



MASSACHUSETTS
GENERAL HOSPITAL



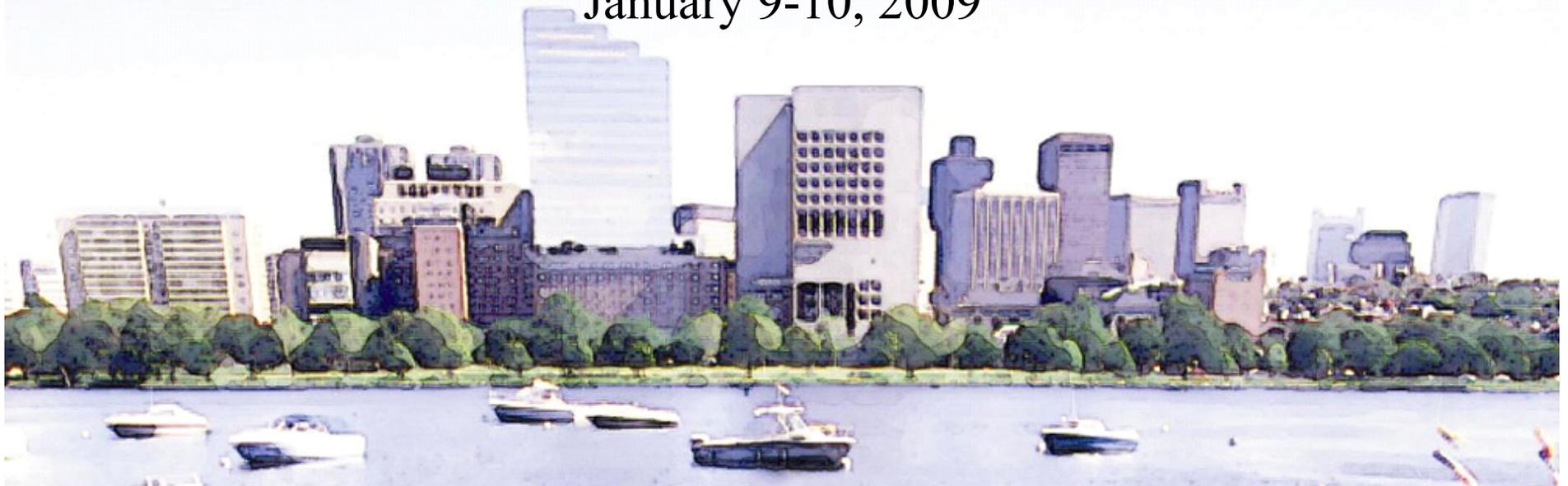
HARVARD
MEDICAL SCHOOL

*How Doctors Choose Medicines
when Treating Patients with Type 2 Diabetes*

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Endocrine Society Beta Cell meeting

January 9-10, 2009



Outline

- Background
- Observed Prescription Patterns
- National Survey of PCPs and Endocrinologists



