

Tradeoffs Between Pain Relief and the Risk of Side Effects in the Treatment of OA: The Patient's Perspective

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Background

- Current OARS recommendations for the treatment of OA:
 - NSAIDs/Coxibs should be used at the lowest effective dose
 - Long-term use should be avoided if possible
 - NSAIDs with gastroprotective agents or Coxibs should be used in patients at increased risk of GI complications
 - NSAIDs/Coxibs should be used with caution in patients at increased CV risk

Background

- Current recommendations do not specify how patient preferences might be considered in therapeutic decisions.
- Therapeutic decisions in OA often involve tradeoffs between the risk of side effects and pain relief.
- Patients are willing to trade risks for benefits.
- Side effects are important in determining treatment preferences.
- Factors such as age, gender or SES have been inconsistently associated with treatment preferences.
- Quantitative data about the risk levels patients are willing to accept are limited.

Objectives

- To quantify patients' maximal acceptable risk for different adverse effects from typical OA medications, given a specified benefit from the medication
- To determine if the maximal acceptable risks are affected by specific aspects of the tradeoff situation and patient characteristics

Methods

- Trade-off characteristics (specified by design):
 - Type of side effect
 - Baseline risk level
 - Pain benefit
 - Final pain level
- Patient characteristics:
 - Demographic (age and sex)
 - Socio-economic (income, education)
 - Clinical (pain, function, health status)
 - Psychological (locus of control and decisional conflict)

Methods

- Maximal acceptable risk increments (MARI) were measured with a probabilistic threshold technique (TT) in a face-to-face interview.
- TT tasks were performed for 5 side effects (dyspeptic symptoms, fluid retention, hypertension, stomach bleed, and heart attack / stroke)
- Pain benefit was either 2 or 5 points on a 0-10 scale.
- Each patient was randomly allocated to one of 4 protocols with different baseline risk and different target pain levels.

Threshold Technique Protocol: MARI for stomach bleed

Condition	Option A	Option B
Pain while taking pills daily on a 0 – 10 scale	5	3
Risks and Side Effects:		
Dyspepsia	20%	20%
Fluid retention	5%	5%
Heart attack / stroke	1%	1%
High blood pressure	10%	10%
Stomach bleed	2%	Increase from 2% to max

Definitions of Side Effects

Dyspepsia:

Nausea, heartburn, stomach pain. These symptoms will disappear if you stop your arthritis medication.

Definitions of Side Effects

High blood pressure:

Increase in blood pressure. This may be more severe in patients who already have high blood pressure, heart disease, or kidney problems. Treatment usually requires long-term medication, but will disappear if you stop your arthritis medication.

Definitions of Side Effects

Fluid retention:

Swelling ankles or legs. This side effect will disappear if you stop your arthritis medication.

Definitions of Side Effects

Stomach bleed:

Feeling unwell, vomiting blood. Treatment involves hospitalization, sedation for tests, a tube inserted down the throat, and blood transfusion. Hospital stay will be 2–7 days. You will be tired for about 3–4 weeks, on medication for 6 months. A small proportion of people may die from stomach bleeding.

Definitions of Side Effects

Heart attack/stroke:

These conditions usually require hospitalization and may cause long-term disability. About 1 in 10 to 1 in 5 patients will die after heart attack/stroke.

Methods

- Demographic and socio-economic characteristics were assessed using a self-administered questionnaire
- Clinical and psychological variables were measured using standardized scales
 - SF-36
 - WOMAC
 - Decisional Conflict Scale
 - Multidimensional Health Locus of Control scale

Methods

Eligibility

- Diagnosed with OA of the hip or knee according to standard ACR criteria
- Age 45-74
- Able to understand English
- Mentally competent
- No co-morbid conditions associated with chronic pain

Methods

- Recruitment
 - Newspaper advertising - 50%
 - Referred by rheumatologists - 38%
 - Referred by orthopedic surgeons - 12%
- Stratification by disease severity
 - Mild
 - Moderate
 - Severe

Results Sample Description

Variable	N (%)
Female	110 (56)
Male	86 (44)
High school or less	42 (22)
College	53 (27)
University	99 (51)
\$0-19,999	20 (10)
\$20-39,999	38 (20)
\$40-59,999	45 (23)
\$60-99,999	49 (26)
\$100,000+	40 (21)
Age (Mean, SD)	61 (8)

Results Sample Description

Variable	N (%)
Prescription drugs	80 (41)
Over-the-counter drugs	94 (48)
Herbal remedies	95 (48)
Mild pain	63 (32)
Moderate pain	77 (39)
Severe pain	55 (28)
Duration of OA (years)	12 (13)

