Student Name: Annemarie Erich, SPT			Search Conducted: 2/10/16- 3/15/16		
Title: Non-exercise Interventions for Knee OA, an Update.				Databases: Clinahl, PubMed, Embase	
Author/Year	Purpose/Design Subjects/Inclusion Criteria	Intervention	Outcome Measures	Conclusion	Limitations
Viscosupplementation					
Anne W.S. Rutjes et al. / 2012	Purpose: Assess risk benefit ratio of Viscosupplementation in adults with symptomatic knee OA Design: Systematic Review and Meta Analysis- 89 RCT Subjects: N=12,667 with symptomatic knee OA Inclusion Criteria: intra-articular (IA) Viscosupplementation with hyaluronic acid or a derivative	Experimental- Viscosupplementation Control- Sham or nonintervention	Pain measures- included VAS and WOMAC subscores (used highest ranking measure on previously described hierarchies) Safety outcomes- Defined as "flare-ups" noted as hot, painful, swollen knee within 24-72 hours after injection	Viscosupplementation had minimal effects on pain and function but increased risk for serious adverse events	Adverse data are poorly reported and trials included were generally of low quality
F Navarro-Sarabia et. al/ 2011	Purpose: Compare efficacy and safety of repeated hyaluronic acid injections to placebo and effects on disease progression over 40 months	Experimental: Patients received four cycles of 5 IA HA injections	VAS for pain Clinical response measured with OARSI 2004, patients were classified as	Adverse reactions were rare, usually of mild-moderate intensity, and short lasting. Repeated cycles of HA injections improve knee OA	-Drop out rate in experimental and control groups were 26.8% and 38.2% respectively

	Design: RCT Subjects: n=306 patients Inclusion criteria: Must have grade II-III and joint space width of ≥2mm, over age 45, score 5.5 or higher on the VAS for pain scale	Control: Placebo injections in the same manner	responders if pain or physical function improved at least 50%	symptoms with results lasting up to 1 year after final injection. This does not prove whether this is true disease remission or just a modification of the natural disease course	-The use of emergency medication as NSAIDS was not controlled (Patients were questioned about use at each follow-up but this method has inherent inaccuracy)
Chen-Ti Wang et al./ 2004	Purpose: To clarify the therapeutic efficacy and safety of IA injection of HA for knee OA Design: Meta-analysis Subjects: 20 trials with total of 1647 randomly assigned knees Inclusion criteria: Trials were single-blind or double-blind RCTs comparing IA injection of HA with placebo for treatment of knee OA	Experimental: IA injection of various HA products Control: placebo	Outcome "end points" of pain with activity, pain without activities, and function were measured using a modified Craen et al. method to find the change in sum of pain intensity difference% (SPID). These numbers were then used to create a SPID – versus-time	Confirms that cross-linked and non-cross linked HA can decrease symptoms of knee OA with few adverse events However, patients over 65 years of age with advanced stages are less likely to benefit from HA injections	-Many trials included were industry funded -Unpublished trials were not searched and trials with negative results tend to be unpublished -Not all outcome measures used in included studies fit neatly into the

			curve.		"end-point" categories used for the data analysis
J. David Evanich/ 2001	Purpose: To define the efficacy of and elucidate favorable response factors of HA IA injections based on the authors' initial clinical experience Design: Retrospective review Subjects: The first 100 knees to receive viscosupplementation at the author's clinic. (Only 80 knees were available for clinical follow-up Inclusion criteria: Patients with knee OA grade I-III, treated at authors' clinic, available for follow-up	Experimental- 3 HA IA injections. (Did not expound on process) Control-none	Patients evaluated pre and post injection with the Hospital for Special Surgery (HSS) knee score-Max of 100 total points in 6 categories: pain, function, range of motion, strength, flexion deformity, and instability Subtractions are made for walking aids, extension lag and varus or valgus deformity	HA injections are not appropriate for all patients with knee OA. Only 50% of patients had satisfactory results with only 35% reporting increased activity 12% reporting adverse events and 28% undergoing TKA within 7 months after injection trials	-No control group -Convenience sampling -Author owns the clinical setting -No discussion of limitations or mention of measures to control for confounding variables
Intra-articular Corticosteroids					
C. Tate Hepper et al./ 2009	Purpose: To determine the efficacy and duration of pain reduction provided by IA corticosteroid (and which type) injection for	Experimental- single IA corticosteroid injection	VAS pain scale	Current evidence demonstrates that corticosteroids can decrease pain by approximately 1/3 as	-Few studies exist to choose from -Diversity of

