

# İnfeksiyon Hastalıklarında Tedavi Rehberleri Uygulanıyor...

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Klinik Mikrobiyoloji Anabilim Dalı**



# Özet

Kılavuzlar

Günlük Pratik



# Klinisyenler Hastalarını Nasıl Tedavi Etmeli?

- **Eski moda (!)**

- Yerel fikir liderleri
- Çok okunan derleme türü makaleler

- **Yeni moda (!)**

- Klinik uygulama kılavuzları
  - Sistematik derlemeler yoluyla hazırlanmış
  - Bilimsel derneklerin onayladığı
  - Dikkatle incelenmiş ve kanıta dayalı
  - Uluslararası kabul görmüş

# Hastalar İin Olası En Kaliteli Tedavi Hizmeti



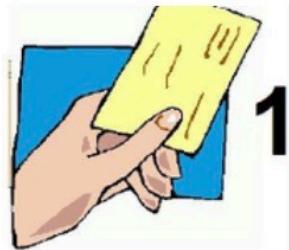
# Kılavuzlara İlişkin Yararlar ve Sorunlar

## Yararlar

- Literatür verilerinin uzmanlar tarafından sentez edilmesi
- Bilimsel kanıt kliniğe uyarlama konusunda açık öneriler

## Sorunlar

- Sürekli güncelleme
- Yoğun içerik ve erişim zorluğu
- Farklı disiplinler arası koordinasyon
- Çıkar çatışmaları
- Çoklu komorbiditesi olan hastalara uyarlama zorluğu



1

Selection of topic



2

Identifying key questions

6



Peer review

5



Formulating and grading the recommendations



3

Identifying & selecting the evidence

4



Evaluating the evidence



Read about [our approach to COVID-19](#)

Home >

# Developing NICE guidelines: the manual

Process and methods [PMG20] Published: 31 October 2014 Last updated: 18 January 2022

Process

[Tools and resources](#)

**Toplam 250 sayfa**

[Download \(PDF\)](#)

- 1 Introduction
- 2 The scope
- 3 Decision-making committees
- 4 Developing review questions and planning the evidence review
- 5 Identifying the evidence: literature searching and evidence submission
- 6 Reviewing research evidence
- 7 Incorporating economic

## Process and methods

### 9 Writing the guideline

- [9.1 Interpreting the evidence to make recommendations](#)
- [9.2 Wording the recommendations](#)
- [9.3 Supporting shared decision-making](#)
- [9.4 Formulating research recommendations](#)
- [9.5 References and further reading](#)

