부록 1: 지침 제정 참여자

1. 개발 위원회

김상완, 서울의대 보라매병원, 내분비내과

글루코코르티코이드 유발 골다공증 진료 지침 위원회 위원장

고정민, 울산의대 서울아산병원, 내분비내과

김태환, 한양의대 한양대학교병원, 류마티스내과

박동아, 한국보건의료연구원 (NECA)

박소영, 경희의대 경희대학교병원, 내분비내과

성윤경, 한양의대 한양대학교병원, 류마티스내과

이신석, 전남의대 빛고을전남대학교병원, 류마티스내과

2. 실무위원회

공현식, 서울의대 분당서울대학교 병원, 정형외과

김경민, 서울의대 분당서울대학교 병원, 내분비내과

김담, 연세의대 강남세브란스병원, 류마티스내과

김하영, 원광의대 산본병원, 내분비내과

박소영, 경희의대 경희대학교병원, 내분비내과

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전찬홍, 순천향의대 부천병원, 류마티스내과

주지현, 가톨릭의대 서울성모병원, 류마티스내과

부록 2: 방법론

1. 방법론 개요

본 진료지침은 한국보건의료연구원의 임상진료지침 프로토콜(Guidance for development of clinical practice guidelines Ver. 1.0)에 따라 개발되었다.

- 진료지침 개발 과정

제1부. 기획

1단계: 진료지침 주제 선정

2단계: 진료지침 개발그룹 구성

3단계: 기존 진료지침 검토

4단계: 개발 계획 수립

5단계: 핵심질문 결정

제2부. 개발

6단계: 근거의 검색

7단계: 근거의 평가

8단계: 근거의 종합

9단계: 권고안 작성, 권고등급 결정

10단계: 합의안 도출

제3부. 최종화

11단계: 외부검토 및 갱신계획

12단계: 진료지침 출판

2. 지침 제정 참여자 및 역할

글루코코르티코이드 유발 골다공증 진료지침 위원회는 개발위원회와 실무위원회로 구성되어

있다. 위원회 구성원의 자세한 내용은 부록2를 참고한다.

1) 개발위원회

□ 구성: 대한류마티스학회와 대한골대사학회에서 추천한 7인 및 방법론 전문가 1인

□ 역할

- 진료지침 개발 기획 및 개발 방법 결정
- 진료지침 검색과 선별, 평가 등 상세 수용개작 과정에 대한 전체 방법론 마련
- 실무위원회 자문 및 개발 과정 검토
- 진료지침의 보급 및 실행 전략 마련

2) 실무위원회

□ 대한류마티스학회와 대한골대사학회 중심의 실무위원회 구성

- 가이드라인 개발 계획 공유 및 의견 수렴, 수용 개작을 담당할 실무위원회 구성
- 개발 우선순위가 높은 분야 선정

□ 가이드라인 개발 범위에 따른 핵심질문 결정

- 우선 개발할 분야 선정에 따른 핵심질문 결정

3. 이해상충공개서

진료지침 개발에 참여한 모든 위원들이 진료지침 개발 활동과 관련된 실제적, 명시적 이해 관계를 공개했다. 개발 위원회와 실무위원회에 소속되어 있는 성윤경 교수는 본 진료지침 개발 전 2년 이내에 화이자로부터 연구비를 받은 적이 있다. 개발 위원회에 소속되어 있는 박동아 연구원은 두통 임상진료지침 개발에 방법론 자문에 참여한 적이 있다. 그 외, 본 진료지침의 개발 위원장을 포함한 다른 위원들은 본 진료지침 개발 전에 개발 대상으로 검토 중인 진료지침의 개발이나 승인과정에 참여한 경력이 없으며, 진료 지침 개발 전 2년 이내에 진료 지침 주제와 관련이 있는 의약품, 재화 및 서비스 관련 회사와 관계를 맺고 있지 않다. 연구비를 받고 있는 경우에는 해당 회사 약제의 토론시에는 토론 밑 표결에 참여하지

않았다. 대한류마티스학회 및 대한골대사학회 이외의 기관이나 단체로부터 재정 재원을 받지 않았다.

4. 진료지침 개발 목적과 사용 대상자

본 진료 지침은 국내 임상 상황에서 글루코코르티코이드를 사용하거나 사용할 계획인 환자들을 진료하는 모든 임상의들에게 글루코코르티코이드 유발 골다공증의 일차적 예방 및 치료에 대한 표준화된 진료지침을 제시하여 효율적인 치료를 증진시킬 목적으로 개발되었다.

본 진료 지침이 다루는 인구 집단은 19세 이상의 글루코코르티코이드를 사용하거나 사용할 계획인 환자 전체 (남녀 모두, 동반 질환 포함)이다.

본 진료지침의 사용 대상자는 국내에서 글루코코르티코이드를 사용하거나 사용할 계획인 환자를 진료하는 모든 임상 의사를 주 대상으로 하였고, 정부관계자, 환자, 일반인 등도 사용할 수 있도록 개발되었다.

5. 지침 제정 방법

(1) 핵심질문 선정

미국, 프랑스, 스페인, 일본, 브라질, 그리고 International Osteoporosis Foundation – European Calcified Tissue Society(IOF-ECTS) 에서 개발된 진료지침 총 6개를 검토하여 일차적으로 14가지의 주제를 선택하였다. 핵심질문 및 관련 검색어를 실무위원회에서 일차적으로 작성 후 개발위원회에서 취합하여 검토 후 최종 선정하였다. 핵심질문은 대상 환자·인구집단(P, patient population), 중재법(I, intervention), 비교 중재법(C, comparator), 중재결과(O, outcome) 내용을 구체적으로 포함하여 최종적으로 7가지의 핵심 질문을 결정하였다.

- 핵심질문1. 글루코코르티코이드를 사용하는 환자에서 비약물적 치료가 글루코코르티코이드 유발 골다공증 예방과 치료에 효과적인가?
- 핵심질문2. 40세 미만 성인에서 어떤 약물 치료가 글루코코르티코이드 유발 골다공증

예방과 치료에 효과적인가?

- 2-1. 40세 미만 성인에서 칼슘과 비타민 D 보충은 글루코코르티코이드 유발 골다공증 예방과 치료에 효과적인가?
- 2-2. 40세 미만 성인에서 비스포스포네이트 사용은 글루코코르티코이드 유발 골다공증 예방과 치료에 효과적인가?
- 2-3. 40세 미만 성인에서 테리파라티드 사용은 글루코코르티코이드 유발 골다공증 예방과 치료에 효과적인가?
- 2-4. 40세 미만 성인에서 데노수맙 사용은 글루코코르티코이드 유발 골다공증 예방과 치료에 효과적인가?

□ 핵심질문3. 40세 이상 성인에서 어떤 약물 치료가 글루코코르티코이드 유발 골다공증 예방과 치료에 효과적인가?

- 3-1. 40세 이상 성인에서 칼슘과 비타민 D 보충은 글루코코르티코이드 유발 골다공증 예방과 치료에 효과적인가?
- 3-2. 40세 이상 성인에서 비스포스포네이트 사용은 글루코코르티코이드 유발 골다공증 예방과 치료에 효과적인가?
- 3-3. 40세 이상 성인에서 테리파라티드 사용은 글루코코르티코이드 유발 골다공증 예방과 치료에 효과적인가?
- 3-4. 40세 이상 성인에서 데노수맙 사용은 글루코코르티코이드 유발 골다공증 예방과 치료에 효과적인가?
- 3-5. 폐경 후 여성에서 선택적 에스트로겐 수용체 조절제 사용은 글루코코르티코이드 유발 골다공증 예방과 치료에 효과적인가?

□ 핵심질문4. 임신을 계획하고 있는 여성에서 치료 약제 사용은 안전한가?

□ 핵심질문5. 글루코코르티코이드 유발 골다공증 환자에서 신체계측/영상학적/생화학적 방법을 이용하여 얼마간의 간격으로 모니터링 할 것인가?

□ 핵심질문6. 글루코코르티코이드 유발 골다공증 치료 중 골절 위험도를 재평가하여 낮은 골절 위험도로 확인되었을 경우 치료 중단을 고려할 수 있는가?

□ 핵심질문7. 글루코코르티코이드 유발 골다공증 치료 실패를 어떻게 정의할 것인가?

(2) 진료지침 검색

개발위원회에서 핵심질문과 관련된 진료지침의 체계적 검색을 수행하였다. 주요 정보원으로 국외 정보원(MEDLINE, EMBASE), 국내 정보원(KoreaMed, KMbase) 및 임상진료지침 주요 정보원(NGC, G-I-N, KoMGI)을 이용하였고, 골다공증 등 관련분야 가이드라인 수기 검색도 시행하였다.

(3) 진료지침 선정

실무위원회에서 검색된 결과에서 핵심질문에 적합한 진료 지침을 선정하였다. 진료지침 선정 과정은 1차, 2차 선정배제 과정을 거쳐 선택된 진료 지침들을 대상으로 질 평가를 수행하여 최종 진료지침을 선정하였다. 선정기준과 1차, 2차 선정배제기준은 아래와 같다.

□ 선정기준

1) - 핵심질문과 일치하는 PICO를 포함하는 진료지침
2) - 근거기반 진료지침(체계적 문헌검색의 보고가 있고, 권고와 지지 근거 사이에 명확한 연계가 있는 것)
3) - 동료검토가 이루어진 진료지침
4) - 한국어 또는 영어로 출판된 진료지침
5) - 2010년 이후 출판된 진료지침

□ 1차 선정 배제기준

- 골다공증/골감소증를 연구하지 않은 문헌
- 스테로이드를 사용하는 환자들에 대한 연구를 포함하지 않은 문헌

- 암이나 내분비질환(쿠싱증후군 제외), HIV infection 등 특정 환자군만을 대상으로 한 문헌
- 권고 또는 지침이 아닌 문헌

  단순한 종설(review), 개별 임상연구, critical Pathway(진료계획표)

  대표성 없는 단일저자가 작성한 진료지침 등
- 중복으로 게재된 경우

□ 2차 선정 배제기준

- 골다공증/골감소증를 연구하지 않은 문헌
- 스테로이드를 사용하는 환자들에 대한 연구를 포함하지 않은 문헌
- 암이나 내분비질환(쿠싱증후군 제외), HIV infection 등 특정 환자군만을 대상으로 한 문헌
- 권고 또는 지침이 아닌 문헌

  단순한 종설(review), 개별 임상연구, critical Pathway(진료계획표)

  대표성 없는 단일저자가 작성한 진료지침 등
- 근거기반 방법으로 작성되지 않은 경우

  체계적 근거검색(systematic search) 없이 합의만으로 작성한 지침의 경우
- 영어 또는 한국어로 보고되지 않은 지침
- 동료검토가 이루어지지 않은 진료지침
- 중복으로 게재된 경우

  동일 내용으로 다른 저널에 게재 혹은 출판형태만 차이가 있는 경우 배제
- 원문확보가 불가능한 경우

1차 선정배제는 사전에 정의한 1차 선정배제기준을 기준으로 검색된 문헌의 제목 및 초록을 검토하여 수행하였다. 두 연구자가 수행하여 의견 불일치 시 퇴의 후 합의 과정을 거쳐 27개의 진료 지침을 선정하였다. 2차 선정배제는 사전에 정의한 2차 선정배제기준을 기준으로 1차 선정배제된 진료지침의 원문을 검토하여 수행하였다. 두 연구자가 수

행하여 의견 불일치시 토의 후 합의 과정을 거쳐 7개의 진료지침을 선정하였으며, 배제 시 배제 사유를 기입하였다. 진료지침 검색에 대한 자세한 선정 가이드는 부록3, 지침 선정 과정은 부록4를 참고한다. 2차 선정배제 과정을 거친 선택된 7가지 진료지침들은 개발위원회에 제공되었다. 7가지 진료지침은 다음과 같다.