	treatment of knee OA. Design: systematic review Subjects: N= 259 Inclusion Criteria: English, prospective RCTs that directly compare IA corticosteroids to placebo	Control- Placebo 5 of 6 trials used normal saline solution. The remaining trial used polysorbate sorbitol, benzyl alcohol, and water		measured by VAS pain scale, but benefit only maintained for 1 wk. There appears to be no prolonged benefit. Clinicians should consider other treatments for long-term relief Specific patterns and trends cannot be observed in comparing various corticosteroids for knee OA	clinical assessment used in included studies -Concomitant use of NSAIDs or other pharmaceuticals for the duration of the studies was not controlled
Ty Jones et al./ 2014	Purpose: To investigate the efficacy and safety of IA corticosteroid injections for treatment of knee OA. Design: Meta-analysis of 13 RCTs Subjects: 641 (62% women, age range 60-71) Inclusion Criteria: comparison studies must include patients with knee OA and test IA corticosteroids against placebo	Experimental- single corticosteroid injection Control- Placebo	Pain, function, ROM, and walking distance, adverse events as infection and hyperglycemia	IA corticosteroid injections can reduce pain by 20% for the short term (1-3wks) in those with knee OA. These injections can cause joint infections (incidence rates vary greatly for 1 in 14,000 to 1 in 77,000) and hyperglycemia for 2-3 days after injection in patients with DM. Injections should not	- No discussion of limitations -Minimal baseline demographic given about subjects -Minimal description of RCTs included

				be given more often than every three months.	
Bellamy N Campbell et al./ 2005	Purpose: To evaluate the efficacy and safety of IA corticosteroid injections for treatment of knee OA. Design: Systematic review Subjects: n=1721, 26 trials Inclusion Criteria: Randomized control trials of IA corticosteroids for patients with knee OA: single/double blind, placebo-based/comparative studies, reports at least one core OMERACTIII outcome measure.	Experimental: IA corticosteroid injection Comparison groups: placebo, IA HA injection, joint lavage, and other types of IA corticosteroid injections	Various measures of Pain, efficacy, global assessment, and safety	Some efficacy was detected for IA corticosteroids and decreasing pain between 1-3wks. HA products have slower onset of pain relief, but affects are more durable than IA corticosteroids. If short-term pain relief and inflammation reduction is the goal IA corticosteroids may be appropriate.	-Review may have missed negative trials that were not submitted for publication
Platelet Rich Plasma					
Amir Khoshbin et al./ 2013	Purpose: To synthesize available literature on Platelet Rich Plasma (PRP) as a therapeutic intervention for symptomatic knee OA Design: Systematic Review Subjects: n=577, 6 studies Inclusion Criteria: RCTs and	Experimental: Multiple (2-4) PRP injections were given at varied volumes, intervals, and locations Control: In 5/6 studies HA	WOMAC, VAS pain scale, International Knee Documentation Committee (IKDC) knee evaluation form, patient reported	Multiple, sequential PRP injections may have beneficial effects in treating adults with mild to moderate knee OA as seen at 6 months. However, there appears to be increased incidence of	-RCTs were pooled which increases risk of selection bias -Differences in reported effect sizes due despite use of