Background

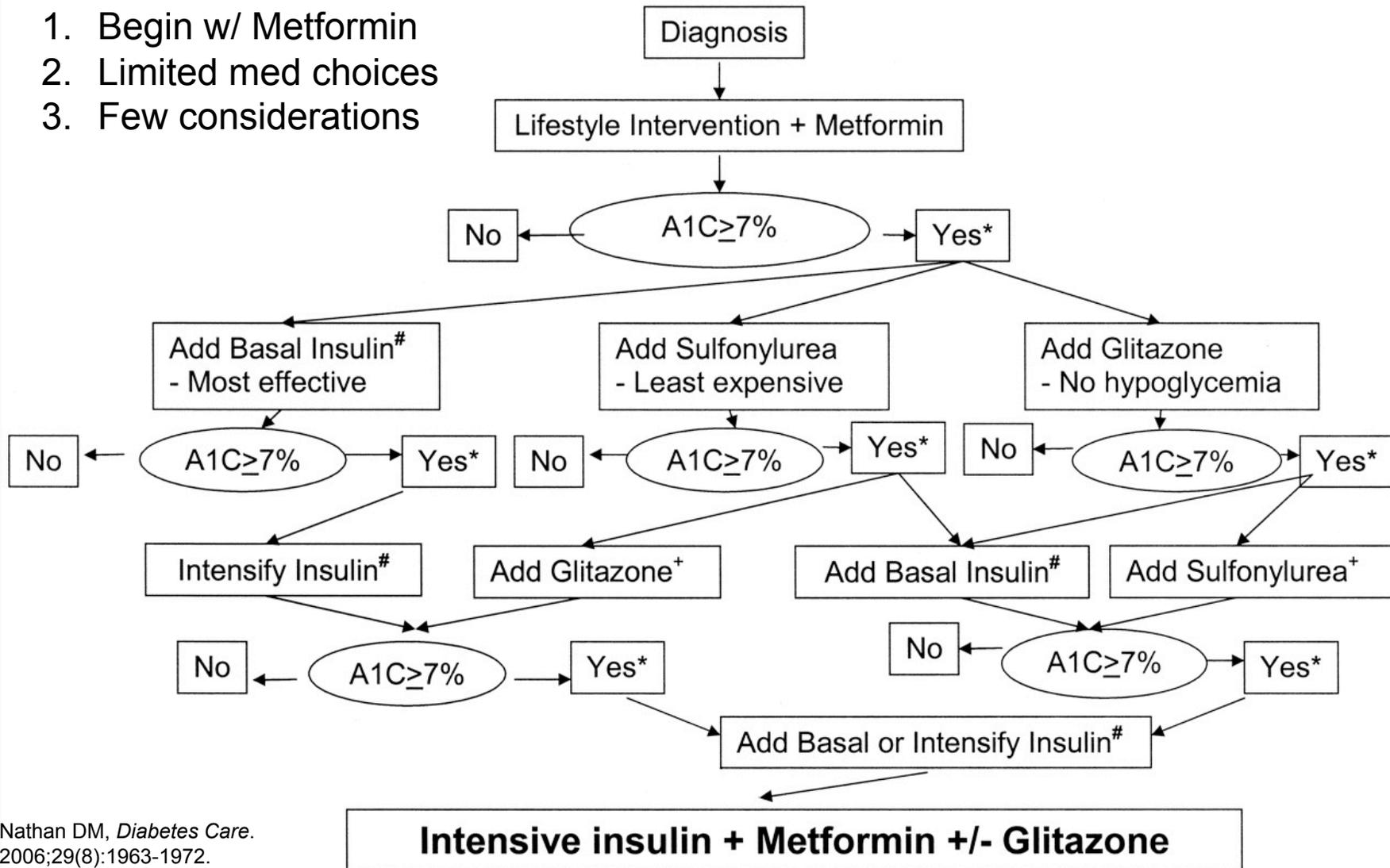
- Glycemic control in type 2 diabetes remains a challenge
- Plethora of drug choices
 - Currently 30 drugs from 9 classes
 - New (and expensive) agents on the horizon
- Sparse evidence regarding which drugs to use and in what order
 - Recent guideline mostly expert opinion
 - Empiric evidence is that there is wide variation in practice



“The Algorithm”

Unless contraindicated:

1. Begin w/ Metformin
2. Limited med choices
3. Few considerations



Nathan DM, *Diabetes Care*.
2006;29(8):1963-1972.

Intensive insulin + Metformin +/- Glitazone



What is the extent of practice variation in medicine prescribing?

1. First Medicine
2. Second Medicine
3. Third Medicine



Prescription Sequences

- All prescriptions for hypoglycemic medications ordered via EMR within Partners HealthCare, January 2000 – December 2006
 - 224,722 prescriptions
 - 18,410 patients
- Limit to “new initiators”
 - First DM med at least 6 mos after other med
 - N = 5856 patients
 - 3708 = 1 med only
 - 2148 = 2 sequential medicines
 - 510 = sequence of 3 or more meds