- 2010 American College of Rheumatology recommendations for the prevention and treatment of glucocorticoid-induced osteoporosis.
- 2012 A framework for the development of guidelines for the management of glucocorticoid-induced osteoporosis (IOF-ECTS)
- 2012 Guidelines for the prevention and treatment of glucocorticoid-induced osteoporosis (Brazil)
- 2014 update of recommendations on the prevention and treatment of glucocorticoid-induced osteoporosis (French)
- Guidelines on the management and treatment of glucocorticoid-induced osteoporosis of the Japanese Society for Bone and Mineral Research: 2014 update (Japan)
- 2010 clinical practice guidelines for the diagnosis and management of osteoporosis (Canada)
- 2016 Guidelines for the diagnosis, prevention and management of osteoporosis (Italy)

(4) 진료지침 평가

개발위원회는 실무위원회에서 2차 선정배제 후 선택된 7가지 진료 지침에 대한 1차 질 평가를 수행하였다. 진료지침의 질 평가는 진료 지침당 3명의 위원이 참여하였으며, K-AGREE를 이용하였다. 평가자들의 평가결과를 공유하며, 평가자 간 4점 이상 점수 차이가 나는 경우 결과를 수정할 수 있는 재검토 과정을 거쳤다. K-AGREE는 범위와 목적, 이해당사자의 참여, 개발의 엄격성, 명확성과 표현, 적용성, 편집 독립성으로 총 6영역으로 나뉘어져 있으며,

개발의 엄격성 영역이 표준화 점수 50%이상인 진료지침을 최종 선정하였다. 질 평가 결과가 낮더라도 실무위원회에서 판단하여 예외적인 사항이 있는 경우에는 지침을 선정하였다. 1차 질 평가를 통해 7가지 지침 중 4가지 진료지침이 선정되었다.

본 진료지침 개발 과정 중 최종 선정된 1가지 진료 지침이 업데이트되었고, 글루코코르티코이드 유발 골다공증에 대한 새로운 진료 지침이 추가로 발표되어 이 진료지침들에 대한 2차 질평가 시행 후 최종적으로 5가지 진료 지침을 선정하였다. 5가지 진료 지침은 다음과 같다.

- 2017 American College of Rheumatology Guideline for the Prevention and Treatment of Glucocorticoid-Induced Osteoporosis
- 2012 A framework for the development of guidelines for the management of glucocorticoid-induced osteoporosis (IOF-ECTS)
- 2014 update of recommendations on the prevention and treatment of glucocorticoid-induced osteoporosis (French)
- 2010 clinical practice guidelines for the diagnosis and management of osteoporosis (Canada)
- 2017 National Osteoporosis Guideline Group 2017 Clinical guideline for the prevention and treatment of osteoporosis

질평가 과정과 결과에 대한 자세한 설명은 부록5, 최종 선정된 진료 지침에 대한 정리는 부록6를 참고한다.

실무위원회에서 최종 선정된 5가지 진료지침의 최신성과 권고의 수용성 및 적용성을 평가하였으며, 해당 내용은 부록7를 참고한다.

(5) 핵심질문별 권고 및 근거 정리

실무위원회에서 진료지침 평가가 완료된 진료지침의 권고 및 근거를 핵심질문별로 정리하

였다. 권고 정리는 핵심질문별로 권고의 내용과 권고 등급을 정리하여 각 진료지침의 권고 내용을 비교하였다. 근거 정리는 핵심질문별로 지침의 권고와 관련된 근거들은 정리하였다. 이에 대한 자세한 내용은 부록8을 참고한다.

(6) 권고문 초안 작성

핵심질문별로 종합 근거수준을 결정하여 권고문 초안을 작성하였다.

□ 근거 수준

구분	의미
높음 (Ⅰ)	다른 연구가 효과 추정에 대한 신뢰를 바꾸는 경우가 거의 없음 (무작위대조시험, 무작위대조시험의 체계적 검토)
중등도 (Ⅱ)	다른 연구가 효과 추정에 대한 본 위원회의 신뢰에 중요한 영향을 미칠 수 있으며 추정에 대한 신뢰정도가 변할 수 있음 (I에 해당되지 않으나, 전향적 디자인의 관찰 연구, 환자-대조군 연구가 있는 경우)
낮음 (Ⅲ)	다른 연구가 효과 추정에 대한 본 위원회의 신뢰에 매우 중요한 영향을 미칠 수 있으며 추정에 대한 신뢰정도가 변할 수 있음 (후향적 디자인의 관찰연구, 환자-대조군 연구)
매우 낮음 (IV)	본 위원회의 추정값에 대한 신뢰정도를 확신하지 않음 (해당 연구 없음)
전문가 합의	근거 문헌은 없으나 본 위원회 전문가의 공식적 합의 절차를 통해 현재 수준에서 임상적으로 적용하기에 적절함

□ 권고등급

Grading	내 용	의 미
A	시행하는 것을 권고함	해당 중재는 원하는 효과에 대한 충분한 근거가 있어 시행할 것을 권고함.
B	(조건부) 시행하는 것을 권고함	해당 중재의 원하는 효과에 대한 근거는 중등도와 충분한 사이임 중재(검사)를 선택적으로 제공하거나, 전문가의 판단에 따라 특정 개인에게 시행할 것을 권고함.

C	시행하지 않는 것을 권고함	해당 중재의 원하지 않는 효과에 대한 충분한 근거가 있어, 시행하는 것을 권고하지 않음(시행하지 않을 것을 권고함)
I	권고 없음 (no recommendation)	해당 중재의 효과가 있다거나 없다는 것에 대한 근거는 불충분하고, 효과에 대한 추가적인 연구가 필요함. 해당 중재의 효과에 대한 확신도가 매우 낮아 권고등급 결정 자체가 의미가 없다고 판단됨.

(7) 권고 합의 및 권고등급 결정

골다공증 분야 전문의 및 관련 임상분야 전문가인 내분비내과 의사, 류마티스내과 의사, 정형외과 의사로 구성된 실무위원회에서 권고안 초안을 검토하여 최종 합의 과정을 진행하였다. 최종 합의 과정은 80% 이상의 합의를 원칙으로 하되, 최종적으로 실무위원회의 전원의 동의를 얻어 결정하였다.

(8) 권고문 최종안 도출 및 외부 검토

최종 권고문은 실무위원회에서 작성하여 취합한 하여 개발위원회에서 최종 검토하여 문서화하였다. 대한내분비학회검토를 거쳐 가이드라인 최종본을 확정한다

부록 3: 진료지침검색 선정 가이드

글루코코르티코이드 유발 골다공증 지침 검색 전략과 선정 과정

지침 검색 관련

1) 주요 정보원

- 국외 정보원: OVID-MEDLINE 혹은 PubMed, OVID-EMBASE
- 국내 정보원: KoreaMed, KMbase
- 임상진료지침 주요 정보원: NGC, G-I-N, KoMGI

2) 검색전략

Patient 와 가이드라인 검색어를 활용하여 포괄적으로 검색 시행

① PubMed

검색일: 2017.03.15

연번	검색어	검색결과
1	steroids[MeSH Terms]	786444
2	steroid*[tiab] OR glucocorticoid*[tiab]	256875
3	#1 or #2	919511
4	osteoporosis[MeSH Terms]	49321
5	osteoporos*[tiab] OR osteopenia[tiab]	60410
6	“bone loss” or “bone losses”	29424

7	#4 or #5 or #6	96508
8	#3 and #7	14223
9	Practice guideline[pt] OR Guideline[pt] OR Guideline*[ti] OR Recommendation*[ti] OR standard*[ti]	180369
10	#8 AND #9	230
11	animals [MeSH Terms] NOT humans [MeSH Terms]	4306851
12	10 not 11	224
13	limit 12 to yr="2000 -Current")	201

② OVID-EMBASE (1974 to 2017 Mar 06)

검색일: 2017.03.15

연번	검색어	검색결과
1	steroids.mp. or exp steroid/	1396294
2	glucocorticoids.mp. or exp glucocorticoid/	654602
3	(steroid* or glucocorticoid*).tw.	337435
4	#1 OR #2 OR #3	1460713
5	osteoporosis.mp. or exp osteoporosis/	131032
6	osteoporos*.tw.	83386
7	osteopenia.mp. or exp osteopenia/	19630

8	osteopenia.tw.	12553
9	bone loss.mp. or exp bone loss/	79402
10	bone loss*.tw.	29445
11	#5 or #6 or #7 or #8 or #9 or #10	194329
12	#4 and #11	42779
13	(guideline* or recommendation*).ti.	117599
14	#12 and #13	646
15	animals/ NOT humans/	1221015
16	14 NOT 15	646
17	limit #16 to yr="2000-current"	583

③ 국내 검색원

구분	연번	검색어	검색결과
KoreaMed (검색일: 3/16)	1	(glucocorticoid* AND osteoporos*) AND (guideline* OR recommendation*)	2
	2	(steroid* AND osteoporos*) AND (guideline* OR recommendation*)	0
	3	limit 1 to Humans, published from 2000 to current	2
KMbase (검색일:	1	[ABSTRACT=glucocorticoid*] AND [ABSTRACT=osteoporos*]	50

3/16)	2	[ABSTRACT=steroid*] AND [ABSTRACT=osteoporos*]	70
	3	#1 OR #2	108
	4	([TITLE=guideline*] OR [TITLE=recommendation*])	1316
	5	#3 AND #4	2
	6	limit 3 to Humans, publish year 2000-2017	2
	7	[ABSTRACT=스테로이드 AND 골다공증]	31
	8	(([TITLE=가이드라인] OR [TITLE=지침]) OR [TITLE=권고])	647
	9	#7 AND #8	0
	10	limit 7 to Humans, publish year 2000-2017	0
	11	#5 OR #10	2

⑤ 임상진료지침 검색원

검색일: 2017.03.06

구분	검색어	검색결과
NGC	1. glucocorticoid* AND osteoporos*	13
	2. steroid* AND osteoporos*	34
	3. #1 OR #2	38

	1차 수기검토	0
G-I-N	1. glucocorticoid*	1
	2. steroid*	8
	3. osteoporos*	57
	1차 수기검토	1
KoMGI	등록된 56개 수기검토	0

1~5의 database에서 검색: 중복 제거하고 총 659건 검색

그 중 2010년 이후의 자료: 309건

3) 진료지침 선정

□ 실무위원회에서 검색된 결과에서 핵심질문에 적합한 지료지침을 선정한다

□ 선정기준

- 핵심질문과 일치하는 PICO를 포함하는 진료지침
- 근거기반 진료지침(체계적 문헌검색의 보고가 있고, 권고와 지지 근거 사이에 명확한 연계가 있는 것)
- 동료검토가 이루어진 진료지침

- 한국어 또는 영어로 출판된 진료지침

- 2010년 이후 출판된 진료지침

□ 1차 선정배제기준

1	골다공증/골감소증를 연구하지 않은 문헌
2	스테로이드를 사용하는 환자들에 대한 연구를 포함하지 않은 문헌
3	암이나 내분비질환(쿠싱증후군 제외), HIV infection 등 특정 환자군만을 대상으로 한 문헌
4	권고 또는 지침이 아닌 문헌 - 단순한 종설(review), 개별 임상연구, critical Pathway(진료계획표) - 대표성 없는 단일저자가 작성한 진료지침 등
5	중복 출판된 연구