	prospective cohort studies that evaluated the clinical efficacy of PRP vs control injection for knee OA	injections were the control and varied as PRP above. The remaining study used saline solution as control	satisfaction, adverse events	adverse events among those treated with PRP as compared to other IA treatments.	random-effects model
Pourcho AM et al./ 2014	Purpose: Outline variables involved in use of PRP and summarize current literature on it's application in knee OA. Design: Systematic Review Subjects: n=1337 Inclusion Criteria: Original articles (case series, non-randomized cohort studies, and RCTs) from 1970-2013 specific to use of PRP in knee OA	Experimental: IA PRP injections, varied from 1-4 injections Control: IA HA injections (very non-specific as to procedure) for both groups	Primary measures: VAS for Pain, function, and ADLs, WOMAC,	The available literature suggests that IA PRP is a better option than HA for many with knee OA However, this is treatment is not considered standard as research is still in it's infancy	- Not all studies mention controlling for use of NSAIDs or other pharmaceuticals
Lawrence P. Lai et al./ 2015	Purpose: To explore effectiveness of PRP in treating cartilage degenerative pathology in the knee joint Design: Systematic review and meta-analysis Subjects: n=1543, 8 studies Inclusion Criteria: single arm-prospective, quasi-experimental, and RCT	Experimental: IA PRP injections Control: single-arm studies=none, 2 quasi-experimental and 4 RCTs= HA injection, 1RCT= normal saline injection, 1 quasi-	IKDC, knee injury OA Outcome Score (KOOS), WOMAC	PRP intervention demonstrates significant improvement (of pain, function, and QOL) in patients with knee cartilage degenerative pathologies. PRP is likely superior to HA with longer effective	-Many trials are of low methodological quality -Heterogeneity across included studies which lacked key factors needed for stratification

	studies that used PRP to treat chondral lesions of the knee	experimental= compared single vs double spinning approach using PRP		duration. Patients who benefit most have a lower degree of degenerative lesions.	-Variability of included levels and pathology of chondral lesions
Ke-Vin Chang et al./ 2014	Purpose: Analyze literature on use of PRP and efficacy in treatment of knee OA Design: Systematic Review Subjects: n=1543, 16 studies Inclusion Criteria: human subjects, prospective clinical studies, full-text articles published in English	26 total treatment arms Experimental: 18 arms= PRP injections (1-3 injections done using varied procedures) Comparison: 7 arms= compared with HA, 1 arm= compared with normal saline	Patient reported stiffness, QOL, physical function, WOMAC, VAS pain scale	PRP may be effective as an alternative treatment for knee OA However, studies are inconclusive regarding efficacy due to low quality of trials. Higher degrees of knee joint degeneration experience less benefit of treatment	-Methodological quality of included studies (lack of consideration for varying contents of the PRP mixture as WBC count, RBC count, and platelet percentages)
Autologous Chondrocyte Implantation					
Elizaveta Kon et al./ 2009	Purpose: To compare clinical outcome of patients treated with 2nd generation ACI versus microfracture repair technique at 5 year follow-up Design: Cohort study Subjects: n=80	ACI group- n=40, second generation using Hyalograft C surgical technique Microfracture group- n=40,	IKDC for knee function, Tegner for return to sport	Both interventions were shown to have satisfactory clinical outcomes at medium-term (5year) follow-up. Second generation ACI is a good and potentially durable	-Not specific to OA pathology -Not randomized -High incidence of previous ACL and/or meniscal surgeries

	Inclusion Criteria: age 16-60, showing clinical symptoms (swelling, knee pain) grade III-IV chondral lesions on femoral condyle or trochlea from 1-5cm^2	Steadman technique		option for treatment of cartilage defects	-Hard to generalize results to older patients as most were young, active individuals with contained lesions
Joshua D. Harris et al./ 2010	Purpose: To determine if literature supports ACI (and which generation) over other cartilage procedures in regard to clinical outcome, MRI, arthroscopic assessment, and durability of treatment. Also, to see which patient and defect specific outcomes after ACI compared to other cartilage repair procedures. Design: Systematic Review Subjects: n=917, 13 studies Inclusion Criteria: comparisons of ACI against other procedures, intergenerational comparisons, human	Experimental: ACI Comparison Groups: microfracture, OATS, and 1st vs 2nd generation ACI, marrow stimulation, many different ACI techniques	KOOS, SF-36, IKDC, Lysholm, Tegner, ICRS, and modified Cincinnati	High-level evidence suggest ACI is superior to microfracture while no conclusion can be drawn about ACI vs OATS. No difference found between 1st and 2nd generation ACI. Young active patients with shorter duration of pre-op symptoms, no malignment, smaller isolated lesions on the medial femoral condyle, no ligamentous instability, or meniscal deficits can expect the best	-Treatment effect may be over or underestimated due to lack of natural control group -Studies included patients with previous surgeries with increases the failure rate of ACI by 3-fold. -Number of patients per group were