Grant RW et al, abstract
67th Scientific Sessions, 2007



Descriptive Results

1. First drug prescribed (n = 5856)

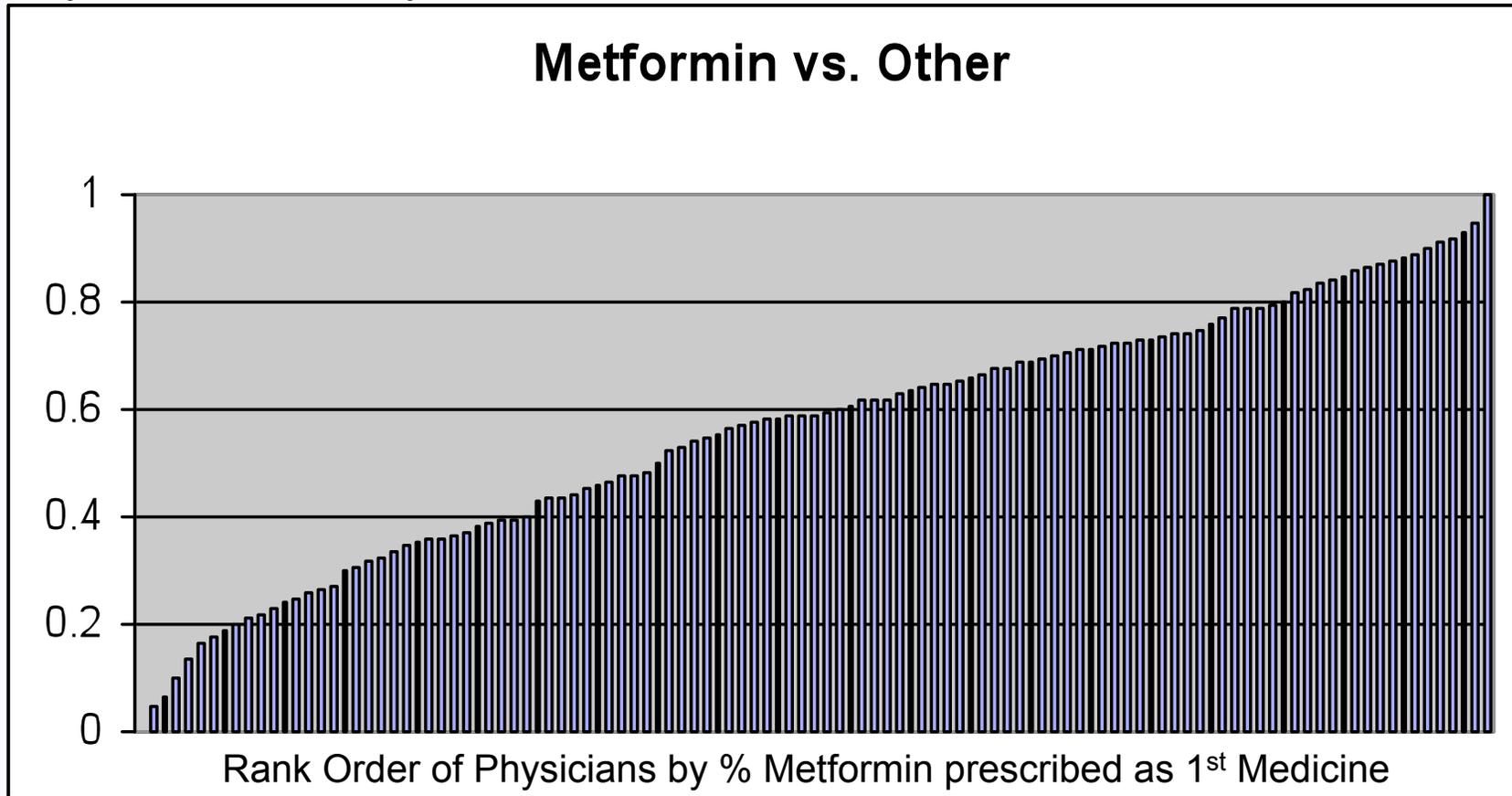
- | | | | |
|--------------|------|---|-----|
| • Metformin | 53% | } | 79% |
| • SFU | 26% | | |
| • Insulin | 17% | | |
| • Glitazones | 3% | | |
| • Other | 0.4% | | |

2. Choice of first two drugs (n = 2148) (20/20 possible combos)

- | | | | |
|--------------------------------------|-----|---|-----|
| 1. Metformin \Rightarrow SFU | 37% | } | 63% |
| 2. SFU \Rightarrow Metformin | 26% | | |
| 3. Metformin \Rightarrow Glitazone | 10% | | |
| 4. Metformin \Rightarrow insulin | 6% | | |
| 5. Other combos (n = 16) | 21% | | |



Physician Variability: First Prescribed Medicine



Proportion of patients per physician prescribed Metformin as first medicine, among physicians with 10 or patients (n = 173)



