Antibiyotik Direnç Çalışmalarında Araştırma Planlama ve Sunum Teknikleri

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Tıpta Araştırma Yayınları

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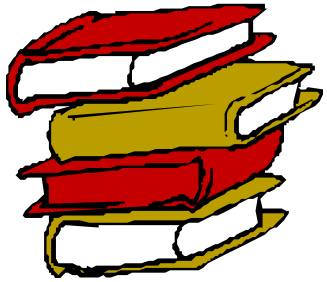

%90

Altman DG. The scandal of poor medical research. BMJ 1994:308;283-4

NEDEN?

- **Uygun olmayan veya yanlış araştırma tasarımı**
- Küçük örneklem
- Temsiliyet değeri olmayan örneklem
- Yanlış analiz
- Yanlış yorumlama ve çıkarımlar

İyi araştırma

- Doğru tasarım
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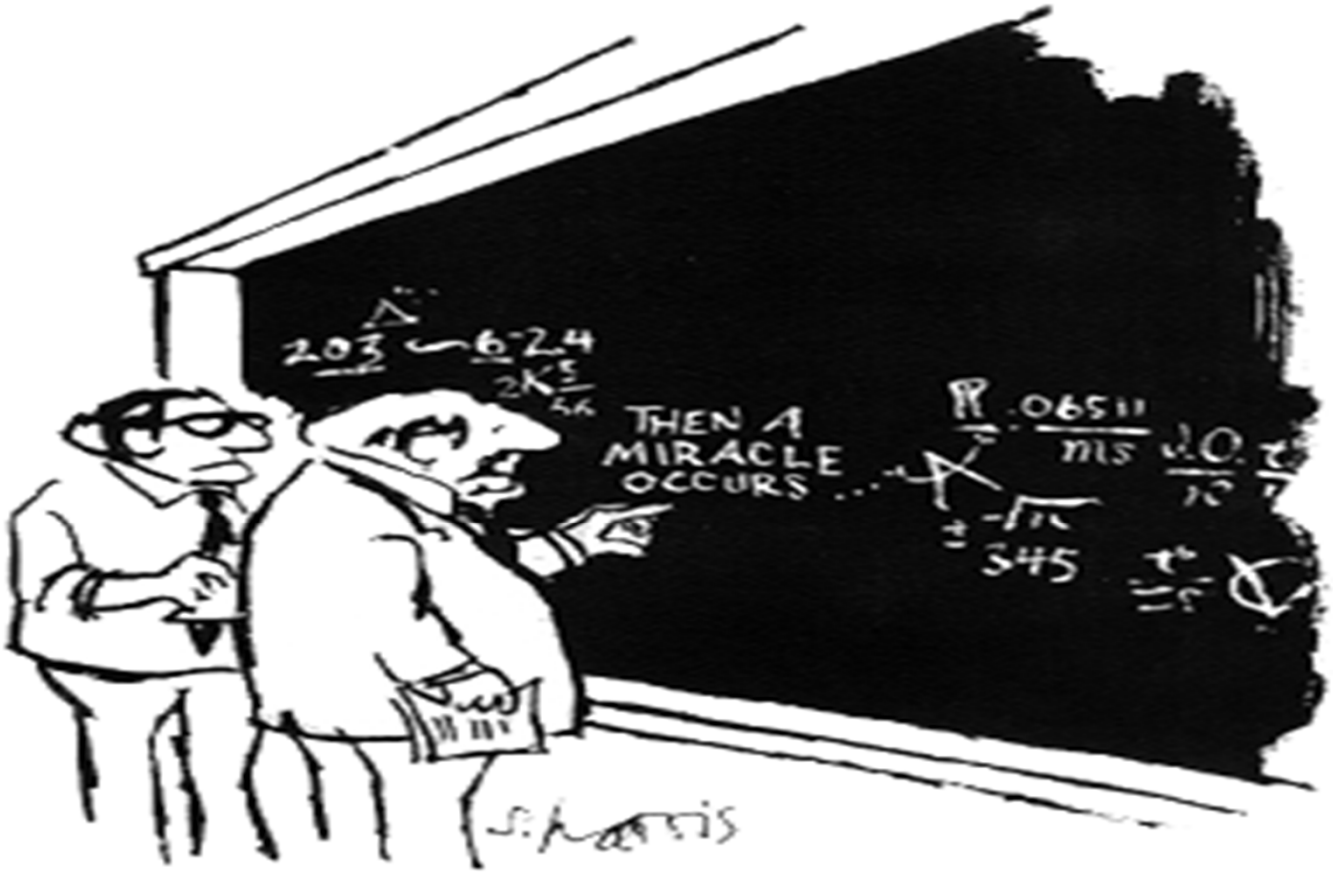
- Doğru tasarım
- Doğru analiz



"I think you should be more explicit here in step two."

Araştırma tasarımları:
Tanımlayıcı vs Analitik

Tanımlayıcı çalışmalar

- Vaka raporları
- Vaka serileri
- Sürveyans
  - Kayıt sistemleri (Registry)
  - Laboratuvar sonuçlarının yayınlanması

Vaka raporları/serileri/sürveyans

Çalışmada karşılaştırma kullanılmış mı?

1. Deneyimleri dokümante etmek ve paylaşmak: yeni, bilinmeyen, az rastlanan.....
2. Soru sormaya başlamak
3. **Neden-sonuç ilişkisine yanıt aranmamalı!**

➢ **Yararlı olduğu yerler**

- "İstisnaların" kaideleri bozduğu yerler
- Yeni hastalıklar
- Salgınlar
- Trend göstermek (sürveyans)

Chicken Soup Rebound and Relapse of Pneumonia: Report of a Case

Nancy L. Caroline, M.D., and Harold Schwartz, M.D.***

A case is reported in which a previously healthy individual, having received an inadequate course of chicken soup in treatment of mild pneumococcal pneumonia, experienced a severe relapse, refractory to all medical treatment and eventually requiring thoracotomy. The pharmacology of chicken soup is reviewed and the dangers of abrupt termination of therapy are stressed.

Chicken soup has long been recognized to possess unusual therapeutic potency against a wide variety of viral and bacterial agents. Indeed, as early as the twelfth century, the theologian, philosopher and physician, Moses Maimonides wrote, "Chicken soup . . . is recommended as an excellent food as well as medication."[1] Previous anecdotal reports regarding the therapeutic efficacy of this agent, however, have failed to provide details regarding the appropriate length of therapy. What follows is a case report in which abrupt withdrawal of chicken soup led to severe relapse of pneumonia.

Case Report

The patient is a 47-year-old male physician who had been in excellent health until 8 days prior to admission, when he experienced the sudden onset of rigors followed by fever to 105°F (40.5 C). He was seen by a physician at that time, when physical examination revealed a severely toxic man, unable to raise his head from the bed. Pertinent physical findings were limited to the chest, where rales were heard over the right middle lobe. Chicken soup was immediately begun in doses of 500 ml po q 4 hours. Defervescence occurred in 36 hours and a chest x-ray film taken 5 days prior to admission was entirely normal. Because he felt symptomatically improved, the patient declined further chicken soup after this time. He continued to feel well and remained afebrile until the night prior to admission, when he developed right upper quadrant pain, nausea and vomiting while on a visit to Vermont. His vomiting persisted through the night, and the following morning he boarded a plane for Cleveland. En route, he became severely dyspneic, and by the time he deplaned in Cleveland, he was cyanotic and in severe respiratory distress.

He was brought immediately to hospital where physical examination revealed an acutely ill man, febrile to 104°F (40.0°C), breathing shallowly 60 times per minute, with a pulse of 140. Physical findings were again chiefly limited to the chest, where bilateral pleural friction rubs, bibasilar rales and egophony over the right middle lobe were heard. Chest x-ray examination showed consolidation of the right middle lobe, infiltrates at both bases and a questionable right pleural effusion. White cell count was 7700 without a shift to the left. Electrolytes were within normal limits. Arterial blood gases on 6 liters/min of nasal oxygen were pH=7.51, P_{CO_2}=20 torr and P_{O_2}=50 torr. Gram stain of the sputum showed swarming diplococci, and multiple cultures of sputum and blood subsequently grew out type 4 Pneumococcus.

Chicken soup being unavailable, the patient was started on one million units q 6 hours of intravenous penicillin. Failure to respond led to increases of the dose up to 30 million units daily. Nonetheless, the patient remained febrile and his chest x-ray film showed progressive effusion and infiltration. On the twelfth hospital day he was taken to the operating room for a right thoracotomy. He thereafter made an uneventful recovery, maintained on 30 million units of penicillin daily during his postoperative course, and was discharged on the 25th hospital day.

Discussion

The therapeutic efficacy of chicken soup was first discovered several thousand years ago when an epidemic highly fatal to young Egyptian males seemed not to affect an ethnic minority residing in the same area. Contemporary epidemiologic inquiry revealed

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that the diet of the group not afflicted by the epidemic contained large amounts of a preparation made by boiling chicken with various vegetables and herbs. It is notable in this regard that the dietary injunctions given to Moses on Mount Sinai, while restricting consumption of no less than 19 types of fowl, exempted chicken from prohibition.[2] Some scholars[3] believe that the recipe for chicken soup[4] was transmitted to Moses on the same occasion, but was relegated to the oral tradition when the Scriptures were canonized. Chicken soup was widely used in Europe for many centuries, but disappeared from commercial production after the Inquisition. It remained as a popular therapy among certain Eastern European groups, however, and was introduced into the United States in the early part of this century. While chicken soup is now widely employed against a variety of organic and functional disorders, its manufacture remains largely in the hands of private individuals, and standardization has proved nearly impossible.

Preliminary investigation into the pharmacology of chicken soup (Bohbymycetin®) has shown that it is readily absorbed after oral administration, achieving peak serum levels in two hours and persisting in detectable levels for up to 24 hours. Parenteral administration is not recommended. The metabolic fate of the agent is not well understood, although varying proportions are excreted by the kidneys, and dosage should be appropriately adjusted in patients with renal failure. Chicken soup is distributed widely throughout body tissues and breakdown products having antimicrobial efficacy cross the blood-brain barrier. Untoward side effects are minimal, consisting primarily of mild euphoria which rapidly remits on discontinuation of the agent.

While chicken soup has been employed for thousands of years in the treatment of viral and bacterial illnesses, there have been no systematic investigations into the optimal course of therapy. The present case illustrates a possible hazard of abrupt chicken soup withdrawal: a previously healthy man, having received what proved to be an inadequate course of chicken soup for clinical signs of pneumonia, experienced a virulent relapse into severe bacterial pneumonia. It was not possible in this case to determine whether the relapse was caused by resistant organisms, as chicken soup was unavailable at the time treatment had to be restarted, and a synthetic product of lesser potency was used instead. Further study is needed to determine the most efficacious regimen for chicken soup. Pending such investigation, it would probably be more prudent to give a ten day course at full dosage, with gradual tapering thereafter and immediate resumption of therapy at the first sign of relapse.

References

1 Rosner F: Studies in Judaica: The Medical Aphorisms of Moses Maimonides. New York, Yeshiva University Press. 1971. Treatise 20, aphorism 67

2 Leviticus 11:13-19

3 Caroline Mrs Z (my mother). Personal communication

4 Bellin MG: Jewish Cookbook. New York, Garden City Books, 1958, pp 19-20 (recipe)

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MMWR Weekly

June 5, 1981 / 30(21);1-3

Epidemiologic Notes and Reports

Pneumocystis Pneumonia --- Los Angeles

In the period October 1980-May 1981, 5 young men, all active homosexuals, were treated for biopsy-confirmed *Pneumocystis carinii* pneumonia at 3 different hospitals in Los Angeles, California. Two of the patients died. All 5 patients had laboratory-confirmed previous or current cytomegalovirus (CMV) infection and candidal mucosal infection. Case reports of these patients follow.

Patient 1: A previously healthy 33-year-old man developed *P. carinii* pneumonia and oral mucosal candidiasis in March 1981 after a 2-month history of fever associated with elevated liver enzymes, leukopenia, and CMV viruria. The serum complement-fixation CMV titer in October 1980 was 256; in may 1981 it was 32.* The patient's condition deteriorated despite courses of treatment with trimethoprim-sulfamethoxazole (TMP/SMX), pentamidine, and acyclovir. He died May 3, and postmortem examination showed residual *P. carinii* and CMV pneumonia, but no evidence of neoplasia.

Patient 2: A previously healthy 30-year-old man developed *p. carinii* pneumonia in April 1981 after a 5-month history of fever each day and of elevated liver-function tests. CMV

International Journal of Antimicrobial Agents 34 (2009) 407–413

Contents lists available at ScienceDirect

International Journal of Antimicrobial Agents

journal homepage: http://www.elsevier.com/locate/ijantimicag

The ARESC study: an international survey on the antimicrobial resistance of pathogens involved in uncomplicated urinary tract infections

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ARTICLE INFO

ABSTRACT

Available online at www.sciencedirect.com
ScienceDirect
Diagnostic Microbiology and Infectious Disease 65 (2009) 414–426
DIAGNOSTIC MICROBIOLOGY AND INFECTIOUS DISEASE
www.elsevier.com/locate/diagmicrobio

Summary trends for the Meropenem Yearly Susceptibility Test Information Collection Program: a 10-year experience in the United States (1999–2008)

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Received 27 July 2009; accepted 28 August 2009

medical centers (2000–2008). The annual study protocols differed slightly over the testing years but, in general, dictated specific quotas of isolates among Gram-negative and Gram-positive pathogens to be submitted, up to a total of 200 isolates per medical center all originating from serious clinical infections in hospitalized patients. Due to intrinsic or

The Meropenem Yearly Susceptibility Test Information Collection (MYSTIC) Program was a longitudinal antimicrobial resistance surveillance study initiated in 1997; the program expanded to include other geographic regions and, for its final year (2008), had greater than 100 participant medical centers worldwide, located in Europe, North

Laboratuvara dayalı sürveyans

- **Biased sampling (hatalı örnekleme)**
  - Aynı hastadan alınan tekrarlı kültürler
  - Kolonizasyon vs infeksiyon etkeni
  - Hastaneden vs toplumdan kazanılmış
  - Hastane büyüklüğü, ağır hasta oranları
  - Doktora, servise, hastalığa bağlı oversampling
  - YBÜ
  - Salgınlar
- **Temsiliyet??**
- **Örneklem büyüklüğü**
  - Trend saptamak
  - Bir infeksiyon etkeni olarak farklı bakterilerin/suşların saptanması

Uluslararası sürveyans çözüm mü?

