Update in Hospital Medicine 2019

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Financial disclosures

None

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Objectives

1. Critique recent literature relevant to the care of a hospitalized internal medicine patient.

2. Present new research in hospital medicine that may impact your practice.

3. Focus on studies with broad application.

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Literature selection

- Sept 2018 to Sept 2019
- Studies relevant to hospital medicine
- Case based scenarios

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Outline

- Antibiotic treatment trends
- Expanding indications for DOACs
- VTE prophylaxis
- Delirium
- Disposition options
- Quick hits + flavor of High Value Care

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Which of the following occurred on the first Thursday in March 2019

A) Justin Bieber's birthday
B) National Corn Dog Day
C) National Landline day
D) Nationality Grammar Da
E) National Hospitalist Day

y March 1st
March 16th
March 10th
March 4th
rs March 7th!!

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Case #1

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A 67yo M with a prosthetic AV is admitted for MSSA endocarditis. He undergoes valve surgery.

What is the best strategy for treating his endocarditis?

A) 6 week course of inpatient IV antibiotics
B) 6 week course of outpatient IV antibiotics
C) Inpatient and then outpatient IV antibiotics
D) Inpatient IV followed by oral antibiotics
E) Oral antibiotics only

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Background

- Infective endocarditis has a high rate of morbidity and mortality if untreated
- Current guidelines recommend 6 weeks IV antibiotics
- PICC line + outpatient infusion not without complications or logistical issues

- Efficacy of IV to oral antibiotic step-down approach not known

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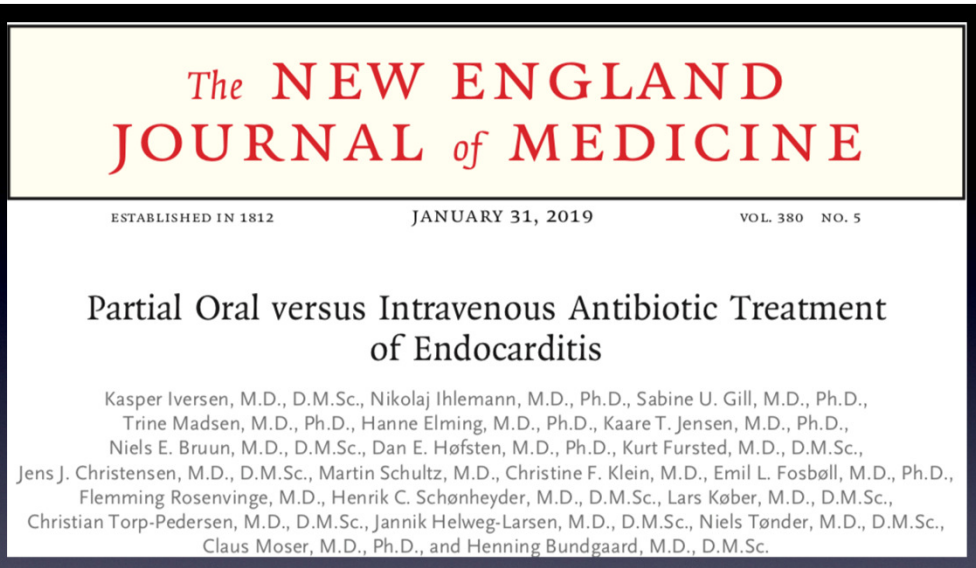

Country of origin?... Denmark

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Design

- Randomized, multi-center, noninferiority
- IV vs. IV→oral strategy

- Left sided endocarditis
- *Streptococcus, Enterococcus, Staph aureus,* Coag-neg *Staph*

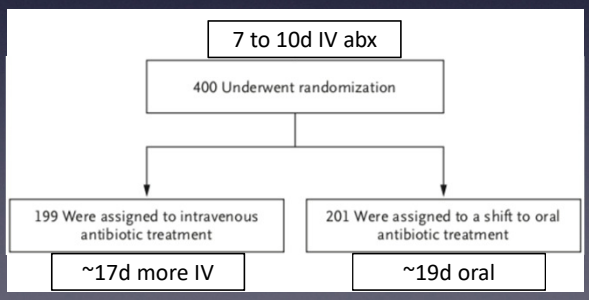

Table 1. Characteristics of the Patients at Baseline.*

Characteristic	Intravenous Treatment (N=199)	Oral Treatment (N=201)
Mean age — yr	67.3±12.0	67.6±12.6
Female sex — no. (%)	50 (25.1)	42 (20.9)
Body temperature — °C	36.9±0.45	37.0±0.44
Coexisting condition or risk factor — no. (%)		
Diabetes	36 (18.1)	31 (15.4)
Renal failure	25 (12.6)	21 (10.4)
Dialysis	13 (6.5)	15 (7.5)
COPD	17 (8.5)	9 (4.5)
Liver disease	7 (3.5)	6 (3.0)
Cancer	14 (7.0)	18 (9.0)
Intravenous drug use	3 (1.5)	2 (1.0)
Pathogen — no. (%)†		
Streptococcus	104 (52.3)	92 (45.8)
Enterococcus faecalis	46 (23.1)	51 (25.4)
Staphylococcus aureus‡	40 (20.1)	47 (23.4)
Coagulase-negative staphylococci	10 (5.0)	13 (6.5)
Laboratory results at randomization		
Hemoglobin — mmol/liter	6.3±1.1	6.5±1.0
Leukocytes — $\times 10^{-9}$/liter	7.6±3.6	7.2±2.6
C-reactive protein — mg/liter	24.3±18.4	19.9±16.7
Creatinine — μmol/liter	124±112	141±164
Preexisting prosthesis, implant, or cardiac disease — no. (%)		
Prosthetic heart valve	53 (26.6)	54 (26.9)
Pacemaker	15 (7.5)	20 (10.0)
Other known valve disease	82 (41.2)	90 (44.8)
Cardiac involvement at randomization — no. (%)§		
Mitral-valve endocarditis	65 (32.7)	72 (35.8)
Aortic-valve endocarditis	109 (54.8)	109 (54.2)
Mitral-valve and aortic-valve endocarditis	23 (11.6)	20 (10.0)
Endocarditis in other locations§	2 (1.0)	0
Pacemaker endocarditis	6 (3.0)	8 (4.0)
Vegetation size >9 mm	7 (3.5)	11 (5.5)
Moderate or severe valve regurgitation	19 (9.5)	23 (11.4)
Valve surgery during current disease course	75 (37.7)	77 (38.3)