Physician Variability: Two Prescribed Medicines

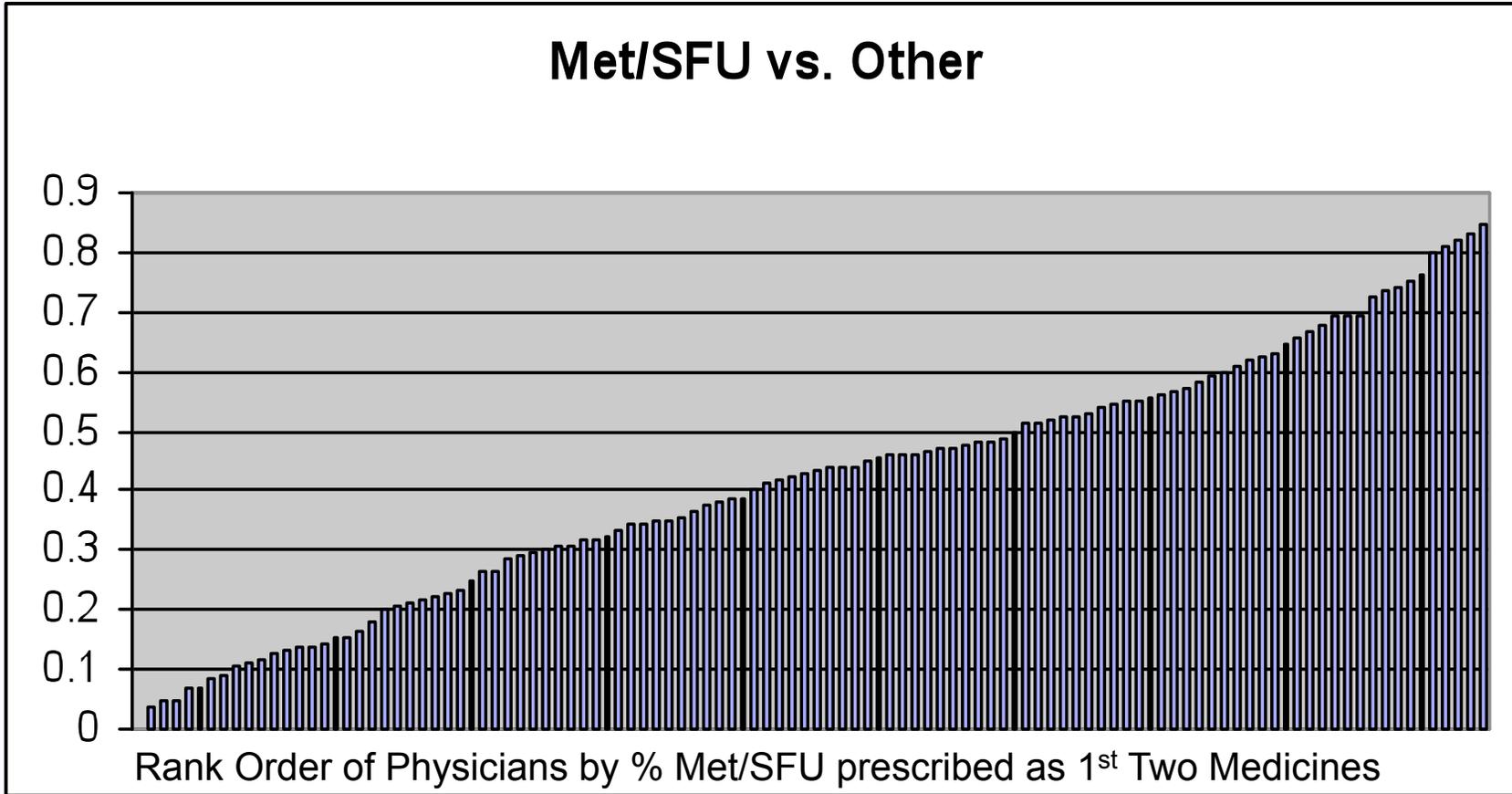


Figure Legend: Proportion of patients per physician prescribed Metformin and SFU as first two medicines, among physicians with 10 or patients (n = 173)



Sequence of three medicines

41 out of 60 possible combinations seen:

| | | |
|-------------------------------|-----|-------|
| Met/SFU followed by Glitazone | 32% | } 60% |
| Met/SFU followed by Insulin | 28% | |
| <hr/> | | |
| Remaining combos (n = 39) | 40% | |

“Common pathways” vs. rarer combinations



What is the source of this practice variation?