- Yukarıdaki sorunlara çözüm getirmiş olmalı!
- Yazılım var, laboratuvar kalitesine yönelik denetleme var ama epidemiyolojik metod yok
- EARS?
- SENTRY?
- MYSTIC ?
- Hastaya dayalı NNIS
- **Dirençli suşların *overrepresantation***
- **Antibiyotik kullanım direnç ilişkisi aranmamalı**

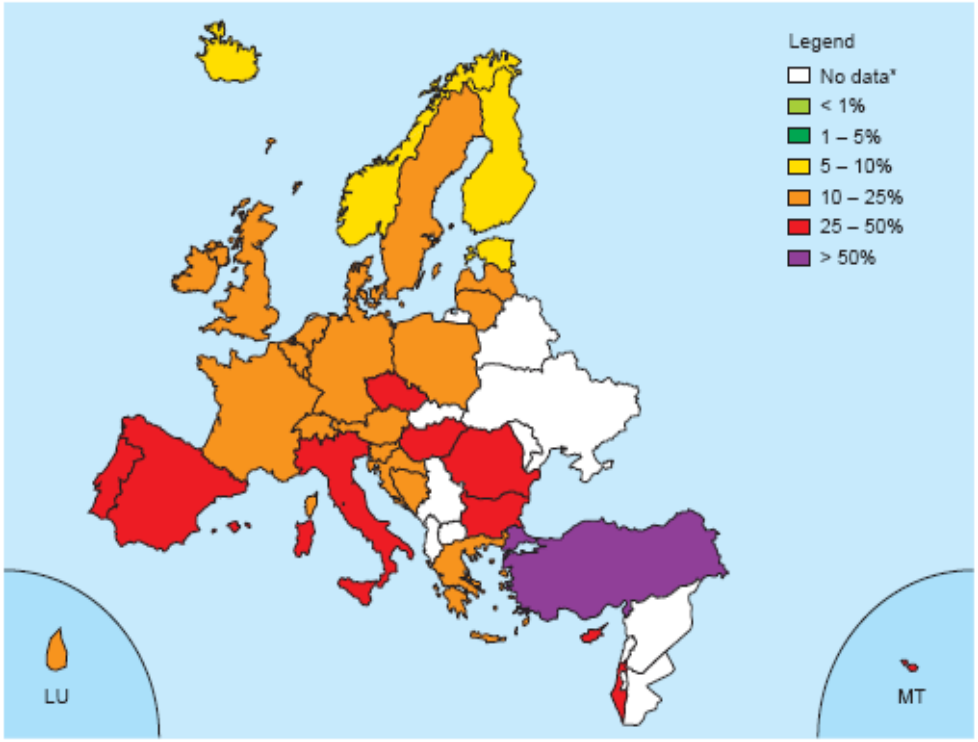
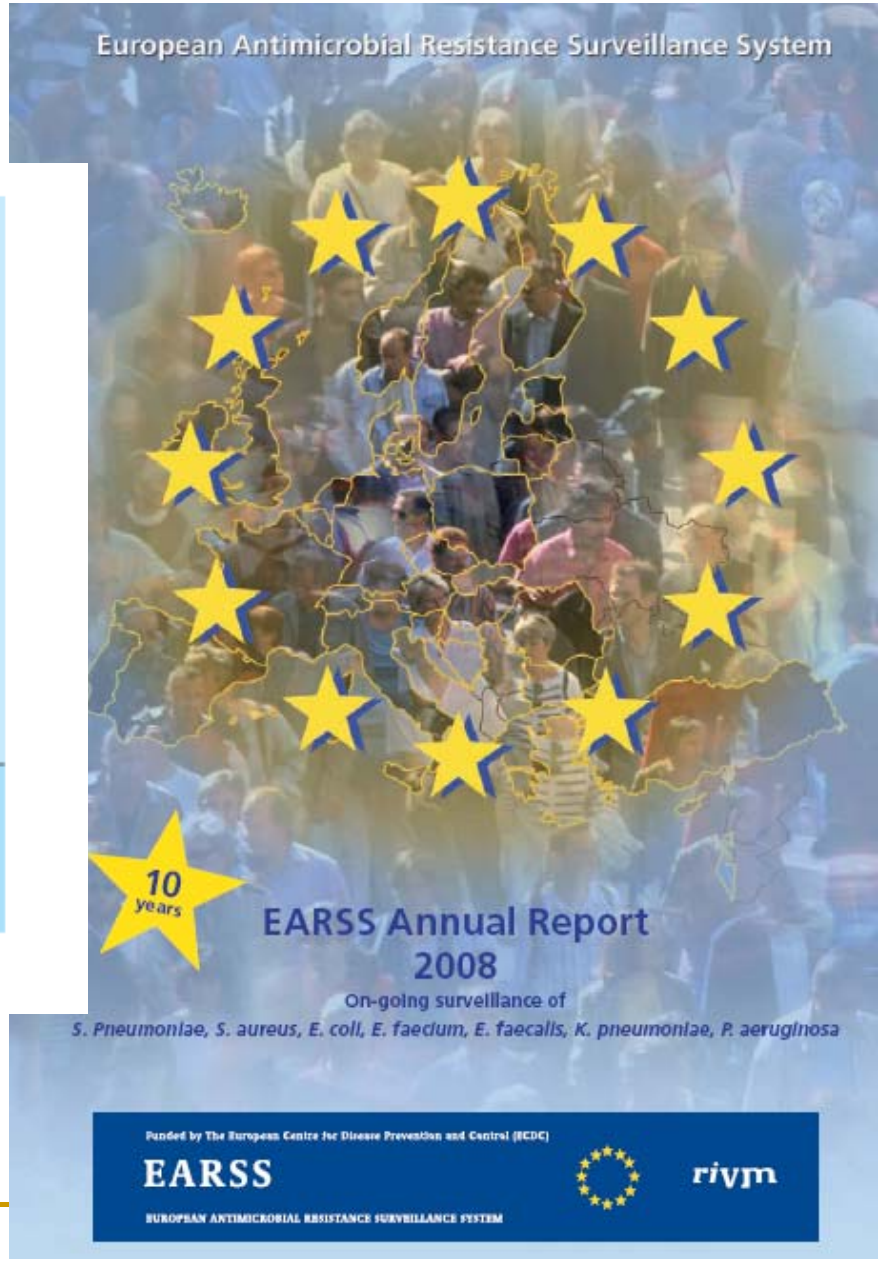


Figure 5.15. *Escherichia coli*: proportion of invasive isolates with resistance to fluoroquinolones in 2008.
* These countries did not report any data or reported less than 10 isolates.



To ensure sufficient representativeness of AST data within each country, atter given to the following minimum criteria for the selection of laboratories.

1) Laboratories from diverse regions

The laboratories that are selected should cover different regions and thereby represent the geographical diversity in terms of population density, socio-economic, ethnical and confessional mix of each country.

2) Reasonable coverage of population and hospital bed-days

Laboratories should be encouraged to participate in order to obtain a sufficiently large catchment area with a coverage which should exceed 20% of the national population.

3) Representative sample of hospitals

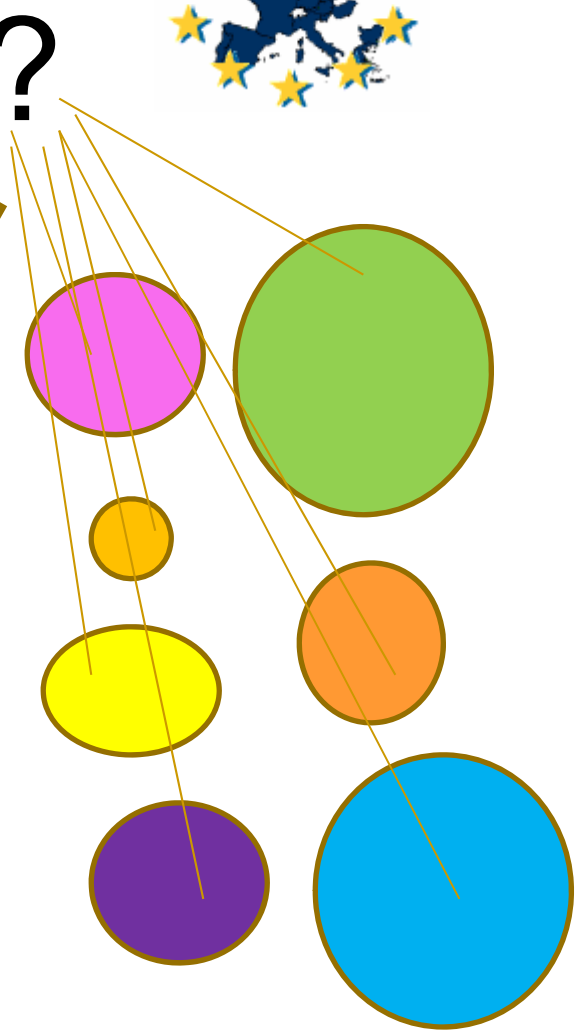
The laboratories selected should represent the distribution of both academic and non-academic hospitals i.e. tertiairy as well as secondary care (general) hospitals. Furthermore, in some countries other health care facilities like nursing homes deliver a substantial part of health care (to the elderly) and should also be included in the institutions under surveillance if possible.

Laboratories are asked to report the first isolate from blood or cerebrospinal fluid per patient per quarter

Uygun sürveyans nasıl?

- Tabakalandırarak örnek
  - Zaman
  - Her h
  -
  -
  -
  - Kalış süresi, altta yatanı vs vs
  - Salgınları fark edip o dönemlere çözüm

