίβεια (precision)
Η έλλειψη τυχαίου σφάλματος

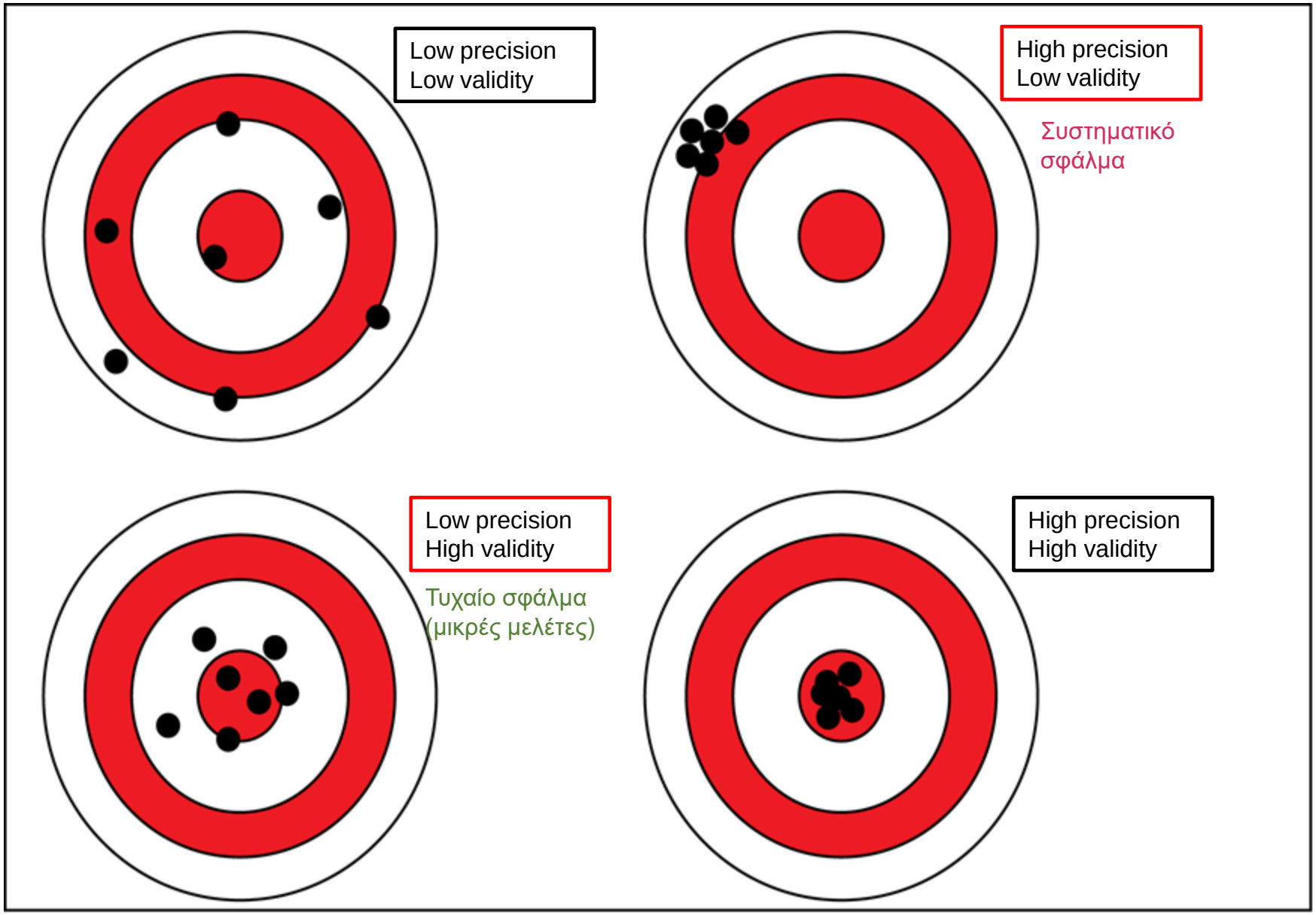
- Σφάλμα τύπου I
- Σφάλμα τύπου II

Εγκυρότητα (validity)
Η έλλειψη συστηματικού σφάλματος

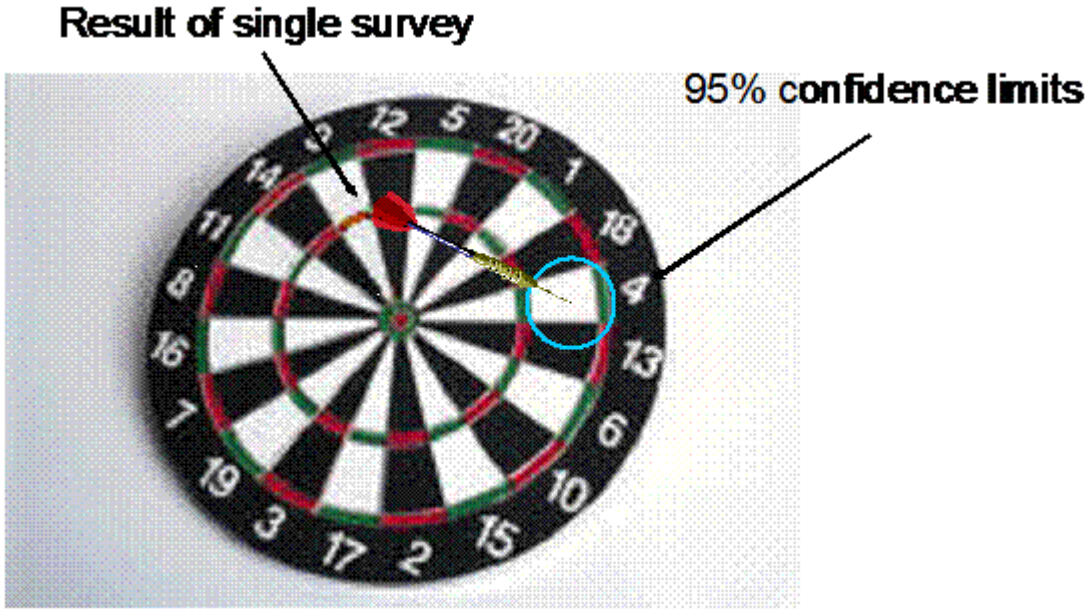
Τυχαίο σφάλμα (random error) vs. συστηματικό σφάλμα (bias)

- Τυχαίο σφάλμα: σφάλμα το οποίο δεν έχει κατεύθυνση, οφείλεται στην τύχη, στη δειγματοληψία

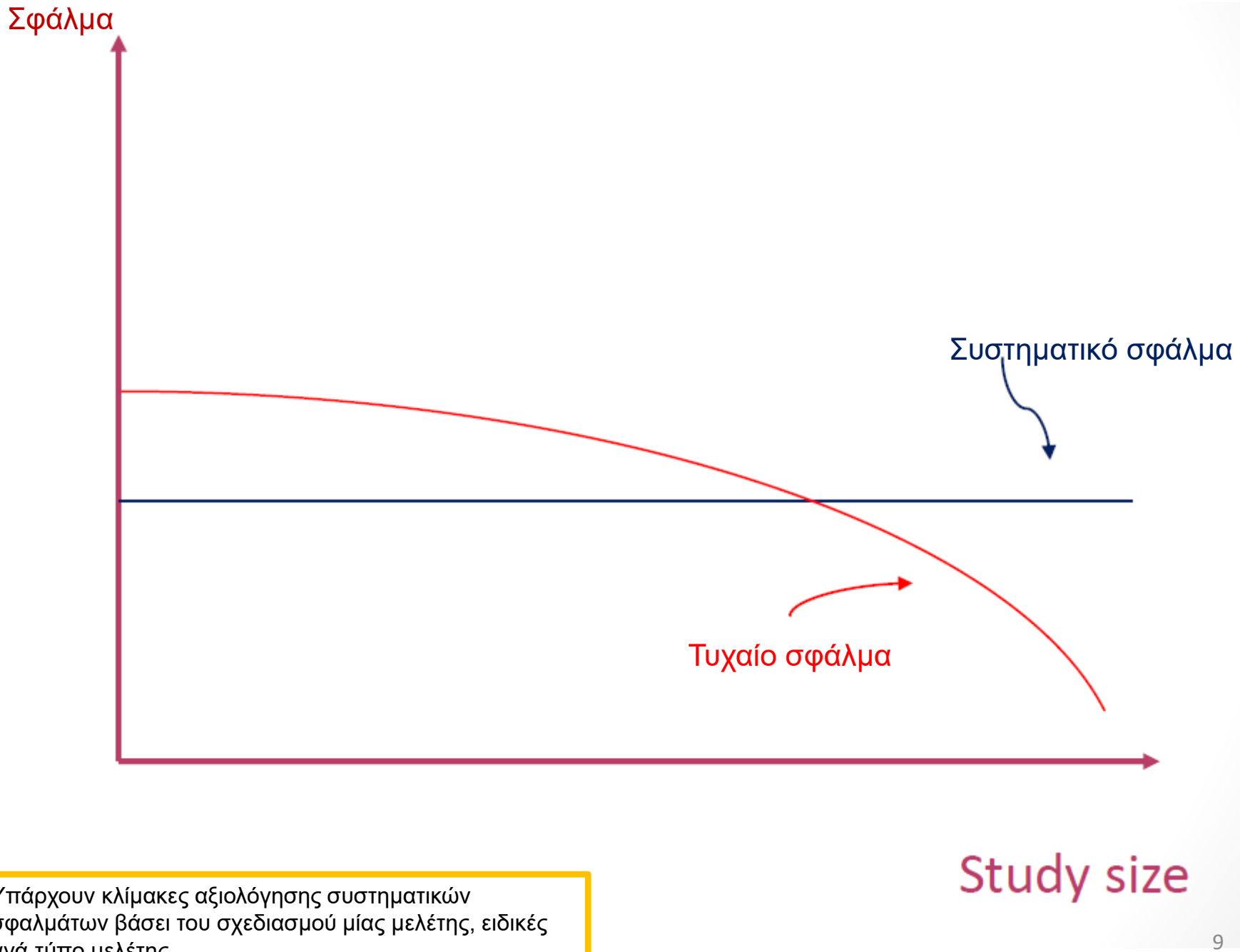
- Συστηματικό σφάλμα: έχει **κατεύθυνση** (υπερεκτίμηση ή υποεκτίμηση της συσχέτισης/διαφοράς), σχετίζεται με το **σχεδιασμό** της μελέτης