두 연구자의 합의로 27개의 문헌을 선정함. 원문 확보 단계

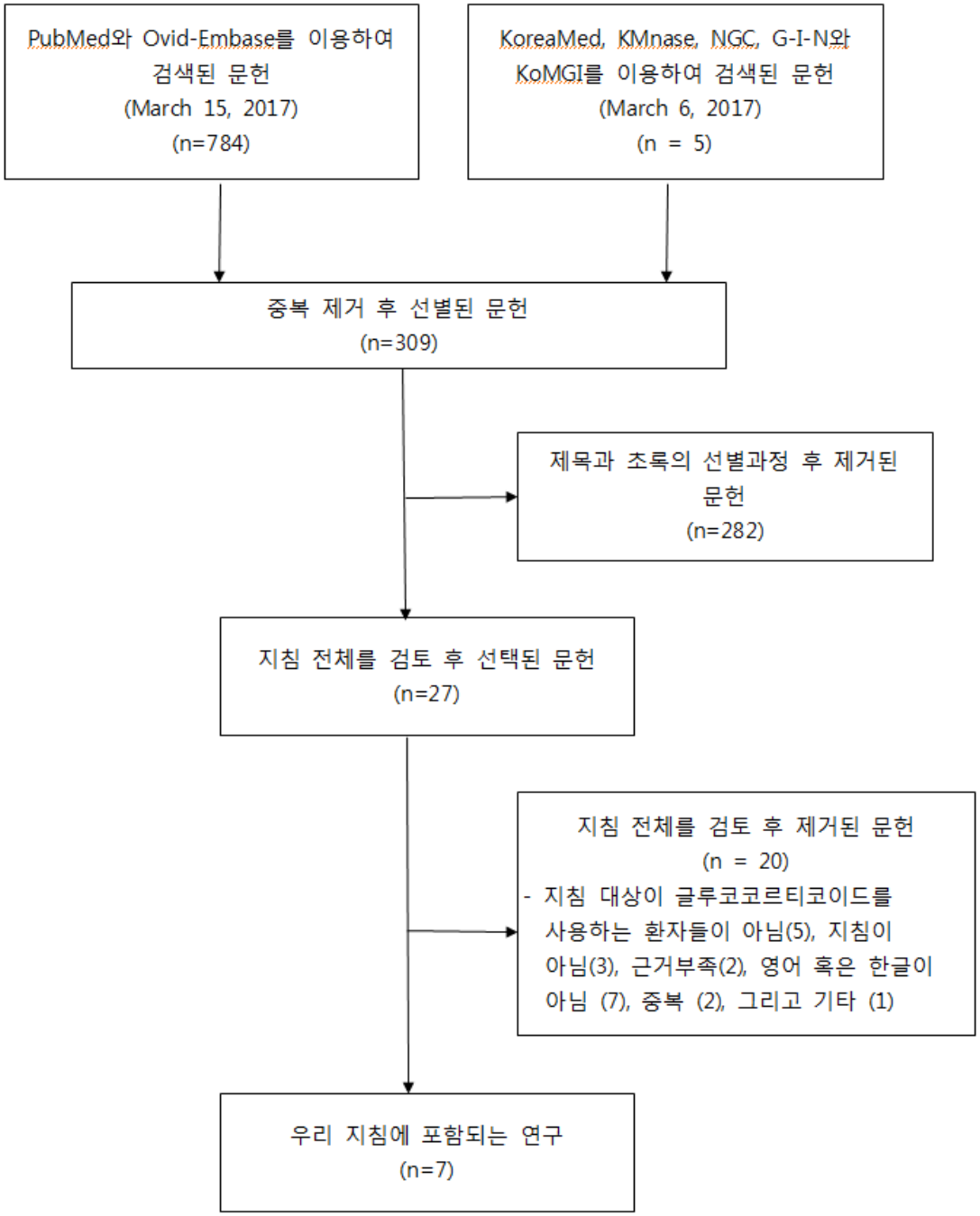
□ 2차 선정배제 기준

1	골다공증/골감소증를 연구하지 않은 문헌 0
2	스테로이드를 사용하는 환자들에 대한 연구를 포함하지 않은 문헌 5
3	암이나 내분비질환(쿠싱증후군 제외), HIV infection 등 특정 환자군만을 대상으로 한 문헌 0
4	권고 또는 지침이 아닌 문헌 3 - 단순한 종설(review), 개별 임상연구, critical Pathway(진료계획표) - 대표성 없는 단일저자가 작성한 진료지침 등
5	근거기반 방법으로 작성되지 않은 경우 2 - 체계적 근거검색(systematic search) 없이 합의만으로 작성한 지침의 경우

6	영어 또는 한국어로 보고되지 않은 지침 7
7	동료검토가 이루어지지 않은 진료지침 0
8	중복으로 게재된 경우 2 - 동일 내용으로 다른 저널에 게재 혹은 출판형태만 차이가 있는 경우 배제
9	원문확보가 불가능한 경우 1

두 연구자의 합의로 최종 7개의 문헌 선정

부록 4. 글루코코르티코이드 유발 골다공증 임상진료지침의 수용개작을 위한 문헌검색과 선정 흐름.



부록 5: 질평가

진료지침 질평가 도구로 K-AGREE를 사용하였다. K-AGREE 서식은 다음과 같다.

1. K-AGREE

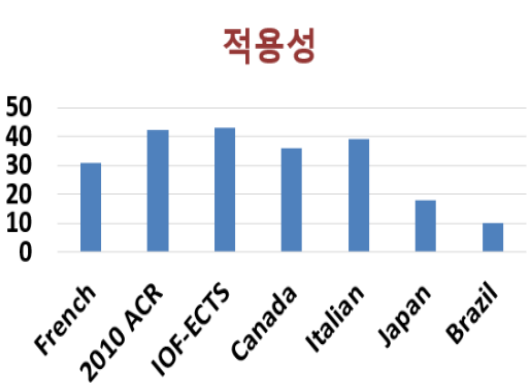
		←전혀 동의안함						매우 동의함→	
		1	2	3	4	5	6	7	NA
영역 1. 범위와 목적									
1	지침의 전반적인 목적을 구체적으로 기술하였다.								
2	진료지침에서 다루고자 하는 건강관련 질문(임상질문)들이 구체적으로 서술되어 있다.								
3	진료지침을 적용할 인구집단(환자, 일반인 등)이 구체적으로 서술되어 있다.								
영역 2. 이해당사자의 참여									
4	지침개발그룹은 모든 관련 전문가집단을 포함하고 있다.								
5	대상인구집단의 관점과 선호도를 포함하였다.								
6	진료지침 사용자가 명백하게 규정되어 있다.								
영역 3. 개발의 엄격성									
7	근거검색에 체계적인 방법을 사용하였다.								
8	근거선택의 기준이 분명하게 서술되어 있다.								

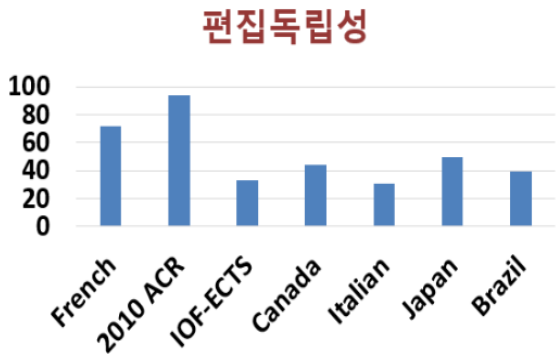
9	근거 자료의 강도와 한계가 분명하게 서술되어 있다								
10	권고도출의 방법이 서술되어 있다.								
11	권고도출에 건강상 편익, 부작용, 위험을 고려하였다.								
12	권고안과 이를 뒷받침하는 근거를 명확하게 연결지을 수 있다.								
13	진료지침은 출판 전에 외부 전문가들에 의한 검토 과정이 있었다.								
14	진료지침의 갱신 절차가 제시되어 있다.								
영역 4. 명확성과 표현									
15	권고안이 특이적이며 모호하지 않다.								
16	임상 상태나 건강 이슈를 관리하기 위한 다양한 대안이 분명하게 표현되어 있다.								
17	주요 권고안은 쉽게 확인할 수 있다.								
영역 5. 적용성									
18	진료지침은 이를 실행하는데 있어 장애요인과 촉진요인을 서술하고 있다.								
19	진료지침은 권고안이 의료현장에서 실제 사용될 수 있도록 도와주는 조언과 도구를 제시하고 있다.								
20	권고를 적용할 때 발생할 수 있는 비용 문제를 고려하였다.								

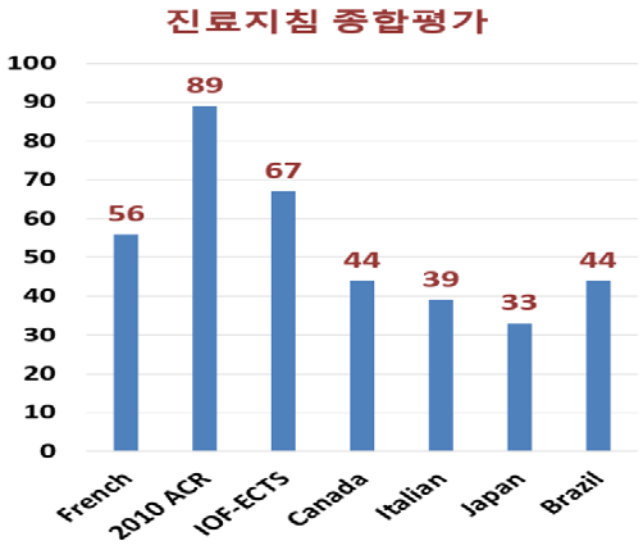
21	지침 시행 정도를 모니터링하고 평가할 수 있는 주요 기준이 제시되었다.								
영역 6. 편집 독립성									
22	재정후원단체의 의견이 진료지침의 내용에 영향을 주지 않았다.								
23	진료지침 개발에 참여한 구성원들의 이해관계가 기록되어 있고 그 내용이 언급되어 있다.								
전반적 평가									
1	진료지침의 전반적인 질 평가								
2	진료지침 사용의 추천여부	□ 사용을 추천함 □ 사용을 추천함(수정필요) □ 사용을 추천안함							

2. 질평가 결과

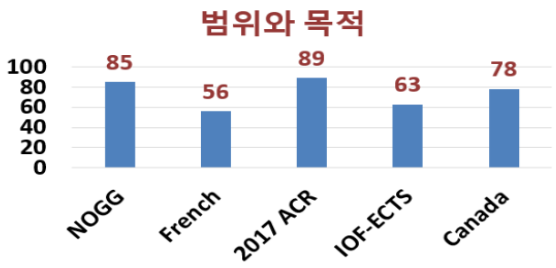
□ 1차 질평가

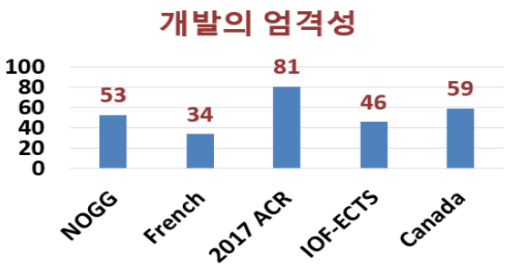


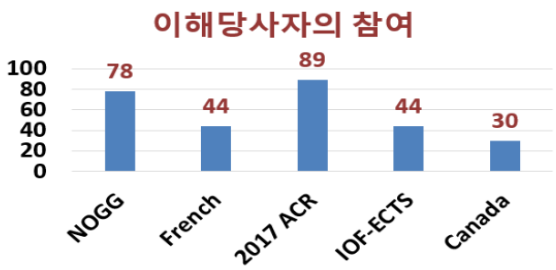



진료지침 종합평가
100
90
80
70
60
50
40
30
20
10
0
56
89
67
44
39
33
44
French
2010 ACR
IOF-ECTS
Canada
Italian
Japan
Brazil