Randomize çalışma metodolojisi örnek alınmalı

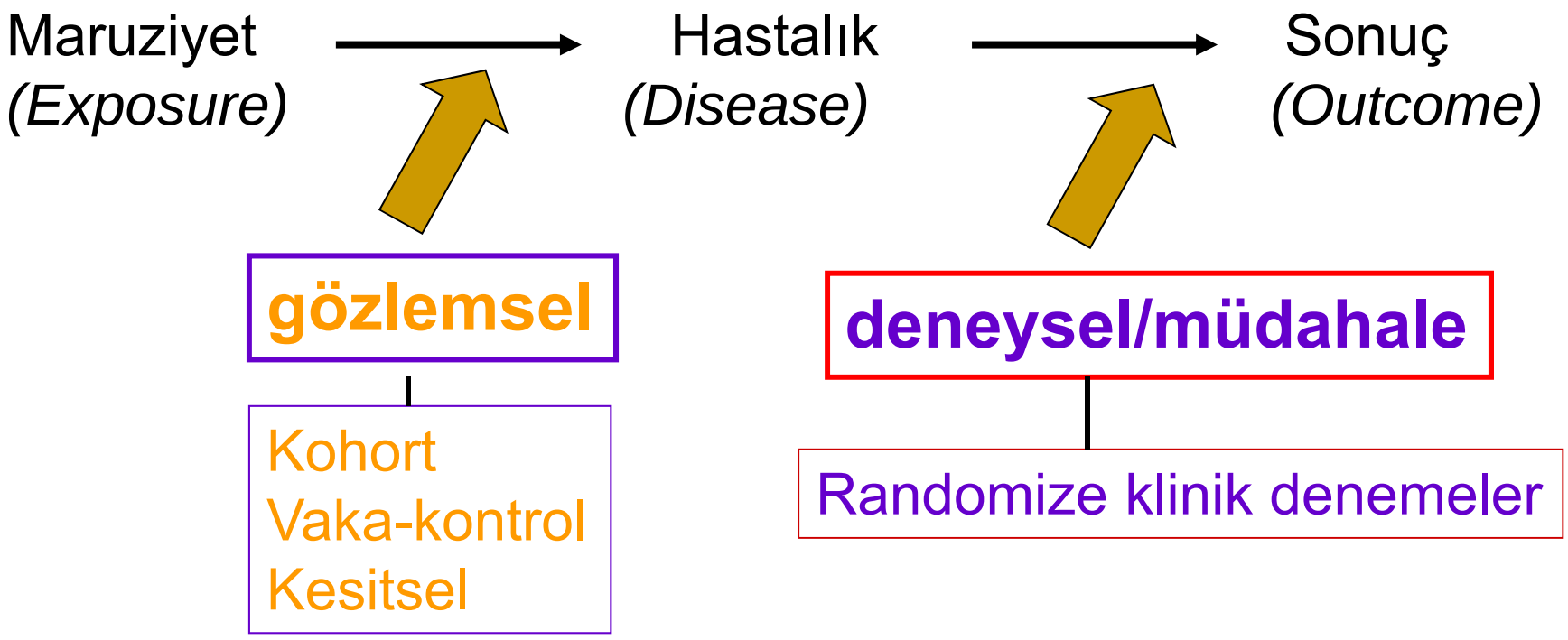


Araştırma tasarımları

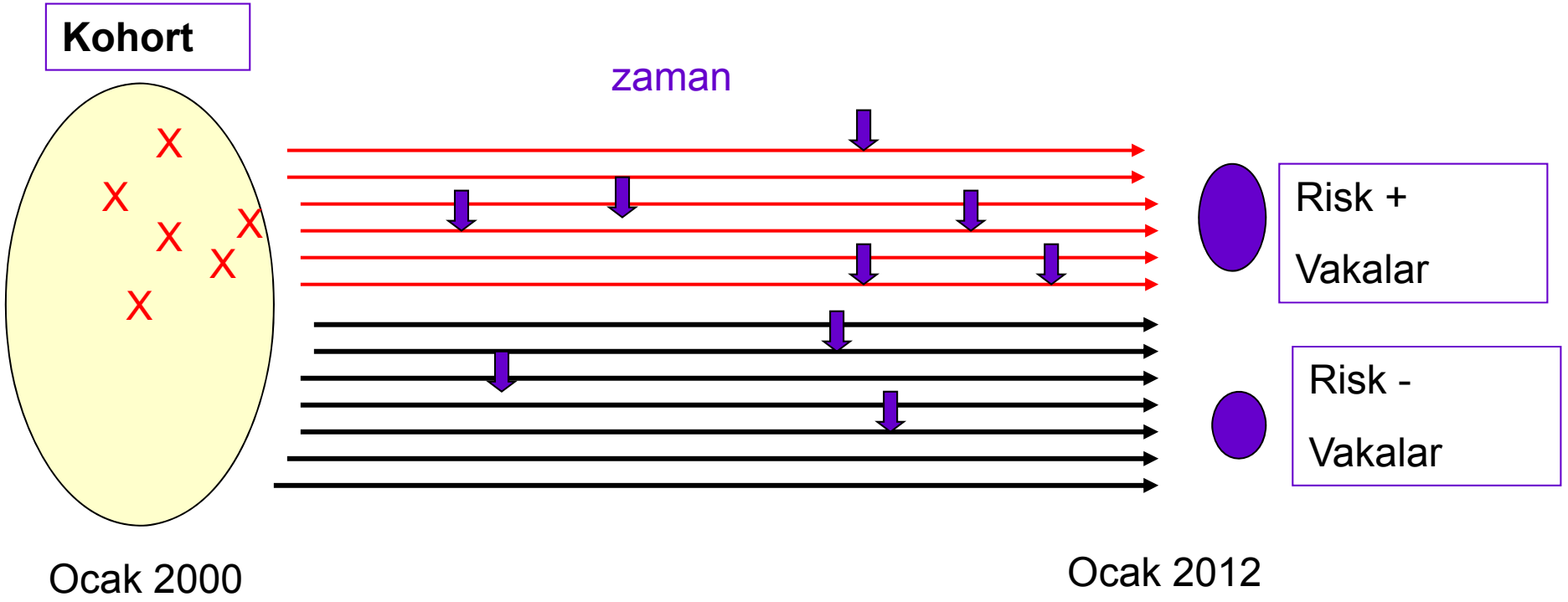
Analitik çalışmalar

- **Gözlemsel araştırmalar (Observational Studies)**
  - Kohort araştırmaları
  - Vaka-kontrol araştırmaları
  - Kesitsel araştırmalar
- **Müdahale araştırmaları (Interventional Studies)**
  - Randomize klinik denemeler (Randomized clinical trials)
  - Preventif saha çalışmaları
  - Yarı-deneysel çalışmalar (Quasi-experimental studies)
- **Metodolojik araştırmalar (Methodological Studies)**
  - Geçerlilik, güvenilirlik (validity/reliability) araştırmaları
  - Matematik modeller

Epidemiyoloji



Prospektif Kohort



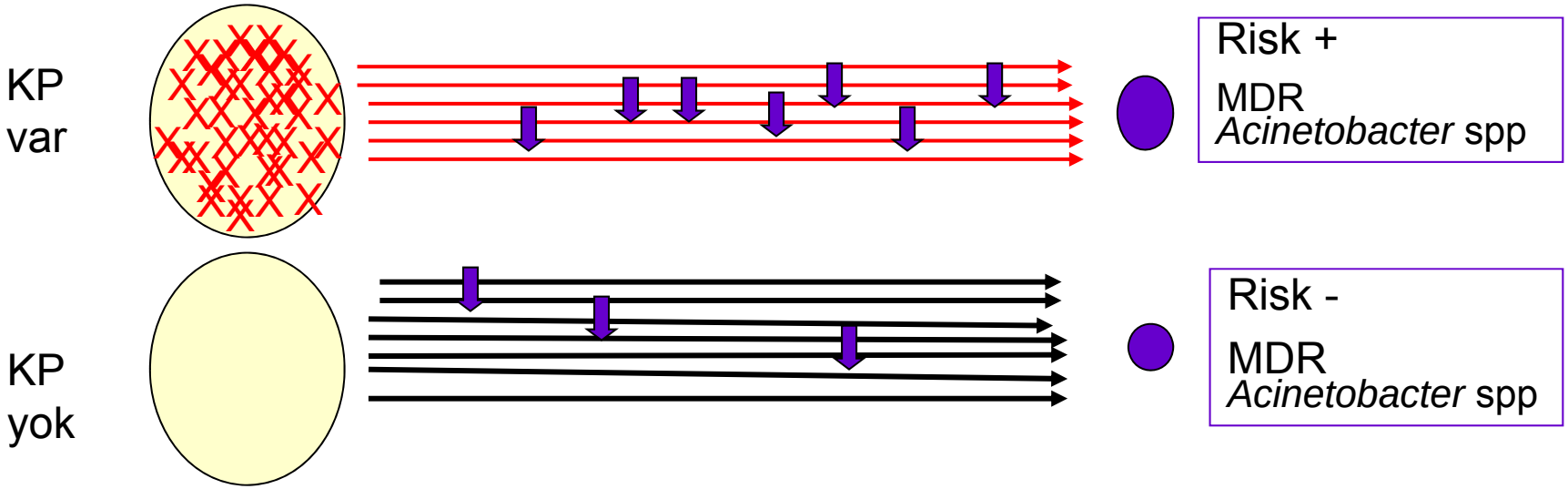
Kohort: Ortak bir özellikleri olan topluluk, çalışma grubu

Hasta değiller! Başlangıçta hasta olanlar çıkarılır.

Araştırılan hastalığa yakalanmaları mümkün = “At risk population”

Bazılarında risk faktörü VAR = maruziyet = *exposed*

Prospektif Kohort

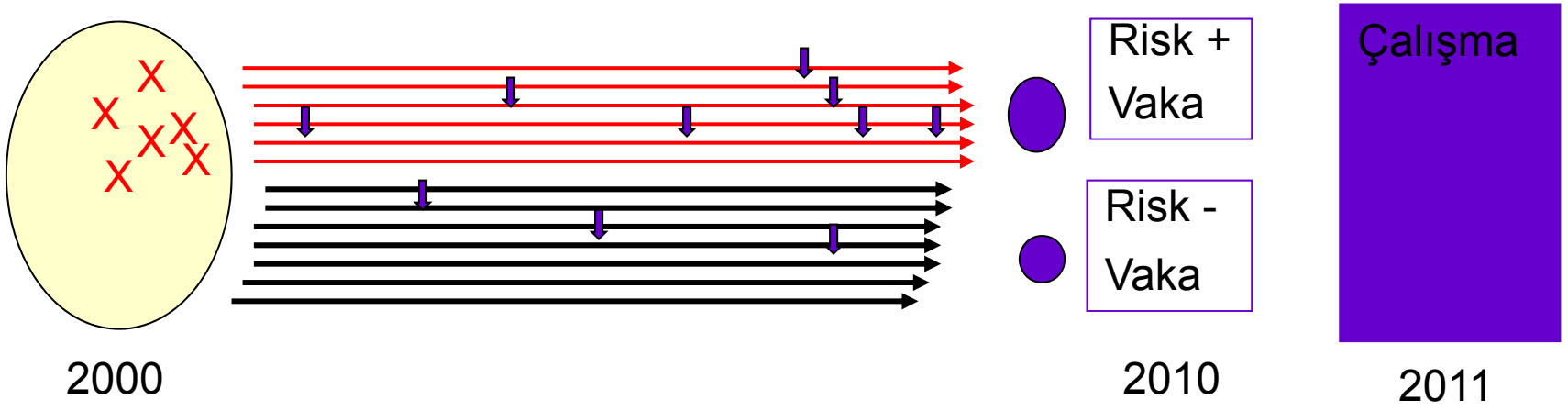


- 200 abx alan, 200 abx almayan hastayı izle
  - Kadın/erkek, yaş, altta yatan vb diğer risk faktörleri
- Maruziyet: Karbapenem alan vs karbapenem almayan
- Çalışma sonunda, her iki grupta MDR *Ab* infeksiyon oranları karşılaştırılır

Sonuç: MDR AB $_{\text{KP alanlarda}}$/ MDR AB $_{\text{KP ALMAyanlarda}}$ = **5**

95% CI: (2.1 - 7.8)

Retrospektif kohort



- Çalışma başladığında hastalık ortaya çıkmış olabilir
- Çalışma başlangıç ve bitiş tarihi belirlenir
- Hastalar, maruziyete göre (geçmiş) zaman içinde izlenir
- İyi kayıt varsa yapılabilir!

mrngrp	acctgrp	date	hospserv	stgen	ndgen	rdgen	amino	antistaph	bli	blipseud	carbepm	macrolid	clinda	metro	othbeta
1	40108	15-Oct-99	MEI	0	1	0	0	0	0	0	0	1	0	0	0
1	40108	16-Oct-99	MEI	0	1	0	0	0	0	0	0	1	0	0	0
1	40108	17-Oct-99	MEI	0	1	0	0	0	0	0	0	1	0	0	0
1	40108	18-Oct-99	MEI	0	0	0	0	0	0	0	0	1	0	0	0
2	35127	12-Feb-99	CDI	0	0	0	1	1	0	0	0	0	0	0	0
2	35127	13-Feb-99	CDI	0	0	0	1	1	0	0	0	0	0	0	0
2	35127	14-Feb-99	CDI	0	0	0	1	1	0	0	0	0	0	0	0
2	35127	15-Feb-99	CDI	0	0	0	0	0	0	0	1	0	0	0	0
20888	18488	7-Nov-96	GSI	0	0	0	0	0	0	0	1	0	0	0	0
20888	18488	8-Nov-96	GSI	0	0	0	0	0	0	0	0	0	0	0	0
20888	18488	9-Nov-96	GSI	0	0	0	0	0	0	0	0	0	0	0	0
20888	18488	10-Nov-96	GSI	0	0	0	0	0	0	0	0	0	0	0	0
20888	29437	1-May-98	MEI	0	0	0	0	0	0	0	0	0	0	0	0
20889	29437	2-May-98	MEI	0	0	0	1	0	0	0	0	0	0	0	0
20889	29437	3-May-98	MEI	0	0	0	1	0	0	0	0	0	0	0	0
20889	29437	4-May-98	MEI	0	0	1	0	0	0	0	0	0	1	0	0
20889	29437	5-May-98	MEI	0	0	1	0	0	0	0	0	0	1	0	0
20889	29437	6-May-98	MEI	0	0	1	0	0	0	0	0	0	1	0	0
20889	29437	7-May-98	MEI	0	0	1	0	0	0	0	0	0	0	0	0
20889	29437	8-May-98	MEI	0	0	1	0	0	0	0	0	0	0	0	0
20889	29437	9-May-98	MEI	0	0	0	0	0	0	0	0	0	0	0	0
20889	29437	10-May-98	MEI	0	0	0	0	0	0	0	0	0	0	0	0
20889	29437	11-May-98	MEI	0	0	0	0	0	0	0	0	0	0	0	0
20890	39646	27-Sep-99	CDI	0	0	0	0	0	0	0	0	0	0	0	0
20890	39646	28-Sep-99	CDI	0	0	0	0	0	0	0	0	0	0	0	0
20890	39646	29-Sep-99	CDI	0	0	0	0	0	0	0	0	0	0	0	0
20890	39646	30-Sep-99	CDI	0	0	0	0	0	0	0	0	0	0	0	0
20890	39646	1-Oct-99	CDI	0	0	0	0	0	0	0	0	0	0	0	0
20891	19007	9-Dec-96	OSI	1	0	0	0	0	0	0	0	0	0	0	0
20891	19007	10-Dec-96	OSI	1	0	0	0	0	0	0	0	0	0	0	0
20891	19007	11-Dec-96	OSI	1	0	0	0	0	0	0	0	0	0	0	0

Kohort Çalışma

- Hastanın aldığı her antibiyotik (*Collateral damage)*
- Altta yatan hastalıklar
- Hastalığın ağırlığı
- Bulaş
- Salgınlar
- Popülasyon düzeyinde kullanılan antibiyotik miktarı
  - Antibiyotik kullanımının indirek etkisi

Table 2: Hazard ratios showing the association between acquisition of a resistant strain and the use of main selecting antibiotic, at the individual- and ward-level. (Ward-level hazard ratio shows the increase in the hazard of having a resistant isolate for an additional 10% increase in use during the last 30 days in the ward where the patient was hospitalized)

	Selecting antibiotic		
Type of organism	**Use by a patient without previous sensitive culture (95% CI)**	**Use by a patient after a sensitive culture (95% CI)**	**Use in the ward (95% CI)**
Gram-positive			
MRSA	0·85 (0·39-1·84)	0·73 (0·32-1·67)	1·39 (0·87-2·22)
VRE	1·37 (0·87-2·17)	1·70 (0·81-3·57)	1·40 (1·07-1·83)
Gram-negative			
CAZ res. EB	2·30 (1·42-3·73)	11·17 (5·67-22·02)	1·24 (0·98-1·57)
CIP res. PA	2·08 (1·17-3·69)	4·41 (2·14-9·08)	1·05 (0·81-1·36)
IMP res. PA	3·02 (1·80-5·06)	7·92 (4·35-14·43)	1·40 (1·08-1·83)

EB: *Enterobacter* spp., **PA**: *P. aeruginosa*, **MRSA:** Methicillin resistant *S. aureus*, **VRE:** Vancomycin resistant *Enterococcus* spp., **CAZ**: Ceftazidime, **CIP**: Ciprofloxacin, **IMP**: Imipenem, **Res:** Resistant

Ascioglu, Lipsitch, Samore. 2012

Table 3: Association between the acquisition of a resistant strain and the use of antibiotics other than the selecting agent. (Ward-level hazard ratio shows the increase in the hazard of having a resistant isolate for an additional 10% increase in use during the last 30 days in the ward where the patient was hospitalized)