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Outcome

- Primary composite: death, unplanned surgery, embolic event or relapse of bacteremia

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Results

	IV group	Oral group	OR
Composite outcome	24 (12.1%)	18 (9.0%)	.72 [0.37-1.36]

Table 2. Distribution of the Four Components of the Primary Composite Outcome.*

Component	Intravenous Treatment (N=199)	Oral Treatment (N=201)	Difference	Hazard Ratio (95% CI)
	number (percent)		*percentage points (95% CI)*	
All-cause mortality	13 (6.5)	7 (3.5)	3.0 (−1.4 to 7.7)	0.53 (0.21 to 1.32)
Unplanned cardiac surgery	6 (3.0)	6 (3.0)	0 (−3.3 to 3.4)	0.99 (0.32 to 3.07)
Embolic event	3 (1.5)	3 (1.5)	0 (−2.4 to 2.4)	0.97 (0.20 to 4.82)
Relapse of the positive blood culture†	5 (2.5)	5 (2.5)	0 (−3.1 to 3.1)	0.97 (0.28 to 3.33)

Overall: Oral strategy non-inferior to IV strategy

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Commentary

When I first heard about this study…

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Commentary

- Intriguing and worthwhile
- Appropriate strategy for selected stable patients

- Low rate of MRSA and IVDA limit generalizability to Oregon and USA
- Need more data before making practice change

What's this?...

…a giant grain of salt

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A 67yo M with a prosthetic AV is admitted for MSSA endocarditis. He undergoes valve surgery.

What is the best strategy for treating his endocarditis?

A) 6 week course of inpatient IV antibiotics
B) 6 week course of outpatient IV antibiotics
C) Inpatient and then outpatient IV antibiotics
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E) Oral antibiotics only

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You are paged by the inpatient pharmacist because you ordered Metformin for your patient to continue in the hospital.

How do you respond?:

A) Apologize and stop Metformin
B) Consider the renal function
C) Continue Metformin, lactic acidosis be damned!
D) "$H*&#@!!

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JAMA Internal Medicine | Original Investigation

Association of Metformin Use With Risk of Lactic Acidosis Across the Range of Kidney Function

A Community-Based Cohort Study

Benjamin Lazarus, MBBS, MPH; Aozhou Wu, MHS; Jung-Im Shin, MD, PhD; Yingying Sang, MS; G. Caleb Alexander, MD, MS; Alex Secora, MPH; Lesley A. Inker, MD, MS; Josef Coresh, MD, PhD; Alex R. Chang, MD, MS; Morgan E. Grams, MD, PhD

- N=75,400 over 5.7 years
- Single center, Geisinger Health System
- Any hospitalization for "acidosis" not DKA

GFR level	HR acidosis	95% CI
45-59 ml/min	1.16	0.95-1.41
30-44 ml/min	1.09	0.95-1.08
<30 ml/min	2.07	1.33-3.22

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Case #2

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The 67yo man from first case returns to hospital with infected prosthetic hip joint and osteomyelitis of the femur. He undergoes appropriate surgical drainage and washout.

What is the best strategy to treat his osteomyelitis?

A) 6 week course of inpatient IV antibiotics
B) 6 week course of outpatient IV antibiotics
C) Inpatient and then outpatient IV antibiotics
D) Inpatient IV followed by oral antibiotics
E) Oral antibiotics only

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Background

- Surgery + 6 week IV abx current standard for complex bone and joint infections
- Based on 1970s article
- Risks to IV therapy
- Meta-analysis* 180 patients x 1 year→no advantage IV over PO treatment

*Conterno LO, Turchi MD. "Antibiotics for treating chronic osteomyelitits in adults. " Cochrane Database Syst Rev 2013; 9

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ORIGINAL ARTICLE

Oral versus Intravenous Antibiotics for Bone and Joint Infection

H.-K. Li, I. Rombach, R. Zambellas, A.S. Walker, M.A. McNally, B.L. Atkins, B.A. Lipsky, H.C. Hughes, D. Bose, M. Kümin, C. Scarborough, P.C. Matthews, A.J. Brent, J. Lomas, R. Gundle, M. Rogers, A. Taylor, B. Angus, I. Byren, A.R. Berendt, S. Warren, F.E. Fitzgerald, D.J.F. Mack, S. Hopkins, J. Folb, H.E. Reynolds, E. Moore, J. Marshall, N. Jenkins, C.E. Moran, A.F. Woodhouse, S. Stafford, R.A. Seaton, C. Vallance, C.J. Hemsley, K. Bisnauthsing, J.A.T. Sandoe, I. Aggarwal, S.C. Ellis, D.J. Bunn, R.K. Sutherland, G. Barlow, C. Cooper, C. Geue, N. McMeekin, A.H. Briggs, P. Sendi, E. Khatamzas, T. Wangrangsimakul, T.H.N. Wong, L.K. Barrett, A. Alvand, C.F. Old, J. Bostock, J. Paul, G. Cooke, G.E. Thwaites, P. Bejon, and M. Scarborough, for the OVIVA Trial Collaborators*

Li et al. "Oral versus Intravenous Antibiotics for Bone and Joint Infection." *NEJM* Jan 2019 Vol 380 (5); 425-36

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Design

- Multi-center non-blinded randomized controlled non-inferiority
- IV antibiotics (N=527) vs. PO antibiotics (N=527) for >4 weeks
- Antibiotic choice at discretion of physician
- Primary outcome: Treatment failure at one year defined by one or more:
  - ❖ Draining sinus tract or pus
  - ❖ Deep-tissue microbiologic isolation same as index infection
  - ❖ Histology of ongoing infection