□ 2차 질평가


범위와 목적
100
80
60
40
20
0
85
56
89
63
78
NOGG
French
2017 ACR
IOF-ECTS
Canada


개발의 엄격성
100
80
60
40
20
0
53
34
81
46
59
NOGG
French
2017 ACR
IOF-ECTS
Canada


이해당사자의 참여
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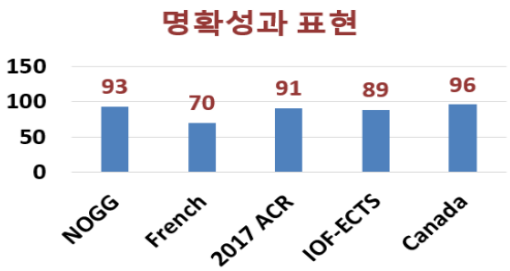
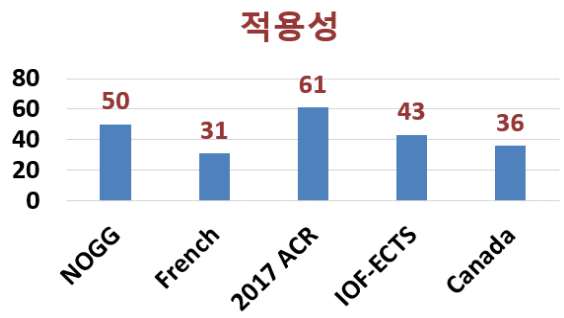
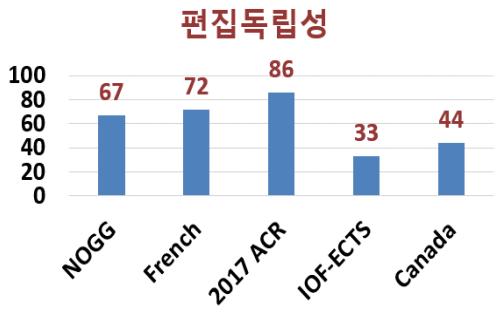
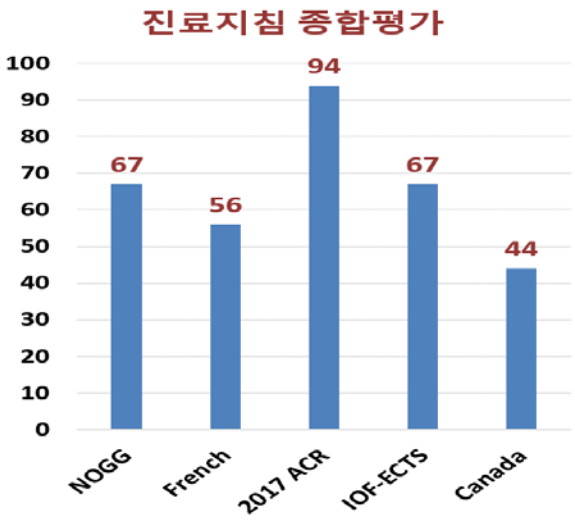
80
60
40
20
0
78
44
89
44
30
NOGG
French
2017 ACR
IOF-ECTS
Canada


명확성과 표현
150
100
50
0
93
70
91
89
96
NOGG
French
2017 ACR
IOF-ECTS
Canada







3. 최종 선정 진료지침

진료지침 질평가 후 최종적으로 5가지의 진료 지침이 선택되었다. 최종 진료 지침은 다음과 같다.

- 2017 American College of Rheumatology Guideline for the Prevention and Treatment

of Glucocorticoid-Induced Osteoporosis

- 2012 A framework for the development of guidelines for the management of glucocorticoid-induced osteoporosis (IOF-ECTS)
- 2014 update of recommendations on the prevention and treatment of glucocorticoid-induced osteoporosis (French)
- 2010 clinical practice guidelines for the diagnosis and management of osteoporosis (Canada)
- 2017 National Osteoporosis Guideline Group 2017 Clinical guideline for the prevention and treatment of osteoporosis

부록 6: 선택지침

선택 지침 1.

지침 제목	2017 American College of Rheumatology Guideline for the Prevention and Treatment of Glucocorticoid-Induced Osteoporosis
발표일	2017, September
Adaptation	자체 개발, revision of American College of Rheumatology Guideline in 2002
지침 개발자	American College of Rheumatology
재원	American College of Rheumatology
저자구성	Rhumatologists
COI	공시
해당질병	Glucocorticoid-Induced Osteoporosis (GIOP)
지침범주	진단, 평가, 관리, 예방, 치료, 치료 반응 평가, 추적 관찰
Clinical Speciality	내과학, 내분비학, 류마티스학, 정형외과학
지침 목적	To develop recommendations for prevention and treatment of GIOP.
사용자	patients with or at risk for GIOP and their clinicians
대상 모집단	average or typical glucocorticoid(GC)-treated patients
주요 결과	the assessment, prevention and treatment of OP and fractures in children and adults taking glucocorticoids (prednisone dose of > 2.5 mg of prednisone for ≥ 3 months), including patients with organ transplant who are treated with GCs.
비용분석	예
근거확보방법	수기검색(이차), 전자 DB 검색
질평가방법	Cochrane risk of bias tool (http://handbook.cochrane.org/)

<table>
<tr><td>지침 제목</td><td>2017 American College of Rheumatology Guideline for the Prevention and Treatment of Glucocorticoid-Induced Osteoporosis</td></tr>
<tr><td>근거수준</td><td>
<table>
<tr><td>Level</td><td>Type of Evidence</td></tr>
<tr><td>High quality</td><td>Further research is very unlikely to change our confidence in the estimate of effect.</td></tr>
<tr><td>Moderate quality</td><td>Further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate</td></tr>
<tr><td>Low quality</td><td>Further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate.</td></tr>
<tr><td>Very low quality</td><td>We are very uncertain about the estimate.</td></tr>
</table>
</td></tr>
<tr><td>근거분석방법</td><td>systematic review</td></tr>
<tr><td>권고안 도출</td><td>전문가 합의, voting process using Poll Everywhere software (http://www.polleverywhere.com/)</td></tr>
<tr><td>권고등급</td><td>
<table>
<tr><td>Grade</td><td>Type of Evidence - Nature of Recommendations</td></tr>
<tr><td>A strong recommendation</td><td>The Panel was confident that the desirable effects of following the recommendation outweigh the undesirable effects (or vice versa), so the course of action would apply to all or almost all patients, and only a small proportion would not want to follow the recommendation.</td></tr>
<tr><td>A conditional recommendation</td><td>The Panel believed the desirable effects of following the recommendation probably outweigh the undesirable effects, so the course of action would apply to the majority of the patients, but some may not want to follow the recommendation. Because of this, conditional recommendations are preference sensitive and always warrant a shared decision-making approach.</td></tr>
</table>
</td></tr>
</table>

지침 제목	2017 American College of Rheumatology Guideline for the Prevention and Treatment of Glucocorticoid-Induced Osteoporosis
	A good practice recommendation: Although the Panel believed the benefits of proceeding according to the guidance far outweigh the harms, the supporting evidence is indirect, and the Panel did not formally assess the relevant evidence.

타당도평가	내외부 동료검토
알고리즘	예
실행계획	예
원문사용	예

선택지침 2

지침 제목	A framework for the development of guidelines for the management of glucocorticoid-induced osteoporosis
발표일	2012. Februray
Adaptation	자체개발
지침 개발자	the International Osteoporosis Foundation(IOF) and the European Calcified Tissue Society
재원	the International Osteoporosis Foundation(IOF) and the European Calcified Tissue Society
저자구성	endocrinologist, rhematologist, physician, orthopedist
COI	공시
해당질병	Glucocorticoid-Induced Osteoporosis (GIOP_
지침범주	역학, 병태생리, 진단, 평가, 관리, 예방, 치료, 치료 반응 평가, 추적 관찰
Clinical Speciality	내과학, 내분비학, 류마티스학, 정형외과학
지침 목적	the management of glucocorticoid-induced osteoporosis
사용자	physicians in primary and secondary care
대상 모집단	men and women aged 18 years and over in whom oral glucocorticoid therapy is considered for 3 months or longer
주요 결과	Epidemiology of GIO, Pathophysiology of GIO, Assessment of fracture risk, Management of glucocorticoid-induced osteoporosis, Intervention thresholds, Cost-effectiveness of the treatment of GIO, Safety of treatments in GIO, Monitoring
비용분석	예
근거확보방법	수기검색(이차), 전자 DB 검색
질평가방법	Jadad score

<table>
<tr><td>지침 제목</td><td>A framework for the development of guidelines for the management of glucocorticoid-induced osteoporosis</td></tr>
<tr><td>근거수준/권고등급</td><td>
<table>
<tr><td>Level of grade of evidence/type of evidence recommendation</td><td>studies</td></tr>
<tr><td>Ia/A</td><td>Meta-analysis of RCTs</td></tr>
<tr><td>Ib/A</td><td>At least one RCT</td></tr>
<tr><td>IIa/B</td><td>At least one well-designed, controlled study but without randomization</td></tr>
<tr><td>IIb/B</td><td>At least one well-designed, quasi-experimental study</td></tr>
<tr><td>III/B</td><td>At least one well-designed, non-experimental descriptive study (e.g. comparative studies, correlation studies, case studies)</td></tr>
<tr><td>IV/C</td><td>Expert committee reports, opinions and/or experience of respected</td></tr>
</table>
</td></tr>
<tr><td>근거분석방법</td><td>systematic review</td></tr>
<tr><td>권고안 도출</td><td>전문가 합의</td></tr>
<tr><td>타당도평가</td><td>내외부 동료검토</td></tr>
<tr><td>알고리즘</td><td>예</td></tr>
<tr><td>수행계획</td><td>예</td></tr>
<tr><td>원문사용</td><td>예</td></tr>
</table>

선택지침 3

지침 제목	2014 update of recommendations on the prevention and treatment of glucocorticoid-induced osteoporosis
발표일	2014 July
Adaptation	자체개발, update the recommendations on the prevention and treatment of glucocorticoid-induced osteoporosis issued in 2003 by the French National Authority for Health (HAS).
지침 개발자	the Bone Section of the French Society for Rheumatology (SFR) and Osteoporosis Research and Information Group (GRIO)
재원	the Bone Section of the French Society for Rheumatology (SFR) and Osteoporosis Research and Information Group (GRIO)
저자구성	National Organization of Teaching Primary-Care Physicians, Osteoporosis Research and Information Group, French National Society for Gastroenterology, French National Society forInternal Medicine, Nephrology Society and French Society for Rheumatology
COI	공시
해당질병	Glucocorticoid-Induced Osteoporosis
지침범주	pathophysiology, risk factors, prevetion and treatment, patient follow-up, safety of osteoporosis drugs
Clinical Speciality	내과학, 내분비학, 류마티스학, 소화기학, 신장학, 정형외과학
지침 목적	to improve the quality of care delivered to patients on long-termglucocorticoid therapy, in order to decrease the risk of fracture
사용자	all physicians involved in the management of patients who are scheduled to start, or are taking, long-term glucocorticoid therapy (≥ 3 months) in any dose and for any reason
대상 모집단	
주요 결과	pathophysiology, risk factors, prevetion and treatment, patient follow-up, safety of osteoporosis drugs