Στόχος: η αληθής τιμή (συσχέτιση/διαφορά) στον πληθυσμό



Μικρό τυχαίο σφάλμα δεν σημαίνει ορθή εκτίμηση της τιμής στον πληθυσμό (μπορεί να υπεισέρχεται συστηματικό σφάλμα)



Υπάρχουν κλίμακες αξιολόγησης συστηματικών σφαλμάτων βάσει του σχεδιασμού μίας μελέτης, ειδικές ανά τύπο μελέτης

Εφαρμογές της κλίμακας

Η NOS χρησιμοποιείται για την βαθμολόγηση της ποιότητας / αξιολόγηση συστηματικών σφαλμάτων:

- Προοπτικών μελετών
- Μελετών ασθενών – μαρτύρων
- Συγχρονικών μελετών (cross-sectional)

Αξιολόγηση της ποιότητας μελέτης ασθενών-μαρτύρων: η κλίμακα Newcastle-Ottawa

NEWCASTLE - OTTAWA QUALITY ASSESSMENT SCALE
CASE CONTROL STUDIES

Note: A study can be awarded a maximum of one star for each numbered item within the Selection and Exposure categories. A maximum of two stars can be given for Comparability.

Selection

1) Is the case definition adequate?
   a) yes, with independent validation ✵
   b) yes, eg record linkage or based on self reports
   c) no description

2) Representativeness of the cases
   a) consecutive or obviously representative series of cases ✵
   b) potential for selection biases or not stated

3) Selection of Controls
   a) community controls ✵
   b) hospital controls
   c) no description

4) Definition of Controls
   a) no history of disease (endpoint) ✵
   b) no description of source

Αξιολόγηση της ποιότητας μελέτης ασθενών-μαρτύρων: η κλίμακα Newcastle-Ottawa

Comparability

1) Comparability of cases and controls on the basis of the design or analysis
   a) study controls for _____ (Select the most important factor.) ✱
   b) study controls for any additional factor ✱ (This criteria could be modified to indicate specific control for a second important factor.)

Exposure

1) Ascertainment of exposure
   a) secure record (eg surgical records) ✱
   b) structured interview where blind to case/control status ✱
   c) interview not blinded to case/control status
   d) written self report or medical record only
   e) no description

2) Same method of ascertainment for cases and controls
   a) yes ✱
   b) no

3) Non-Response rate
   a) same rate for both groups ✱
   b) non respondents described
   c) rate different and no designation

- Σκεφτείτε κριτικά και διασυνδέστε με τους τύπους συστηματικών σφαλμάτων

- Υπενθύμιση: Πώς ελέγχουμε τους συγχυτικούς παράγοντες στην Επιδημιολογία;

Αντιμετώπιση των συγχυτικών παραγόντων στην Επιδημιολογία

Α. Κατά το σχεδιασμό μιας μελέτης

- Τυχαιοποίηση (randomization):

✓ κάθε άτομο έχει την ίδια πιθανότητα να αποδοθεί π.χ. σε κάθε χορηγούμενη αγωγή.
Περιορισμός: εφαρμόζεται στις κλινικές μελέτες.

✓ Χρήσιμη για την εξάλειψη γνωστών και άγνωστων συγχυτικών παραγόντων

- Περιορισμός (restriction):

π.χ. διεξαγωγή μίας μελέτης μόνο σε καπνιστές

- Εξομοίωση (matching):

π.χ. σε μελέτες ασθενών μαρτύρων επιλογή των μαρτύρων

1:1 (ή 1:n, m:n) ίδιας ηλικίας, ίδιου φύλου κλπ.

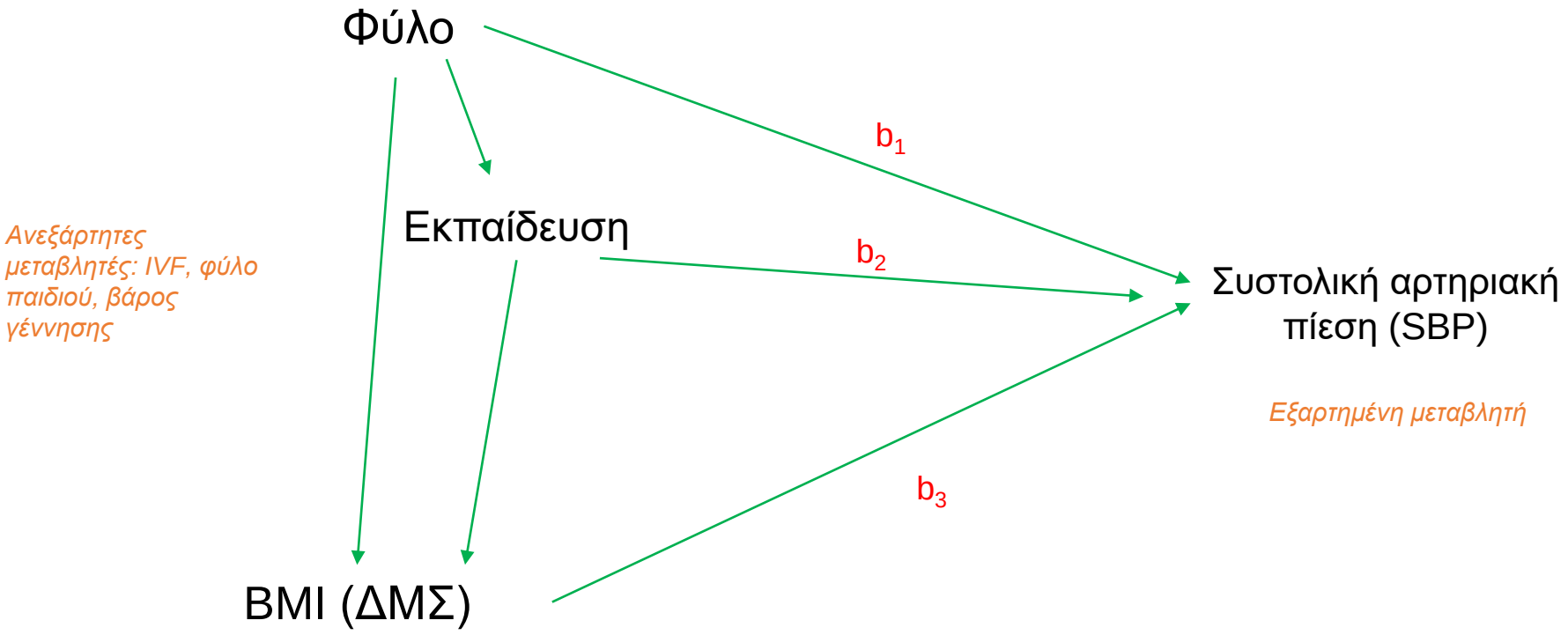
Αφορούν σε γνωστούς συγχυτικούς παράγοντες

Αντιμετώπιση των συγχυτικών παραγόντων στην Επιδημιολογία

Β. Κατά την ανάλυση μιας μελέτης

- Διαστρωμάτωση (stratification)
- Προτύπωση (standardization): αναγωγή σε πρότυπο πληθυσμό
- Πολυμεταβλητή ανάλυση (multivariate adjustment, *πολυμεταβλητή «προσαρμογή»*)

Πολυπαραγοντική γραμμική παλινδρόμηση (multivariate linear regression)



- Τα b_1 ,b_2 ,b_3 είναι “adjusted” (προσαρμοσμένα)

π.χ. το b_1 είναι *προσαρμοσμένο (adjusted)* για την επίδραση της εκπαίδευσης και του BMI (δηλώνει την επίδραση του φύλου στη συστολική αρτηριακή πίεση *ανεξάρτητα από το επίπεδο εκπαίδευσης και το BMI*)

το b_2 δηλώνει την επίδραση του επιπέδου εκπαίδευσης στη συστολική αρτηριακή πίεση, είναι *προσαρμοσμένο (adjusted)* για την επίδραση του φύλου και του BMI, κ.ο.κ.