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Design

Table 1. Baseline Characteristics of the Trial Participants.*

Characteristic	Intravenous Group (N=527)	Oral Group (N=527)	Total (N=1054)
Age — yr			
Median (interquartile range)	61 (49–70)	60 (49–70)	60 (49–70)
Range	18–92	18–91	18–92
Male sex — no. (%)	320 (60.7)	358 (67.9)	678 (64.3)
Baseline surgical procedure — no. (%)			
No implant or device present; débridement of chronic osteomyelitis performed	153 (29.0)	169 (32.1)	322 (30.6)
No implant or device present; débridement of chronic osteomyelitis not performed	25 (4.7)	29 (5.5)	54 (5.1)
Débridement and implant retention	124 (23.5)	123 (23.3)	247 (23.4)
Removal of orthopedic device for infection	89 (16.9)	78 (14.8)	167 (15.8)
Prosthetic joint implant removed	68 (12.9)	67 (12.7)	135 (12.8)
Prosthetic joint implant, one-stage revision	47 (8.9)	43 (8.2)	90 (8.5)
Surgery for diskitis, spinal osteomyelitis, or epidural abscess; débridement performed	8 (1.5)	5 (0.9)	13 (1.2)
Surgery for diskitis, spinal osteomyelitis, or epidural abscess; débridement not performed	13 (2.5)	13 (2.5)	26 (2.5)
Organisms identified — no./total no. (%)§			
Staphylococcus aureus	196/500 (39.2)	182/503 (36.2)	378/1003 (37.7)
Coagulase-negative staphylococcus	137/500 (27.4)	135/503 (26.8)	272/1003 (27.1)
Streptococcus species	72/500 (14.4)	73/503 (14.5)	145/1003 (14.5)
Pseudomonas species	28/500 (5.6)	23/503 (4.6)	51/1003 (5.1)
Other gram-negative organisms	84/500 (16.8)	84/503 (16.7)	168/1003 (16.7)
Culture negative	77/500 (15.4)	78/503 (15.5)	155/1003 (15.5)

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Results

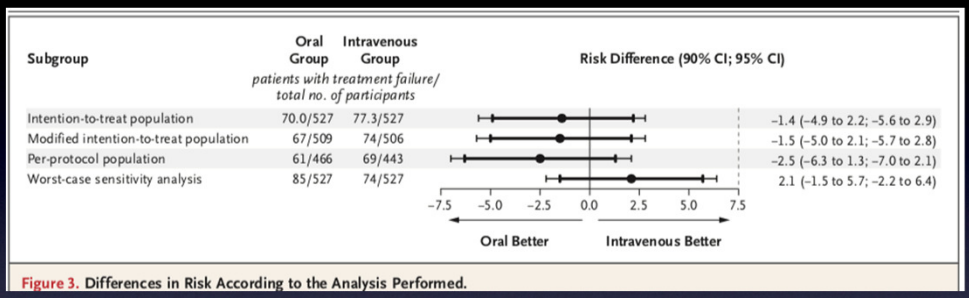

Figure 3. Differences in Risk According to the Analysis Performed.

- 75% of participants had abx at least 6 weeks
- Tried different mathematical models to “break” non-inferiority.
- PO was still non-inferior to IV
- Oral therapy had shorter hospital length of stay

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Commentary

- Largest RCT to date for this issue
- Challenges long held dogma about treating complex orthopedic infections
- Study design mimics “real world”
- Oral therapy could be considered in selected cases

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The 67yo man from first case returns to hospital with infected prosthetic hip joint and osteomyelitis of the femur. He undergoes appropriate surgical drainage and washout.

What is the best strategy to treat his osteomyelitis?

A) 6 week course of inpatient IV antibiotics
B) 6 week course of outpatient IV antibiotics
C) Inpatient and then outpatient IV antibiotics
D) Inpatient IV followed by oral antibiotics
E) Oral antibiotics only

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Didn't I hear something about oral therapy for appendicitis?

JAMA | Original Investigation

Five-Year Follow-up of Antibiotic Therapy for Uncomplicated Acute Appendicitis in the APPAC Randomized Clinical Trial

Paulina Salminen, MD, PhD; Risto Tuominen, MPH, PhD; Hannu Paajanen, MD, PhD; Tero Rautio, MD, PhD; Pia Nordström, MD, PhD; Markku Aarnio, MD, PhD; Tuomo Rantanen, MD, PhD; Saija Hurme, MSc; Jukka-Pekka Mecklin, MD, PhD; Juhani Sand, MD, PhD; Johanna Virtanen, MD, PhD; Airi Jartti, MD, PhD; Juha M. Grönroos, MD, PhD

Group	5yr Complication	Recurrent appendicitis
Appendectomy (n=273)	24.4%	NA
Antibiotic only (n=257)	6.5%	34% at 2 years 35.2% at 3 years 39% at 5 years

Conclusion: Oral antibiotics safe for uncomplicated appendicitis

Salminen et al "Five-Year Follow-up of Antibiotic Therapy for Uncomplicated Acute Appendicitis in the APPAC Randomized Clinical Trial" *JAMA*. 2018; 320(12):1259-1265 Sept 2018

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Case #3

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75yo F with newly diagnosed cancer is about to start chemotherapy. She has no history of venous thromboembolism.

What is the best strategy to prevent VTE in this patient?

A) Warfarin
B) Low molecular weight heparin
C) Factor Xa inhibitor
D) ASA + Plavix
E) Compression hosiery

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Background

- Low molecular weight heparin is current standard of care for VTE treatment and prevention in patients with cancer
- VTE is common in cancer patients, possibly interrupting treatment
- Factor Xa inhibitors ("DOAC", "NOAC") have been FDA approved for anticoagulant use in Afib, Stroke, PE/DVT treatment and prevention
- Initial studies of Factor Xa inhibitors had patients with cancer but small volume and methodological issues with studies

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Clinical question

- *What is the role of Factor Xa inhibitors in VTE prevention in patients with cancer?*
- *Is primary prevention of VTE warranted in "high risk" cancer patients?*

"Khorana score"

Patient characteristics		Risk score points
Site of cancer		
Very high risk (stomach, pancreas)		2
High risk (lung, lymphoma, gynecologic, genitourinary excluding prostate)		1
Pre-chemotherapy platelet count $\geq$350,000/mm^3		1
Hemoglobin level less than <10 g/dl or use of red cell growth factors		1
Pre-chemotherapy leukocyte count >11,000/mm^3		1
BMI 35 $\geq$ 35 kg/m^2		1
Risk score (points)	**Risk category**	**Rates of sVTE according to scores (%)**
0	Low	0.3–0.8
1–2	Intermediate	1.8–2.0
$\geq$3	High	6.7–7.1