지침 제목	2014 update of recommendations on the prevention and treatment of glucocorticoid-induced osteoporosis
비용분석	아니오.
근거확보방법	method developed by the HAS, 구체적인 기술 없음.
질평가방법	method developed by the HAS, 구체적인 기술 없음.
근거수준	구체적인 기술 없음
근거분석방법	SR
권고안 도출	전문가 합의
권고등급	구체적인 기술 없음
타당도평가	내외부 동료검토
알고리즘	예
수행계획	아니오
원문사용	예

선택지침 4

<table>
<tr><td>지침 제목</td><td>2010 clinical practice guidelines for the diagnosis and management of osteoporosis in Canada: summary</td></tr>
<tr><td>발표일</td><td>2010, November</td></tr>
<tr><td>Adaptation</td><td>자체개발, revision of the Osteoporosis Canada guidelins in 2002</td></tr>
<tr><td>지침 개발자</td><td>the Scientific Advisory Council of Osteoporosis Canada</td></tr>
<tr><td>재원</td><td>the Scientific Advisory Council of Osteoporosis Canada</td></tr>
<tr><td>저자구성</td><td>소아과의사, 내과의사, 가정의학과의사, 내분비내과 의사, 영상의학과 의사</td></tr>
<tr><td>COI</td><td>공시</td></tr>
<tr><td>해당질병</td><td>osteoporosis</td></tr>
<tr><td>지침범주</td><td>risk assessment, treatment, monitoring</td></tr>
<tr><td>Clinical Speciality</td><td>내과, 가정의학과, primary case physician</td></tr>
<tr><td>지침 목적</td><td>management of osteoporosis</td></tr>
<tr><td>사용자</td><td>primary care physicians, patients, osteoporosis specialists from various disciplines, radiologists, allied health professionals and health policy-makers to identify priorities</td></tr>
<tr><td>대상 모집단</td><td>women and men over age 50, because of the overall burden of illness in that age group.
children and young adults, as well as high-risk groups such as transplant recipients</td></tr>
<tr><td>주요 결과</td><td>assessment for osteoporosis and fracture risk, treatment, adverse events, management in special group, monitoring, stop or use combination therapy</td></tr>
<tr><td>비용분석</td><td>아니오</td></tr>
<tr><td>근거확보방법</td><td>수기검색(이차), 전자 DB 검색</td></tr>
<tr><td>질평가방법</td><td>구체적인 기술 없음</td></tr>
<tr><td>근거수준</td><td>
<table>
<tr><td>Level</td><td>criteria</td></tr>
<tr><td colspan="2">Studies of diagnosis</td></tr>
<tr><td>1</td><td>I. Independent interpretation of test results
ii. Independent interpretation of the diagnostic standard</td></tr>
</table>
</td></tr>
</table>

지침 제목	2010 clinical practice guidelines for the diagnosis and management of osteoporosis in Canada: summary

	iii. Selection of people suspected, but not known to have the disorder iv. Reproducible description of the test and diagnostic standard v. At least 50 people with and 50 people without the disorder
2	Meets 4 of the Level 1 criteria
3	Meets 2 of the Level 1 criteria
4	Meets 1 or 2 of the Level 1 criteria
Studies of treatment and intervention	
1+	Systematic overview of meta-analysis of randomized controlled trials
1	1 randomized controlled trial with adequate power
2+	Systematic overview or meta--analysis of Level 2 randomized controlled trials
2	Randomized controlled trial that does not meet Level 1 criteria
3	Non-randomized controlled trial or cohort study
4	Before-after study, cohort study with non-contemporaneous controls, case-control study
5	Case series without controls
6	Case report or case series of < 10 patients
Studies of prognosis	
1	i. Inception cohort of patients with the condition of interest, but free of the outcome of interest ii Reproducible inclusion and exclusion criteria iii Follow-up of at least 80% of participants iv. Statistical adjustment for confounders v. Reproducible description of the outcome measures
2	Meets criterion I and 3 of the 4 of the Level 1 criteria
3	Meets criterion I and 2 of the 4 of the Level 1 criteria

지침 제목	2010 clinical practice guidelines for the diagnosis and management of osteoporosis in Canada: summary

근거분석방법	systematic review
권고안 도출	a modified RAND/University of California, Los Angeles Delphi method
권고등급	<table><tr><td>grade</td><td>criteria</td></tr><tr><td>A</td><td>Need supportive level 1 or 1+ evidence plus consensus*</td></tr><tr><td>B</td><td>Need supportive level 2 or 2+ evidence plus consensus*</td></tr><tr><td>C</td><td>Need supportive level 3 evidence plus consensus</td></tr><tr><td>D</td><td>Any lower level of evidence supported by consensus</td></tr><tr><td colspan="2">*As appropriate level of evidence was necessary, but not sufficient to assign a grade in recommendation; consensus was required in addition.</td></tr></table>
타당도평가	전문가 검토
알고리즘	예
수행계획	아니오
원문사용	예

선택지침 5

지침 제목	National Osteoporosis Guideline Group 2017 Clinical guideline for the prevention and treatment of osteoporosis
발표일	2017, March
Adaptation	자체개발, updates those previously developed by the Royal College of Physicians [RCP 1999, 2000] and the National Osteoporosis Guideline Group [Compston et al 2009, Compston et al 2013].
지침 개발자	National Osteoporosis Guideline Group
재원	No funding source/body was involved in the development of this guideline.
저자구성	bone specialist, Primary Care Physician, endocrinologist, rheumatologist
COI	공시
해당질병	osteoporosis
지침범주	the assessment and diagnosis of osteoporosis, the therapeutic interventions available and the manner in which these can be used to develop management strategies for the prevention of osteoporotic fracture in postmenopausal women and in men age 50 years or over
Clinical Speciality	내과학, 내분비학, 류마티스학, 소화기학, 신장학, 정형외과학
지침 목적	the management of glucocorticoid-induced osteoporosis
사용자	all healthcare professionals involved in the management of osteoporosis
대상 모집단	postmenopausal women and in men age 50 years or over
주요 결과	definition and diagnosis of osteoporosis, fracture risk assessment, lifestyle measures in the management of osteoporosis, pharmacological interventions, duration and monitoring of bisphosphonate therapy, glucocorticoid-induced osteoporosis, osteporosis in men, post-fracture care and Fracture Liaison Services, Case finding and intervension thresholds, recommendations for training, recommendations for commissioners of healthcare and the Department of Health, Review criteria for audit
비용분석	아니오
근거확보방법	수기검색(이차), 전자 DB 검색
질평가방법	AMSTAR

<table>
<tr><td>지침 제목</td><td>National Osteoporosis Guideline Group 2017 Clinical guideline for the prevention and treatment of osteoporosis</td></tr>
<tr><td>근거수준</td><td>
<table>
<tr><td colspan="2">Levels of evidence for studies of intervention are defined as follows:</td></tr>
<tr><td>Ia</td><td>from meta-analysis of randomised controlled trials (RCTs)</td></tr>
<tr><td>Ib</td><td>from at least one RCT</td></tr>
<tr><td>IIa</td><td>from at least one well designed controlled study without randomisation</td></tr>
<tr><td>IIb.</td><td>from at least one other type of well-designed quasi-experimental study</td></tr>
<tr><td>III.</td><td>from well-designed non-experimental descriptive studies, e.g. comparative studies, correlation studies, case-control studies</td></tr>
<tr><td>IV.</td><td>from expert committee reports or opinions and/or clinical experience of authorities</td></tr>
<tr><td colspan="2">The validity of candidate risk factors is also assessed by an evidence-based approach:</td></tr>
<tr><td>Ia</td><td>Systematic reviews or meta-analysis of level I studies with a high degree of homogeneity</td></tr>
<tr><td>Ib</td><td>Systematic reviews or meta-analysis with moderate or poor homogeneity</td></tr>
<tr><td>Ic</td><td>Level I studies (with appropriate populations and internal controls)</td></tr>
<tr><td>IIa</td><td>Systematic reviews or meta-analysis of level II studies</td></tr>
<tr><td>IIb</td><td>Level II studies (inappropriate population or lacking an internal control)</td></tr>
<tr><td>IIIa</td><td>Systematic reviews or meta-analysis of level III studies</td></tr>
<tr><td>IIIb</td><td>Case-control studies</td></tr>
<tr><td>IV</td><td>Evidence from expert committees without explicit critical scientific analysis or that based on physiology, basic research or first principles</td></tr>
</table>
</td></tr>
<tr><td>근거분석방법</td><td>SR</td></tr>
<tr><td>권고안 도출</td><td>전문가 합의</td></tr>
</table>

<table>
<tr><td>권고등급</td><td>
<table>
<tr><td colspan="2">The quality of the guideline recommendations is similarly graded to indicate the levels of evidence on which they are based:</td></tr>
<tr><td>GRADE A</td><td>evidence levels Ia and Ib</td></tr>
<tr><td>GRADE B</td><td>evidence levels IIa, IIb and III</td></tr>
<tr><td>GRADE C</td><td>evidence level IV</td></tr>
<tr><td colspan="2">Risk factors can also be categorised according to evidence for reversible risk:</td></tr>
<tr><td>GRADE A</td><td>Validated by use as inclusion criteria in randomized controlled trials</td></tr>
<tr><td>GRADE B</td><td>Do not adversely affect fracture outcomes in randomized controlled trials</td></tr>
<tr><td>GRADE C</td><td>Untested or adversely affect intervention outcomes</td></tr>
</table>
</td></tr>
<tr><td>타당도평가</td><td>내외부 동료검토</td></tr>
<tr><td>알고리즘</td><td>예</td></tr>
<tr><td>수행계획</td><td>예</td></tr>
<tr><td>원문사용</td><td>예</td></tr>
</table>

부록 7: 권고근거 정리

▣ 핵심질문 1.

글루코코르티코이드를 사용하는 환자에서 비약물적 치료가 글루코코르티코이드 유발 골다공증 예방과 치료에 효과적인가?

▣ PICO

Patients	Intervention	Comparators	Outcomes
글루코코르티코이드를 사용하는 환자	비약물적 치료		글루코코르티코이드 유발 골다공증 예방과 치료 효과

▣ 권고비교표

	지침 1 (ACR)	지침 2 (IOF-ESTS)	지침 3 (FRENCH)	지침 4 (CANADA)	지침 5 (NOGG)

출판년도	2017	2012	2014	2010	2017
AGREE 평가점수	89	67	56	44	67
권고문	All adults taking prednisone at a dose of ≥2.5 mg/day for ≥3 months Optimize calcium intake (800–1,000 mg/day) and vitamin D intake (600–800 IU/day) and lifestyle modifications (balanced diet, maintaining weight in the recommended range, smoking cessation, regular weight-bearing or resistance training exercise, limiting	Tobacco use and alcohol abuse should be avoided, and appropriate levels of physical exercise should be encouraged.	Encourage smoking cessation and a decrease of excessive alcohol use to a reasonable level	1. Exercises involving resistance training appropriate for the individual's age and functional capacity and/or weightbearing aerobic exercises are recommended for those with osteoporosis or at risk for osteoporosis [grade B]. 2. Exercises to enhance core stability and thus to compensate for weakness or postural abnormalities are recommended	Regular weight-bearing exercise should be advised, tailored according to the needs and abilities of the individual patient.

	alcohol intake to 1–2 alcoholic beverages/day) over no treatment or over any of these treatments alone.			for individuals who have had vertebral fractures [grade B]. 3. Exercises that focus on balance, such as tai chi, or on balance and gait training should be considered for those at risk of falls [grade A].	
근거수준,권고등급	III/B	전문가합의/B	III/B	III/B	전문가합의/B

▣ 근거 내용 정리

[지침1] ACR 2017

- **Reference**

	문헌정보	연구유형	연구대상자수 (치료군/비교군)