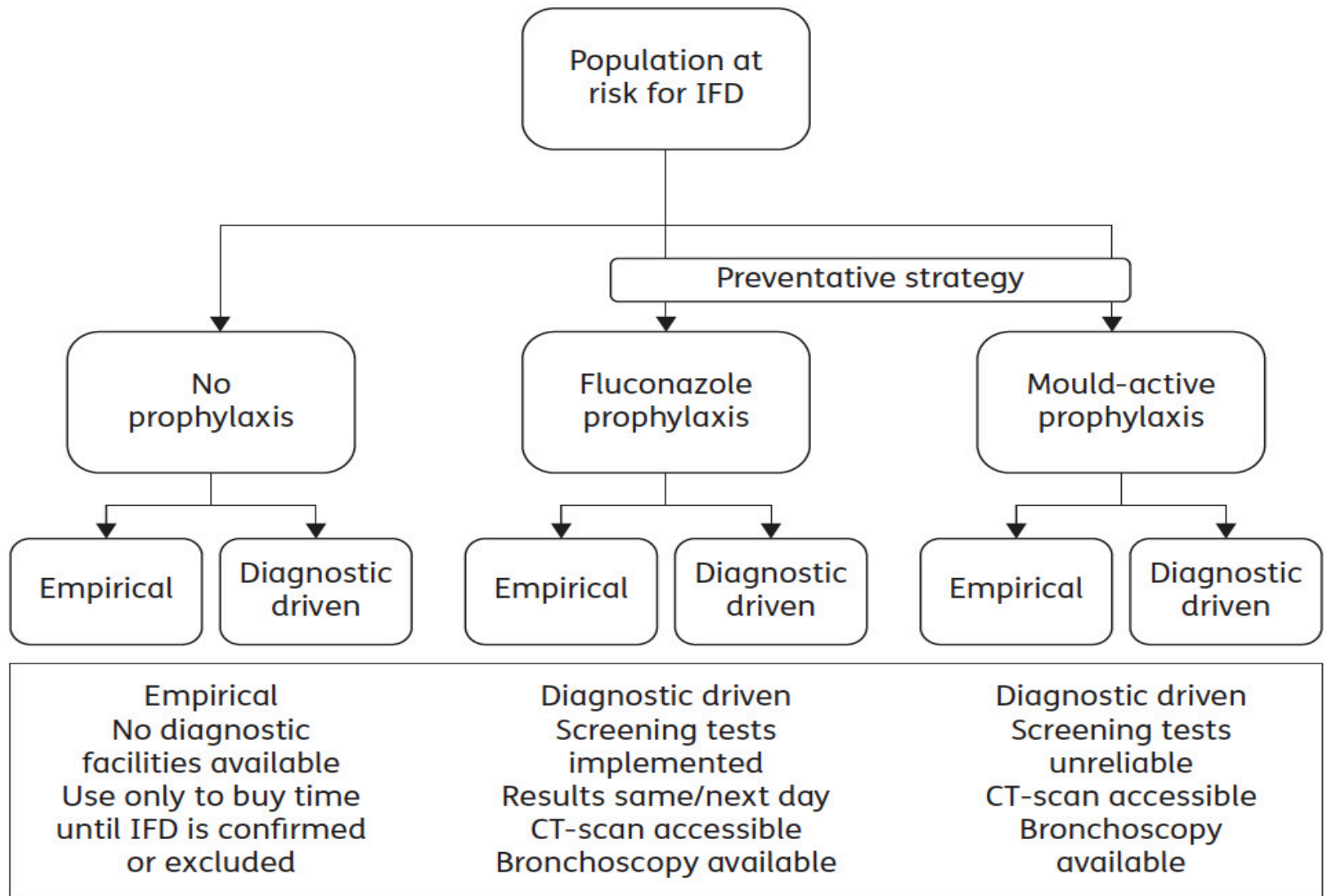


# Kişisel Kılavuzlar (!)

- Bireysel risk faktörlerini irdeleyen
- Yarar zarar dengesini irdeleyen araçlar
- **Sınırlılıkları**
  - Elde etmek zor veya mümkün değil
    - Hastaya özgül veri
    - Valide edilmiş yöntemler
  - Hasta değerlendirme üzerine etkileri



# IFI Gelişme Riski Olan Hastalarda Antifungal Stratejiler



# The Online TST/IGRA Interpreter

Version 3.0

The following tool estimates the risk of active tuberculosis for an individual with a tuberculin skin test reaction of  $\geq 5$ mm, based on his/her clinical profile. It is intended for adults tested with standard tuberculin (5 TU PPDS, or 2 TU RT-23) and/or a commercial Interferon Gamma release assay (IGRA). For more details about the algorithm used, go to the [About](#) page. The current version of the algorithm contains modifications of the original version, which was detailed in a paper by [Menzies, et al. \(2008\)](#). For further information see [references](#), or contact [dick.menzies@mcgill.ca](mailto:dick.menzies@mcgill.ca)

Please select the best response for each field:

TST Size:

5-9 mm

IGRA Result:

Positive

Age:

31

Age at immigration (if person immigrated to a low TB incidence country):

N/A

Country of birth:

Turkey

BCG status: Vaccinated age < 2 years

For more info, visit: [BCG World Atlas](#).

Recent contact with active TB: No Contact

Please select all the conditions that currently apply (If none of these conditions apply, please leave boxes unchecked)

- |  |   |
|--|---|
| <input type="checkbox"/> AIDS  | <input type="checkbox"/> Abnormal chest   |
| <input type="checkbox"/> Abnormal chest x-ray: fibronodular disease  | <input type="checkbox"/> Carcinoma of h   |
| <input type="checkbox"/> Chronic renal failure requiring hemodialysis  | <input type="checkbox"/> Cigarette smok   |
| <input type="checkbox"/> Diabetes Mellitus (all types)   | <input type="checkbox"/> HIV infection  |
| <input type="checkbox"/> Recent TB infection (TST conversion $\leq$ 2 years ago)                             | <input type="checkbox"/> Transplantation (requiring immune-suppressant therapy)                             |
| <input type="checkbox"/> Silicosis   | <input type="checkbox"/> Treatment with glucocorticoids   |
| <input checked="" type="checkbox"/> Tumor Necrosis Factor (TNF)-alpha inhibitors(e.g. Infliximab/Etanercept) | <input type="checkbox"/> Underweight (< 90 per cent ideal body weight or a body mass index (BMI) $\leq$ 20) |
| <input type="checkbox"/> Young age when infected (0-4 years)   |   |

## Results

[Printable version](#)

Below are the results for a patient with a TST reaction of **5-9 mm** and a **Positive** QFT Test, who is **31** years old, born in **Turkey**, whose BCG status is **Vaccinated age < 2 years**, who has had **no contact** with active TB, and who can be characterized by:

- **Tumor Necrosis Factor (TNF)-alpha inhibitors(e.g. Infliximab/Etanercept)**

The likelihood that this is a true positive test (PPV) is: **99.08%**

The annual risk of development of active tuberculosis disease is estimated to be **0.53%**.

The cumulative risk of active tuberculosis disease, up to the age of 80, is: **25.97%**

If treated with INH, the probability of clinically significant drug-induced hepatitis is **0.3%**, and the associated probability of hospitalization related to drug-induced hepatitis is **0.1%**.

Refresh

# Building better guidelines with BRIDGE-Wiz: development and evaluation of a software assistant to promote clarity, transparency, and implementability

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## ABSTRACT

**Objective** To demonstrate the feasibility of capturing the knowledge required to create guideline recommendations in a systematic, structured, manner using a software assistant. Practice guidelines constitute an important modality that can reduce the delivery of inappropriate care and support the introduction of new knowledge into clinical practice. However, many guideline recommendations are vague and underspecified, lack any linkage to supporting evidence or documentation of how they were developed, and prove to be difficult to transform into systems that influence the behavior of care providers.

**Methods** The BRIDGE-Wiz application (Building Recommendations In a Developer's Guideline Editor) uses a wizard approach to address the questions: (1) under what circumstances? (2) who? (3) ought (with what level of obligation?) (4) to do what? (5) to whom? (6) how and why? Controlled natural language was applied to create and populate a template for recommendation statements.

**Results** The application was used by five national panels to develop guidelines. In general, panelists agreed that the software helped to formalize a process for authoring guideline recommendations and deemed the application usable and useful.

**Discussion** Use of BRIDGE-Wiz promotes clarity of recommendations by limiting verb choices, building active voice recommendations, incorporating desirability

contributed mightily to the development of evidence-based medicine.<sup>2</sup> At the same time, many practice guidelines have become de facto repositories of the best knowledge about 'ideal' clinical practice.