	Antibiotics other than the main selecting agent		
Type of organism	**Antibiotics**	**Use by the patient (95% CI)**	**Use at the ward HR (95% CI)**
Gram-positives			
MRSA	Carbapenems	1·45 (1·07-1·97)	1·19 (0·99-1·43)
	Quinolones	1·77 (1·3-2·42)	0·95 (0·76-1·20)
VRE	3rd Generation cephalosporins	1·80 (1·19-2·72)	1·36 (1·02-1·80)
Gram-negatives			
CAZ res. EB	Carbapenems	0·47 (0·27-0·83)	1·32 (1·03-1·69)
	Quinolones	0·26 (0·13-0·54)	0·78 (0·55-1·12)
	BLI combinations	1·61 (0·81-3·22)	2·24 (1·12-4·49)
CIP res. PA	Vancomycin	1·73 (1·03-2·90)	1·06 (0·84-1·33)
IMP res. PA	Aminoglycosides	1·95 (1·17-3·25)	1·20 (0·92-1·57)

EB: *Enterobacter* spp., **PA**: *P. aeruginosa*, **MRSA**: Methicillin resistant *S. aureus*, **VRE**: Vancomycin resistant *Enterococcus* spp., **BLI**: ß-lactamase inhibitor, **CAZ**: Ceftazidime, **CIP**: Ciprofloxacin, **IMP**: Imipenem, **Res**: Resistant

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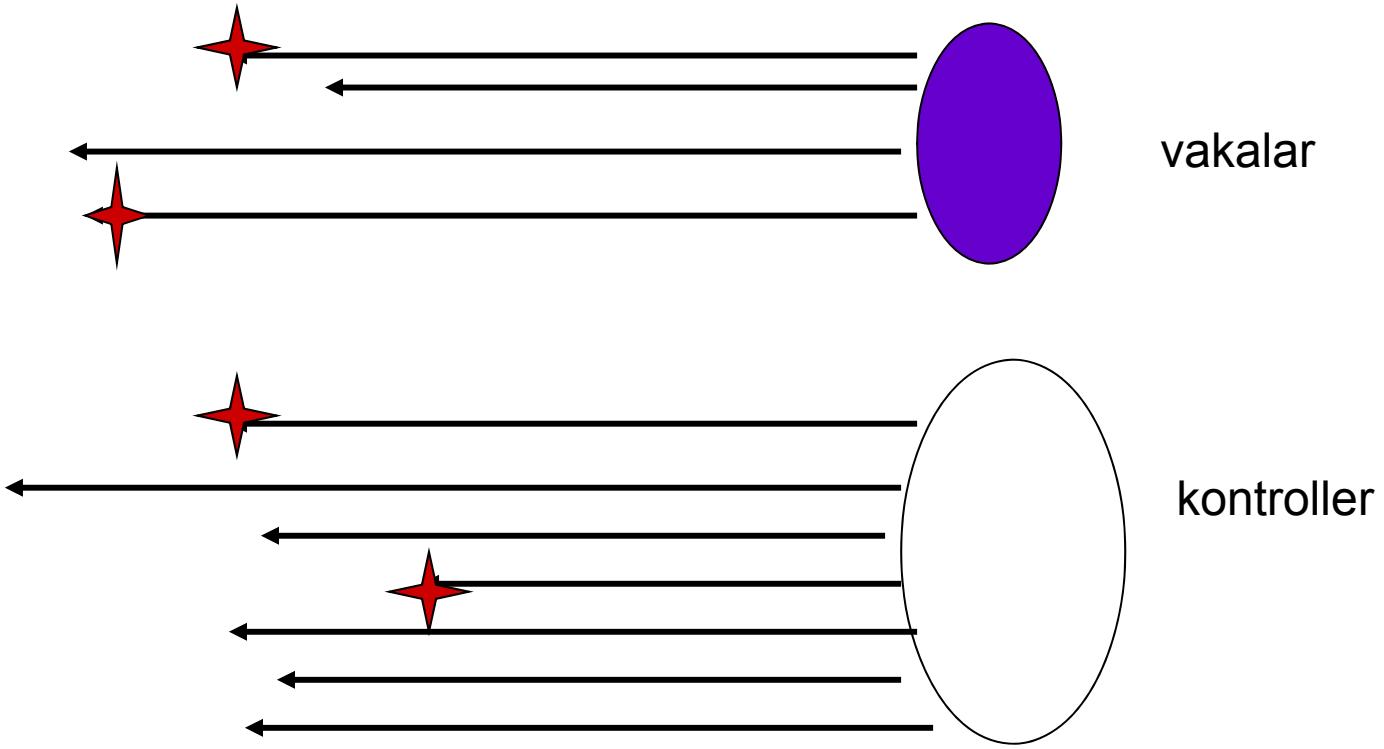
Vaka-Kontrol çalışmaları

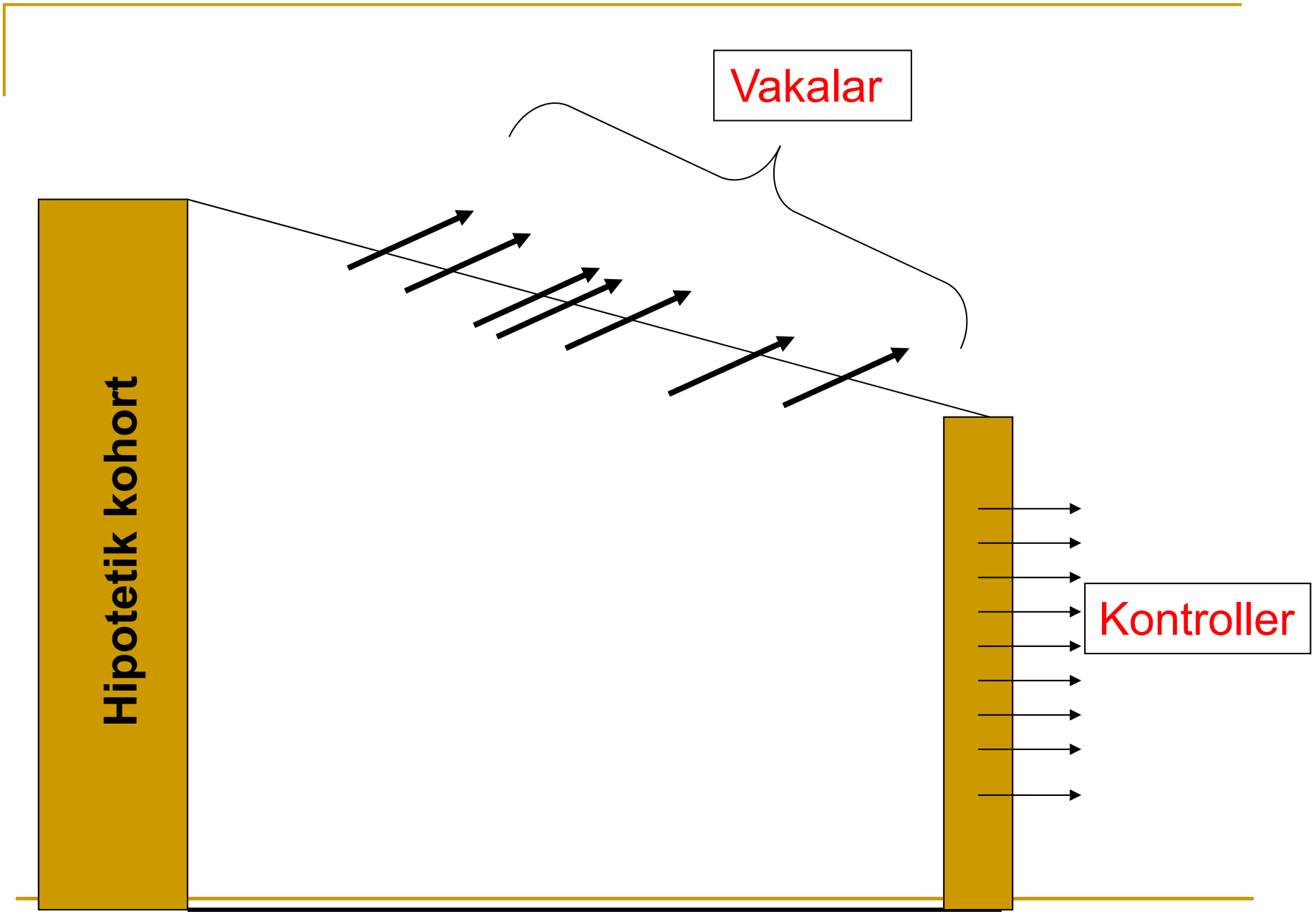


- Kontroller, tüm kohortu temsil etmelidir
- Maruziyetten tümüyle bağımsız olarak seçilmelidir
- Birden fazla kontrol seçilebilir, max: 4

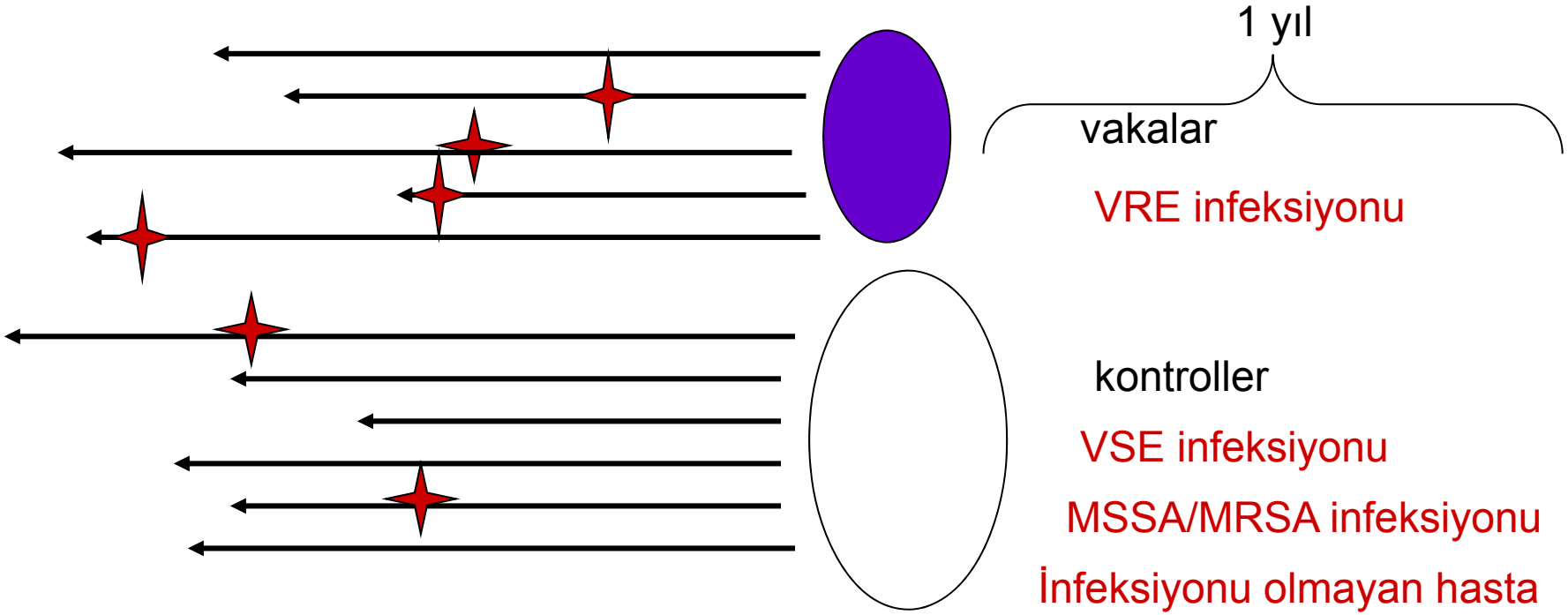
Vaka-kontrol çalışmalarda hatanın önlenmesi

- Vakalar ve kontroller aynı “hipotetik” popülasyondan gelmeli
- Kontroller vakaların içinden çıktığı referans popülasyonu temsil etmeli

D. L. Sackett
“I would trust only 6 people in the world to do a proper case-control study”

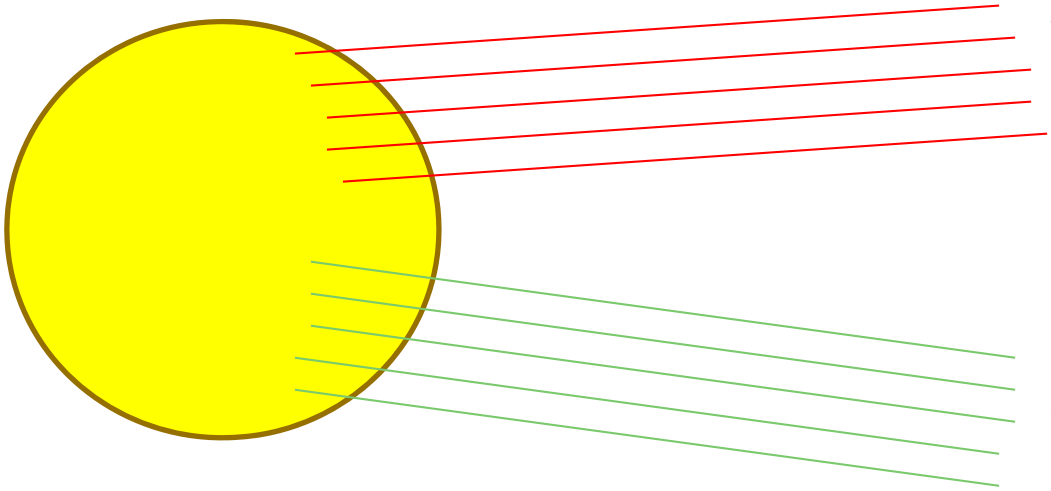

Vakalar
Hipotetik kohort
Kontroller

Vaka-Kontrol çalışmaları



- Karbapenem kullanımı VRE infeksiyonu için risk faktörü müdür?
- **Vaka**: 1 yıl boyunca, VRE infeksiyonu olan150 hasta
- **Kontrol**: Aynı süre boyunca VRE infeksiyonu olmayan 300 hasta
- Yaş, altta yatan hastalık eşleştirilebilir ama.....