Αναλυτική Επιδημιολογία: έρευνες ασθενών-μαρτύρων (case-control studies)

Διάκριση με κριτήριο αν έχουν προσβληθεί ή όχι από το υπό μελέτη νόσημα:

- Α) Ομάδα ατόμων που πάσχει από το νόσημα (ασθενείς)
- Β) Ομάδα ατόμων που δεν πάσχει από το νόσημα (μάρτυρες)

- Σύγκριση των δύο ομάδων: με βάση τη συχνότητα του πιθανολογούμενου αιτιολογικού παράγοντα στις δύο ομάδες

Αξιολόγηση της ποιότητας μελέτης ασθενών-μαρτύρων: η κλίμακα Newcastle-Ottawa

Comparability

1) Comparability of cases and controls on the basis of the design or analysis
   a) study controls for _____ (Select the most important factor.) ✱
   b) study controls for any additional factor ✱ (This criteria could be modified to indicate specific control for a second important factor.)

Έλεγχος για τους συγχυτικούς παράγοντες (confounding)

Exposure

1) Ascertainment of exposure
   a) secure record (eg surgical records) ✱
   b) structured interview where blind to case/control status ✱
   c) interview not blinded to case/control status
   d) written self report or medical record only
   e) no description

2) Same method of ascertainment for cases and controls
   a) yes ✱
   b) no

3) Non-Response rate
   a) same rate for both groups ✱
   b) non respondents described
   c) rate different and no designation

Selection #1: Case definition

Selection

1) Is the case definition adequate?
   a) yes, with independent validation ✵
   b) yes, eg record linkage or based on self reports
   c) no description

CODING MANUAL FOR CASE-CONTROL STUDIES

SELECTION

1) Is the Case Definition Adequate?

a) Requires some independent validation (e.g. >1 person/record/time/process to extract information, or reference to primary record source such as x-rays or medical/hospital records) ☆
b) Record linkage (e.g. ICD codes in database) or self-report with no reference to primary record
c) No description

Selection #1: Case definition

Selection

1) Is the case definition adequate?
   a) yes, with independent validation ✵
   b) yes, eg record linkage or based on self reports
   c) no description

CODING MANUAL FOR CASE-CONTROL STUDIES

SELECTION

1) Is the Case Definition Adequate?

a) Requires some independent validation (e.g. >1 person/record/time/process to extract information, or reference to primary record source such as x-rays or medical/hospital records) ☆
b) Record linkage (e.g. ICD codes in database) or self-report with no reference to primary record
c) No description

MATERIALS AND METHODS

Participants included 67 patients with RVO, 39 with CRVO and 28 with BRVO, who were recruited at the Retina Department, 2nd Department of Ophthalmology, University of Athens, Athens, Greece. Individuals with corneal abnorm-

Ασθενείς από τα αρχεία της Β’ Πανεπιστημιακής Οφθαλμολογικής Κλινικής.

Selection 2# Representativeness of the cases

2) Representativeness of the cases
   a) consecutive or obviously representative series of cases ✵
   b) potential for selection biases or not stated

2) Representativeness of the Cases

a) All eligible cases with outcome of interest over a defined period of time, all cases in a defined catchment area, all cases in a defined hospital or clinic, group of hospitals, health maintenance organisation, or an appropriate sample of those cases (e.g. random sample) ☆
b) Not satisfying requirements in part (a), or not stated.

Selection 2# Representativeness of the cases

2) Representativeness of the cases
   a) consecutive or obviously representative series of cases *
   b) potential for selection biases or not stated

2) Representativeness of the Cases

a) All eligible cases with outcome of interest over a defined period of time, all cases in a defined catchment area, all cases in a defined hospital or clinic, group of hospitals, health maintenance organisation, or an appropriate sample of those cases (e.g. random sample) ☆
b) Not satisfying requirements in part (a), or not stated.

MATERIALS AND METHODS

Participants included 67 patients with RVO, 39 with CRVO and 28 with BRVO, who were recruited at the Retina Department, 2nd Department of Ophthalmology, University of Athens, Athens, Greece. Individuals with corneal abnorm-

Δεν αναγράφεται ότι οι ασθενείς ήταν αλληλοδιάδοχοι σε συγκεκριμένη χρονική περίοδο

Selection 3#: Selection of controls

3) Selection of Controls

a) community controls *

b) hospital controls

c) no description

3) Selection of Controls

This item assesses whether the control series used in the study is derived from the same population as the cases and essentially would have been cases had the outcome been present.

a) Community controls (i.e. same community as cases and would be cases if had outcome) ☆

b) Hospital controls, within same community as cases (i.e. not another city) but derived from a hospitalised population

c) No description

Selection 3#: Selection of controls

3) Selection of Controls
   a) community controls *
   b) hospital controls
   c) no description

3) Selection of Controls

This item assesses whether the control series used in the study is derived from the same population as the cases and essentially would have been cases had the outcome been present.

a) Community controls (i.e. same community as cases and would be cases if had outcome) ☆
b) Hospital controls, within same community as cases (i.e. not another city) but derived from a hospitalised population
c) No description

3) Selection of controls: _____
   a) Community controls *(one star)*
   b) Hospital controls
   c) No description ✓

Δεν υπάρχει αναφορά για το πως επιλέχθηκαν οι μάρτυρες.

Selection 4#: Definition of Controls

4) Definition of Controls
   a) no history of disease (endpoint) ✱
   b) no description of source

4) Definition of Controls

a) If cases are first occurrence of outcome, then it must explicitly state that controls have no history of this outcome. If cases have new (not necessarily first) occurrence of outcome, then controls with previous occurrences of outcome of interest should not be excluded. ☆
b) No mention of history of outcome

Selection 4#: Definition of Controls

4) Definition of Controls
   a) no history of disease (endpoint) *
   b) no description of source

4) Definition of Controls

a) If cases are first occurrence of outcome, then it must explicitly state that controls have no history of this outcome. If cases have new (not necessarily first) occurrence of outcome, then controls with previous occurrences of outcome of interest should not be excluded. ☆
b) No mention of history of outcome

4) Definition of controls: _____
   a) No history of disease (endpoint) ***(one star)*** ✓
   b) No description of source

and psychiatric diseases were excluded. In addition, 70 age- and sex-matched controls without RVO or other ocular disease related to the above-mentioned exclusion criteria were also enrolled in the study. All procedures were in accordance with

Δεν υπήρχε ιστορικό απόφραξης φλέβας στους μάρτυρες.

Comparability

Comparability

1) Comparability of cases and controls on the basis of the design or analysis
   a) study controls for _____ (Select the most important factor.) ✵
   b) study controls for any additional factor ✵ (This criteria could be modified to indicate specific control for a second important factor.)

COMPARABILITY

1) Comparability of Cases and Controls on the Basis of the Design or Analysis

A maximum of 2 stars can be allotted in this category

Either cases and controls must be matched in the design and/or confounders must be adjusted for in the analysis. Statements of no differences between groups or that differences were not statistically significant are not sufficient for establishing comparability. Note: If the odds ratio for the exposure of interest is adjusted for the confounders listed, then the groups will be considered to be comparable on each variable used in the adjustment.

There may be multiple ratings for this item for different categories of exposure (e.g. ever vs. never, current vs. previous or never)

Age =☆ , Other controlled factors = ☆

Comparability

Comparability

1) Comparability of cases and controls on the basis of the design or analysis
   a) study controls for _____ (Select the most important factor.) ✵
   b) study controls for any additional factor ✵ (This criteria could be modified to indicate specific control for a second important factor.)

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There may be multiple ratings for this item for different categories of exposure (e.g. ever vs. never, current vs. previous or never)
Age =☆ , Other controlled factors = ☆

Table 2. Results of the multivariate logistic regression analysis, examining factors associated with retinal vein occlusion.

	Category/Increment	Odds ratio (95%CI)	*p*-Value
Educational level	University vs. Secondary school	11.31 (3.64–35.13)	**<.001**
Smoking	Yes vs. No	28.35 (6.51–123.24)	**<.001**
Exercise	Mild/Moderate vs. No	0.07 (0.02–0.29)	**<.001**
Dyslipidaemia	Yes vs. No	5.51 (1.51–20.09)	**.010**
Thyroidopathy	Yes vs. No	9.47 (1.79–50.00)	**.008**

Η μελέτη πραγματοποιεί εξομοίωση για ηλικία και φύλο, καθώς επίσης πολυπαραγοντική ανάλυση. Αν θεωρήσουμε κύριο συγχυτικό παράγοντα την ηλικία → δύο αστεράκια

Exposure #1: Ascertainment of exposure

Exposure

1) Ascertainment of exposure
   a) secure record (eg surgical records) ✵
   b) structured interview where blind to case/control status ✵
   c) interview not blinded to case/control status
   d) written self report or medical record only
   e) no description

EXPOSURE

Ascertainment of Exposure

Allocation of stars as per rating sheet

Exposure #1: Ascertainment of exposure

Exposure

1) Ascertainment of exposure
   a) secure record (eg surgical records) ✵
   b) structured interview where blind to case/control status ✵
   c) interview not blinded to case/control status
   d) written self report or medical record only
   e) no description

EXPOSURE

Ascertainment of Exposure

Allocation of stars as per rating sheet

Demographic (age, sex, marital status and education level) and lifestyle data (smoking, alcohol consumption, exercise), medical history and comorbidities (hypertension, diabetes mellitus, thyroidopathy, cardiovascular diseases, coagulation disorders) were recorded.