- US National Survey of Physicians
- What factors guide physicians' choices of which medications to prescribe?
- Assess “major considerations” at three key stages of therapy:
 - A. Medication Initiation
 - B. Use of Glitazones
 - C. Adding Insulin

Grant RW et al, Diabetes Care
2007, 30:1448-1453



Methods

- Compare responses between academic generalists (SGIM) and diabetes specialists (ADA)
- Web-based questionnaire e-mailed to “Fellow SGIM” and “Fellow ADA” members



How do you choose which glycemic medicine to prescribe first?

1. To what extent do you consider each of the following factors when choosing **which medicine to prescribe FIRST** (e.g. metformin vs. sulfonylurea vs. insulin, etc) for glycemic control in Type 2 Diabetes [assume no medical contra-indications]:

| | Major Consideration | Minor Consideration | Not a Consideration |
|---|--------------------------|--------------------------|--------------------------|
| Patient's tendency to complain about side effects | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> |
| Your usual practice with similar prior patients | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> |
| Expert guidelines or hospital algorithm | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> |
| Patient's adherence behavior | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> |
| Extent of HbA1c elevation | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> |
| Patient's weight | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> |
| Patient's age | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> |
| Your assessment of patient's health status and co-morbid conditions | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> |
| Patient's out-of-pocket expense | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> |
| Patient's specific medication request | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> |



Listed Considerations

Physician-related factors:

- usual/prior practice, guidelines/algorithm, assessment of health status & co-morbidities
 - *Glitazones*: lipid profile, insulin resistance, delay/avoid insulin (MD)
 - *Insulin*: strength of therapeutic relationship

Subjective patient factors:

- adherence behavior, pt medication request
- tendency to complain about side effects
 - *Glitazones*: delay/avoid insulin injection (pt)
 - *Insulin*: motivation to improve



Listed Considerations (cont)

Objective clinical data

- age, weight, HbA1c
 - *Insulin*: pattern of measured glucoses

Non-clinical factors

- medication costs



Academic Generalists

- 449 responses/1524 eligible e-mails sent
 - 30% response rate
- Academic attending physicians
 - Most graduated within past 15 yrs
 - 41% saw > 100 patients w/ DM in past year
 - 9% saw < 20 patients w/ DM in past year



ADA Respondents

- 427 responses/1926 eligible e-mails sent
 - 22% response rate
- Attending physicians
 - 40% academic, 38% private practice
 - Most graduated within past 25 yrs
 - 67% saw > 100 patients w/ DM in past year
 - 5% saw < 20 patients w/ DM in past year



Results – First Med Choice

- Top 3 major considerations
 - SGIM: your assessment (85%), HbA1c (64%), pt wt (64%)
 - ADA: your assessment (93%), HbA1c (86%), pt wt (70%)
- Other major
 - SGIM: pt adherence (57%), usual practice (54%), \$\$ (52%), algorithm (47%)
 - ADA: usual practice (68%), pt adherence (59%), \$\$ (49%)
- Not Major
 - SGIM: pt request, pt age, pt tendency to complain
 - ADA: **algorithm**, pt request, pt age, pt tendency to complain



Table 1—Major considerations when choosing initial hypoglycemic medical therapy

| Major considerations | Specialist (n = 379) | Academic generalist (n = 440) | P |
|--|-------------------------|----------------------------------|--------|
| Assessment of patient's health and comorbid conditions | 93 (1) | 85 (1) | <0.001 |
| Extent of A1C elevation | 86 (2) | 64 (2) | <0.001 |
| Patient's weight | 70 (3) | 63 (3) | 0.06 |
| Physician's usual practice | 68 (4) | 54 (5) | <0.001 |
| Patient's adherence behavior | 59 (5) | 57 (4) | 0.7 |
| Patient's out-of-pocket costs | 49 (6) | 52 (6) | <0.001 |
| Expert guideline/hospital algorithm | 37 (8) | 47 (7) | 0.01 |
| Patient's age | 38 (7) | 22 (9) | <0.001 |
| Patient's request | 16 (10) | 26 (8) | <0.001 |
| Patient's tendency to complain about side effects | 22 (9) | 18 (10) | 0.003 |

Data are percentage (rank) of specialists vs. academic generalists listing each major consideration. Considerations are listed in order of overall combined rank.