	subjects, minimum follow-up of 12 months, evaluation of knee joint only, human subjects, Grade III or IV focal defects			outcome	drastically unequal -Selection bias was introduced via alternating consecutive-selection randomization
J. Bruce Moseley et al./ 2010	Purpose: To observe long-term durability of ACI in US patients. Design: Case series, observational study Subjects: n=72 Inclusion Criteria: Patients must have history of ACI treated full-thickness lesion on distal femur, completed follow-up between 1- ≤5 years, signed HIPPA form, ACI performed before Dec 31, 1996	Observations at ACI post-op follow-up were made between 1-5 years and again at 6-10 years	Baseline measurements taken with Cincinnati Knee Rating System for overall condition, pain, and swelling	ACI for large symptomatic, full-thickness lesions of distal femur with low baseline scores can show significant, durable improvement. Benefits were maintained up to 10 years in some cases.	-No natural historical control group -Confounding factors of BMI, age, workers' comp status, and lesion size could affect interpretability of results.
Osteochondral Autologous Transplantation					
James C.Y. Chow et al./ 2004	Purpose: Evaluate medium term results of OATs procedure Design: Case series, Retrospective analysis Subjects: n=30	OATS procedure performed with graphs from graphs harvested from superior lateral intercondylar notch	Lysholm, IKDC, knee joint radiographs	Arthroscopic OATS procedure is safe and effective for treating symptomatic chondral defects in appropriately	-Follow-up is not enough to assess effect in modifying the development of knee joint OA.

	Inclusion Criteria: full-thickness chondral and osteochroal defects demonstrated by arthroscopy, defect of medial or lateral femoral condyle from 1-2.5cm diameter, radiographic evidence of physeal closure of distal femur and proximal tibia			selected patients	-No comparison to alternative methods
Caro, Fancesca De et al./2015	Purpose: Provide an updated literature review for the OA(allographs)T procedure for treating large defects in the knee Design: Systematic Review Subjects: 374 knees, 11 articles Inclusion Criteria: Level I-IV clinical studies, basic science articles, articles published in past 5 yr, English, n≥10, 1 yr of follow-up	Patients had received osteochondral allografts (either fresh or frozen) applied to the femoral condyle, tibial plateau, or patellofemoral joint	IKDC, WOMAC, and various measure of cellularity, matrix content, and structural prosperities	Fresh osteochondral allografts of the knee result in good functional outcomes persisting to longer-term follow-up	-Quality of articles was low and lack homogeneity preventing meta-analysis -Associated knee procedures were common among patients included in selected studies
Rimtautas Guadas et al./ 2005	Purpose: Compare outcomes of mosaic OAT and microfracture	Randomly divided to undergo OAT or microfracture	HSS, International Cartilage Repair	In the short-term (avg of 37.1 months) OAT procedure showed	-Excluded those with OA

	procedures in treating articular cartilage defects of young athletes Design: Prospective RCT Subjects: n=57 Inclusion Criteria: competitive athletes, 1-4cm^2 lesion present on weight bearing area of medial or lateral femoral condyle, under 40 years of age	between 1998-2002	Society (ICRS), radiograph, MRI, and clinical assessment, histological evaluation (at 12.4 months post-op	superiority to microfracture of for repair of articular cartilage in the knee	-Small sample size
Rimautas Guadas et al./ 2012	Purpose: To update clinical results at 10 year follow-up of above study Design: Prospective RCT follow-up Subjects: n=57 Inclusion Criteria: those patients included in above study	Observe /evaluate patients 10 years following OAT or MR procedure.	ICRS, Tegner activity score, radiographs, MRI	OAT technique allows for higher rate of return to sport than microfracture at 10-year follow-up.	- No discussion of limits, but those of previous study are inherent in this follow-up