Δεν παρέχονται πληροφορίες για τον τρόπο καταγραφής των εκθέσεων.

Exposure #2: Method of ascertainment

2) Same method of ascertainment for cases and controls
   a) yes *
   b) no

EXPOSURE

Ascertainment of Exposure

Allocation of stars as per rating sheet

Exposure #2: Method of ascertainment

2) Same method of ascertainment for cases and controls
   a) yes ✵
   b) no

EXPOSURE

Ascertainment of Exposure

Allocation of stars as per rating sheet

Demographic (age, sex, marital status and education level) and lifestyle data (smoking, alcohol consumption, exercise), medical history and comorbidities (hypertension, diabetes mellitus, thyroidopathy, cardiovascular diseases, coagulation disorders) were recorded.

Δεν συνάγεται διαφορά ανάμεσα στον τρόπο καταγραφής σε ασθενείς και μάρτυρες (ωστόσο θα ήταν καλό να είχε δηλωθεί ξεκάθαρα).

Exposure #3: Non-Response Rate

3) Non-Response rate
   a) same rate for both groups ❋
   b) non respondents described
   c) rate different and no designation

Non-Response Rate

Allocation of stars as per rating sheet

Exposure #3: Non-Response Rate

3) Non-Response rate
   a) same rate for both groups ✵
   b) non respondents described
   c) rate different and no designation

Non-Response Rate

Allocation of stars as per rating sheet

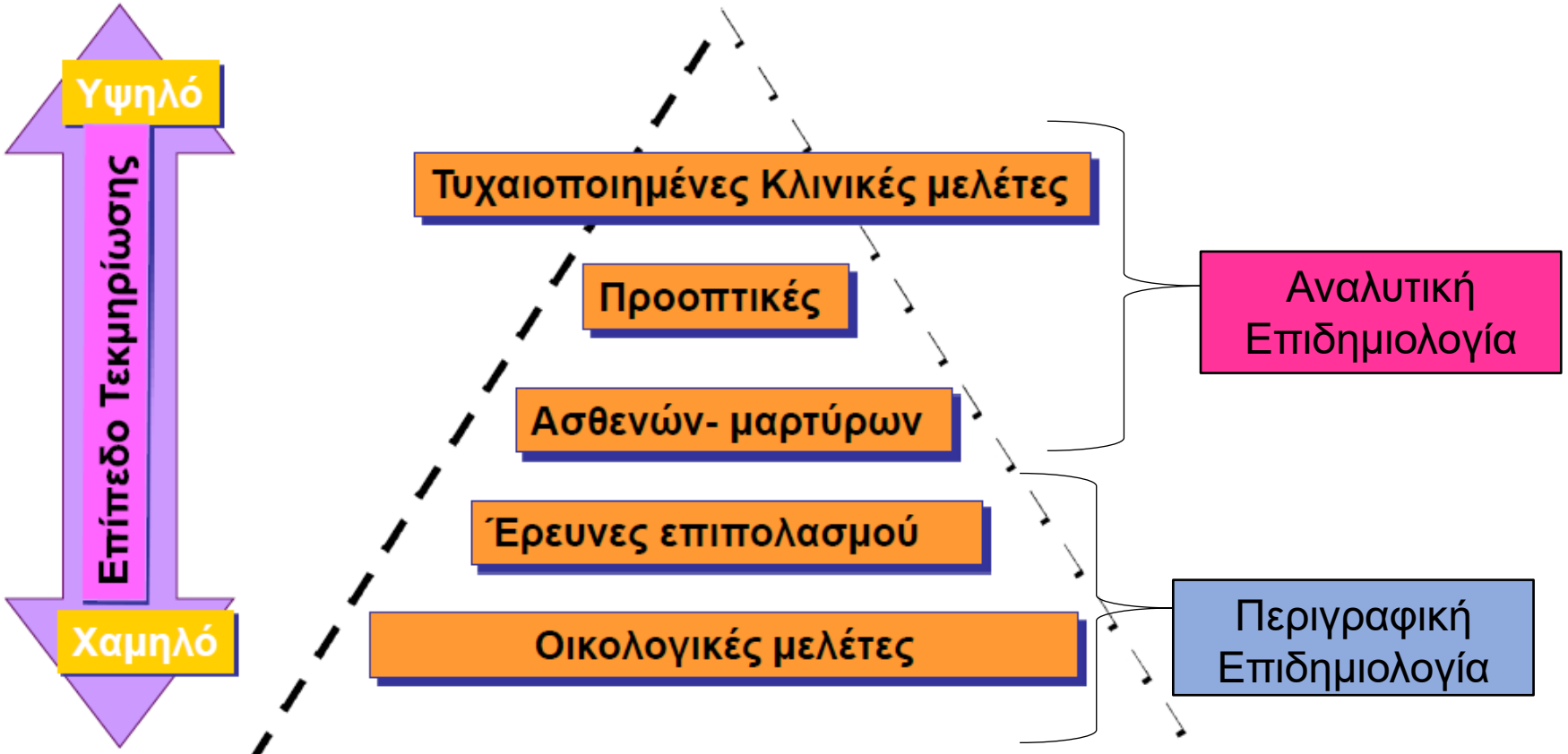
Δεν υπάρχουν πληροφορίες αναφορικά με τη μη απαντητικότητα σε ασθενείς και μάρτυρες.

Παράδειγμα αξιολόγησης μελέτης ασθενών-μαρτύρων

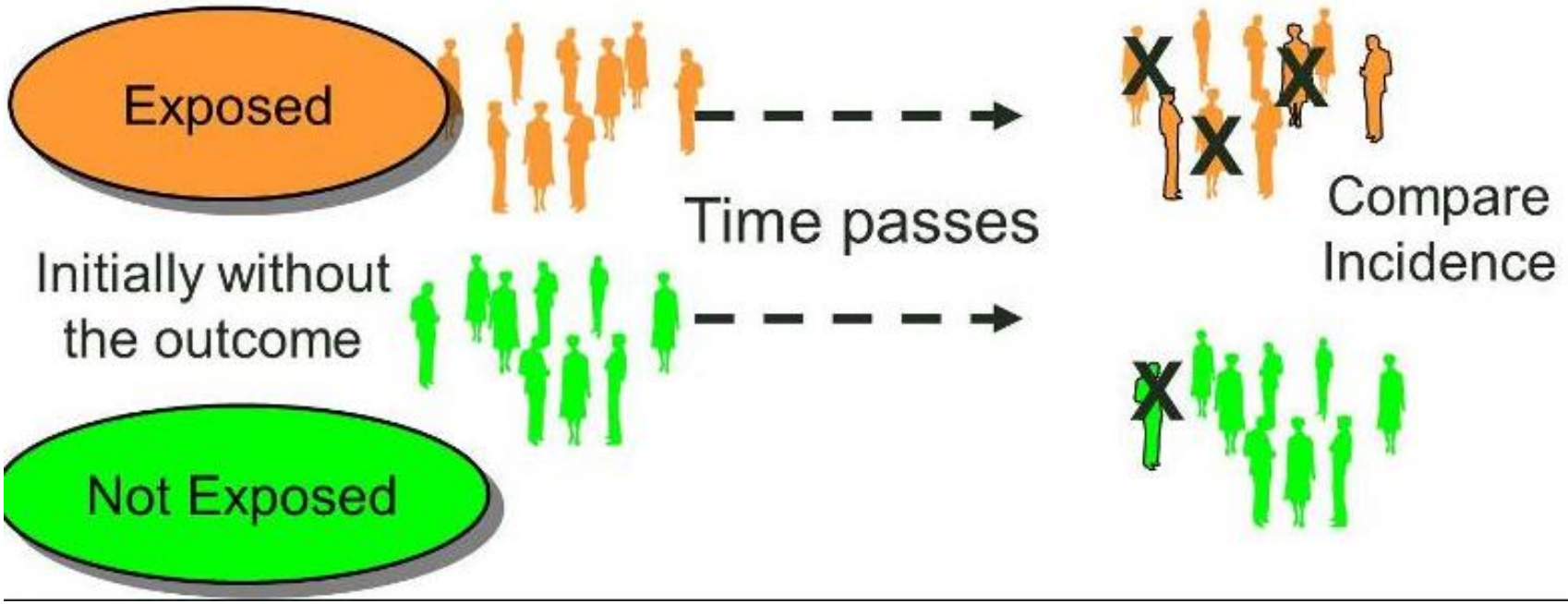
	Selection				Comparability		Exposure			Total
	Case definition	Representativeness of the cases	Selection of controls	Definition of controls	On …age	On other factors	Ascertainment of exposure	Same method of ascertainment in cases and controls	Non-response rate	
Chatzirallis et al (2021)	1	0	0	1	1	1	0	1	0	5