Antibiyotik direnç çalışmalarında kontrol grubu seçimi



- Kontrol grubu infekte olmayan hastalar olmalı
- İkinci bir vaka grubu olarak VSE hastaları olabilir
- Her iki vaka grubunu infekte olmayanlarla karşılaştır
  - Vaka-vaka-kontrol tasarımı

Örnek 2

- Dahiliye yoğun bakımda çoklu dirençli *Acinetobacter* spp'e bağlı VİP salgını
- Kontrolleri kimlerden seçelim?
  - Duyarlı *Acinetobacter* spp. VİP'i olan vakalar?
  - Yan taraftaki Cerrahi YB'da VİP olan hastalar?
  - O dönem içinde Dahiliye YB'da VİP'i olmayan hastalar?
  - O dönem içinde Dahiliye YB'da yatan ve ventilatöre bağlı fakat VİP'i olmayan hastalar?

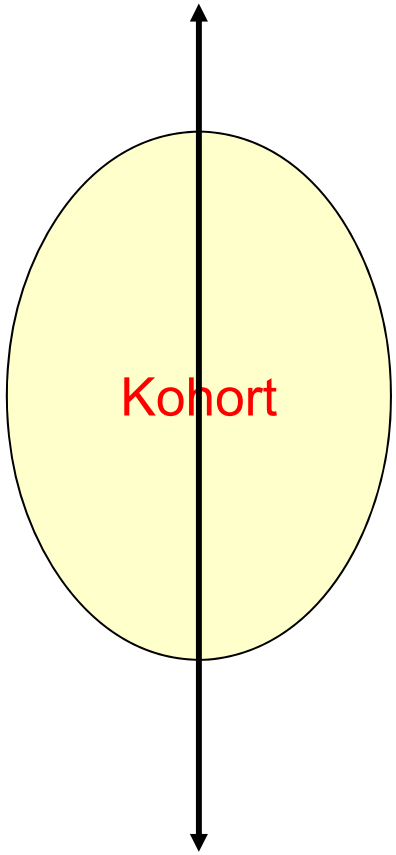
KOHORT

- Hastalığın insidansı/riski bulunur (relatif risk hesaplanabilir)
- Yanlılık ve hata daha azdır
- Ölçümler kayıtlar iyidir
- Birden fazla hastalık çalışılabilir
- Zor
- Pahalı
- Uzun süre alır

VAKA-KONTROL

- Çabuk
- Kolay
- Küçük
- Tek hastalık çalışılabilir
- Relatif risk hesaplanamaz
  - Bazı koşullar sağlanırsa OR relatif riski tahminin ettirir
- İnsidans hesaplanamaz
- Hata, yanlılık çok kolay

Kesitsel çalışmalar



- Kohort'un fotoğrafı çekilir
- Maruziyet ve hastalık aynı anda belirlenir
- Sadece prevelans saptanabilir
- Politika belirleme, maliyet vb

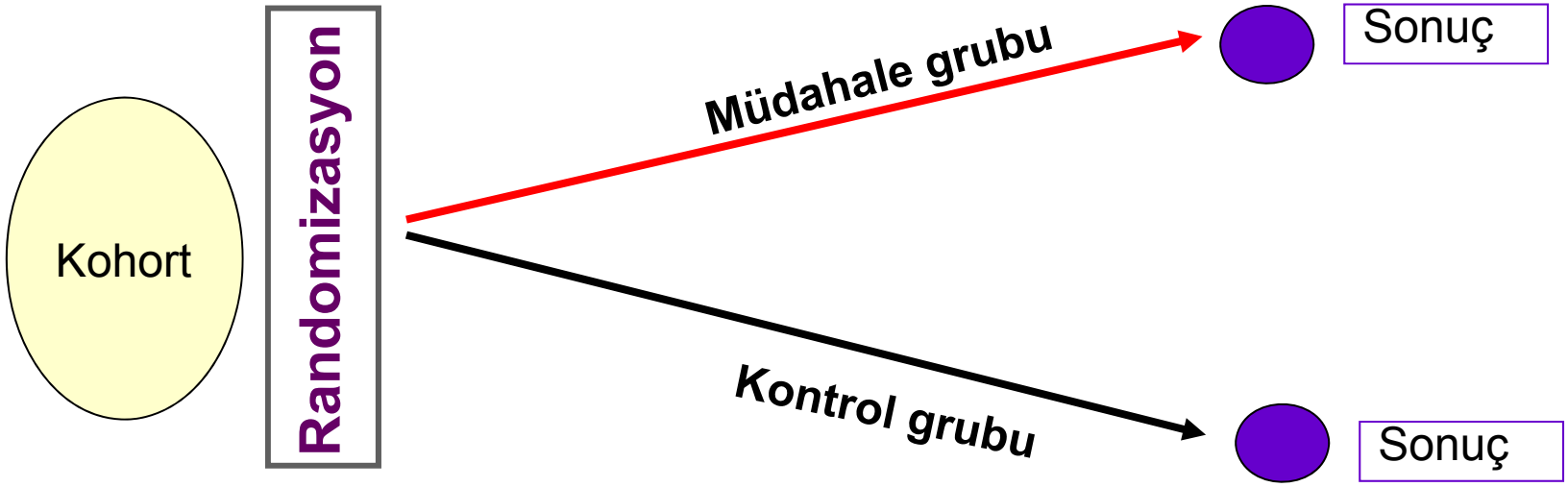
Araştırma tasarımları

Analitik çalışmalar

- **Gözlemsel araştırmalar (Observational Studies)**
  - Kohort araştırmaları
  - Vaka-kontrol araştırmaları
  - Kesitsel araştırmalar
- **Müdahale araştırmaları (Interventional Studies)**
  - Randomize klinik denemeler (Randomized clinical trials)
  - Preventif saha çalışmaları
  - Yarı-deneysel çalışmalar (Quasi-experimental studies)
- **Metodolojik araştırmalar (Methodological Studies)**
  - Geçerlilik, güvenilirlik (validity/reliability) araştırmaları
  - Matematik modeller

Randomize kontrollü klinik denemeler

"*Randomized controlled clinical trials*"



- İlaç ve tedavi çalışmalarında ALTIN STANDARD!
- Prospektif kohortun bir tipi
- Hastaların hangi tedavi grubunda olacağı randomizasyonla belirlenir
  - Yeni ilaç vs standard tedavi (plasebo)

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Intervention to Reduce Transmission of Resistant Bacteria in Intensive Care

W. Charles Huskins, M.D., Charmaine M. Huckabee, M.S., Naomi P. O'Grady, M.D., Patrick Murray, Ph.D., Heather Kopetskie, M.S., Louise Zimmer, M.A., M.P.H., Mary Ellen Walker, M.S.N., Ronda L. Sinkowitz-Cochran, M.P.H., John A. Jernigan, M.D., Matthew Samore, M.D., Dennis Wallace, Ph.D., and Donald A. Goldmann, M.D., for the STAR*ICU Trial Investigators*

ABSTRACT

BACKGROUND

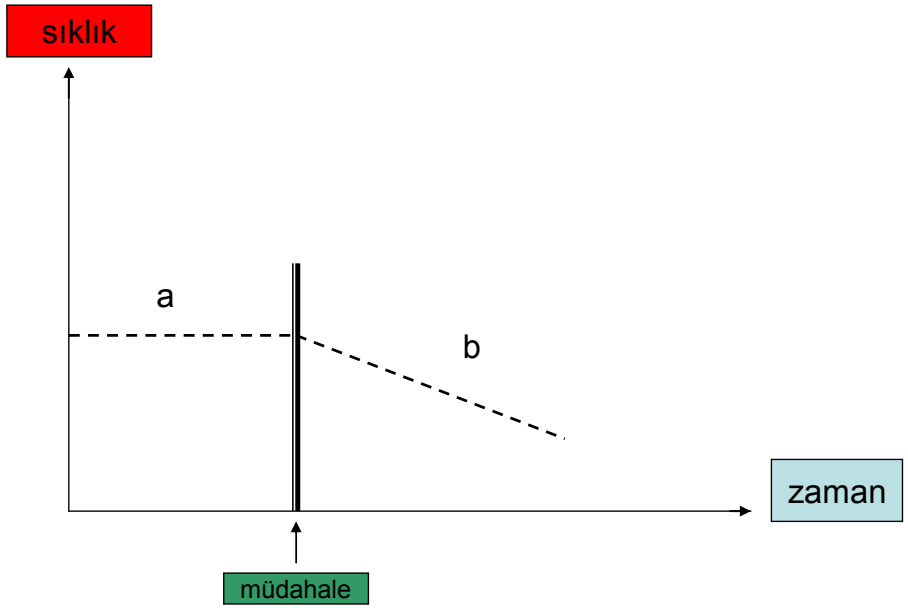
Intensive care units (ICUs) are high-risk settings for the transmission of methicillin-resistant *Staphylococcus aureus* (MRSA) and vancomycin-resistant enterococcus (VRE).

METHODS

In a cluster-randomized trial, we evaluated the effect of surveillance for MRSA and VRE colonization and of the expanded use of barrier precautions (intervention) as compared with existing practice (control) on the incidence of MRSA or VRE colonization or infection in adult ICUs. Surveillance cultures were obtained from patients in all participating ICUs; the results were reported only to ICUs assigned to the intervention. In intervention ICUs, patients who were colonized or infected with MRSA or VRE were assigned to care with contact precautions; all the other patients were assigned to care with universal gloving until their discharge or until surveillance cultures obtained at admission were reported to be negative.

Yarı-deneysel çalışmalar

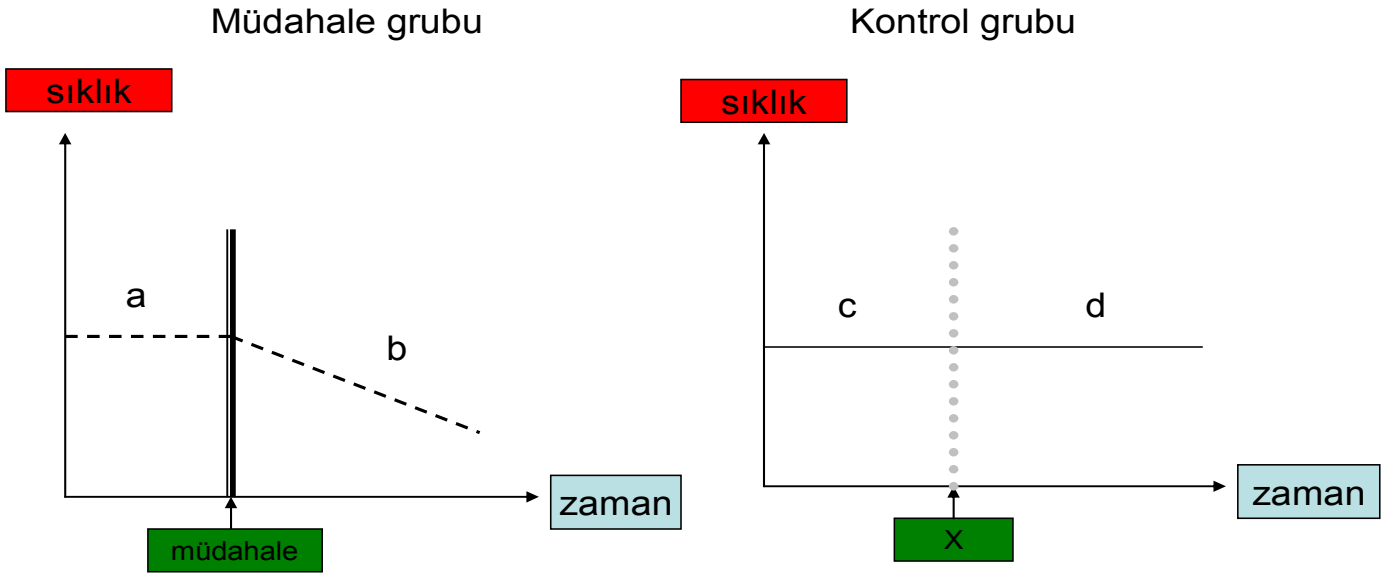
YBÜ`de el antiseptiği kullanımı



a müdahale öncesi VRE görülme sıklığı
b müdahale sonrası VRE görülme sıklığı

Yarı-deneysel çalışmalar

Şekil 6



a Dahili yoğun bakımda müdahale öncesi VRE görülme sıklığı

b Dahili yoğun bakımda müdahale sonrası VRE görülme sıklığı

c Cerrahi yoğun bakımda VRE görülme sıklığı

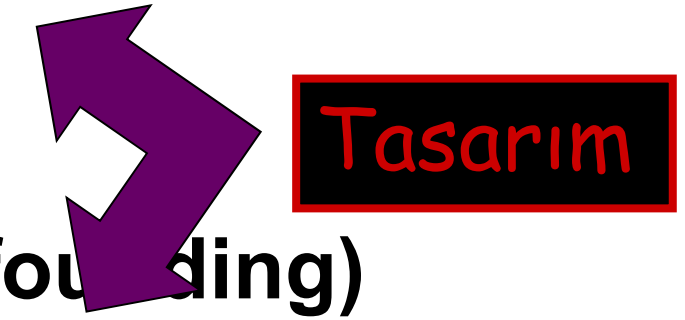
d Cerrahi yoğun bakımda VRE görülme sıklığı

x Dahili yoğun bakımdaki müdahale zamanı

Karıştırıcı Etken (Confounding)