Results Sample Description

Variable	Score Mean (SD)
SF-36 Physical Health	54 (20)
SF-36 Mental Health	69 (19)
WOMAC Pain	37 (20)
WOMAC Function	35 (20)
WOMAC Stiffness	45 (22)
WOMAC Total	37 (19)

Results MARI for Dyspepsia

Side Effects	Pain Relief (0 – 10)	Initial Risk Levels (%)	Mean MARI (95% CI)	Median MARI
	2 Points	0	23.4 (17.3, 29.6)	10.5
		20	30.1 (26.3, 33.8)	23.5
Dys-pepsia	5 Points	0	30.9 (24.0, 37.9)	12.5
		20	34.6 (30.1, 39.1)	25.5

MARI = Maximum Acceptable Risk Increments

Results MARI for Hypertension

Side Effects	Pain Relief (0 – 10)	Initial Risk Levels (%)	Mean MARI (95% CI)	Median MARI
High Blood Pressure	2 Points	0	13.4 (8.4, 18.4)	4.5
		10	17.9 (15.1, 20.7)	11.5
	5 Points	0	17.1 (11.5, 22.6)	5.5
		10	20.8 (17.2, 24.3)	13.5

MARI = Maximum Acceptable Risk Increments

Results MARI for Fluid Retention

Side Effects	Pain Relief (0 – 10)	Initial Risk Levels (%)	Mean MARI (95% CI)	Median MARI
	2 Points	0	26.1 (19.6, 32.5)	10.5
		5	21.8 (17.0, 26.6)	10.5
Fluid Retention	5 Points	0	33.1 (25.8, 40.4)	15.5
		5	24.6 (19.3, 29.8)	10.5

MARI = Maximum Acceptable Risk Increments

Results MARI for Stomach Bleed

Side Effect	Pain Relief (0 – 10)	Initial Risk Levels (%)	Mean MARI (95% CI)	Median MARI
	2 Points	0	5.7 (2.9, 8.5)	0.0
		2	5.4 (4.2, 6.5)	3.5
Stomach Bleed	5 Points	0	8.1 (4.8, 11.4)	3.5
		2	7.2 (5.5, 8.9)	4.5

MARI = Maximum Acceptable Risk Increments

Results MARI for Heart Attack/Stroke

Side Effects	Pain Relief (0 – 10)	Initial Risk Levels (%)	Mean MARI (95% CI)	Median MARI
Heart Attack/Stroke	2 Points	0	3.0 (1.2, 4.8)	0.0
		1	3.9 (3.0, 4.9)	1.5
	5 Points	0	4.4 (2.0, 6.8)	0.0
		1	5.0 (3.7, 6.3)	2.5

MARI = Maximum Acceptable Risk Increments

Results: Regression analysis Pain Difference = 2 Points

	Dyspepsia	Fluid retention	Hypertension	Stomach bleed	Heart attack / stroke
Initial risk	0.37		0.43	0.54	0.75
Income			0.20		
Uncertainty	-0.16				
Unclear values			-0.18		
Model r-squared	0.10	0.05	0.14	0.06	0.17

Only variables significant in at least one model ($p < 0.05$) are shown. Each model included additional variables selected in univariate analysis ($P < 0.25$).

Results: Regression analysis Pain Difference = 5 Points

	Dyspepsia	Fluid retention	Hypertension	Stomach bleed	Heart attack / stroke
Initial risk			0.29		0.57
Income	0.21	0.23	0.24		
Uncertainty			-0.18		
Model r-squared	0.12	0.13	0.14	0.03	0.10

Only variables significant in at least one model ($p < 0.05$) are shown. Each model included additional variables selected in univariate analysis ($P < 0.25$).

Conclusions

- Patients with OA vary widely in the level of risk they would accept for a given level of pain relief.
- Acceptable levels of risk depend on the type of side effect and pain benefit.
- For some patients the levels of risks & benefits typically associated with NSAIDs are unacceptable, whereas others would accept much higher levels of risk.
- Those whose baseline risk is already elevated are more likely to accept the extra risk.

Conclusions

- Acceptance of risk associated with side effects is not explained by age, gender, education, physical or mental functioning, pain, or locus of control.
- Higher income is associated with higher risk acceptance for dyspepsia, fluid retention, and hypertension.
- Uncertainty and lack of clarity about values may be associated with lower risk acceptance for some side effects.

Implications

These observations may be important for the development of practice guidelines for physicians and patients' decision aids that can foster individualized, evidence-based yet preference-sensitive care for patients with OA.

Questions

- To what extent should treatment be individualized according to patient preferences?
 - Are stated preferences consistent with the actual choices patients make?
 - Are the levels of risk that seem acceptable/unacceptable to patients also acceptable/unacceptable to clinicians?
 - Should practice guidelines reflect the fact that patient at higher risk of complications tend to accept higher levels of additional risk?

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