Αξιολόγηση συστηματικών σφαλμάτων στις προοπτικές μελέτες

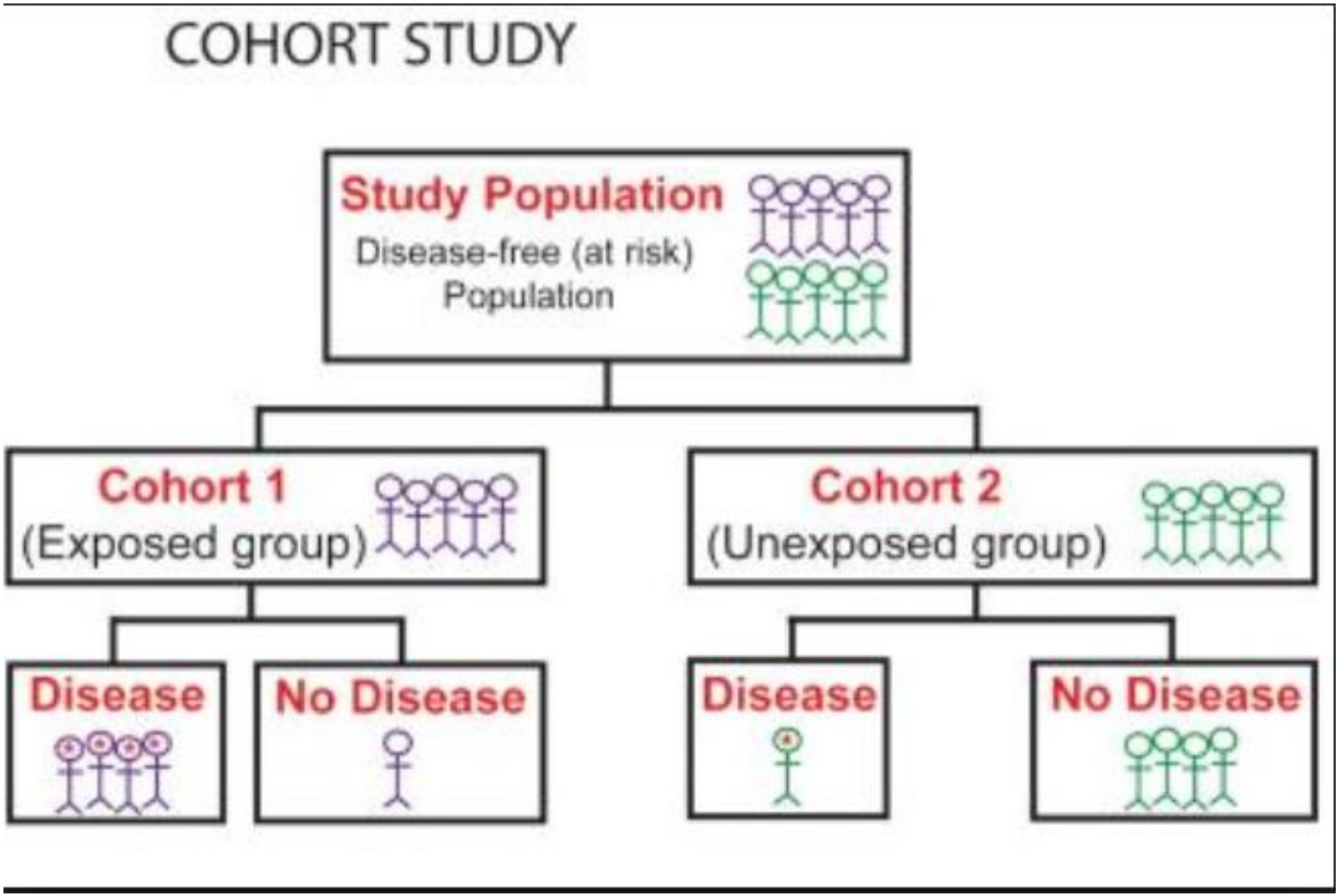
Τύποι επιδημιολογικών ερευνών ανάλογα με τη δυνατότητα τεκμηρίωσης μιας αιτιολογικής συσχέτισης



Αναλυτική Επιδημιολογία – Προοπτικές μελέτες



Αναλυτική Επιδημιολογία – Προοπτικές μελέτες



Τι σημαίνει «cohort»