BMI body mass index, *sVTE* symptomatic VTE

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Primary prevention vs. placebo…

"CASSINI"

Rivaroxaban for Thromboprophylaxis in High-Risk Ambulatory Patients with Cancer

A.A. Khorana, G.A. Soff, A.K. Kakkar, S. Vadhan-Raj, H. Riess, T. Wun, M.B. Streiff, D.A. Garcia, H.A. Liebman, C.P. Belani, E.M. O'Reilly, J.N. Patel, H.A. Yimer, P. Wildgoose, P. Burton, U. Vijapurkar, S. Kaul, J. Eikelboom, R. McBane, K.A. Bauer, N.M. Kuderer, and G.H. Lyman, for the CASSINI Investigators*

"AVERT"

Apixaban to Prevent Venous Thromboembolism in Patients with Cancer

Marc Carrier, M.D., Karim Abou-Nassar, M.D., Ranjeeta Mallick, Ph.D., Vicky Tagalakis, M.D., Sudeep Shivakumar, M.D., Ariah Schattner, M.D., Philip Kuruvilla, M.D., Danny Hill, M.D., Silvana Spadafora, M.D., Katerine Marquis, M.D., Mateya Trinkaus, M.D., Anna Tomiak, M.D., Agnes Y.Y. Lee, M.D., Peter L. Gross, M.D., Alejandro Lazo-Langner, M.D., Robert El-Maraghi, M.D., Glenwood Goss, M.D., Gregoire Le Gal, M.D., David Stewart, M.D., Timothy Ramsay, Ph.D., Marc Rodger, M.D., Debra Witham, B.Sc.N., and Philip S. Wells, M.D., for the AVERT Investigators*

Secondary prevention vs. LMWH…

Comparison of an Oral Factor Xa Inhibitor With Low Molecular Weight Heparin in Patients With Cancer With Venous Thromboembolism: Results of a Randomized Trial (SELECT-D)

Annie M. Young, Andrea Marshall, Jenny Thirlwall, Oliver Chapman, Anand Lokare, Catherine Hill, Danielle Hale, Janet A. Dunn, Gary H. Lyman, Charles Hutchinson, Peter MacCallum, Ajay Kakkar, F.D. Richard Hobbs, Stavros Petrou, Jeremy Dale, Christopher J. Poole, Anthony Maraveyas, and Mark Levine

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Design

	CASSINI	AVERT	SELECT-D
Type	DBRCT	DBRCT	
Population	Ambulatory Cancer	Ambulatory Cancer	
Size	~400 patients each arm	~275 patients each arm	
Comparison	6 mo Rivaroxaban vs. Placebo	6 mo Apixiban vs. Placebo	
Outcome	DVT/PE or Death	VTE	

Khorana et al "Rivaroxaban for Thromboprophylaxis in High-Risk Ambulatory Patients with Cancer". *NEJM*. Feb 2019: 380 (8)
Carrier et al "Apixaban to Prevent Venous Thromboembolism in Patients with Cancer" *NEJM. Feb* 2019; 380(8)
Young et al "Comparison of an Oral Factor Xa inhibitor with low molecular weight heparin in patients with cancer with venous thromboembolism". *J Clin Oncology* 36:2017-2023

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Results: CASSINI and AVERT

Table 1. Cumulative Analysis of the AVERT and CASSINI Trials.*

Outcome	CASSINI Trial		AVERT Trial		Cumulative Values				
	Rivaroxaban	Placebo	Apixaban	Placebo	DOACs	Placebo	Relative Risk (95% CI)	Absolute Difference	No. Needed to Treat or Harm†
			number/total number (percent)					*percentage points*	
Primary efficacy outcome									
ITT analysis	25/420 (6.0)	37/421 (8.8)	12/288 (4.2)	28/275 (10.2)	37/708 (5.2)	65/696 (9.3)	0.56 (0.38–0.83)	−4.1	24
Analysis during treatment period	11/420 (2.6)	27/421 (6.4)	3/288 (1.0)	20/275 (7.3)	14/708 (2.0)	47/696 (6.8)	0.29 (0.16–0.53)	−4.8	21
Symptomatic VTE: ITT analysis	15/420 (3.6)	19/421 (4.5)	9/288 (3.1)	22/275 (8.0)	24/708 (3.4)	41/696 (5.9)	0.58 (0.35–0.94)	−2.5	40
Major bleeding	8/405 (2.0)	4/404 (1.0)	10/288 (3.5)	5/275 (1.8)	18/693 (2.6)	9/679 (1.3)	1.96 (0.88–4.33)	1.3	77
Death from any cause	84/420 (20.0)	100/421 (23.8)	35/288 (12.2)	27/275 (9.8)	119/708 (16.8)	127/696 (18.2)	0.92 (0.73–1.16)	−1.4	71

* In the AVERT trial, the modified intention-to-treat analysis was the primary analysis (574 patients underwent randomization). DOACs denotes direct oral anticoagulants, ITT intention to treat, and VTE venous thromboembolism.
† The number needed to treat is shown for all outcomes except major bleeding (number needed to harm).

Agnelli "Direct Oral Anticoagulants for Thromboprophylaxis in Ambulatory Patients with Cancer". *NEJM*. Feb 2019: 380 (8)

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Results: SELECT-D

	Rivaroxaban	Dalteparin
Risk of VTE	3.94%	8.86%
RR	.44	
ARR	4.92%	
NNT	20	
Risk of Major Bleeding	5.4%	2.9%
RR	1.86	
NNH	40	

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Commentary

- DOACs are emerging as alternative to LMWH in cancer patients for primary or secondary prevention
- Costs, risk:benefit, patient preference may play role in choice
- Might require guideline update before broad practice change occurs

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75yo F with newly diagnosed cancer is about to start chemotherapy. She has no history of venous thromboembolism.

What is the best strategy to prevent VTE in this patient?

A) Warfarin
B) Low molecular weight heparin
C) Factor Xa inhibitor
D) ASA + Plavix
E) Compression hosiery

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Case #4

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You are admitting a patient to the ICU who is deemed "high risk" for VTE development. The patient is not on any VTE prophylaxis.