A longstanding informatics challenge has been to develop efficient mechanisms whereby valid medical knowledge can be translated accurately and transparently into recommendations about appropriate care. However, the gulf between raw knowledge and clear, transparent, and implementable recommendation statements is broad.

To date, much of the effort in knowledge translation has been focused on extracting knowledge from guidelines that have been finalized and published.<sup>3-5</sup> This paper describes a novel software application intended to support and facilitate the development of clinical practice guidelines. BRIDGE-Wiz (Building Recommendations In a Developer's Guideline Editor) captures the knowledge required to create guideline recommendations in a systematic, structured, manner using a software wizard. In this paper, we will (1) describe the need for such an application and the environment in which its development and testing occurred, (2) present key design objectives, (3) describe the function of the BRIDGE-Wiz application, (4) report the evaluation of the program's usefulness and usability and (5) discuss lessons learned from the

# İki Farklı Klinik Senaryo

## İlki...

- 80 yaşında, relaps ve dirençli AML'si olan hasta
  - Nötropeni ateş nedeniyle geniş spektrumlu antibakteriyel tedaviye rağmen devam eden ateş
  - Serebral kanama nedeniyle komada
  - Serum galaktomannan  $>1$  ve artıyor
  - CT'de multiple nodüler lezyonlar ve kavitasyon

## İkincisi...

- **18 yaşına, ALL'si olan ve indüksiyon kemoterapisi alan hasta**
  - Antibakteriyel tedaviye rağmen süren ateş
  - Serum galaktomannan  $>1$  ve artıyor
  - CT'de nodül, halo belirtisi ve kavite

# **Kılavuzlar:**

## ***Sorular ve Sorunlar***

- **Öneri için yeterli kanıt var mı?**
- **Ne kadar etkililer?**
- **Ayrı ayrı hastalar için uygulanabilirler mi?**
- **Neden hepsi klinik pratiğe uygulanamıyor ?**

# Kalb Yetmezliđi Örneđi

- **NICE dökümanı:**
  - Tüm öneriler uygulanırsa  
£19.000/100.000 kar
- **ABD verisi:**
  - Eğer klinisyenler kronik kalb yetmezliđ tedavisinde önerler 6 öneriyi uygularsa ,  
67.996 ölüm önlenebilir