1	Ross AC, Manson JE, Abrams SA, Aloia JF, Brannon PM, Clinton SK, et al. The 2011 report on dietary reference intakes for calcium and vitamin D from the Institute of Medicine: what clinicians need to know. J Clin Endocrinol Metab 2011;96:53–8 [1]	review	

- **일차연구문헌 근거표** – 없음

[지침2] 2012 IOF-ECTS

- **Reference** – 없음

- **일차연구문헌 근거표** – 없음

[지침3] 2014 FRENCH

- **Reference**

	문헌정보	연구유형	연구대상자수 (치료군/비교군)
1	El-Khoury F, Cassou B, Charles MA,et al. The effect of fall prevention exercise programmes on fall induced injuries community dwelling older adults: systematic review and meta-analysis of randomised controlled trials. BMJ2013;347:f6234 [2]	meta-analysis	17trials involving 4305 participants

- **일차연구문헌 근거표** – 없음

[지침4] 2010 CANADA

- **Reference**

	문헌정보	연구유형	연구대상자수 (치료군/비교군)
1	LiWC,ChenYC,YangRS,etal. Effects of exercise programmes on quality of life in osteoporotic and osteopenic postmenopausal women: a systematic review and meta-analysis. Clin Rehabil 2009;23:888-96 [3]	review and meta-analysis	

2	Moayyeri A. The association between physical activity and osteoporotic fractures: a review of the evidence and implications for future research. Ann Epidemiol 2008;18:827-35 [4]	review	
3	Hip protectors in long-term care policy guidance and implementation. Ottawa(ON): Canadian Agency for Drugs and Technologies in Health, Health Technology Inquiry Service; 2010 [5]	policy guidance	

- **일차연구문헌 근거표** – 없음

[지침5] 2017 NOGG

- **Reference** – 없음

- **일차연구문헌 근거표** – 없음

▣ 핵심질문 2.

40세 미만 성인에서 어떤 약물 치료가 글루코코르티코이드 유발 골다공증 예방과 치료에 효과적인가?

▣ 핵심질문 2-1.

40세 미만 성인에서 칼슘과 비타민 D 보충은 글루코코르티코이드 유발 공다공증 예방과 치료에 효과적인가?

▣ PICO

Patients	Intervention	Comparators	Outcomes
40세 미만 성인	칼슘과 비타민 D 보충		글루코코르티코이드 유발 골다공증 예방과 치료 효과

▣ 권고비교표

	지침1 (ACR)	지침2 (IOF-ECTS)	지침3 (FRENCH)	지침4 (CANADA)	지침5 (NOGG)
출판년도	2017	2012	2014	2010	2017
AGREE 평가점수	89	67	56	44	67
권고문	All adults taking prednisone at a dose of ≥2.5 mg/day for ≥3 months Optimize calcium intake (800–1,000 mg/day) and vitamin D intake (600–800 IU/day) and lifestyle modifications (balanced diet, maintaining weight in the recommended range, smoking cessation, regular weight-bearing or	1. Advise good nutrition especially with calcium and vitamin D 2. Adequate calcium intake should be achieved through dietary intake if possible, with the use of supplements if necessary. 3. An adequate vitamin D status should be maintained, using supplements if required	1. Ensure adequate intakes of calcium (preferably via a balanced diet) and vitamin D 2. Routine prescription of calcium supplements is not recommended 3. The serum level of 25-OH vitamin D should be maintained at the optimal value,which has been set at 30 ng/mL (75 nmoL/L) [52] based on findingsfrom biological and clinical studies that	1. For healthy adults at low risk of vitamin D deficiency, routine supplementation with 400–1000 IU (10–25 µg) vitamin D 3 daily is recommended [grade D]. 2. For individuals receiving pharmacologic therapy for osteo-porosis, measurement of serum 25-hydroxyvitamin D should follow three to four months of adequate	General recommendation (GIOP를 포함한) - A daily calcium intake of between 700 and 1200mg should be advised, if possible achieved through dietary intake, with use of supplements if necessary. It is recommended that in postmenopausal women and men ≥50 years who are at increased risk of

	resistance training exercise, limiting alcohol intake to 1–2 alcoholic beverages/day) over no treatment or over any of these treatments alone.		did not focus specificallyon glucocorticoid-induced osteoporosis 4. In patients with vitamin D insufficiency or deficiency, a loading dose of vitamin D should be given to elevate the serum 25-OH vita-min D level above the target of 30 ng/mL 5. The maintenance dose is 800 to 1200 IU/day (or the equivalent of 100,000 IU every 2–3 months). The currently available data do not support the use of high-dose vitamin D	supplementation and should not be repeated if an optimal level (≥ 75 nmol/L) is achieved [grade D].	fracture, a daily dose of 800 IU of cholecalciferol should be advised(Grade A recommendation). Intermittent administration of large doses of vitamin D e.g. ≥100,000 IU is not advised, based on recent reports of an associated increased risk of fracture and falls

			supplementation (500,000 or 600,000 IU once or twice every year)		
근거수준,권고등급	II / B	II / B	II / B	II / B	II / B

▣ 근거 내용 정리

[지침1] 2017 ACR

- **Reference**

	문헌정보	연구유형	연구대상자수 (치료군/비교군)
1	Braun JJ, Birkenhager-Frenkel DH, Rietveld AH, Juttmann JR, Visser TJ, Birkenhager JC. Influence of 1 alpha-(OH)D3 administration on bone and bone mineral metabolism in patients on chronic glucocorticoid treatment; a double	RCT	14 (7/7)

	blind controlled study. Clin Endocrinol (Oxf). 1983;19(2):265-273 [6]		
2	Adachi JD, Bensen WG, Bianchi F, Cividino A, Pillersdorf S, Sebaldt RJ, et al. Vitamin D and calcium in the prevention of corticosteroid induced osteoporosis: a 3 year follow up. J Rheumatol. 1996;23(6):995-1000 [7]	RCT	62
3	Grant AM, Avenell A, Campbell MK, McDonald AM, MacLennan GS, McPherson GC, et al. Oral vitamin D3 and calcium for secondary prevention of low-trauma fractures in elderly people (Randomised Evaluation of Calcium Or vitamin D, RECORD): a randomised placebo-controlled trial. Lancet. 2005;365(9471):1621-1628 [8]	RCT	5292 (3,940/1,332)
4	Porthouse J, Cockayne S, King C, Saxon L, Steele E, Aspray T, et al. Randomised controlled trial of calcium and supplementation with cholecalciferol (vitamin D3) for prevention of fractures in primary care. BMJ. 2005;330(7498):1003 [9]	RCT	4133 (1,321/ 1,993)
5	Jackson RD, LaCroix AZ, Gass M, Wallace RB, Robbins J, Lewis CE, et al. Calcium plus vitamin D supplementation and the risk of fractures. N Engl J Med. 2006;354(7)669 -683 [10]	RCT	36,282 (18,176/18,106)

6	Salovaara K, Tuppurainen M, Karkkainen M, Rikkonen T, Sandini L, Sirola J, et al. Effect of vitamin D(3) and calcium on fracture risk in 65- to 71-year-old women: a population-based 3-year randomized, controlled trial—the OSTPRE-FPS. J Bone Miner Res. 2010;25(7):1487-1495 [11]	observational cohort study	3195 (1,586/1,609)

- **일차연구문헌 근거표**

Author, Publication year	**J. J. BRAUN et al.** **Clinical Endocrinology (1983) 18,265-273**
Title	INFLUENCE OF 1α-(OH)D3 ADMINISTRATION ON BONE AND BONE MINERAL METABOLISM IN PATIENTS ON CHRONIC GLUCOCORTICOID TREATMENT; A DOUBLE BLIND CONTROLLED STUDY
Methods	a double-blind placebo controlled study
Participants	**N= 14 (중재군/비교군= 7/7)** **Inclusion criteria** - No medication with known influence on bone metabolism was used. - All patients with chronic obstructive lung disease used a P-adrenergic drug and a xanthine-derivative. - Patients were not immobilized. **Exclusion criteria**

	- Renal disease
Interventions	▸(중재군) a daily dose of 2 pg 1α-(OH)D3 ▸(비교군) placebo
Outcomes	**Primary outcome** -Biochemistrical change **Secondary outcomes** -the changes of Bone histontorphometry and Bone mineral content ▸추적기간 - 6 month
Results	▸Two of the 14 patients showed an increased serum immunoreactive parathyroid hormone (iPTH) concentration. ▸Serum 25-hydroxyvitamin D and 1,25-dihydroxyvitamin D (1,25-$(0H)_3$D) were normal but the average 24,25-dihydroxyvitamin D (24,25-(OH)2D) was low. ▸The histomorphometrically determined trabecular bone volume of an iliac crest biopsy appeared to be low in 6 patients ▸The average active bone resorption and osteoid seams were increased, while the average osteoblast seams were within the normal range. ▸Treatment with 1 a-(OH)D3 raised 47Ca2+ intestinal absorption and 24 h urinary Ca2+ excretion

	significantly at 3 and 6 months and at 6 months serum iPTH concentration and 24 h urinary hydroxyproline excretion had fallen significantly in the treated group. During treatment with 1 a-(OH)D3 the serum 1,25-(OH)2D and 24,25-(OH)2D levels increased significantly ▸trabecular bone volume remained constant or even increased in the la-(OH)D3-group ▸In both groups osteoid seams and osteoblast seams did not change significantly

Author, Publication year	**Adachi JD et al.** **J Rheumatol. 1996 Jun;23(6):995-1000.**
Title	Vitamin D and calcium in the prevention of corticosteroid induced osteoporosis: a 3 year followup.
Methods	a minimized double blind, placebo controlled trial
Participants	**N= 62** **Inclusion criteria** - subjects with polymyalgia rheumatica, temporal arteritis, asthma, vasculitis, or systemic lupus erythematosus **Exclusion criteria** **-**
Interventions	▸(중재군) -vitamin D 50,000 units/week and calcium 1,000 mg/day for 36 months

	▸(비교군) -placebo for 36 months
Outcomes	**Primary outcome:** - the percentage change in bone mineral density (BMD) of the lumbar spine in the 2 treatment groups from baseline to 36 months follow up. **Secondary outcomes:** ▸추적기간 - 36 months
Results	▸BMD of the lumbar spine in the vitamin D and calcium treated group decreased by a mean (SD) of 2.6% (4.1%) at 12 mo, 3.7% (4.5%) at 24 mo, and 2.2% (5.8%) at 36 mo. ▸In the placebo group there was a decrease of 4.1% (4.1%) at 12 mo, 3.8% (5.6%) at 24 mo, and 1.5% (8.8%) at 36 mo. ▸The observed differences between groups were not statistically significant. The difference at 36 mo was-0.693% (95% CI -5.34, 3.95).