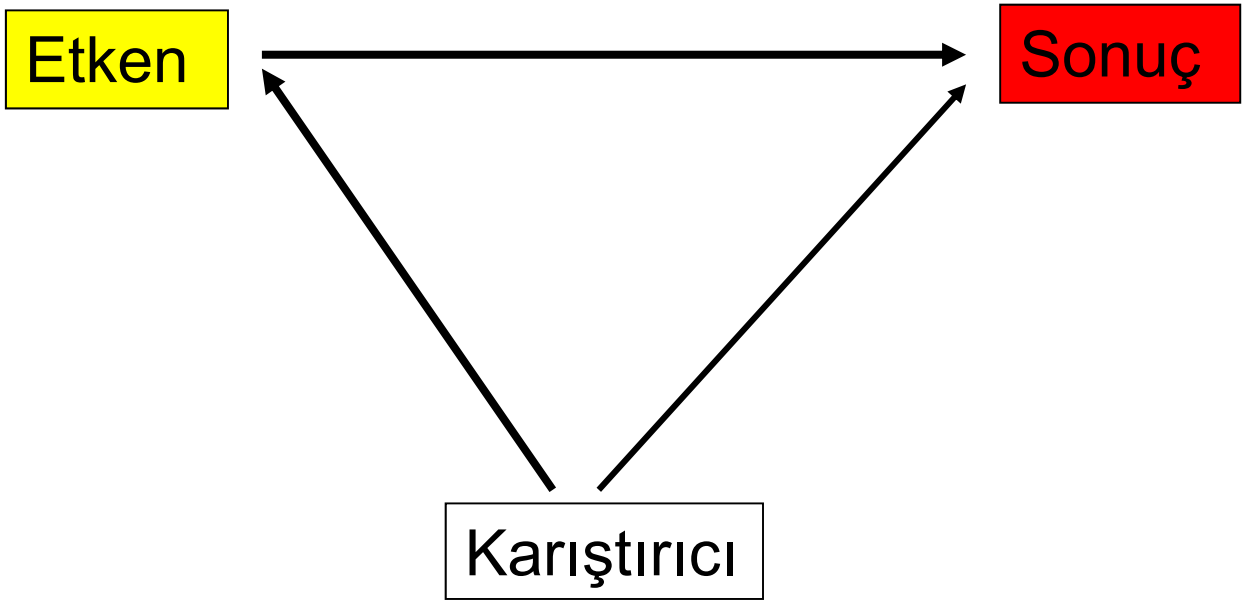
Araştırma sonuçları

1. **Doğru**
2. **Hata/Yanlılık (Bias)**
3. **Karıştırıcı etken (Confounding)**
4. **Şans**



Karıştırıcı Etken (Confounding)

- Baktığınız etkenle sonuç arasında, başka bir etkenden dolayı bir ilişki varmış gibi sonuç çıkması

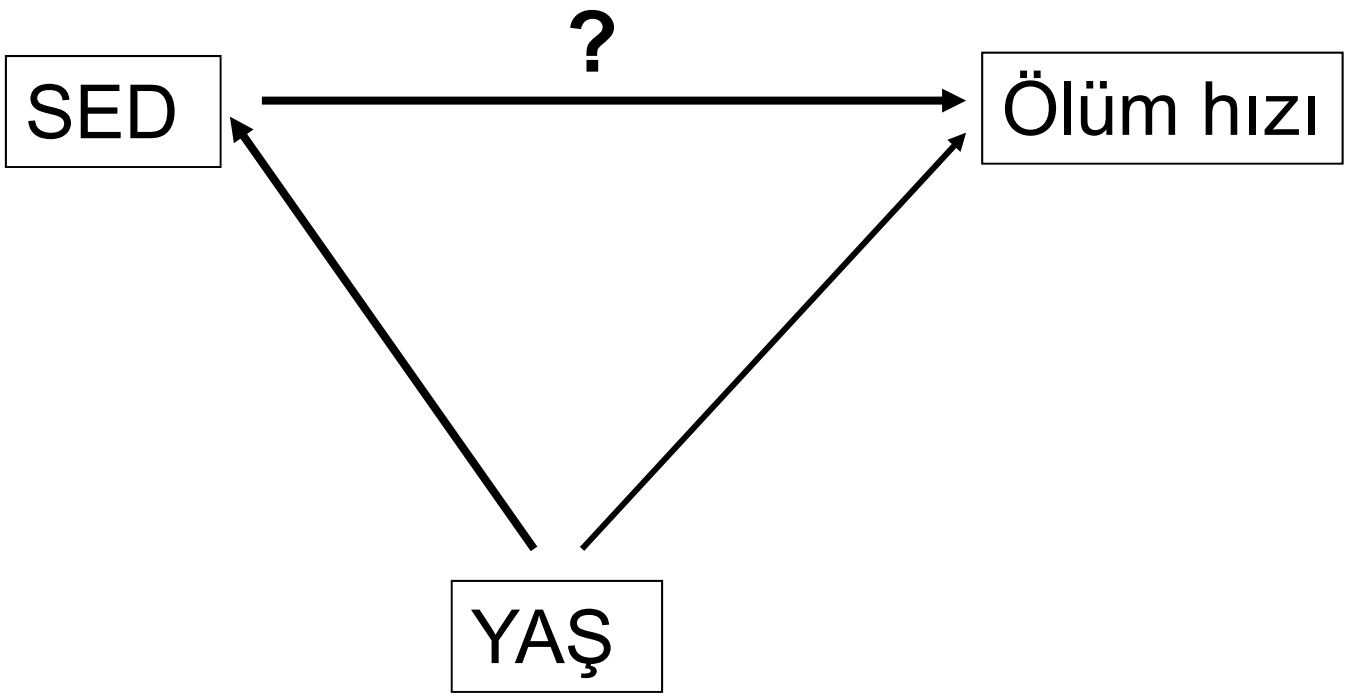


- Araştırmanın amacı:
  - SED vs Mortalite?

- Veri:
  - Kosta Rika: 3.8 / 1000
  - Venezuela: 4.4 / 1000
  - Meksika: 4.9 / 1000
  - Kanada: 7.3 / 1000
  - ABD: 8.7 / 1000

Zenginlik ⟶ ↑ ölüm hızı

Örnek 1



Karıştırıcı etken kontrol edilmiş
Adjusting (controling) for confounding

- Ülkelerin yaş ortalamaları analize katıldığında
  - Kosta Rika: 3.7 / 1000
  - Venezuela: 4.6 / 1000
  - Meksika: 5 / 1000
  - Kanada: 3.2 / 1000
  - ABD: 3.6 / 1000

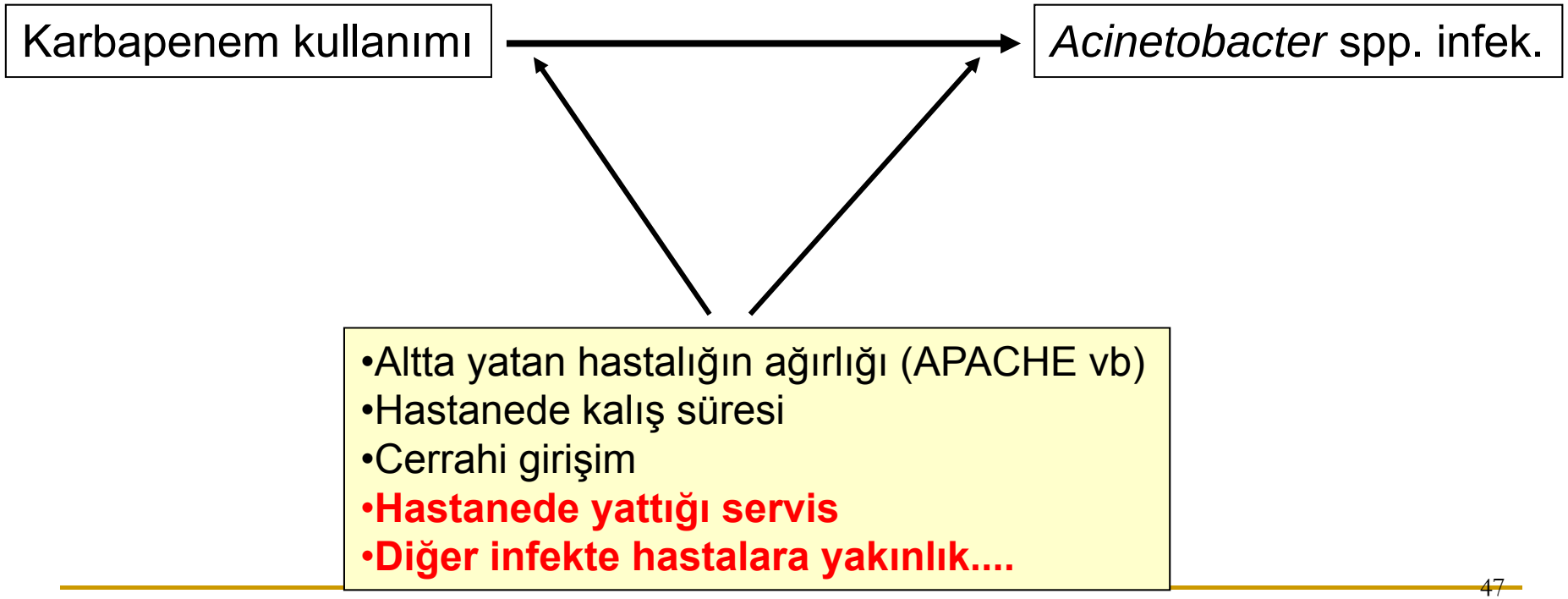
Nasıl başa çıkılır?

- Araştırılan durumla ilgili temel bilgi
- Karıştırıcı etkenle ilgili verinin toplanması
- Araştırma planlanması veya analiz sırasında kontrol

  Randomizasyon
  - Kısıtlama (Restriction)
  - Eşleştirme (Matching)
  - Tabakalama (Stratification)
  - Çoklu değişkenli (Multivariable) analizler
    - Lojistik regresyon
    - Linear regresyon
    - vb.

Örnek 2

- Araştırma sorusu: Çoklu dirençli *Acinetobacter* spp. infeksiyonlarında karbapenem kullanımı risk faktörü müdür?



Sunum

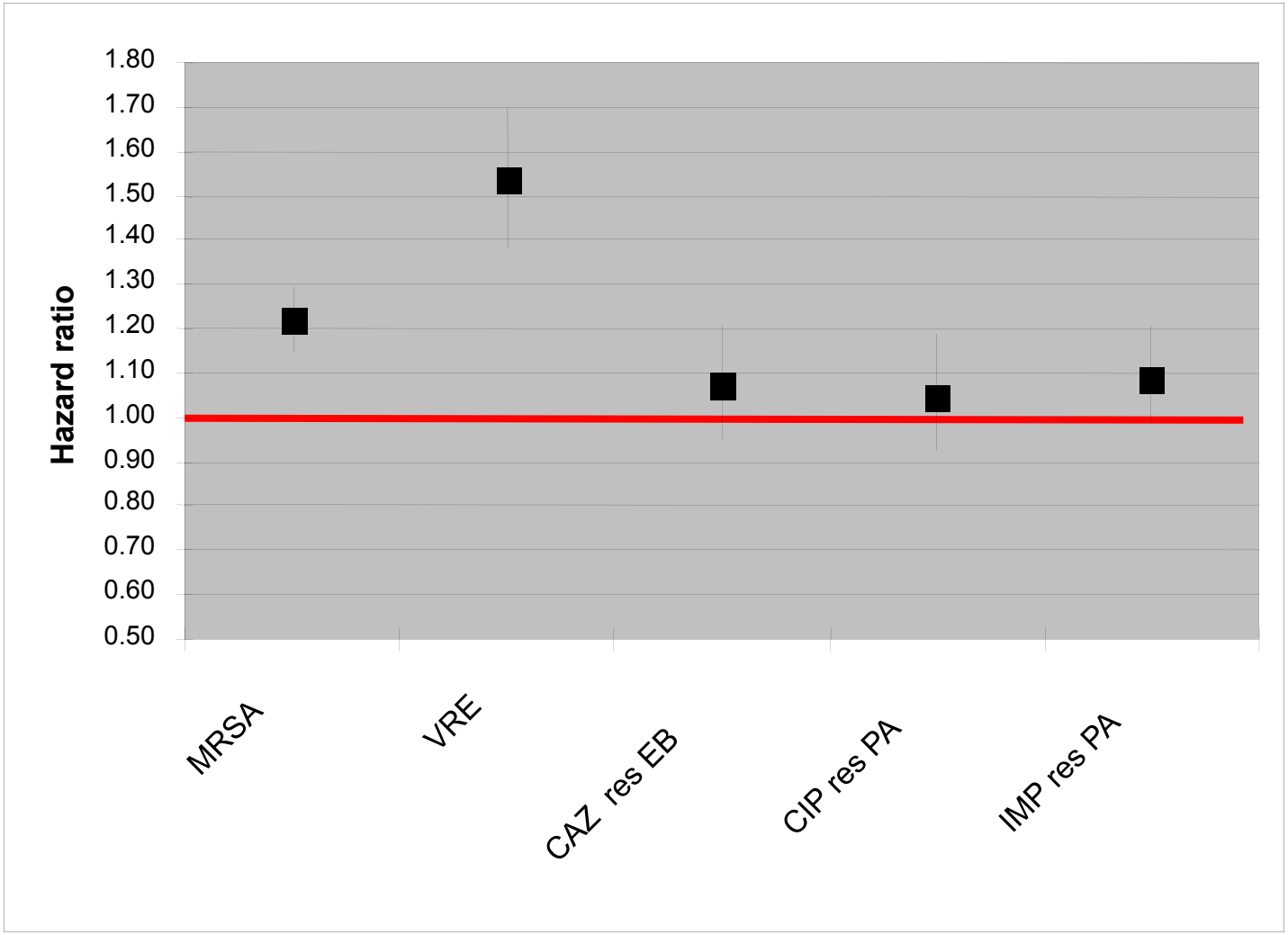
Bazı önemli noktalar

Sonuçlar

- P-değeri
  - Tam değer neyse onu belirtin
  - <0.05 veya >0.05 YAZMAYIN

- Araştırdığınız ilişkiyi özetleyen kestirim parametreleri [95% güven aralığı] kullanın
  - Odds oranı, risk, hazard oranı vs