As you open the chart…

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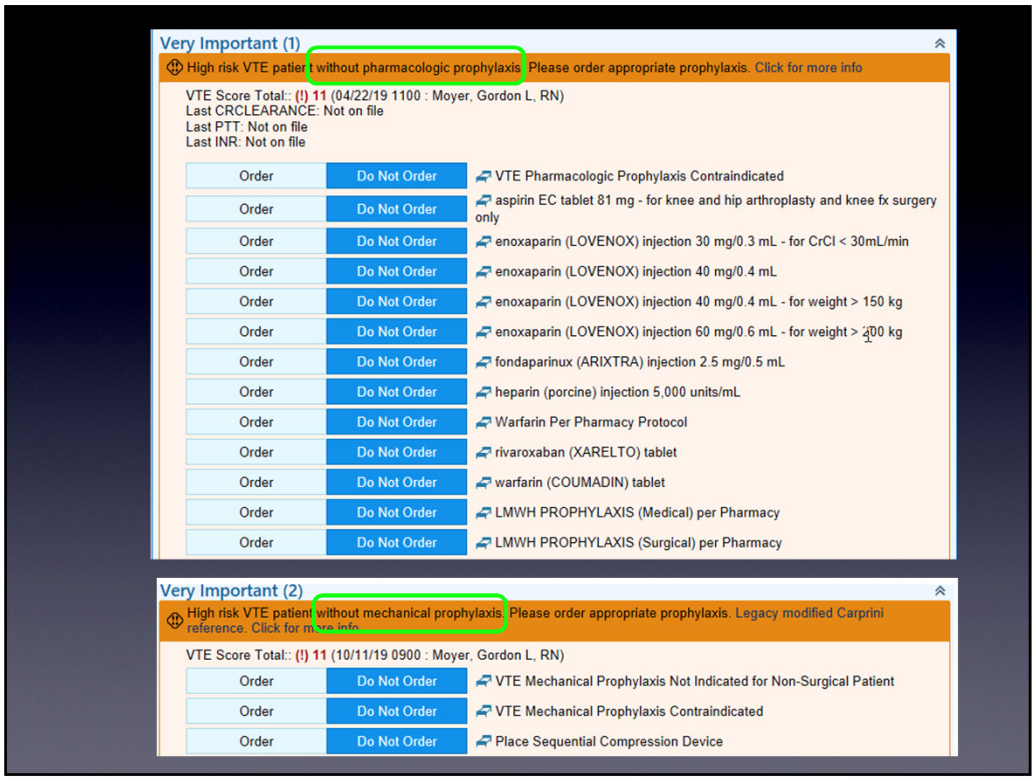

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You are admitting a patient to the ICU who is deemed "high risk" for VTE development. The patient is not on any VTE prophylaxis.

How do you respond?:

A) Order enoxaparin alone
B) Order SCDs alone
C) Order both SCDs and enoxaparin
D) Order TED hose instead
E) No VTE prophylaxis, that stuff is overrated

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Background

- VTE is common in critically ill patients
- 50% reduction in VTE with pharmacologic prophylaxis vs. placebo
  - 5-20% still get VTE even with pharmacologic prophy
- 30% reduction in VTE with pharm + SCD vs. pharm alone—retrospective stroke population
- No RCTs comparing pharm +/- SCDs in critically ill
- Guidelines make mixed recs; therefore…

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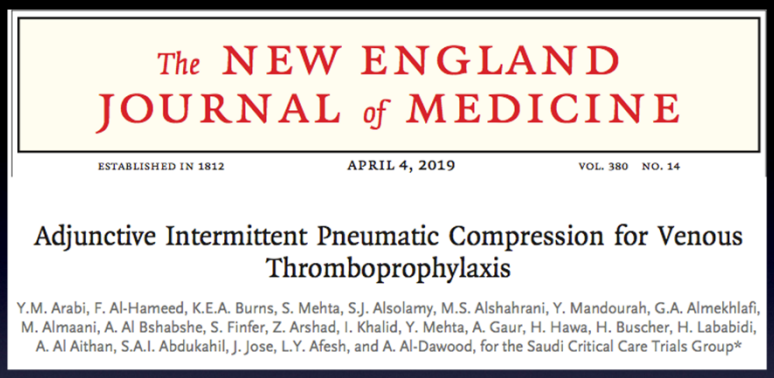

The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812 APRIL 4, 2019 VOL. 380 NO. 14

Adjunctive Intermittent Pneumatic Compression for Venous Thromboprophylaxis

Y.M. Arabi, F. Al-Hameed, K.E.A. Burns, S. Mehta, S.J. Alsolamy, M.S. Alshahrani, Y. Mandourah, G.A. Almekhlafi, M. Almaani, A. Al Bshabshe, S. Finfer, Z. Arshad, I. Khalid, Y. Mehta, A. Gaur, H. Hawa, H. Buscher, H. Lababidi, A. Al Aithan, S.A.I. Abdukahil, J. Jose, L.Y. Afesh, and A. Al-Dawood, for the Saudi Critical Care Trials Group*

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Design

- Multi-site international non-blinded RCT
- Pharmacologic VTE +/- pneumatic compression
- Primary outcome: Incidence of lower limb DVT

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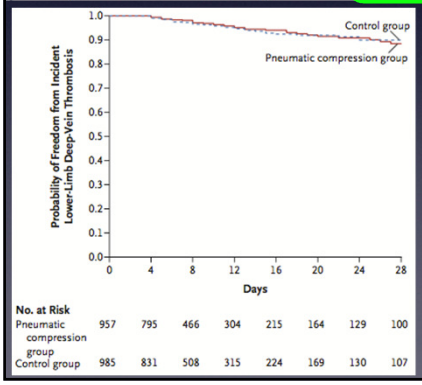
Results

Table 3. Primary Outcome of Incident Proximal Lower-Limb Deep-Vein Thrombosis in the Modified Intention-to-Treat and Per-Protocol Populations.*

Variable	Modified Intention-to-Treat Population		Per-Protocol Population	
	Pneumatic Compression Group (N=991)	Control Group (N=1012)	Pneumatic Compression Group (N=959)	Control Group (N=984)
Incident proximal lower-limb deep-vein thrombosis — no./total no. (%)†	37/957 (3.9)	41/985 (4.2)	35/929 (3.8)	41/957 (4.3)
Relative risk (95% CI)	0.93 (0.60–1.44)‡	Reference	0.88 (0.57–1.37)	Reference
Adjusted relative risk (95% CI)§	0.93 (0.61–1.41)	Reference	0.89 (0.58–1.36)	Reference



No difference in VTE incidence between two groups

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Commentary

- Largest controlled trial to date on topic
- Eliminating SCDs when patients are on LMWH has potential huge cost implications and patient mobility
- Need to address hospital policies to match this new data

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You are admitting a patient to the ICU who is deemed "high risk" for VTE development. The patient is not on any VTE prophylaxis.