Author, Publication year	**Grant AM. et al.** **Lancet. 2005;365(9471):1621-1628.**

Title	Oral vitamin D3 and calcium for secondary prevention of low-trauma fractures in elderly people (Randomised Evaluation of Calcium Or vitamin D, RECORD): a randomised placebo-controlled trial.
Methods	a randomised placebo-controlled trial
Participants	**N= 5292(중재군/비교군= 3940/1332)** **Inclusion criteria** - age 70 years or older who had had a low-trauma, osteoporotic fracture in the previous 10 years were assessed between Feb 1, 1999, and March 31, 2002 **Exclusion criteria** **-** bed or chair bound before fracture - cognitive impairment indicated by an abbreviated mental test score8 of less than seven - cancer in the past 10 years that was likely to metastasise to bone - fracture associated with pre-existing local bone abnormality - those known to have hypercalcaemia; renal stone in the past 10 years - life expectancy of less than 6 months; individuals known to be leaving the UK - daily intake of more than 200 IU vitamin D or more than 500 mg calcium supplements - intake in the past 5 years of fluoride, bisphosphonates, calcitonin, tibolone, hormone-replacement therapy, selective oestrogen-receptor modulators, or any vitamin D metabolite (eg, calcitriol); and vitamin D by injection in the past year
Interventions	▸(중재군) - oral vitamin D3 (800 IU per day) (n=1343)

	- oral calcium (1000 mg per day) (n=1311) - oral vitamin D3 (800 IU per day) combined with calcium (1000 mg per day) (n=1306) ▸(비교군) - placebo (n=1332)
Outcomes	**Primary outcome:** - new low-energy fractures **Secondary outcomes:** - quality of life ▸추적기간 - between 24 months and 62 months
Results	▸The incidence of new, low-trauma fractures did not differ significantly between participants allocated calcium and those who were not (331 [12.6%] of 2617 vs 367 [13.7%] of 2675; hazard ratio (HR) 0.94 [95% CI 0.81-1.09]); between participants allocated vitamin D3 and those who were not (353 [13.3%] of 2649 vs 345 [13.1%] of 2643; 1.02 [0.88-1.19]); or between those allocated combination treatment and those assigned placebo (165 [12.6%] of 1306 vs 179 [13.4%] of 1332; HR for interaction term 1.01 [0.75-1.36]). ▸The groups did not differ in the incidence of all-new fractures, fractures confirmed by radiography, hip fractures, death, number of falls, or quality of life. ▸By 24 months, 2886 (54.5%) of 5292 were still taking tablets, 451 (8.5%) had died, 58 (1.1%) had withdrawn, and 1897 (35.8%) had stopped taking tablets but were still providing data for at least the main

	outcomes. ▸Compliance with tablets containing calcium was significantly lower (difference: 9.4% [95% CI 6.6-12.2]), partly because of gastrointestinal symptoms. However, potentially serious adverse events were rare and did not differ between groups.

Author, Publication year	**Porthouse J et al.** **BMJ. 2005;330(7498):1003.**
Title	Randomised controlled trial of calcium and supplementation with cholecalciferol (vitamin D3) for prevention of fractures in primary care.
Methods	randomised controlled trial
Participants	**N= 4133 (중재군/비교군= 1321/ 1993)** **Inclusion criteria** - We identified women aged 70 and over who had at least one self reported risk factor for hip fracture: low bodyweight (< 58 kg), any previous fracture, maternal history of hip fracture, smoker, and poor or fair health. **Exclusion criteria** - Women were excluded from the study if they could not give written consent or were receiving any calcium supplementation of more than 500 mg a day.

	- We also excluded women with a history of kidney or bladder stones, renal failure, or hypercalcaemia**.**
Interventions	▸(중재군) - daily oral supplementation using 1000 mg calcium with 800 IU cholecaliferol ▸(비교군) - information leaflet on dietary calcium intake and prevention of falls, or leaflet only
Outcomes	**Primary outcome:** -all clinical fractures **Secondary outcomes:** -adherence to treatment, falls, and quality of life (measured with the SF-12). ▸추적기간 - median follow-up of 25 months (range 18 to 42 months)
Results	▸69% of the women who completed the follow-up questionnaire at 24 months were still taking supplements (55% with inclusion of randomised participants known to be alive). ▸After a median follow-up of 25 months (range 18 to 42 months), clinical fracture rates were lower than expected in both groups but did not significantly differ for all clinical fractures (odds ratio for fracture in supplemented group 1.01, 95% confidence interval 0.71 to 1.43). ▸The odds ratio for hip fracture was 0.75 (0.31 to 1.78). ▸The odds of a woman having a fall at six and 12 months was 0.99 and 0.98, respectively. ▸Quality of life did not significantly differ between the groups.

Author, Publication year	**Jackson RD et al.** **N Engl J Med. 2006;354(7)669-683**
Title	Calcium plus vitamin D supplementation and the risk of fractures.
Methods	randomised controlled trial
Participants	**N= 36,282 (중재군/비교군= 18,176/18,106)** **Inclusion criteria** -Eligible women were 50 to 79 years of age at the initial screening and had no evidence of a medical condition associated with a predicted survival of less than three years and no safety, adherence, or retention risks **Exclusion criteria** - hypercalcemia, renal calculi, corticosteroid use, and calcitriol use.
Interventions	▸(중재군) - 1000 mg of elemental calcium + 400 IU of vitamin D3 daily for 9 years ▸(비교군)

	- 1000 mg of elemental calcium + placebo for 9 years
Outcomes	**Primary outcome:** - Hip bone density **Secondary outcomes:** - spine, whole body bone density - fraciture ▸추적기간 - 9 years
Results	▸Hip bone density was 1.06 percent higher in the calcium plus vitamin D group than in the placebo group (P<0.01). ▸Intention-to-treat analysis indicated that participants receiving calcium plus vitamin D supplementation had a hazard ratio of 0.88 for hip fracture (95 percent confidence interval, 0.72 to 1.08), 0.90 for clinical spine fracture (0.74 to 1.10), and 0.96 for total fractures (0.91 to 1.02). ▸The risk of renal calculi increased with calcium plus vitamin D (hazard ratio, 1.17; 95 percent confidence interval, 1.02 to 1.34). ▸Censoring data from women when they ceased to adhere to the study medication reduced the hazard ratio for hip fracture to 0.71 (95 percent confidence interval, 0.52 to 0.97 ▸Effects did not vary significantly according to prerandomization serum vitamin D levels.

Author, Publication year	**Salovaara K. et al.** **J Bone Miner Res. 2010;25(7):1487-1495.**
Title	Effect of vitamin D(3) and calcium on fracture risk in 65- to 71-year-old women: a population-based 3-year randomized, controlled trial—the OSTPRE-FPS.
Methods	observational cohort study.
Participants	**N= 3195 (중재군/비교군= 1586/1609)** **Inclusion criteria** - all women living in the region of northern Savonia, previous Kuopio Province (latitude 628 to 648N), born between 1932 and 1941 **Exclusion criteria** **-** no exclusion criteria
Interventions	▸(중재군) - 800 IU of cholecalciferol + 1000 mg of calcium daily ▸(비교군) -palcebo
Outcomes	**Primary outcome:** - incident fractures

	Secondary outcomes: - serum vitamin D levels during follow-up. ▸추적기간 - 36 months
Results	▸In adjusted Cox proportional hazards models, the risk of any fracture decreased in the vitamin D and calcium group by 17% [adjusted hazard ratio (aHR) ¼ 0.83; 95% confidence interval (CI) 0.61–1.12], and the risk of any nonvertebral fracture decreased by 13% (aHR ¼ 0.87; 95% CI 0.63–1.19). ▸The risk of distal forearm fractures decreased by 30% (aHR ¼ 0.70; 95% CI 0.41–1.20), and the risk of any upper extremity fractures decreased by 25% (aHR ¼ 0.75; 95% CI 0.49–1.16), whereas the risk of lower extremity fractures remained essentially equal (aHR ¼ 1.02; 95% CI 0.58–1.80). None of these effects reached statistical significance.

[지침2] 2012 IOF-ECTS

- **Reference**

	문헌정보	연구유형	연구대상자수 (치료군/비교군)

1	Amin S, LaValley MP, Simms RW, Felson DT (1999) The role of vitamin D in corticosteroid-induced osteoporosis: a meta-analytic approach. Arthritis Rheum 42:1740–1751 [12]	meta-analysis	
2	Reginster JY, Kuntz D, Verdickt W, Wouters M, Guillevin L, Menkes CJ, Nielsen K (1999) Prophylactic use of alfacalcidol in corticosteroid-induced osteoporosis. Osteoporos Int 9:75–8 [13]	RCT	145 (74/71)
3	Sambrook, P. N. et al. Corticosteroid osteoporosis: practical implications of recent trials. J Bone Miner Res 15:1645–1649 [14]	review	
4	Holick MF (2007) Optimal vitamin d status for the prevention and treatment of osteoporosis. Drugs Aging 24:1017–1029 [15]	review	
5	Buckley LM, Leib ES, Cartularo KS, Vacek PM, Cooper SM (1996) Calcium and vitamin D3 supplementation prevents bone loss in the spine secondary to low-dose corticosteroids in patients with rheumatoid arthritis. A randomized, double-blind, placebo-controlled trial. Ann Intern Med 125:961–968 [16]	RCT	66 (31/35)

6	Homik J, Suarez-Almazor ME, Shea B, Cranney A, Wells G, Tugwell P (2000) Calcium and vitamin D for corticosteroid induced osteoporosis. Cochrane Database Syst Rev 2:CD000952 [17]	meta-analysis	

- **일차연구문헌 근거표**

Author, Publication year	**Reginster JY. et al.** **Osteoporos Int. 1999;9(1):75-81.**
Title	Prophylactic use of alfacalcidol in corticosteroid-induced osteoporosis.
Methods	randomized placebo-controlled trial
Participants	**N= 145 (중재군/비교군= 74/71)** **Inclusion criteria** - One hundred and forty-five patients suffering from diseases requiring long-term treatment with high doses

	of corticosteroids (30 mg/day or greater of prednisolone) were recruited to the study. - Patients had to be steroid naive on entry to the study (not more than 15 days of treatment with a corticosteroid within the previous 24 months). **Exclusion criteria** **-** no exclusion criteria
Interventions	▸(중재군) - alfacalcidol 1 microgram/day ▸(비교군) - placebo
Outcomes	**Primary outcome:** - Bone mineral density (BMD) of the lumbar spine **Secondary outcomes:** - Safety, serum calcium ▸추적기간 - 12 months
Results	▸The percentage change in BMD after 6 months' treatment was -2.11% in the alfacalcidol group and –4.00% in the placebo group (p = 0.39). ▸After 12 months the percentage change in BMD was +0.39% (CI: -4.28 to 4.81) in the alfacalcidol group and -5.67% (CI: -8.13 to -3.21) in the placebo group, this difference (6.06%, CI: 0.88 to 11.24) being

	statistically significant (p = 0.02). ▸An intention to treat analysis also showed a significant difference between the two treatment groups in alfacalcidol's favor (3.81%, p = 0.01; CI: 0.92 to 6.70). ▸There was no significant difference between the two treatment groups in the corticosteroid dose at any time point during the study. ▸Serum calcium was measured throughout and there were no significant differences between the two treatment groups at any visit.

Author, Publication year	**Buckley LM et al** **Ann Intern Med. 1996 Dec 15;125(12):961-8.**
Title	Calcium and vitamin D3 supplementation prevents bone loss in the spine secondary to low-dose corticosteroids in patients with rheumatoid arthritis. A randomized, double-blind, placebo-controlled trial.
Methods	A randomized, double-blind, placebo-controlled trial.
Participants	**N= 66 (중재군/비교군= 31/35)** **Inclusion criteria** - Patients were eligible if they were between 18 and 65 years of age and had a diagnosis of rheumatoid arthritis as defined by the revised American College of Rheumatology criteria, serum creatinine level less than 176.8 µmol/L, and

	normal liver function. **Exclusion criteria** - Patients were excluded if they were receiving an anticonvulsant medication, hydrochlorothiazide, bisphosphonates, fluoride, calcitonin, or calcitriol or if they had a history of malabsorption, hyperparathyroidism, immobilization, metabolic bone disease, or thyroid disease with an abnormal thyroid-stimulating hormone
Interventions	▸(중재군) - Calcium carbonate (1000 mg/d) and vitamin D3 (500 IU/d) ▸(비교군) - placebo
Outcomes	**Primary outcome:** - bone densitometry of the lumbar spine **Secondary outcomes:** - bone densitometry of the femur ▸추적기간 - 24 months
Results	▸Patients receiving prednisone therapy who were given placebo lost bone mineral density in the lumbar spine and trochanter at a rate of 2.0% and 0.9% per year, respectively. ▸Patients receiving prednisone therapy who were given calcium and vitamin D3 gained bone mineral density in the lumbar spine and trochanter at a rate of 0.72% (P=0.005) and 0.85% (P=0.024) per year,

respectively.