Figure 1. Hazard ratios showing the effect of previous incidence of infection in the same ward on acquiring a subsequent resistant infection



Tablolar

- Sayılar, yüzdeler ve toplamlar aynı tobloda olmalı VEYA tablodan net olarak hesaplanabilmeli
- Vertikal çizgiler koymayın
- Bilmece yaratmayın
- Noktadan sonraki basamakları minimal tutun
  - Direnç oranları için 1'den fazlaya hiç gerek yok
- Bir pattern varsa onu görünür hale getirin
  - Yıllar içinde artan direnç oranları vb
- Sıfır ve eksik veriyi ayırd edin

Grafikler (Data visualization)

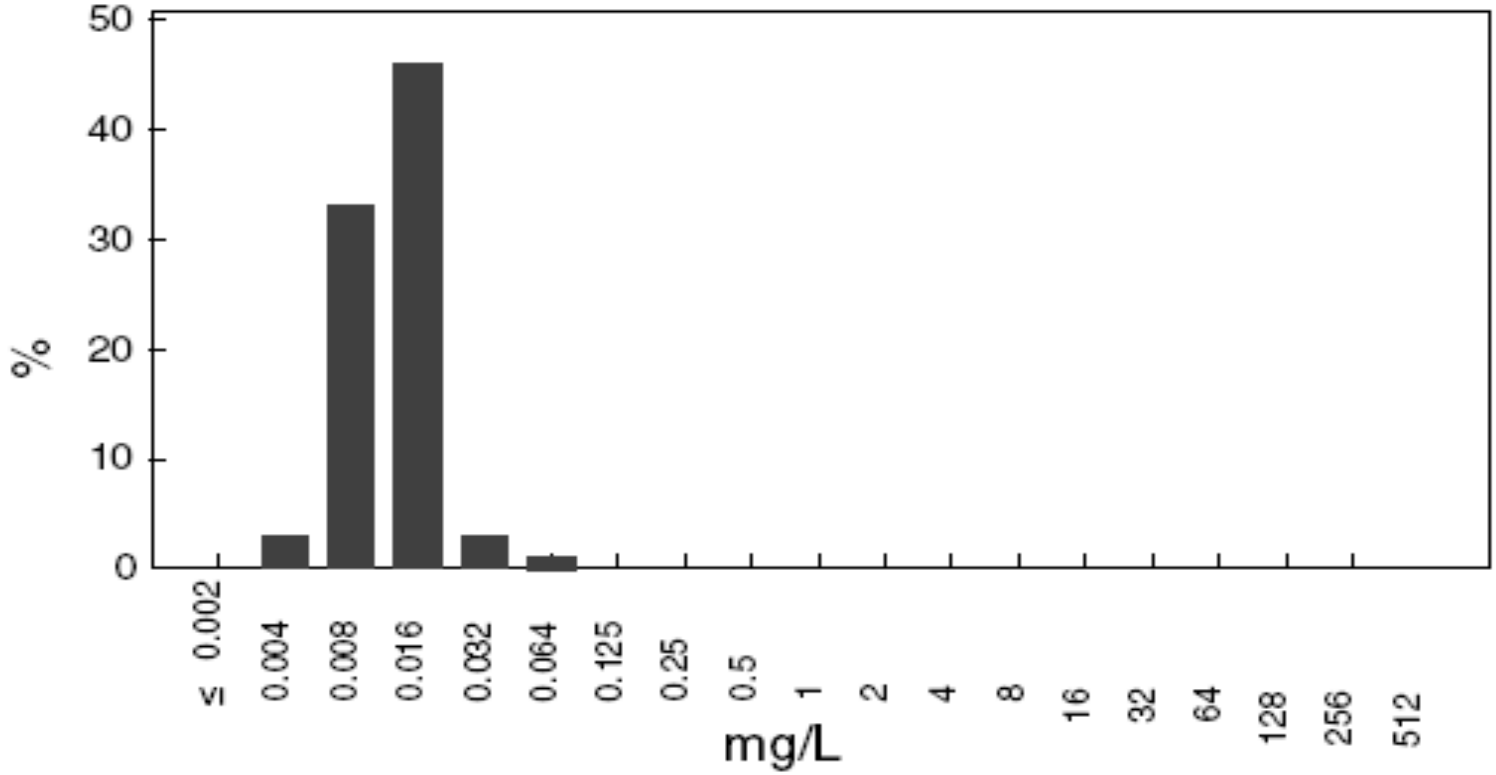
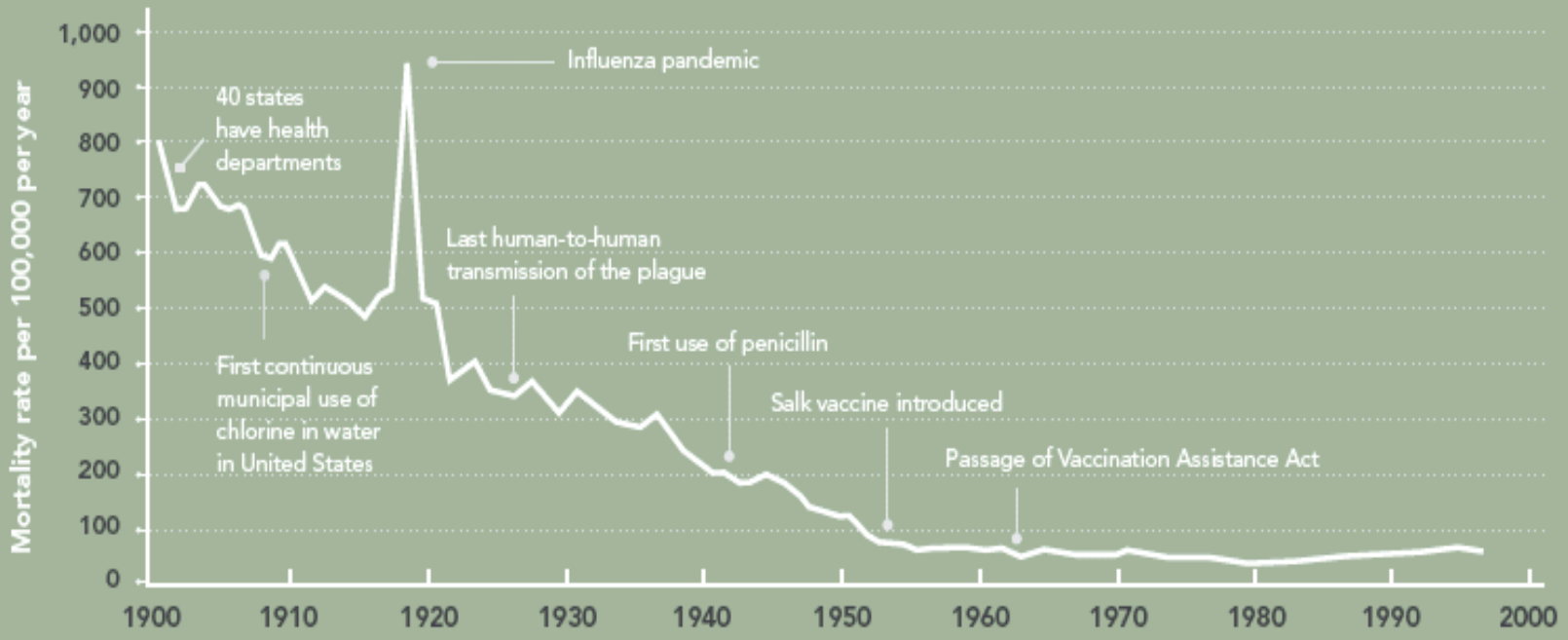


FIGURE 1.1

Crude infectious disease mortality rate in the United States, 1900–1996



Source: Adapted from Armstrong, Conn et al. (1999).

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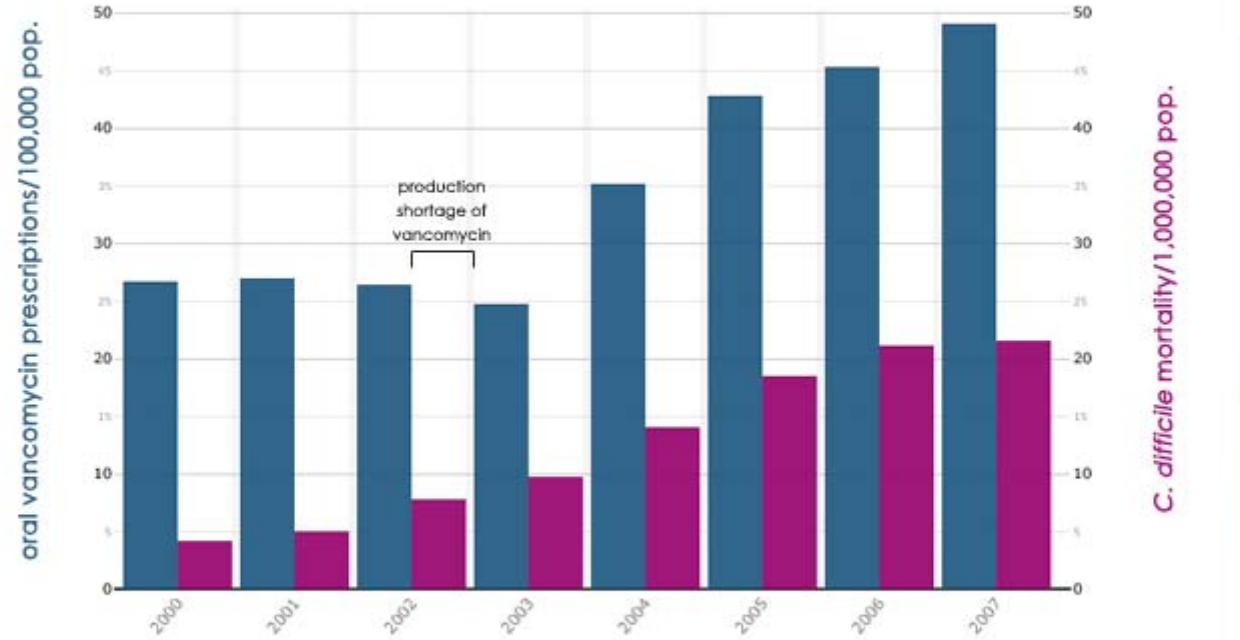
RESOURCES FOR THE FUTURE

Oral vancomycin use increased along with mortality from *C. difficile* infections in the United States, 2000-2007



Sources: Centers for Disease Control and Prevention, National Center for Health Statistics. Compressed Mortality File 1999-2008. CDC WONDER Online Database; Polgreen, Philip M., Yang, M., et al. 2011. Using Oral Vancomycin Prescriptions as a Proxy Measure for Clostridium difficile Infections: A Spatial and Time Series Analysis. *Infection Control and Hospital Epidemiology* (32).Oral vancomycin data obtained under license from IMS Health Xponent ™ (January 2000-December 2007) IMS Health Incorporated. All Rights Reserved. The findings, conclusions and views expressed do not necessarily reflect those of IMS Health or any of its affiliated or subsidiary entities.

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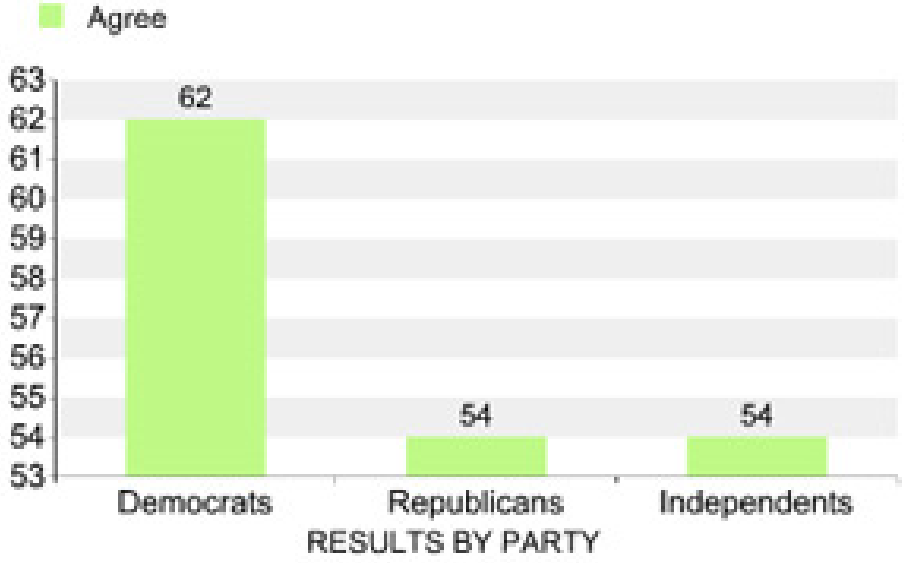
CNN/USA TODAY/GALLUP POLL

Results by party

PREVIOUS NEXT



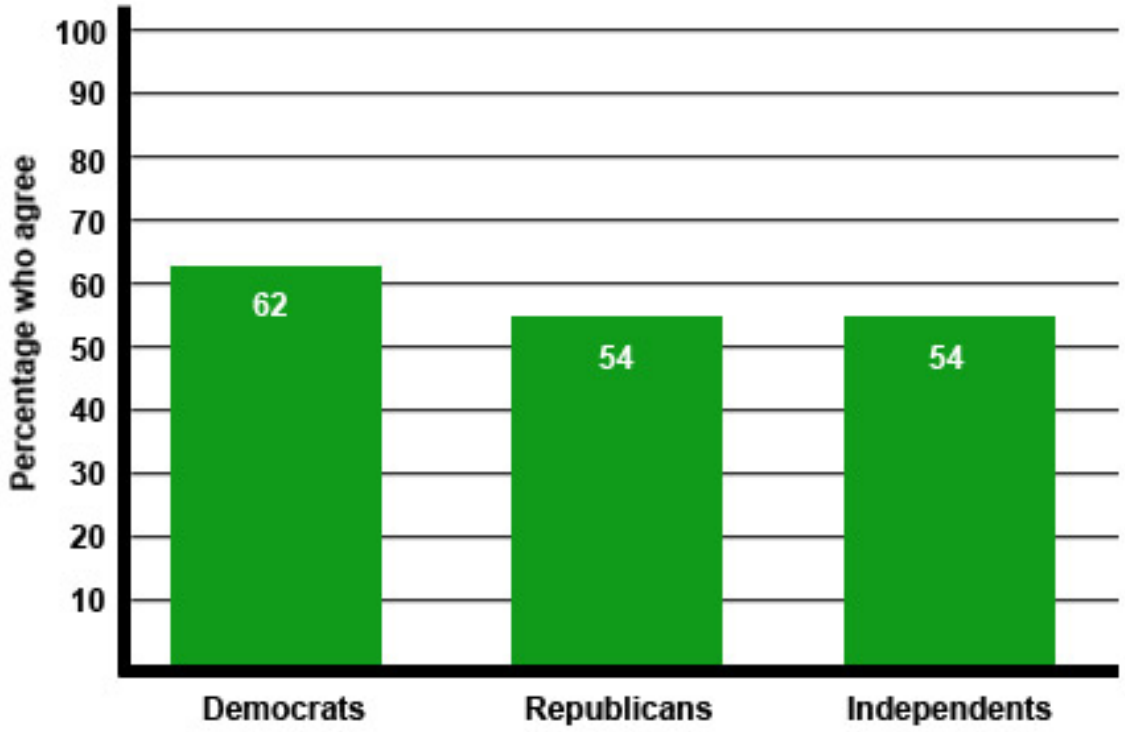
Question 2: Based on what you have heard or read about the case, do you agree with the court's decision to have the feeding tube removed?