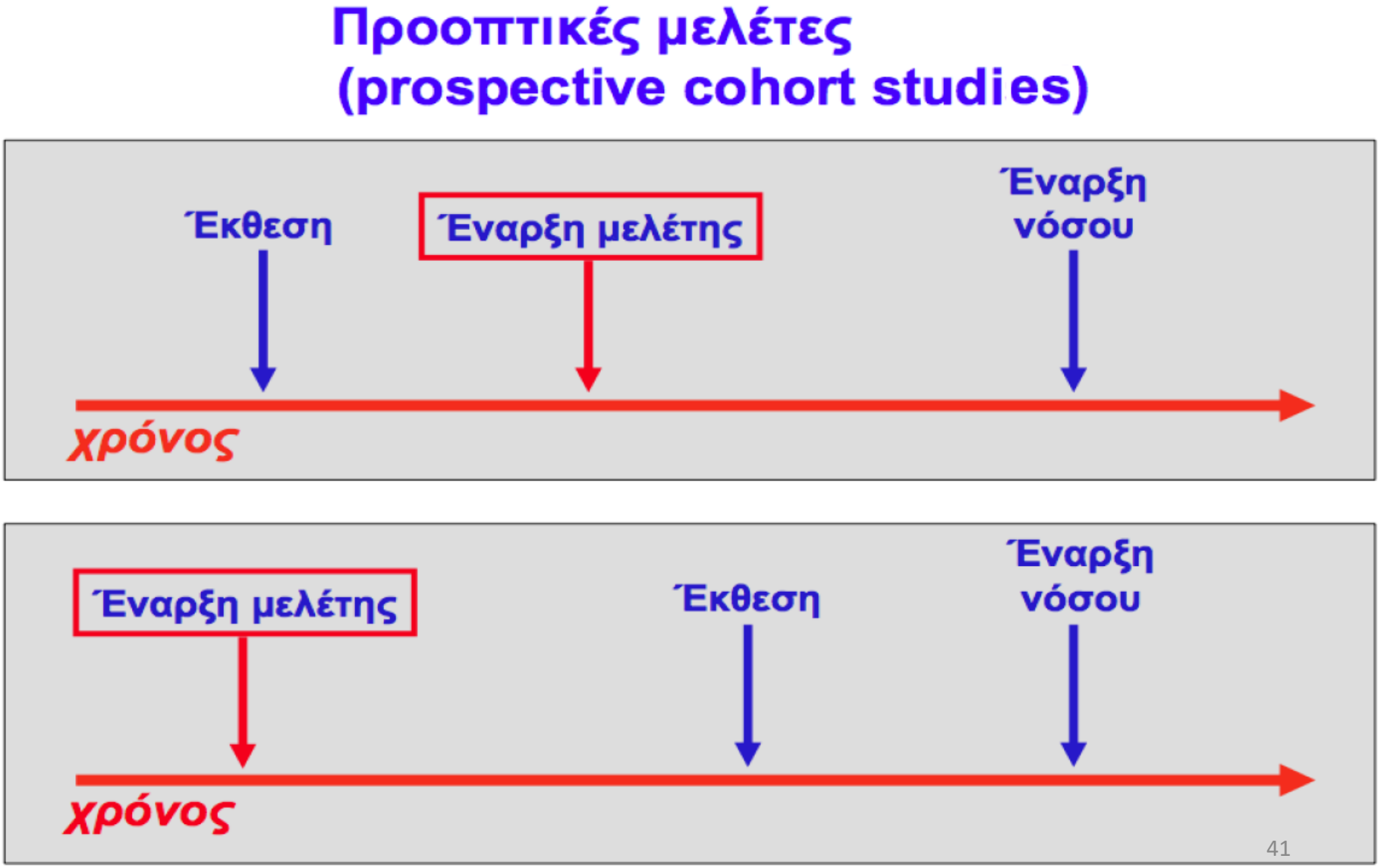
- **Προέλευση όρου:**

  μία από 10 υποδιαιρέσεις των Ρωμαϊκών λεγεώνων με 300 έως 600 λεγεωνάριους

  Λατιν. cohors = αυλή, περίβολος / τάγμα στρατιωτών. Συνδ. hortus = κήπος

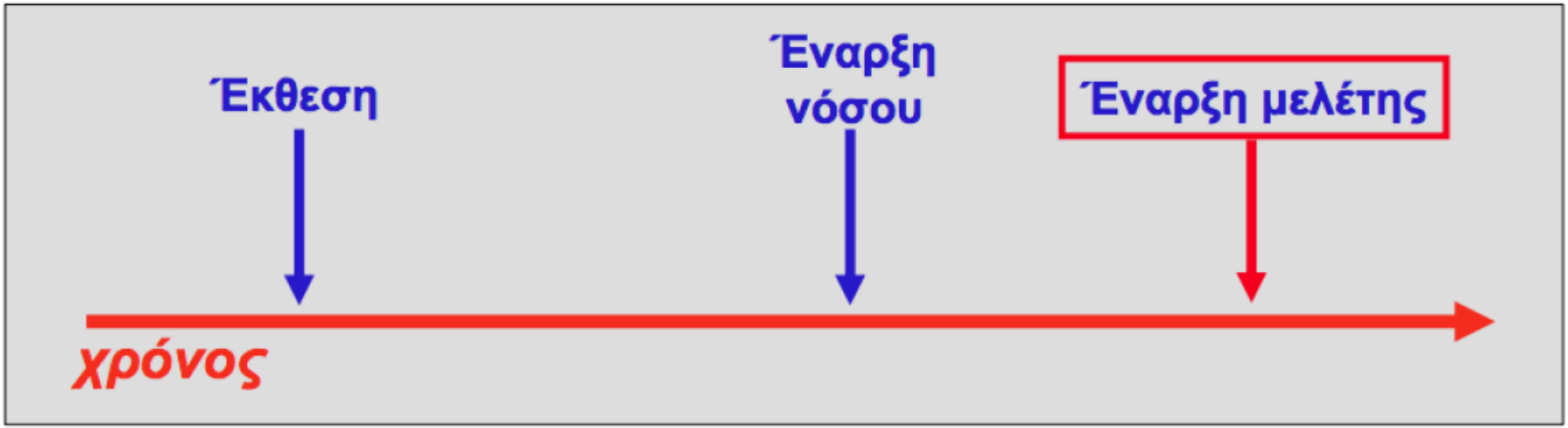
- **Σύνολο ατόμων**
  - **Με κοινή εμπειρία/χαρακτηριστικό**
  - **Πορεύονται μαζί στο χρόνο για καθορισμένο διάστημα**
- **Παραδείγματα**
  - **«Γενιά» ατόμων (γεννήθηκαν ίδια περίοδο - birth cohort)**
  - **«Φουρνιά» μαθητών σχολείου (ίδια τάξη)**
  - **«Σειρά» στο στρατό (παρουσιάστηκαν μαζί)**

Προοπτικές μελέτες «μέλλοντος»



Προοπτικές μελέτες παρελθόντος

(retrospective cohort studies)



Παράδειγμα αξιολόγησης προοπτικής μελέτης

Selection

1) Representativeness of the exposed cohort
   a) truly representative of the average _____ (describe) in the community ✵
   b) somewhat representative of the average _____ in the community ✵
   c) selected group of users eg nurses, volunteers
   d) no description of the derivation of the cohort

2) Selection of the non exposed cohort
   a) drawn from the same community as the exposed cohort ✵
   b) drawn from a different source
   c) no description of the derivation of the non exposed cohort

3) Ascertainment of exposure
   a) secure record (eg surgical records) ✵
   b) structured interview ✵
   c) written self report
   d) no description

4) Demonstration that outcome of interest was not present at start of study
   a) yes ✵
   b) no

Παράδειγμα αξιολόγησης προοπτικής μελέτης

Comparability

1) Comparability of cohorts on the basis of the design or analysis
   a) study controls for _____ (select the most important factor) ✵
   b) study controls for any additional factor ✵ (This criteria could be modified to indicate specific control for a second important factor.)

Outcome

1) Assessment of outcome
   a) independent blind assessment ✵
   b) record linkage ✵
   c) self report
   d) no description

2) Was follow-up long enough for outcomes to occur
   a) yes (select an adequate follow up period for outcome of interest) ✵
   b) no

3) Adequacy of follow up of cohorts
   a) complete follow up - all subjects accounted for ✵
   b) subjects lost to follow up unlikely to introduce bias - small number lost - > ____ % (select an adequate %) follow up, or description provided of those lost) ✵
   c) follow up rate < ____% (select an adequate %) and no description of those lost
   d) no statement

Ποια είναι η έκθεση και ποια η έκβαση;

εκθέσεις

έκβαση

Table 3. Results of the GLS linear regression analysis of retinal layers, potentially affecting visual acuity

Variable	Category/increment	Coefficient (95% CI)	*p* value
CRT thickness	100 µm increase	+0.18 (+0.17 to +0.20)	**<0.001**
GCL thickness	10 µm increase	+0.01 (−0.07 to +0.10)	0.794
IPL thickness	10 µm increase	+0.03 (−0.05 to +0.11)	0.424
INL thickness	10 µm increase	+0.18 (+0.10 to +0.26)	**<0.001**
OPL thickness	10 µm increase	+0.23 (+0.16 to +0.31)	**<0.001**
ONL thickness	10 µm increase	+0.03 (+0.02 to +0.04)	**<0.001**
EZ	Disrupted versus intact	+0.18 (+0.15 to +0.20)	**<0.001**

CRT, central retinal thickness; GCL, ganglion cell layer; IPL, inner plexiform layer; INL, inner nuclear layer; OPL, outer plexiform layer; ONL, outer nuclear layer; EZ, ellipsoid zone; GLS, generalized least squares; CI, confidence interval; SD, standard deviation. Bold values indicate statistical significance.

Generalized Least Squares (GLS) random-effects linear regression analysis was used to assess the potential association between retinal layers and VA since observation may be intercorrelated in such datasets. VA was the dependent variable, while CRT, thickness of GCL, INL, IPL, ONL, OPL, and EZ condition were the independent variables in models adjusted for time (in months) and treatment. The beta coefficients with their 95% confidence intervals (CIs) are given in the manuscript.

Selection #1 Representativeness of the exposed cohort

1) Representativeness of the exposed cohort
   a) truly representative of the average _____ (describe) in the community ✵
   b) somewhat representative of the average _____ in the community ✵
   c) selected group of users eg nurses, volunteers
   d) no description of the derivation of the cohort

1) Representativeness of the Exposed Cohort

Item is assessing the representativeness of exposed individuals in the community, not the representativeness of the sample of women from some general population. For example, subjects derived from groups likely to contain middle class, better educated, health oriented women are likely to be representative of postmenopausal estrogen users while they are not representative of all women (e.g. members of a health maintenance organisation (HMO) will be a representative sample of estrogen users. While the HMO may have an under-representation of ethnic groups, the poor, and poorly educated, these excluded groups are not the predominant users users of estrogen).

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Participants in this prospective study were 110 treatment-naïve patients (110 eyes) with type 2 DM and center involved DME (CI-DME), who were treated with anti-VEGF agents at the Second Department of Ophthalmology, University of Athens, Athens,

Βαθμολογούμε με ένα αστέρι καθώς ο πληθυσμός ων εκτεθειμένων της μελέτης μπορεί να θεωρηθεί *σχετικά αντιπροσωπευτικός* των εκτεθειμένων διαβητικών στην κοινότητα.

Selection #2: Selection of the non-exposed cohort

2) Selection of the non exposed cohort
   a) drawn from the same community as the exposed cohort ✵
   b) drawn from a different source
   c) no description of the derivation of the non exposed cohort

2) Selection of the Non-Exposed Cohort

Allocation of stars as per rating sheet

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Εκτεθειμένοι και μη εκτεθειμένοι έχουν ληφθεί από την ίδια κοινότητα

Selection #3: Ascertainment of exposure

3) Ascertainment of exposure
   a) secure record (eg surgical records) ✵
   b) structured interview ✵
   c) written self report
   d) no description

3) Ascertainment of Exposure

Allocation of stars as per rating sheet

Selection #3: Ascertainment of exposure

3) Ascertainment of exposure
   a) secure record (eg surgical records) ✵
   b) structured interview ✵
   c) written self report
   d) no description

3) Ascertainment of Exposure

Allocation of stars as per rating sheet

Data related to demographic characteristics, DM duration, comorbidities (hypertension, hyperlipidemia), and HbA1c levels were recorded for all included patients. All participants underwent a complete ophthalmological examination at the time of DME diagnosis (baseline), including best corrected visual acuity (BCVA) measurement, slit-lamp biomicroscopy, dilated fundoscopy, SD-OCT, and fluorescein angiography using Spectralis (Spectralis HRA + OCT, Heidelberg Engineering, Germany).

Οι πληροφορίες για την έκθεση ελήφθησαν από νοσοκομειακά αρχεία.

Selection 4#: Demonstration that the outcome was not present in the start of the study

4) Demonstration that outcome of interest was not present at start of study
   a) yes ✵
   b) no

4) Demonstration That Outcome of Interest Was Not Present at Start of Study

In the case of mortality studies, outcome of interest is still the presence of a disease/ incident, rather than death. That is to say that a statement of no history of disease or incident earns a star.