NICE Clinical Guideline 108; 2010

Fonarow GC, et al. Am Heart J 2011;161:1024

# **Klinisyenlerin Hasta Bakımında Karşılaştıkları Güçlükler**

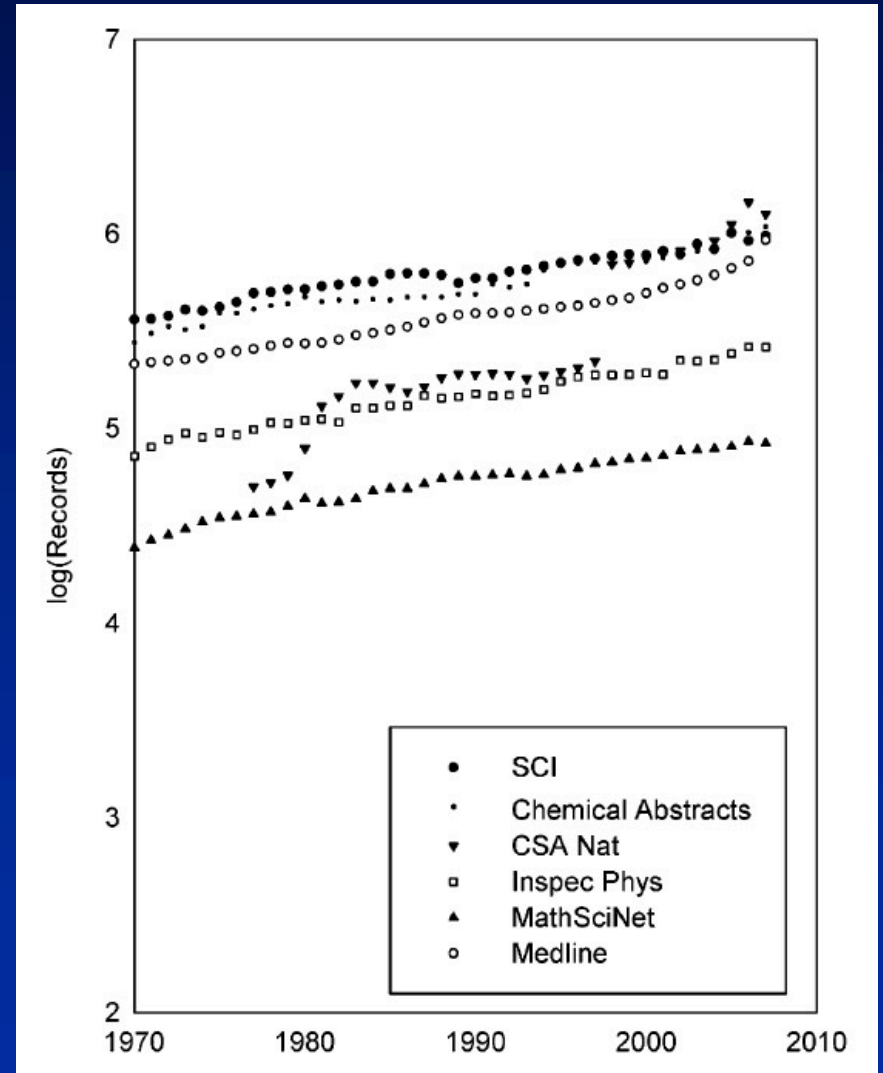
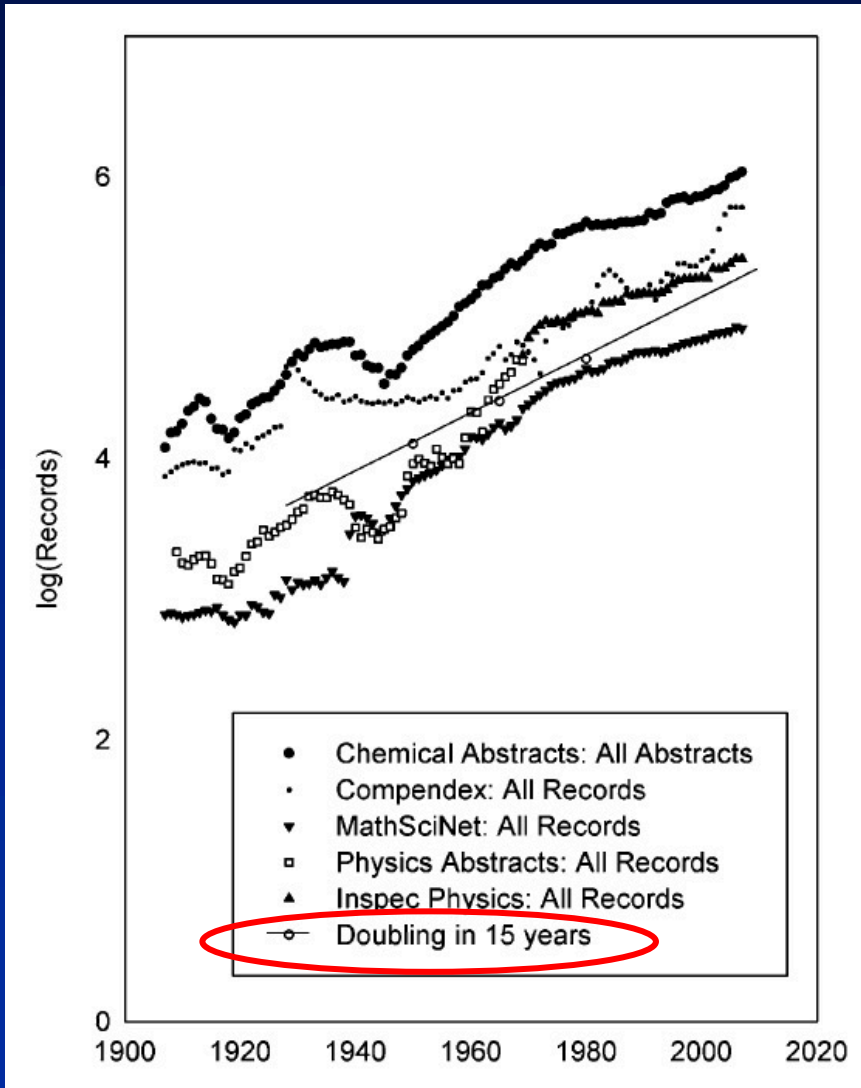
- **Uygun tanı ve tedavi konusunda karar vermede güçlük**
- **Veri ve kanıta ulaşmada güçlük**
  - Tek tek hastanın sorunu yönelik kanıt bulmak
  - Bilgiyi araştırmak için zaman eksikliği
  - Bilginin farklı dergilere dağılmış olması