SAMPLE: Interviews conducted by telephone March 18-20, 2005, with 909 adults in the United States.

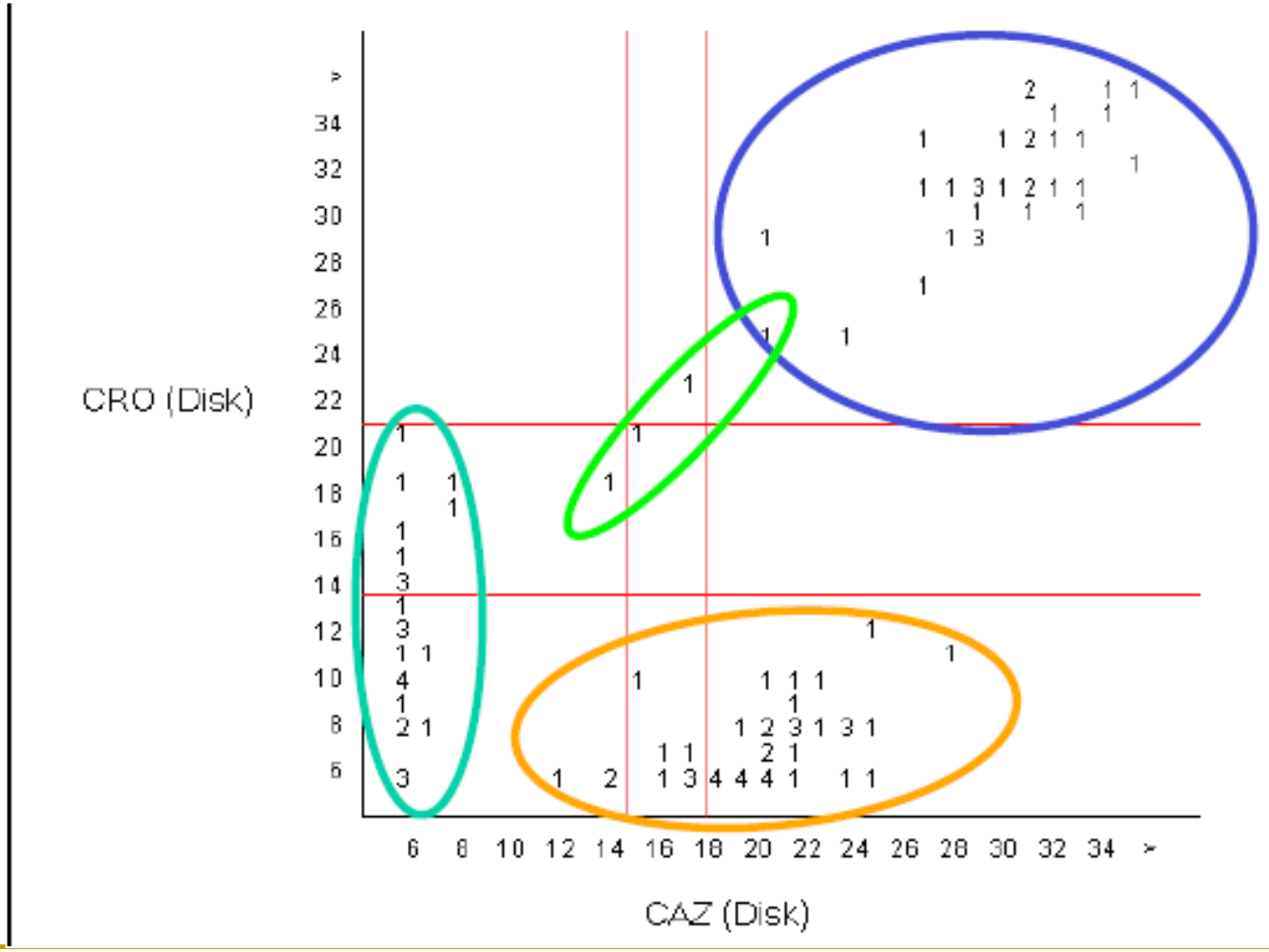
SAMPLING ERROR: +/- 7% pts

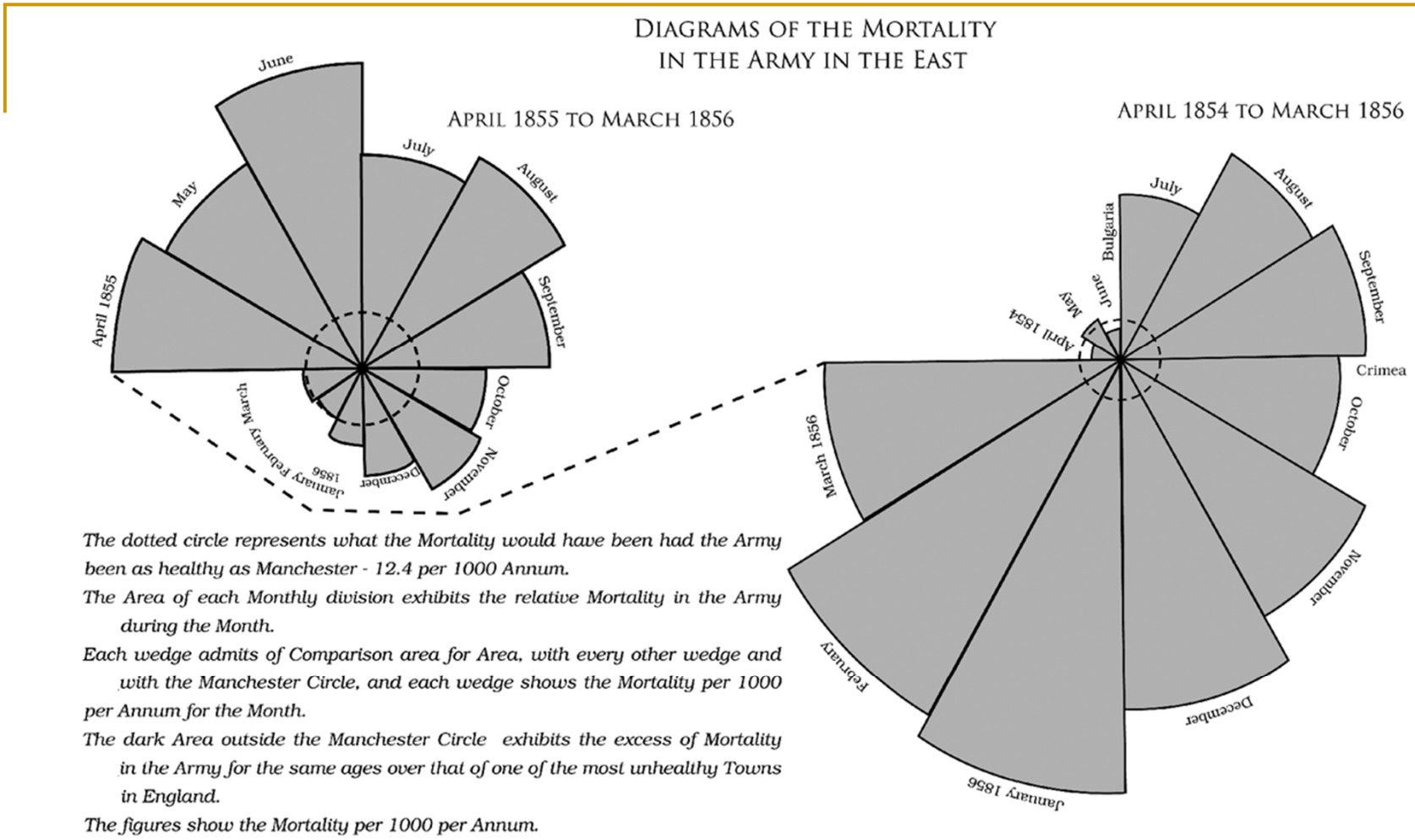
RESULTS BY PARTY: CNN/USA Today/Gallup Poll
Margin of error: +/- 7%

Question 2: Based on what you have heard or read about the case, do you agree with the court's decision to have the feeding tube removed?



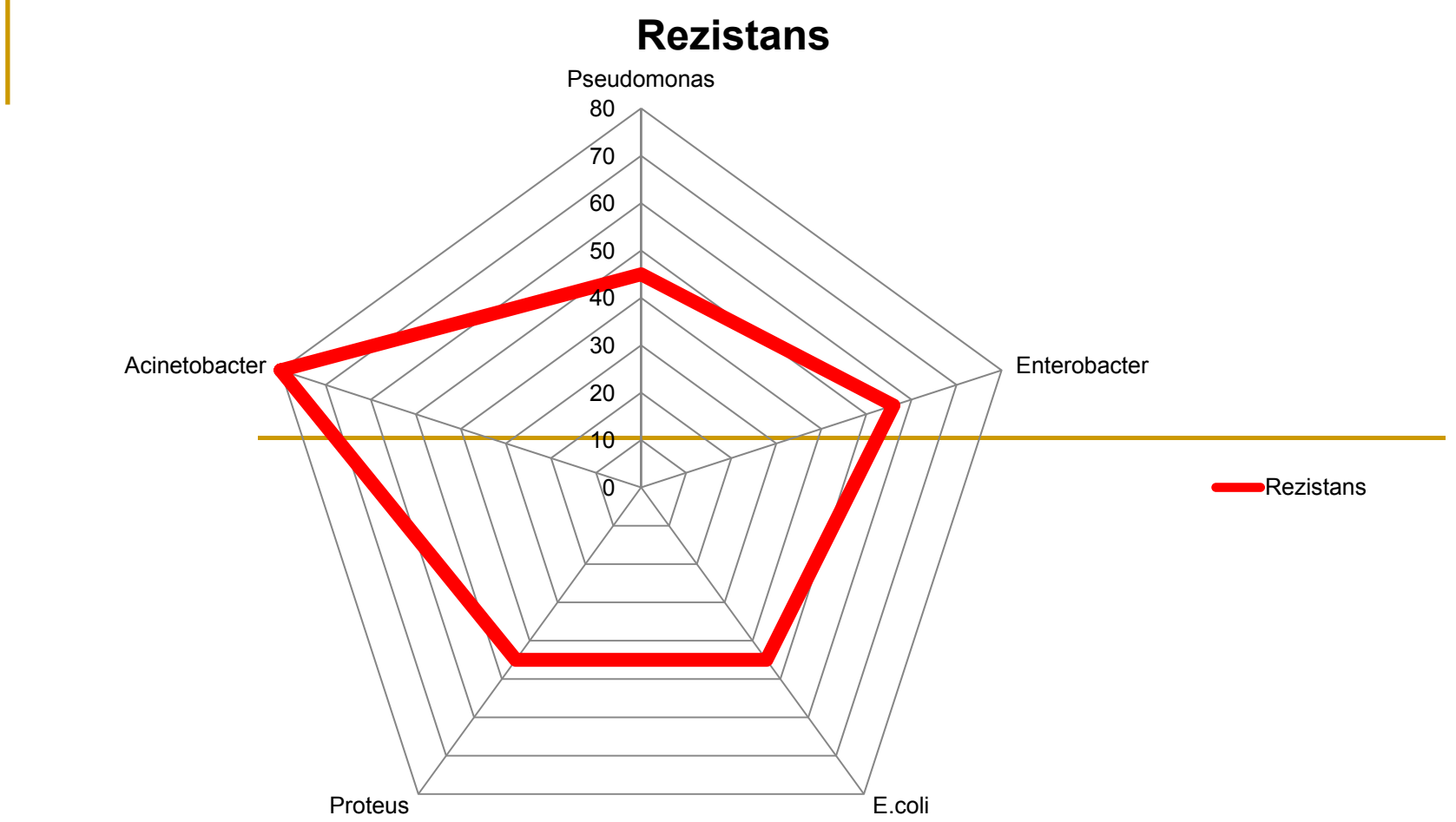
Analitik grafikler





Note: Reproduced from the only available original

Source: Commission (1999, p.158)


Rezistans
Pseudomonas
80
70
60
50
40
30
20
10
0
Enterobacter
E.coli
Proteus
Acinetobacter
Rezistans

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LINEAR ALGEBRA AND ITS APPLICATIONS
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Generators of matrix algebras in dimension 2 and 3

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Received 14 June 1995; accepted 8 May 2006
Available online 8 October 2008
Submitted by T.J. Laffey