How do you respond?:

A) Order enoxaparin alone
B) Order SCDs alone
C) Order both SCDs and enoxaparin
D) Order TED hose instead
E) No VTE prophylaxis, that stuff is overrated

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Case #5

49

85yo female with influenza is admitted to the wards. On HD#3, she is confused, seems to be hallucinating and is picking at her IV and removing her oxygen. She has a fever of 101.4 and SaO2 90% on 2L.
Overnight she has more shortness of breath and is transferred to the ICU with ARDS and respiratory failure. She remains confused.

Which of the following are true?

A) Early treatment with anti-psychotic medications on the wards will shorten her duration of delirium?
B) Early treatment with anti-psychotic medications could have prevented her ICU transfer?
C) Initiation of anti-psychotic medications in the ICU will shorten her days of delirium?
D) None of the above are true

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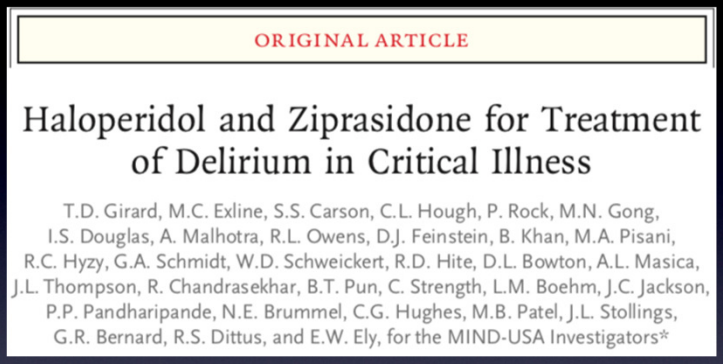
Background

- Delirium is very common in hospitalized patients and associated with poorer outcomes
- Hypoactive (80%) >> Hyperactive (20%) cases
- Conflicting prior data on effectiveness of anti-psychotics in treatment of delirium
- Anti-psychotics continue to be used widely (50-60% cases)

51

Design



ORIGINAL ARTICLE

Haloperidol and Ziprasidone for Treatment of Delirium in Critical Illness

T.D. Girard, M.C. Exline, S.S. Carson, C.L. Hough, P. Rock, M.N. Gong, I.S. Douglas, A. Malhotra, R.L. Owens, D.J. Feinstein, B. Khan, M.A. Pisani, R.C. Hyzy, G.A. Schmidt, W.D. Schweickert, R.D. Hite, D.L. Bowton, A.L. Masica, J.L. Thompson, R. Chandrasekhar, B.T. Pun, C. Strength, L.M. Boehm, J.C. Jackson, P.P. Pandharipande, N.E. Brummel, C.G. Hughes, M.B. Patel, J.L. Stollings, G.R. Bernard, R.S. Dittus, and E.W. Ely, for the MIND-USA Investigators*

52

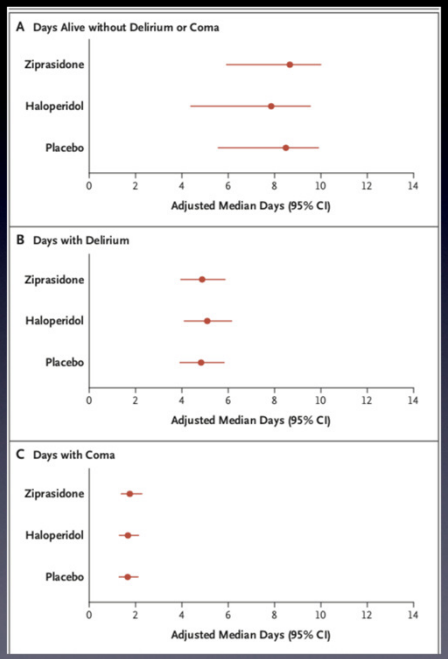
Design

- Multi-center DBRCT
- ICU patients with delirium
- Haldol IV (N=192) vs. Ziprasidone IV (N=190) vs. Placebo (N=184)
- Trained assessments 2x/day with CAM-ICU tool
- Outcome: Number of days with and without delirium

53

Results

No difference in delirium days between the groups



54

Commentary

- Largest DBRCT to date on topic
- Similar findings as prior smaller ICU delirium studies (“MIND” and “Hope-ICU”)
- Reemphasizes need to address underlying factors leading to delirium and be patient for resolution
- TWDFNR=Anti-psychotics for delirium

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Commentary

Journal of Hospital Medicine

FULL MENU | Current Issue | Past Issues | SHM Statements | New Online | Online Only

CHOOSING WISELY: THINGS WE DO FOR NO REASON

Things We Do For No Reason: Use of Antipsychotic Medications in Patients with Delirium

J. Hosp. Med. 2019 September;14(9):565-567. Published online first March 20, 2019.

By: Amit K Pahwa, MD, FAAP, Imran Qureshi, Pharm D, BCPP, Ethan Cumbler, MD, FACP, FHM

Amit K Pahwa, MD, FAAP; E-mail: apahwa1@jhmi.edu; Telephone: 410-502-1934.

Inspired by the ABIM Foundation's Choosing Wisely® campaign, the "Things We Do for No Reason™" (TWDFNR) series reviews practices that have become common parts of hospital care but may provide little value to our patients. Practices reviewed in the TWDFNR™ series do not represent "black and white" conclusions or clinical practice standards but are meant as a starting place for research and active discussions among hospitalists and patients. We invite you to be part of that discussion.