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Στην μελέτη αυτή οι ασθενείς δεν είχαν λάβει ξανά στο παρελθόν θεραπεία με anti-VEGF και το οποίο θεραπευτικό αποτέλεσμα στην οπτική οξύτητα δεν μπορεί να θεωρηθεί υπάρχον στην έναρξη της μελέτης

Comparability

Comparability

1) Comparability of cohorts on the basis of the design or analysis
   a) study controls for _____ (select the most important factor) ✵
   b) study controls for any additional factor ✵ (This criteria could be modified to indicate specific control for a second important factor.)

COMPARABILITY

1) Comparability of Cohorts on the Basis of the Design or Analysis

A maximum of 2 stars can be allotted in this category
Either exposed and non-exposed individuals must be matched in the design and/or confounders must be adjusted for in the analysis. Statements of no differences between groups or that differences were not statistically significant are not sufficient for establishing comparability. Note: If the relative risk for the exposure of interest is adjusted for the confounders listed, then the groups will be considered to be comparable on each variable used in the adjustment.
There may be multiple ratings for this item for different categories of exposure (e.g. ever vs. never, current vs. previous or never)
Age = ☆ , Other controlled factors = ☆

Comparability

Comparability

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   a) study controls for _____ (select the most important factor) ✵
   b) study controls for any additional factor ✵ (This criteria could be modified to indicate specific control for a second important factor.)

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Αν θεωρήσουμε τον αριθμό θεραπειών ως συγχυτικό παράγοντα, μπορούμε να αποδώσουμε δύο αστεράκια

Outcome #1: Assessment of the outcome

Outcome

1) Assessment of outcome
   a) independent blind assessment ✵
   b) record linkage ✵
   c) self report
   d) no description

OUTCOME

1) Assessment of Outcome

For some outcomes (e.g. fractured hip), reference to the medical record is sufficient to satisfy the requirement for confirmation of the fracture. This would not be adequate for vertebral fracture outcomes where reference to x-rays would be required.

a) Independent or blind assessment stated in the paper, or confirmation of the outcome by reference to secure records (x-rays, medical records, etc.) ☆
b) Record linkage (e.g. identified through ICD codes on database records) ☆
c) Self-report (i.e. no reference to original medical records or x-rays to confirm the outcome)
d) No description.

Outcome #1: Assessment of the outcome

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   a) independent blind assessment ✵
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All patients were followed up at a pro re nata basis, with monthly monitoring for at least 12 months. At each monthly visit, all patients underwent BCVA measurement and SD-OCT assessment, while reinjection was performed if the height of macular edema was ≥320 μm and if a decrease in VA ≥ 1 Snellen line was noticed.

Τα αποτελέσματα της μελέτης ελέγχθηκαν μέσω διαγνωστικών εξετάσεων

Outcome #2: Was follow-up long enough?

2) Was follow-up long enough for outcomes to occur
   a) yes (select an adequate follow up period for outcome of interest) ✵
   b) no

2) Was Follow-Up Long Enough for Outcomes to Occur

An acceptable length of time should be decided before quality assessment begins (e.g. 5 yrs. for exposure to breast implants)

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Ο ερευνητής που πραγματοποιεί την ανασκόπηση πρέπει να θέσει ένα χρονικό περιθώριο που θεωρεί ότι αρκεί για να εμφανιστεί το εν λόγω αποτέλεσμα. Εάν στην περίπτωση αυτή θέσουμε το χρονικό περιθώριο αυτό στους 12 μήνες θεωρούμε πως ήταν αρκετό το διάστημα.

Outcome #3: Adequacy of follow-up cohorts

3) Adequacy of follow up of cohorts
   a) complete follow up - all subjects accounted for ✵
   b) subjects lost to follow up unlikely to introduce bias - small number lost - > ____ % (select an adequate %) follow up, or description provided of those lost) ✵
   c) follow up rate < ____% (select an adequate %) and no description of those lost
   d) no statement

3) Adequacy of Follow Up of Cohorts

This item assesses the follow-up of the exposed and non-exposed cohorts to ensure that losses are not related to either the exposure or the outcome.

Allocation of stars as per rating sheet

Outcome #3: Adequacy of follow-up cohorts

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3) Adequacy of Follow Up of Cohorts

This item assesses the follow-up of the exposed and non-exposed cohorts to ensure that losses are not related to either the exposure or the outcome.

Allocation of stars as per rating sheet

Participants in this prospective study were 110 treatment-naïve patients (110 eyes) with type 2 DM and center involved DME (CI-DME), who were treated with anti-VEGF agents at the Second Department of Ophthalmology, University of Athens, Athens, Greece, from November 2015 to November 2018 and had at least 12 months of follow-up.

Σε αυτό το σημείο επίσης ο ερευνητής θέτει ένα ποσοστό των συμμετεχόντων που θεωρεί ότι απαιτείται να παραμείνει μέχρι το τέλος της μελέτης. Στην προκειμένη μελέτη όλοι οι ασθενείς παρακολουθήθηκαν για τουλάχιστον 12 μήνες.

Παράδειγμα αξιολόγησης προοπτικής μελέτης

	Selection				Comparability		Outcome			Total
	Representativeness	Selection of non-exposed	Ascertainment of exposure	Outcome not present at start	On … treatment	On other factors	Assessment of outcome	Long enough follow-up (median ≥1 year)	Adequacy (completeness) of follow-up (>90%)	
Chatziralli et al (2021)	1	1	1	1	1	1	1	1	1	9

Αξιολόγηση συστηματικών σφαλμάτων στις συγχρονικές μελέτες – τροποποίηση της κλίμακας Newcastle-Ottawa (2016)

S1 Text
NEWCASTLE - OTTAWA QUALITY ASSESSMENT SCALE
(adapted for cross sectional studies)

Selection: (Maximum 5 stars)

1) Representativeness of the sample:
    a) Truly representative of the average in the target population. * (all subjects or random sampling)
    b) Somewhat representative of the average in the target population. * (non-random sampling)
    c) Selected group of users.
    d) No description of the sampling strategy.
2) Sample size:
    a) Justified and satisfactory. *
    b) Not justified.
3) Non-respondents:
    a) Comparability between respondents and non-respondents characteristics is established, and the response rate is satisfactory. *
    b) The response rate is unsatisfactory, or the comparability between respondents and non-respondents is unsatisfactory.
    c) No description of the response rate or the characteristics of the responders and the non-responders.
4) Ascertainment of the exposure (risk factor):
    a) Validated measurement tool. **
    b) Non-validated measurement tool, but the tool is available or described.*
    c) No description of the measurement tool.

Comparability: (Maximum 2 stars)

1) The subjects in different outcome groups are comparable, based on the study design or analysis. Confounding factors are controlled.
    a) The study controls for the most important factor (select one). *
    b) The study control for any additional factor. *

Outcome: (Maximum 3 stars)

1) Assessment of the outcome:
    a) Independent blind assessment. **
    b) Record linkage. **
    c) Self report. *
    d) No description.
2) Statistical test:
    a) The statistical test used to analyze the data is clearly described and appropriate, and the measurement of the association is presented, including confidence intervals and the probability level (p value). *
    b) The statistical test is not appropriate, not described or incomplete.

έκβαση

εκθέσεις

TABLE 2. Results of the Univariate Analysis Regarding Factors Potentially Associated With DR Presence