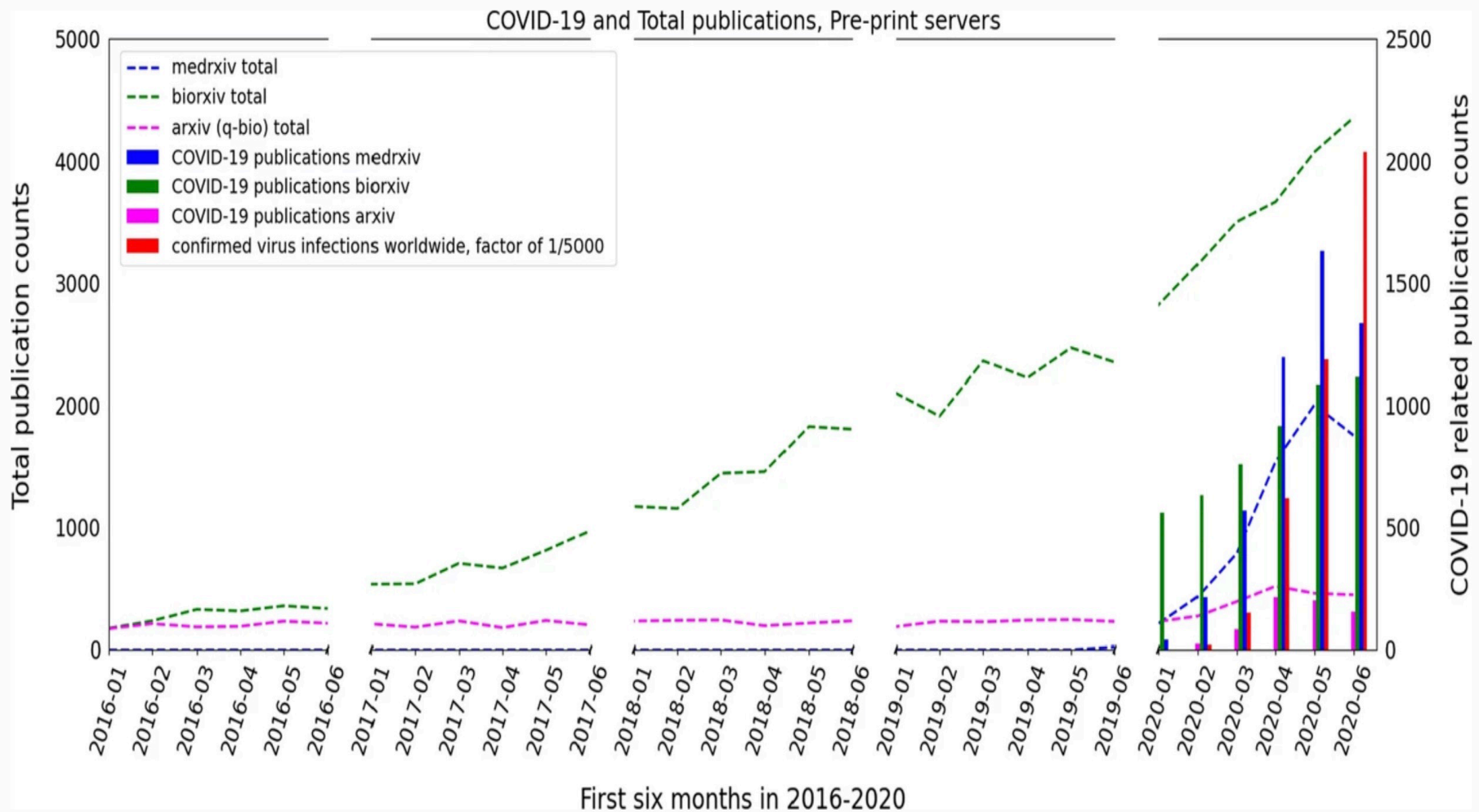


# Bilimsel Yayınların Artış Hızına Dair Tahminler

- WoS'da tahmin edilen yıllık artış hızı %2.5
- 2010 yılında indekslenen hakemli makale sayısı 1.486.000
- 1665'ten bu yana kümülatif yayın sayısı 2009'da >50 milyon

# Bilimsel Makalelerin Artış Hızı





Publication growth in the examined preprint repositories during the first six months of the years 2016–2020. Dotted plots - Total papers published. Bars - COVID-19 related papers, compared with the pandemic spread (factor of 1/5000)



**W. Edwards Deming**  
**1900-1993**

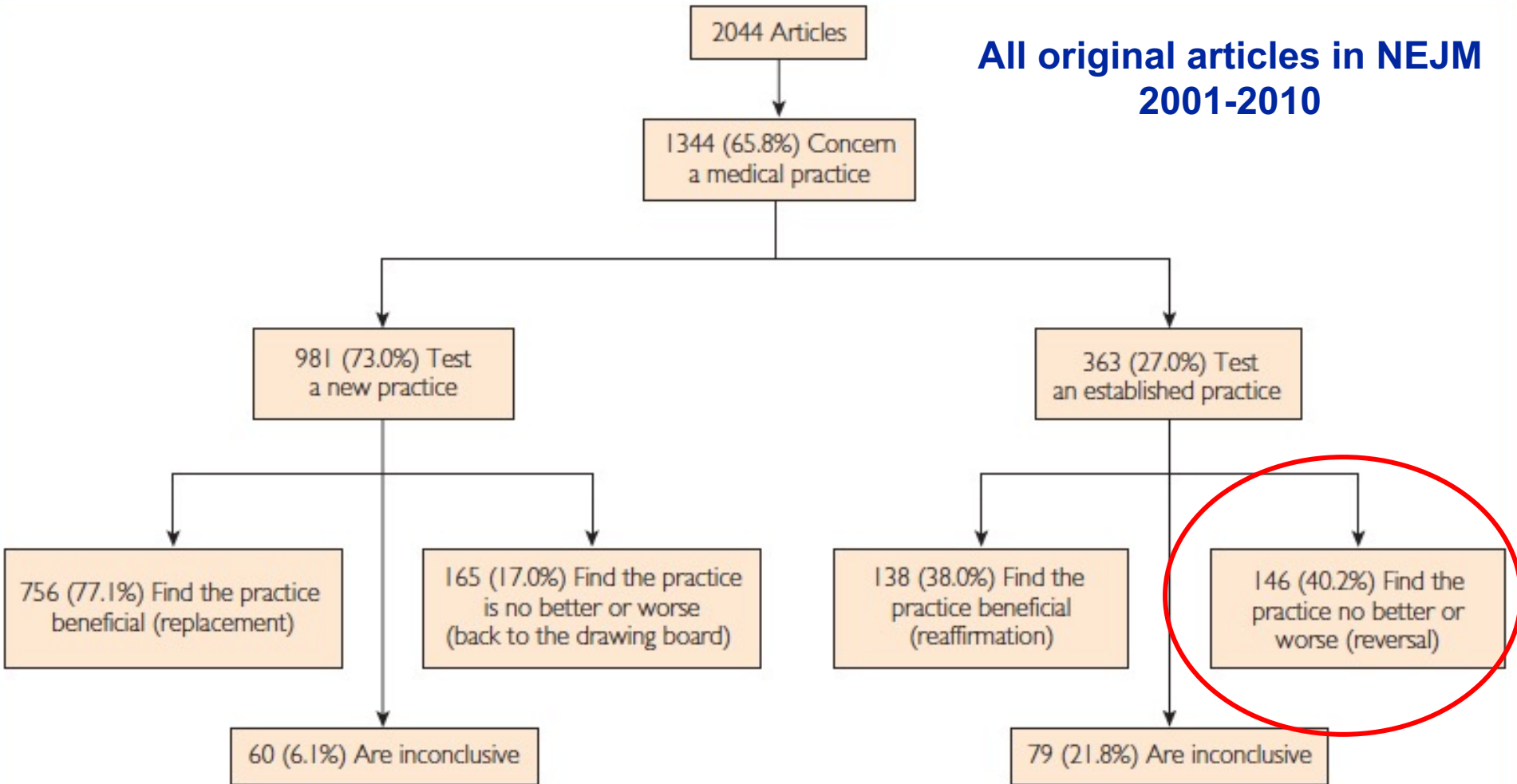
**In God we trust,  
All others must bring data...**