Interpretation

- Very similar factors between generalists & specialists
- “Assessment of health status & co-morbidities” -> MD black box
- Algorithms low on list, especially for specialists



Results – Use of Glitazones

- Frequency of use
 - SGIM: frequently (16%), occasionally (44%)
 - ADA: **frequently (54%)**, occasionally (32%)
- Major Considerations
 - SGIM: pt avoid **insulin** (76%), your assessment (68%), HbA1c (60%), your desire to avoid/delay **insulin**
 - ADA: your assessment (88%), HbA1c (65%), improve lipids/reduce insulin resistance (64%), usual practice (58%), pt weight (53%)



Table 2—Major considerations when choosing to prescribe a glitazone

| Major considerations | Specialist (n = 369) | Academic generalist (n = 403) | P |
|---|-------------------------|----------------------------------|--------|
| Assessment of patient's health and comorbid conditions | 88 (1) | 68 (2) | <0.001 |
| Patient's desire to avoid insulin | 47 (7) | 76 (1) | <0.001 |
| Extent of A1c elevation | 65 (2) | 60 (3) | 0.26 |
| Physician's desire to improve lipid profile/reduce insulin resistance | 63 (3) | 39 (6) | <0.001 |
| Patient's out-of-pocket costs | 50 (6) | 50 (5) | 1.0 |
| Physician's desire to avoid/delay insulin | 36 (8) | 56 (4) | <0.001 |
| Physician's usual practice | 57 (4) | 32 (8) | <0.001 |
| Patient's weight | 53 (5) | 25 (9) | <0.001 |
| Expert guideline/hospital algorithm | 24 (9) | 36 (7) | <0.001 |
| Patient request | 13 (11) | 15 (10) | 0.03 |
| Patient age | 14 (10) | 13 (11) | 0.47 |

Data are percentage (rank) of specialists vs. academic generalists listing each major consideration. Considerations are listed in order of overall combined rank.



Interpretation

- Generalists use 3rd-line agents less often
 - do so to avoid insulin
- Specialist use more often
 - apply pathophysiologic rationales like insulin resistance and dyslipidemia



Results – Use of Insulin

- Top 5 Major considerations
 - SGIM: HbA1c (92%), pt adherence (76%), your assessment (75%), glucose pattern (74%), pt motivation (71%)
 - ADA: HbA1c (94%), your assessment (81%), glucose pattern (83%), pt motivation (67%), pt adherence (60%)



Table 3—Major considerations when choosing to initiate insulin therapy

| Major considerations | Specialist (n = 370) | Academic generalist (n = 434) | P |
|--|-------------------------|----------------------------------|--------|
| Extent of A1C elevation | 93 (1) | 92 (1) | 0.82 |
| Pattern of measured glucose levels | 83 (2) | 74 (4) | 0.012 |
| Assessment of patient's health and comorbid conditions | 81 (3) | 75 (3) | 0.06 |
| Patient's motivation to improve | 67 (4) | 71 (5) | 0.06 |
| Patient's adherence behavior | 60 (5) | 76 (2) | <0.001 |
| Strength of therapeutic relationship with patient | 46 (6) | 38 (6) | <0.001 |
| Expert guideline/hospital algorithm | 26 (7) | 37 (7) | <0.001 |
| Patient's weight | 20 (9) | 24 (8) | <0.001 |
| Patient age | 20 (9) | 20 (9) | 0.92 |
| Patient's out-of-pocket costs | 22 (8) | 24 (8) | 0.65 |

Data are percentage (rank) of specialists vs. academic generalists listing each major consideration. Considerations are listed in order of overall combined rank.



Interpretation

- Generalists & Specialists consider similar criteria in choosing insulin
 - Academic generalists placed greater emphasis on patient adherence
 - 76% vs. 60% of specialists, $P < 0.001$
- Generalists report patient-level barriers
- Specialists indicate clinical resources not a problem



Barriers to Insulin Use

- Major Barriers
 - SGIM: pt fear or resistance to injections (68%), pt preference to continue other rx (68%)
 - ADA: *none*
- Minor Barriers
 - SGIM: concern for wt gain (65%), safety (51%), lack of staff support (40%)
 - ADA: concern for wt gain (57%), pt fear or resistance to injections (51%), pt preference to continue other rx (49%)
- Not Barriers
 - SGIM: experience, time; ADA: experience, time, resources



Qualitative vs. Quantitative

Aggregate scores (scale of 0–10), $P < 0.001$.