Choosing Wisely®

An initiative of the ABIM Foundation

The ABIM Foundation's mission for the Choosing Wisely® campaign is to promote conversations between clinicians and patients by helping patients choose care that is supported by evidence, not duplicative of other tests or procedures already received, free from harm, and truly necessary. Hospitalists can incorporate the Choosing Wisely® recommendation(s) into daily practice. Visit the Choosing Wisely website for a complete overview.

56

85yo female with influenza is admitted to the wards. She is confused, seems to be hallucinating and is picking at her IV and removing her oxygen. She has a fever of 101.4 and SaO2 90% on 2L.
Overnight she has more shortness of breath and is transferred to ICU with ARDS and respiratory failure. She remains confused.

Which of the following are true?

A) Early treatment with anti-psychotic medications on the wards will shorten her duration of delirium?
B) Early treatment with anti-psychotic medications could have prevented her ICU transfer?
C) Initiation of anti-psychotic medications in the ICU will shorten her days of delirium?
D) None of the above are true

57

75yo M with sepsis and acute cholecystitis.

Which of the following has a lower complication rate?

A) Lap chole—get that sucker out of there!
B) Percutaneous drainage

58

Laparoscopic cholecystectomy versus percutaneous catheter drainage for acute cholecystitis in high risk patients (CHOCOLATE): multicentre randomised clinical trial

Charlotte S Loozen,[1] Hjalmar C van Santvoort,[1,2] Peter van Duijvendijk,[3] Marc GH Besselink,[3] Dirk J Gouma,[4] Grard AP Nieuwenhuijzen,[5] Johannes C Kelder,[6] Sandra C Donkervoort,[7] Anna AW van Geloven,[8] Philip M Kruyt,[9] Daphne Roos,[10] Kirsten Kortram,[1] Verena NN Kornmann,[1] Apollo Pronk,[11] Donald L van der Peet,[12] Rogier MPH Crolla,[13] Bert van Ramshorst,[1] Thomas L Bollen,[14] Djamila Boerma[1]

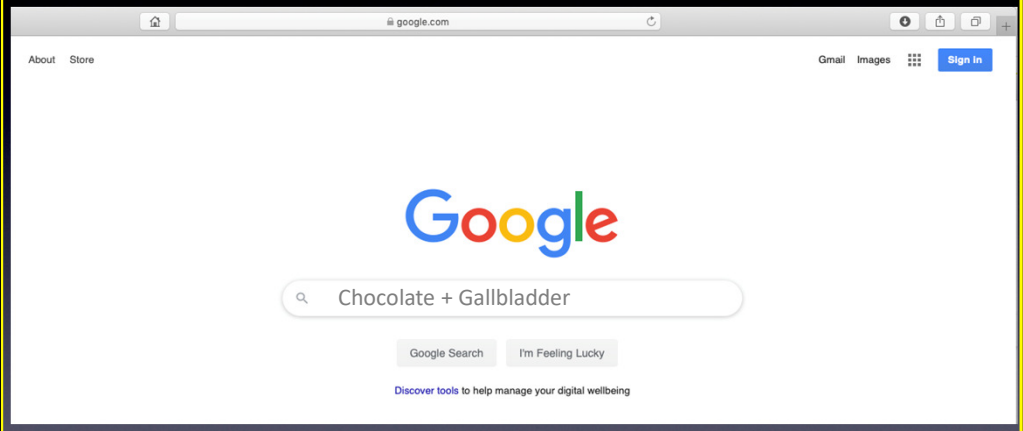
- First RCT
- APACHE score 7-14

Procedure	Complication rate	Death	Healthcare cost
Lap chole (N=66)	12%	3%	-30%
Perc drainage (N=68)	65%	9%	NA

Loozen et al "Laproscopic cholecystectomy versus percutaneous catheter drainage for acute cholecystitis in high risk patients (CHOCOLATE): multicentre randomised clinical trial" BMJ 2018; 363:k3965 Aug 2018

59

When I regretted using Google…



60

Case #6

61

75yo M, who lives independently, is admitted after a fall due to CHF exacerbation. PMH includes COPD, HTN and mild cognitive impairment. He works with PT/OT and is not quite at his functional baseline.

What is the best discharge disposition for him?

A) He should be discharged to home with home health
B) He should be discharged to Skilled nursing
C) He should remain in hospital until fully back to functional baseline
D) Need more information

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Background

- 40% Medicare inpatients get “post-acute” care—90% as Skilled nursing (SNF) or Home health (HH)
- $60 billion per year and rising!
- Prior studies have been small or observational with conflicting results
- HH costs<<SNF costs
- *What about other metrics or clinical outcomes?*

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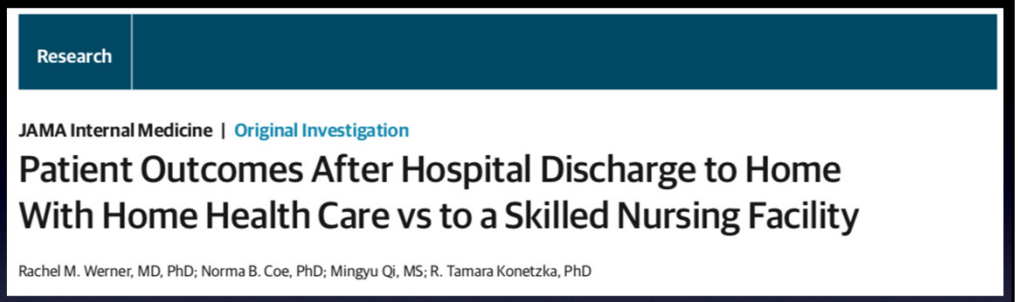
Background


Research

JAMA Internal Medicine | Original Investigation

Patient Outcomes After Hospital Discharge to Home With Home Health Care vs to a Skilled Nursing Facility

Rachel M. Werner, MD, PhD; Norma B. Coe, PhD; Mingyu Qi, MS; R. Tamara Konetzka, PhD

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Design


Research

JAMA Internal Medicine | Original Investigation

Patient Outcomes After Hospital Discharge to Home With Home Health Care vs to a Skilled Nursing Facility