# Yüksek Atıflı Makalelerde Çelişkili Bulgular

- 1990-2003 arası >1000 atıf almış klinik çalışma makaleleri- JAMA, Lancet, NEJM
- 45/49 klinik uygulamanın etkin olduğu rapor etmiş
  - %16'sının daha sonraki çalışmalarda doğru olmadığı gösterilmiş
  - %16'sının sonraki çalışmalarda daha az etkili olduğu saptanmış
  - %44'ü tekrarlanabilmiş
  - %24'ünde başka çalışma yapılmamış

# Contradicted Medical Practice

All original articles in NEJM  
2001-2010



# Evidence Leads Practice...

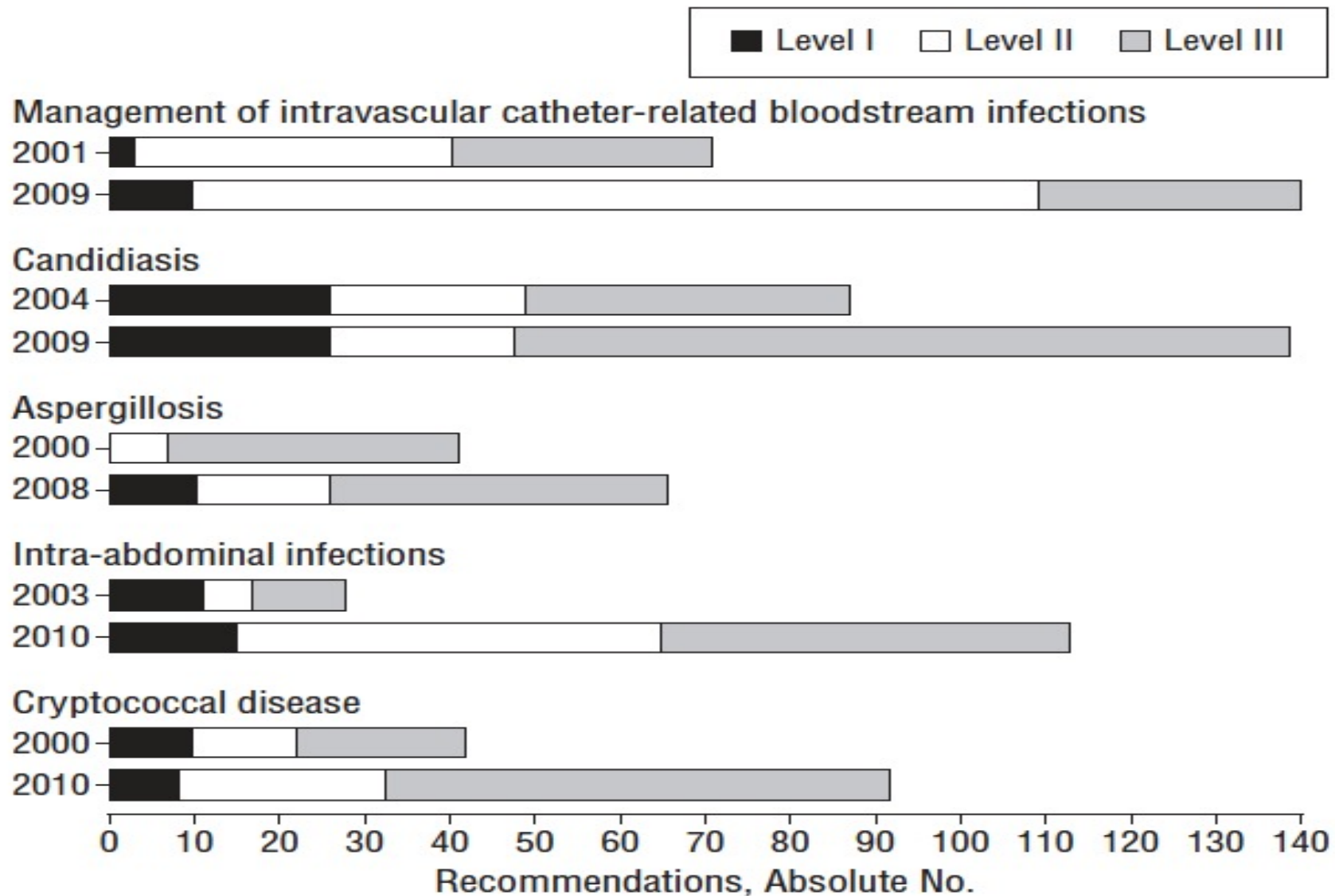


# **IDSA Kılavuzlarında Kanıt Düzeyleri**

- **41 IDSA kılavuzu, 1994 ve 2010 arası**
- **4218 öneri**
  - **Düzyey I (%14)**
  - **Düzyey II (%31)**
  - **Düzyey III (%55)**