- Qualitative factors = 7.3
 - adherence, motivation, overall health assessment
- Quantitative factors = 6.9
 - A1C, age, weight



Summary

Respondents had **5 major considerations** at each stage

Frequently cited major considerations included:

- overall assessment of the patient's health/comorbidity
- A1C level
- patient's adherence behavior
- not expert guidelines/hospital algorithms or patient age



Conclusions

Physicians consider a wide range of qualitative and quantitative factors when making medication choices for hyperglycemia management.

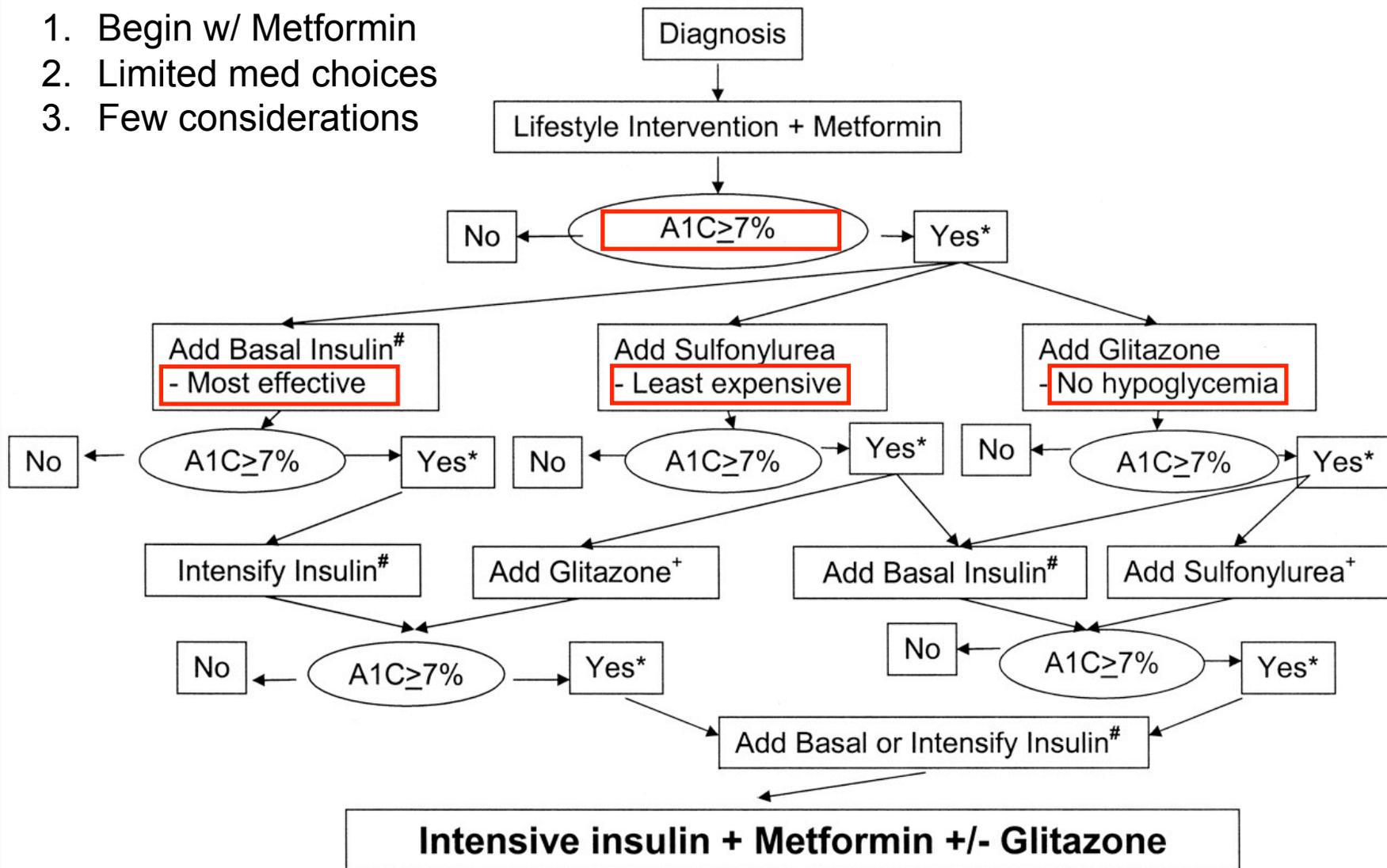
The apparent complexity of the medication choice process contrasts with current evidence-based treatment guidelines.