Rachel M. Werner, MD, PhD; Norma B. Coe, PhD; Mingyu Qi, MS; R. Tamara Konetzka, PhD

- Retrospective cohort Medicare beneficiares
- 17.2 million hospitalizations
- Jan 1, 2010 to Dec 31, 2016

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Outcome measures


Research

JAMA Internal Medicine | Original Investigation

Patient Outcomes After Hospital Discharge to Home With Home Health Care vs to a Skilled Nursing Facility

Rachel M. Werner, MD, PhD; Norma B. Coe, PhD; Mingyu Qi, MS; R. Tamara Konetzka, PhD

- All cause 30 day readmission
- Death within 30 days of discharge
- Functional status change
- Medicare payment for postacute care and total payment at 60 days

66

Results

- Cohort well-matched
- Usual stuff

Table 1. Characteristics of Patients Discharged From the Hospital in Study Cohort

Characteristic	Patients, No. (%)	
	Home Health Care (n = 6 687 339)	SNF (n = 10 548 515)
Age, mean (SD), y	78.7 (7.7)	81.5 (7.9)
Female sex	3 918 245 (58.6)	6 809 443 (64.6)
Race/ethnicity		
White	5 706 387 (85.3)	9 163 361 (86.9)
Black	657 929 (9.8)	959 701 (9.1)
Hispanic	128 577 (1.9)	159 732 (1.5)
Dually enrolled in Medicare and Medicaid	863 159 (12.9)	2 179 823 (20.7)
Enrolled in Medicare Advantage	1 633 387 (24.4)	2 602 358 (24.7)
No. of comorbidities, mean (SD)	3.2 (2.7)	3.3 (2.8)
5 Most common DRGs		
Total knee or hip replacement	856 617 (12.8)	1 178 668 (11.2)
Sepsis	313 046 (4.7)	667 208 (6.3)
Congestive heart failure	456 418 (6.8)	460 914 (4.4)
Pneumonia	293 392 (4.4)	406 087 (3.8)
Urinary tract infection	170 681 (2.6)	434 723 (4.1)

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Results

- Raw data

Table 2. Unadjusted Patient Outcomes and Medicare Payments Among Patients Discharged to Home Health Care and to SNFs

Outcome	Discharge to Home Health Care	Discharge to SNFs	Difference Between Discharge to Home Health Care (vs SNF)
Patient outcomes (all discharges [N = 17 235 854]), %			
Readmission within 30 d	15.8	17.8	−2.0
Death within 30 d	2.3	6.9	−4.6
Improvement in activities of daily living[a]	80.2	29.3	50.9
Medicare payment (fee-for-service Medicare discharges [n = 13 000 109]), mean (SD), $			
Medicare payment to hospital	11 240 (11 231)	11 549 (12 195)	−309
Medicare payment to HHA or SNF	2459 (1520)	11 073 (9414)	−8614
Total Medicare payment in first 60 d after hospital admission	17 088 (14 525)	26 101 (16 426)	−9013

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Results


Research

JAMA Internal Medicine | Original Investigation

Patient Outcomes After Hospital Discharge to Home With Home Health Care vs to a Skilled Nursing Facility

Rachel M. Werner, MD, PhD; Norma B. Coe, PhD; Mingyu Qi, MS; R. Tamara Konetzka, PhD

- After statistical analysis
- 17,235,854 hospitalizations
- 62.2% women, 37.8% men

Outcome	HH (38.8%) vs. SNF (61.2%)	P-value
30d readmission	+5.6%	0.02
30d mortality	-2%	0.12
Functional status	-1.9%	0.71
Cost		
30d	-$5384	<0.001
60d	-$4514	<0.001

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Commentary

- Largest study to date looking at this topic
- 2x more patients to SNF vs. Home—Why?...
  - Clinical factors—old, frail, complicated
  - Non-clinical factors—social support, "easy DC", CCOs, hospitalists, fear of readmission
- Tradeoffs of "risks"—readmissions vs. cost
- Need better Home Health "system" analysis and improvement

- Tip of iceberg sort of study…gets the policy and other conversations going

70

75yo M, who lives independently, is admitted after a fall and CHF exacerbation. PMH includes COPD, HTN and mild cognitive impairment. He works with PT/OT and is not quite at his functional baseline.

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D) Need more information

71

You are co-managing an 83yo F with a right hip fracture after a ground level fall. She has osteoporosis, HTN, cataracts and hypothyroidism. Her pain is well controlled on oral morphine.

Which of the following should NOT be used for prevention of constipation?

A) Docusate oral
B) Sennoside oral
C) Polyethylene glycol (PEG or Miralax)
D) Lactulose
E) Soluble fiber (Psyllium aka “Metamucil”)

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CHOOSING WISELY®: THINGS WE DO FOR NO REASON

Things We Do for No Reason: Prescribing Docusate for Constipation in Hospitalized Adults

Robert J Fakheri, MD[1]*, Frank M Volpicelli, MD[2]

- On balance studies on docusate effectiveness show no difference vs. placebo or other modalities
- Cost of drug and administration--$100 million!*
- Harm in waiting to poop

Recommendation:

- PEG>Lactulose>Psyllium>Sennosides**
- Remove colace from hospital formulary!

Fakheri, RJ "Things we do for no reason: Prescribing Docusate for Constipaiton in Hospitalized Adults" JHM vol 14 (2) Feb 2019
*Lee TC, Pattern of inpatient laxative use: waste not, want not. JAMA Intern Med. 2016;176(8):1216-1217
**Ramkumar D, Efficacy and safety of traditional medical therapies for chronic constipation: systematic review. Am J Gastroenterol. 2005;100(4):936- 971

Summary

START

- Oral antibiotics for selected cases of endocarditis, osteomyelitis and appendicitis
- DOACs as an option in cancer patients
- Cholecystectomy rather than perc drainage for high risk acute cholecystitis
- Redesigning home health to be a more robust discharge option
- Thank a hospitalist 1st Thursday every March

Summary

STOP

- Metformin if GFR<30 ml/min
- SCDs in high risk patients already on pharmacological VTE prophylaxis
- Anti-psychotics in patients with hypOactive delirium
- Colace for constipation

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What Questions Do you have?

Thank you!

kbreger@LHS.org

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CAM-ICU tool from MDCalc.com