# IDSA Kılavuzlarında Kanıt Düzeyleri



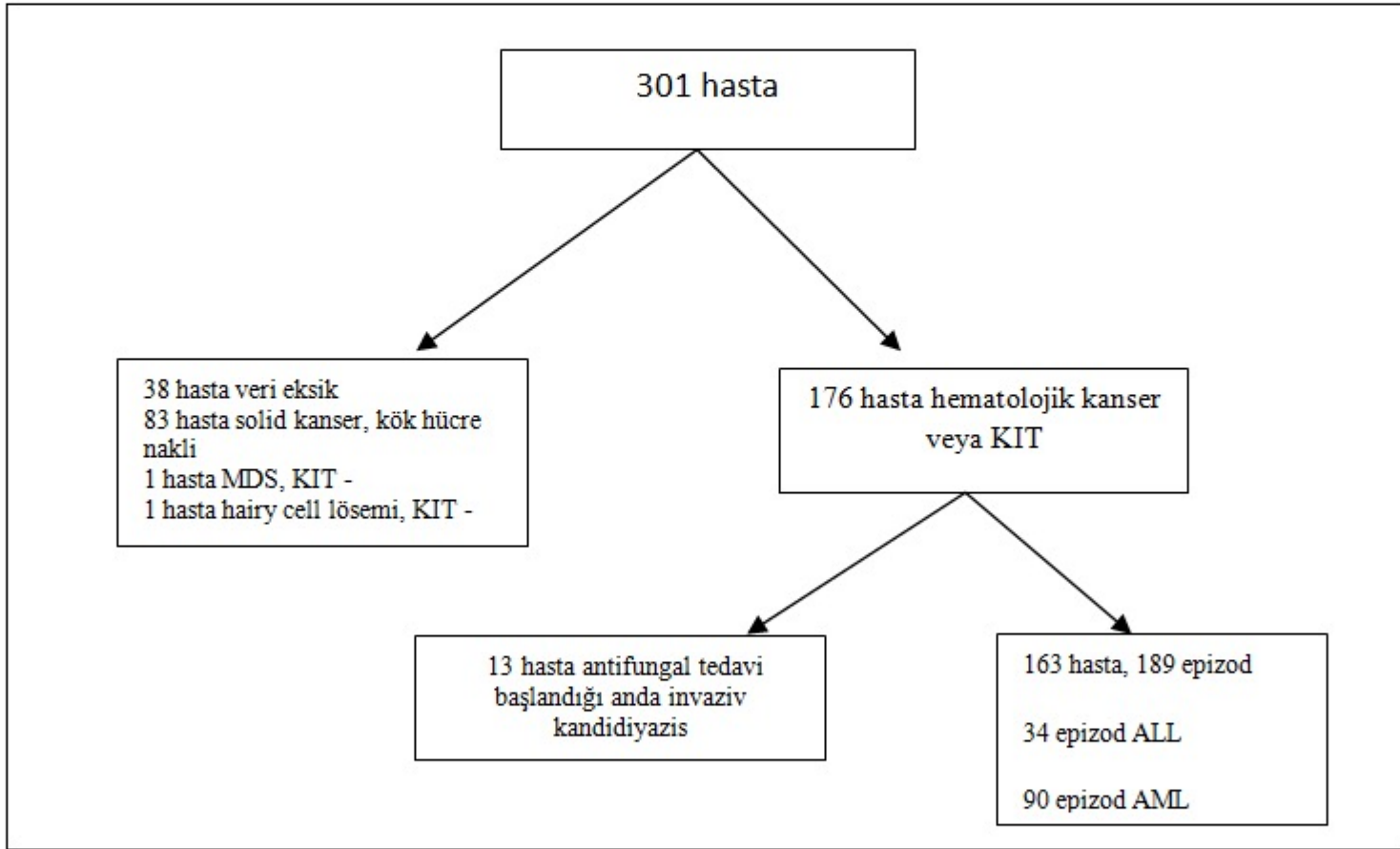
# Kılavuzlarda Randomize Kontrollü Çalışmalara (RKÇ) Atıf

- 191 kılavuz
  - AIM, BMJ, JAMA, Lancet, NEJM, Pediatrics 1979, 1984, 1989, 1994 ve 1999
- RKÇ atıfta bulunan kılavuzlar
  - 1979'da %5 1999'da %47
- 4853 referansın
  - % 8.1'i RKÇ
  - %0.4 sistematik derleme
  - %0.5 RKÇ metaanalizleri

# Uluslararası Kılavuzlara Uyum- SEIFEM 2008B

- 136 AML ve invaziv aspergillozlu hasta
- Kılavuz uyumu
  - ECIL, %28
  - IDSA, %55
- İlk seçenek tedavi başarısı
  - %76 IDSA vs %59 non-IDSA (p=.03)
  - %84 ECIL vs %62 non-ECIL (p=.02)
- 120 günlük sağkalımda fark yok

# Çalışmaya Alınan Hastalar



\*: KIT: kök hücre nakli, OTO KIT: otolog kök hücre nakli, ALLO KIT: allojeneik kök hücre nakli

# 30 Günlük Mortalite ve Kılavuzlara Uygunluk\*

Mortalite	Kılavuza Uygunluk		Toplam
	Uygun	Uygun değil	
Yok	125 (%75.8)	14 (%70.0)	139 (%75.1)
Var	40 (%24.2)	6 (%30.0)	46 (%24.9)
Toplam	165 (%100)	20 (%100)	185 (%100)

\*(p=0.574)