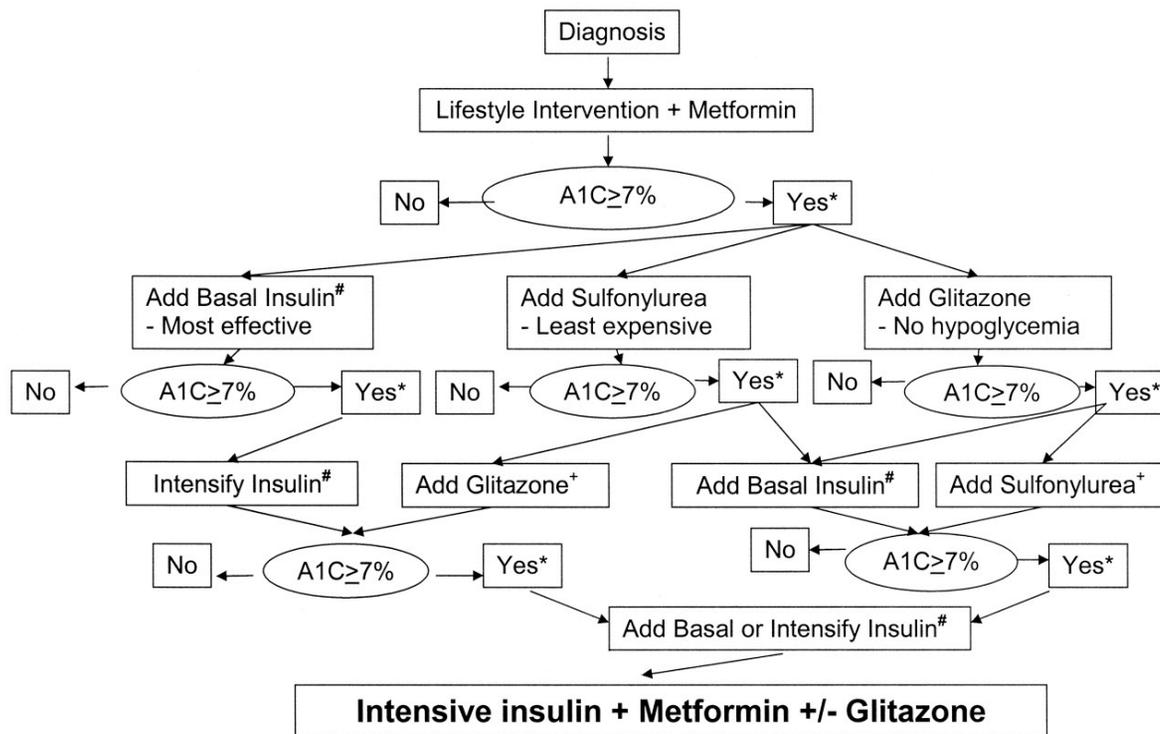


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Nathan DM, *Diabetes Care*. 2006;29(8):1963-1972.

“The Survey”

Unless contraindicated:

1. “Overall patient assessment”
2. Is patient overweight? Motivated? Adherent? Insured?
3. Differences between “Evidence-based” vs. “Physiology” approaches



Thank you!



Table 4—Factors most frequently listed as “not a consideration” at each management stage

| | Specialist | Academic generalist | P |
|---|------------|------------------------|--------|
| When choosing initial hypoglycemic agent | | | — |
| <i>n</i> | 379 | 440 | — |
| Patient tendency to complain about side effects | 16 | 25 | 0.001 |
| Patient’s specific medication request | 15 | 16 | 0.59 |
| Expert guideline/hospital algorithm | 17 | 14 | 0.23 |
| When choosing to prescribe a glitazone | | | — |
| <i>n</i> | 369 | 403 | — |
| Patient’s age | 23 | 27 | 0.22 |
| Patient’s specific medication request | 20 | 27 | 0.23 |
| Expert guideline/hospital algorithm | 25 | 18 | 0.01 |
| When deciding to initiate insulin | | | — |
| <i>n</i> | 370 | 434 | — |
| Patient’s out-of-pocket expenses | 25 | 26 | 0.81 |
| Expert guideline/hospital algorithm | 26 | 15 | <0.001 |
| Patient’s age | 18 | 17 | 0.7 |

Data are percentages.