Variable	Category or Increment	OR (95% CI)	*P* Value
Age	One quartile increase	0.99 (0.87–1.13)	0.873
Sex	Male vs. female	1.58 (1.16–2.14)	**0.004**
Race	Black vs. white	1.11 (0.80–1.53)	0.542
	Asian vs. white	1.00 (0.54–1.86)	>0.999
	Mixed vs. white	1.25 (0.69–2.28)	0.457
Legal partnership	Single/widowed/divorced vs. married/cohabiting	0.96 (0.72–1.30)	0.809
Current employment	Yes vs. no	0.84 (0.62–1.13)	0.247
Smoking	Current vs. never	0.99 (0.66–1.49)	0.978
	Former vs. never	0.77 (0.54–1.06)	0.106
DM duration	≥6 mo vs. <6 mo	1.13 (0.83–1.55)	0.441
Cataract	Yes vs. no	0.90 (0.54–1.50)	0.675
Any cardiovascular event	Yes vs. no	1.65 (1.03–2.65)	**0.039**
Any microvascular*	Yes vs. no	1.26 (0.70–2.27)	0.432
Erectile dysfunction*	Yes vs. no	1.26 (0.83–1.91)	0.274
Body mass index	≥25 vs. <25	0.95 (0.69–1.32)	0.767
Central obesity	Yes vs. no	1.02 (0.64–1.62)	0.945
Hypertension	Yes vs. no	1.04 (0.77–1.40)	0.817
Medications			
Antidiabetic tablets	Yes vs. no	1.20 (0.89–1.63)	0.226
Insulin	Yes vs. no	0.82 (0.33–2.00)	0.657
Statins/fibrates	Yes vs. no	1.29 (0.95–1.76)	0.108
Antihypertensives	Yes vs. no	0.92 (0.68–1.24)	0.578
HbA1c, %	≥7.5 vs. <7.5	1.62 (1.16–2.25)	**0.005**
Triglycerides, mM	≥2.0 vs. <2.0	0.95 (0.67–1.33)	0.751
Total cholesterol, mM	≥5.0 vs. <5.0	1.11 (0.81–1.52)	0.525
HDL, mM	≥1.2 vs. <1.2	0.86 (0.63–1.17)	0.333
LDL, mM	≥3.0 vs. <3.0	1.10 (0.79–1.53)	0.577
WBC, $\times 10^6$	≥11 vs. <11	1.05 (0.48–2.34)	0.896
PLT, $\times 10^3$	≥450 vs. normal	0.76 (0.26–2.24)	0.614
	≤150 vs. normal	0.99 (0.40–2.46)	0.977
Creatinine, μM	≥120 vs. <120	1.37 (0.53–3.51)	0.516
Microalbuminuria	Positive vs. negative	1.56 (0.78–2.73)	0.129
CRP, mg/L	≥5.0 vs. <5.0	0.80 (0.58–1.11)	0.188
IL-1ra, pg/mL	One quartile increase	0.84 (0.73–0.96)	**0.009**
IL-1b, pg/mL	One quartile increase	0.86 (0.75–0.98)	**0.023**
IL-4, pg/mL	One quartile increase	0.91 (0.79–1.03)	0.124
IL-6, pg/mL	One quartile increase	0.80 (0.70–0.92)	**0.001**
IL-10, pg/mL	One quartile increase	0.91 (0.79–1.04)	0.145
VEGF, pg/mL	One quartile increase	1.01 (0.89–1.15)	0.866
Adiponectin, ng/mL	One quartile increase	0.92 (0.80–1.05)	0.209
TNF-α, pg/mL	One quartile increase	0.84 (0.73–0.96)	**0.009**
MCP-1, pg/mL	One quartile increase	1.00 (0.87–1.14)	0.946

Bold values denote statistical significance.
* The OR was derived based only on male patients.

Selection 1#: Representativeness of the sample

Selection: (Maximum 5 stars)

1) Representativeness of the sample:
   a) Truly representative of the average in the target population. * (all subjects or random sampling)
   b) Somewhat representative of the average in the target population. * (non-random sampling)
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This is a population-based, cross-sectional study based on the baseline data from participants of the South London-Diabetes (SOUL-D) study. SOUL-D is a prospective cohort of people newly diagnosed with T2DM, aiming to investigate the role of various biopsychosocial factors on biomedical outcomes over a period of 2 years.[30] Ethical approval was granted by the King's College Hospital Research Ethics Committee (reference 08/H0808/1) and by Lambeth, Southwark, and Lewisham Primary Care Trusts (reference RDLSLB 410). The study was conducted according to the tenets of the Declaration of Helsinki and written informed consent was obtained from all the participants.

Οι συμμετέχοντες είναι άτομα με πρόσφατη διάγνωση ΣΔ τύπου 2. Η επιλογή τους (population-based) έγινε από τη μελέτη SOUL-D. Μπορούν να θεωρηθούν αρκετά αντιπροσωπευτικοί των πρόσφατα διαγνωσθέντων διαβητικών στην Αγγλία.

Selection 2#: Sample Size

2) Sample size:
    a) Justified and satisfactory. *
    b) Not justified.

Selection 2#: Sample Size

2) Sample size:
   a) Justified and satisfactory. *
   b) Not justified.

Table 1 shows the demographic and clinical characteristics, as well as the laboratory findings of our study sample, comprising of 1062 patients with newly diagnosed T2DM. Their mean age was 56.0 ± 10.9 years. 55.1% were male. As far as ethnicity is

Ο ερευνητής αποφασίζει ένα μέγεθος δείγματος που θεωρεί ικανοποιητικό. Στην περίπτωση μπορεί να θεωρηθεί πως >1000 συμμετέχοντες είναι ικανοποιητικός αριθμός, με βάση υπολογισμούς ισχύος.

Selection 3#: Non-respondents

3) Non-respondents:

a) Comparability between respondents and non-respondents characteristics is established, and the response rate is satisfactory. *

b) The response rate is unsatisfactory, or the comparability between respondents and non-respondents is unsatisfactory.

c) No description of the response rate or the characteristics of the responders and the non-responders.

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Δεν υπάρχουν πληροφορίες στο κείμενο για τα άτομα που δεν απάντησαν στο ερωτηματολόγιο.

Selection 4#: Ascertainment of t he exposure

4) Ascertainment of the exposure (risk factor):
   a) Validated measurement tool. **
   b) Non-validated measurement tool, but the tool is available or described.*
   c) No description of the measurement tool.

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   c) No description of the measurement tool.

Demographic and clinical data of patients were collected. Assessment of DR status was performed using digital two-field photography. In addition, HbA_{1c} (%), lipid profile, and urinary albumin were measured at recruitment. The following inflammatory markers were also measured: serum C-reactive protein, white blood cells, platelet, adiponectin, IL-4, IL-6, IL-10, vascular endothelial growth factor, tumor necrosis factor-α (TNF-α), IL-1b, IL-1 receptor antagonist (IL-1RA), and monocyte chemotactic protein-1. Univariate and multivariate

Ο έλεγχος του λιπιδαιμικού προφιλ, της HbA1c καθώς και οι υπόλοιπες αιματολογικές εξετάσεις έγιναν μέσω πιστοποιημένων μεθόδων.

Comparability

Comparability: (Maximum 2 stars)

1) The subjects in different outcome groups are comparable, based on the study design or analysis. Confounding factors are controlled.

a) The study controls for the most important factor (select one). *

b) The study control for any additional factor. *

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TABLE 3. Results of the Multivariate Analysis, Showing Factors Significantly Associated With DR Presence

Variable	Category or Increment	OR (95% CI)	*P* Value
Sex	Male vs. female	1.44 (1.05–1.99)	**0.024**
Any cardiovascular event	Yes vs. no	1.77 (1.09–2.88)	**0.022**
HbA1c, %	≥7.5 vs. <7.5	1.60 (1.13–2.25)	**0.007**
IL-1RA, pg/mL	One quartile increase	0.81 (0.71–0.93)	**0.004**

Bold values denote statistical significance.

Επιλέγουμε ως πιο σημαντικό παράγοντα το φύλο. Έχει γίνει έλεγχος για το φύλο και άλλους παράγοντες, οπότε βαθμολογούμε με 2 αστέρια.

Outcome #1

Outcome: (Maximum 3 stars)

1) Assessment of the outcome:
   a) Independent blind assessment. **
   b) Record linkage. **
   c) Self report. *
   d) No description.

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Ο έλεγχος της ύπαρξης διαβητικής αμφιβληστροειδοπάθειας έγινε μέσω εξέτασης στους συμμετέχοντες.

Outcome #2

2) Statistical test:

a) The statistical test used to analyze the data is clearly described and appropriate, and the measurement of the association is presented, including confidence intervals and the probability level (p value). *

b) The statistical test is not appropriate, not described or incomplete.

Outcome #2

2) Statistical test:
   a) The statistical test used to analyze the data is clearly described and appropriate, and the measurement of the association is presented, including confidence intervals and the probability level (p value). *
   b) The statistical test is not appropriate, not described or incomplete.

Univariate and multivariate analyses of the association of various potential risk factors and DR were conducted. Subjects with missing values for the outcome variables (presence or absence of DR) were excluded from the analysis. At the univariate analysis, ordinal logistic regression was performed; the dependent variable was converted to an ordinal variable with four levels (1: minimum value-25th percentile; 2: 25th percentile-median; 3: median-75th percentile; and 4: 75th percentile-maximum value), where applicable. Nevertheless, when the median was equal to the maximum value of the variable due to markedly skewed distribution, as well as to the presence of numerous ties, the ordinal logistic regression model was obligatorily degenerated to logistic regression model (0: values below median; 1: values equal to median-maximum value). The odds ratios (ORs) with the respective 95% confidence intervals (CIs) are indicated in the text. At the multivariate analysis, only factors proven significant ($P < 0.05$) at the univariate analysis were tested in the stepwise multivariate model as independent variables; in the final model, only the statistically significant variables were retained (i.e., backward-selection statistical procedure). Statistical analysis was performed using STATA/SE 13 statistical software (Stata Corporation, College Station, TX, USA). A P value <0.05 was considered as statistically significant.

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Bold values denote statistical significance.

Υπάρχει πλήρης περιγραφή των στατιστικών μεθόδων που χρησιμοποιήθηκαν και ήταν κατάλληλες.

Παράδειγμα αξιολόγησης συγχρονικής μελέτης

	Selection				Comparability		Outcome		Total
	Representativeness	Sample size	Non-respondents	Asxertainment of the exposure	On … gender	On other factors	Assessment of outcome	Statistical test	
Chatziralli et al (2017)	1	1	0	2	1	1	2	1	9