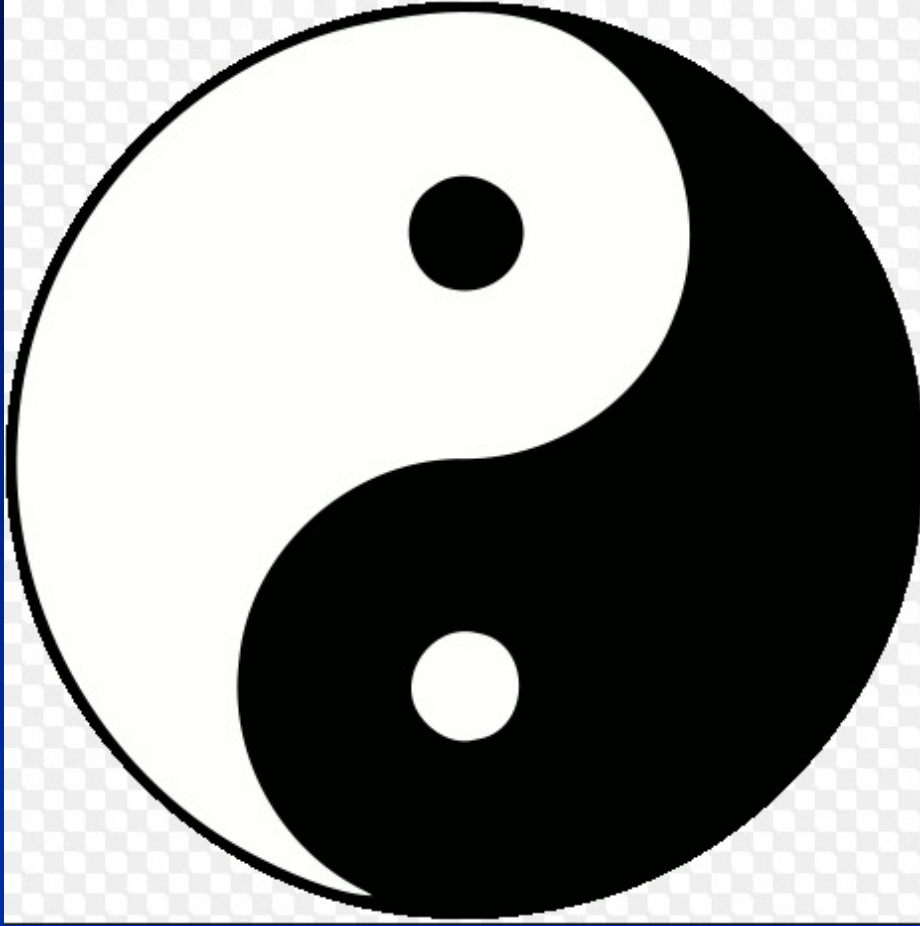
# Kyoto'da Bir Zen Bahçesi...

## Çakıltaşı ile Çevrili 15 Kaya Parçası



- Kılavuzlar en üst düzeyde kanıt sunar
- Ama hastaların kişisel gereksinimlerini gözardı edebilir

# Yin ve Yang



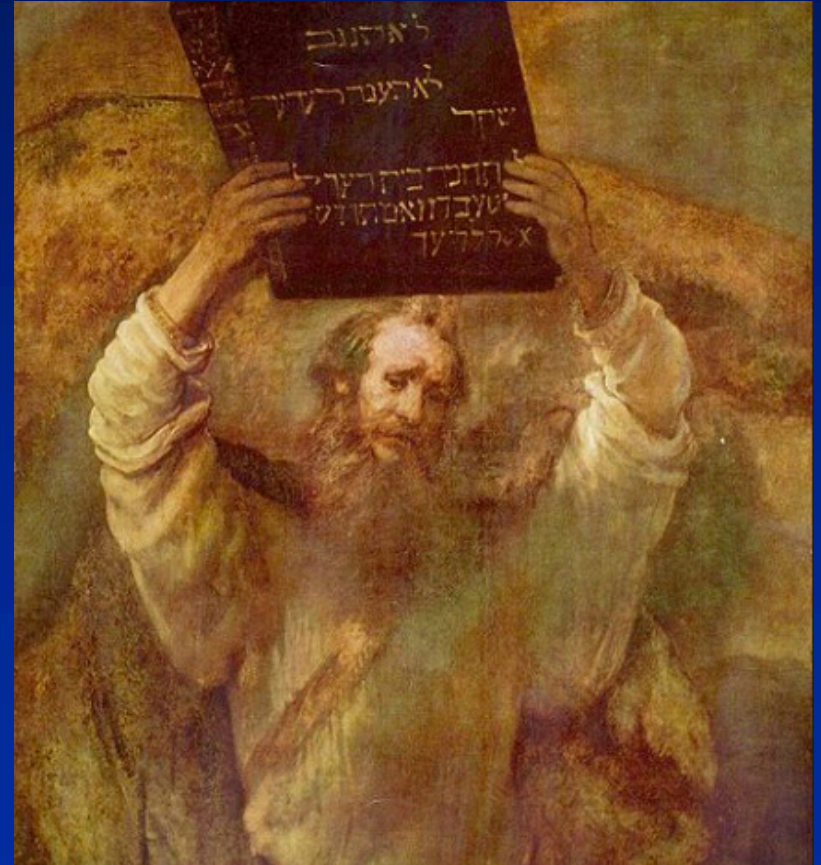
- Evrende herşey iki kutupludur
- Her kutup karşıtını içinde barındırır
- Karşıtlıklar birbirini tamamlayıcıdır

*Taijitu*

'Diagram of the supreme ultimate'

# Kılavuzlar Tanrı Buyruđu Deđil...

- Kılavuzlar öneri, kural deđil
- En az deneyimli olanlar en çok yararlanır
- Daima farklı biçimde tedavi edilebilecek olanlar var olacak





**Teşekkürler...**