▸In patients receiving prednisone therapy, bone mineral densities of the femoral neck and the Ward triangle did not increase significantly with calcium and vitamin D3. Calcium and vitamin D3 did not improve bone mineral density at any site in patients who were not receiving corticosteroids

[지침3] 2014 FRENCH

- **Reference**

	문헌정보	연구유형	연구대상자수 (치료군/비교군)
1	Sanders KM, Stuart AL, Williamson EJ, et al. Annual high dose oral vitamin D and falls and fractures in older women: a randomized controlled trial. JAMA 2010;303:1815–22 [18]	RCT	2256 (1131/1125)

- **일차연구문헌 근거표**

Author, Publication year	**Sanders KM, et al.** **JAMA 2010;303:1815–22.**
Title	Annual high-dose oral vitamin D and falls and fractures in older women: a randomized controlled trial.
Methods	A double-blind, placebo-controlled trial
Participants	**N= 2256 (중재군/비교군= 1131/1125)** **Inclusion criteria** - Patients were eligible if they were between 18 and 65 years of age and had a diagnosis of rheumatoid arthritis as defined by the revised American College of Rheumatology criteria, serum creatinine level less than 176.8 μmol/L, and normal liver function. **Exclusion criteria** - Patients were excluded if they were receiving an anticonvulsant medication, hydrochlorothiazide, bisphosphonates, fluoride, calcitonin, or calcitriol or if they had a history of malabsorption, hyperparathyroidism, immobilization, metabolic bone disease, or thyroid disease with an abnormal thyroid-stimulating hormone
Interventions	▸(중재군) - 500,000 IU of cholecalciferol orally once a year ▸(비교군) - placebo
Outcomes	**Primary outcome:** - fall and fractures

	Secondary outcomes: - serum 25-hydroxycholecalciferol and parathyroid hormone levels ▸추적기간 - 12 months
Results	▸Women in the cholecalciferol (vitamin D) group had 171 fractures vs 135 in the placebo group ▸837 women in the vitamin D group fell 2892 times (rate, 83.4 per 100 person-years) while 769 women in the placebo group fell 2512 times (rate, 72.7 per 100 person-years; incidence rate ratio [RR], 1.15; 95% confidence interval [CI], 1.02-1.30; P = .03). ▸The incidence RR for fracture in the vitamin D group was 1.26 (95% CI, 1.00-1.59; P = 0.047) vs the placebo group (rates per 100 person-years, 4.9 vitamin D vs 3.9 placebo). A temporal pattern was observed in a post hoc analysis of falls. ▸The incidence RR of falling in the vitamin D group vs the placebo group was 1.31 in the first 3 months after dosing and 1.13 during the following 9 months (test for homogeneity; P = .02). ▸In the substudy, the median baseline serum 25-hydroxycholecalciferol was 49 nmol/L. Less than 3% of the substudy participants had 25-hydroxycholecalciferol levels lower than 25 nmol/L. In the vitamin D group, 25-hydroxycholecalciferol levels increased at 1 month after dosing to approximately 120 nmol/L, were approximately 90 nmol/L at 3 months, and remained higher than the placebo group 12 months after dosing.

[지침4] 2010 CANADA

- **Reference**

	문헌정보	연구유형	연구대상자수 (치료군/비교군)
1	Tang BM, Eslick GD, Nowson C, et al. Use of calcium or calcium in combination with vitamin D supplementation to prevent fractures and bone loss in people aged 50 years and older: a meta-analysis. *Lancet* 2007;370:657-66 [19]	meta-analysis	
2	Reid IR, Bolland MJ, Grey A. Effect of calcium supplementation on hip fractures. *Osteoporos Int* 2008;19:1119-23 [20]	meta-analysis	
4	Hanley DA, Cranney A, Jones G, et al.; Guidelines Committee of the Scientific Advisory Council of Osteoporosis Canada. Vitamin D in adult health and disease: a review and guideline [21]	review	

- **일차연구문헌 근거표** – 없음

[지침5] 2017 NOGG

- **Reference**

	문헌정보	연구유형	연구대상자수 (치료군/비교군)
1	Tai V, Leung W, Grey A, Reid IR, Bolland MJ. Calcium intake and bone mineral density: systematic review and meta-analysis. BMJ 2015 Sep 29;351:h4183 [22]	systematic review and meta-analysis.	
2	Shea B, Wells G, Cranney A et al. Meta-analyses of therapies for postmenopausal osteoporosis. VII. Meta-analysis of calcium supplementation for the prevention of postmenopausal osteoporosis. Endocr Rev 2002; 23, 552-9 [23]	meta-analysis	
3	Bolland MJ, Leung W, Tai V et al. Calcium intake and risk of fracture: systematic review. BMJ 2015 Sep 29;351:h4580. doi: 10.1136/bmj.h4580 [24]	systematic review	
4	Tang BM, Eslick GD, Nowson C, Smith C, Bensoussan A. Use of calcium or calcium in combination with vitamin D supplementation to	meta-analysis	

	prevent fractures and bone loss in people aged 50 years and older: a meta-analysis. Lancet 2007 Aug 25;370(9588):657-66 [19]		
5	Avenell A, Mak JCS, O'Connell D. Vitamin D and vitamin D analogues for preventing fractures in post-menopausal women and older men. The Cochrane database of systematic reviews 2014;4, CD000227-CD000227 [25]	systematic review	
6	Bischoff-Ferrari HA, Willett WC, Wong JB et al. Prevention of nonvertebral fractures with oral vitamin D and dose dependency: a meta-analysis of randomized controlled trials. Arch Intern Med 2009a;169:551-61 [26]	meta-analysis	
7	Bischoff-Ferrari HA, Dawson-Hughes B, Staehelin HB et al. Fall prevention with supplemental and active forms of vitamin D: a meta-analysis of randomised controlled trials. BMJ 2009b; 339, b3692-b3692 [27]	meta-analysis	
8	Sanders KM, Stuart AL, Williamson EJ et al. Annual high-dose oral vitamin D and falls and fractures in older women: a randomized controlled trial. JAMA 2010; 303:1815-22 [18]	RCT	2256 (1131/1125)
9	Bischoff-Ferrari HA, Dawson-Hughes B, Orav EJ et al. Monthly high-dose vitamin D treatment for the prevention of functional decline: a	RCT	200 (67/133)

	randomized clinical trial. JAMA Intern Med 2016;176:175-83 [28]		

- **일차연구문헌 근거표**

Author, Publication year	**Sanders KM, et al.** **JAMA 2010;303:1815–22.**
Title	Annual high-dose oral vitamin D and falls and fractures in older women: a randomized controlled trial.
Methods	A double-blind, placebo-controlled trial
Participants	**N= 2256 (중재군/비교군= 1131/1125)** **Inclusion criteria** - Patients were eligible if they were between 18 and 65 years of age and had a diagnosis of rheumatoid arthritis as defined by the revised American College of Rheumatology criteria, serum creatinine level less than 176.8 µmol/L, and normal liver function. **Exclusion criteria** - Patients were excluded if they were receiving an anticonvulsant medication, hydrochlorothiazide, bisphosphonates, fluoride, calcitonin, or calcitriol or if they had a history of malabsorption, hyperparathyroidism, immobilization, metabolic bone disease, or thyroid disease with an abnormal thyroid-stimulating hormone

Interventions	▸(중재군) - 500,000 IU of cholecalciferol orally once a year ▸(비교군) - placebo
Outcomes	**Primary outcome:** - fall and fractures **Secondary outcomes:** - serum 25-hydroxycholecalciferol and parathyroid hormone levels ▸추적기간 - 12 months
Results	▸Women in the cholecalciferol (vitamin D) group had 171 fractures vs 135 in the placebo group ▸837 women in the vitamin D group fell 2892 times (rate, 83.4 per 100 person-years) while 769 women in the placebo group fell 2512 times (rate, 72.7 per 100 person-years; incidence rate ratio [RR], 1.15; 95% confidence interval [CI], 1.02-1.30; P = .03). ▸The incidence RR for fracture in the vitamin D group was 1.26 (95% CI, 1.00-1.59; P = 0.047) vs the placebo group (rates per 100 person-years, 4.9 vitamin D vs 3.9 placebo). A temporal pattern was observed in a post hoc analysis of falls. ▸The incidence RR of falling in the vitamin D group vs the placebo group was 1.31 in the first 3 months after dosing and 1.13 during the following 9 months (test for homogeneity; P = .02).

	▸In the substudy, the median baseline serum 25-hydroxycholecalciferol was 49 nmol/L. Less than 3% of the substudy participants had 25-hydroxycholecalciferol levels lower than 25 nmol/L. In the vitamin D group, 25-hydroxycholecalciferol levels increased at 1 month after dosing to approximately 120 nmol/L, were approximately 90 nmol/L at 3 months, and remained higher than the placebo group 12 months after dosing.

Author, Publication year	**Bischoff-Ferrari HA, et al.** **JAMA Intern Med 2016;176:175-83.**
Title	Monthly high-dose vitamin D treatment for the prevention of functional decline: a randomized clinical trial.
Methods	double-blind, randomized clinical trial
Participants	**N= 200 (중재군/비교군= 133/67)** **Inclusion criteria** - maintaining mobility with or without a walking aid, having the ability to use public transportation to attend the clinic visits, and scoring at least 27 on the Mini-Mental State Examination to ensure that participants understood the study procedures and voluntarily agreed to participate by providing written informed consent.

	Exclusion criteria - supplemental vitamin D use exceeding 800 IU/d and unwillingness to discontinue additional calciumandvitaminDsupplementation
Interventions	▸(중재군) - receiving 60,000 IU of vitamin D3 (60,000 IU group) (n=67) - receiving 24,000 IU of vitamin D3 plus 300 μg of calcifediol (24,000 IU plus calcifediol group) (n=66) ▸(비교군) - 24,000 IU of vitamin D3 (24,000 IU group) (n=67)
Outcomes	**Primary outcome:** - improving lower extremity function (on the Short Physical Performance Battery) and achieving 25-hydroxyvitamin D levels of at least 30 ng/mL at 6 and 12 months **Secondary outcomes:** - monthly reported falls. Analyses were adjusted for age, sex, and body mass index. ▸추적기간 - 12 months
Results	▸Intent-to-treat analyses showed that, while 60,000 IU and 24,000 IU plus calcifediol were more likely than 24,000 IU to result in 25-hydroxyvitamin D levels of at least 30 ng/mL (P = .001), they were not more effective in improving lower extremity function, which did not differ among the treatment groups (P=0.26). ▸However, over the 12-month follow-up, the incidence of falls differed significantly among the treatment

	groups, with higher incidences in the 60,000 IU group (66.9%; 95% CI, 54.4% to 77.5%) and the 24,000 IU plus calcifediol group (66.1%; 95% CI, 53.5%-76.8%) group compared with the 24,000 IU group (47.9%; 95% CI, 35.8%-60.3%) (P = .048). ▸Consistent with the incidence of falls, the mean number of falls differed marginally by treatment group. ▸The 60,000 IU group (mean, 1.47) and the 24,000 IU plus calcifediol group (mean, 1.24) had higher mean numbers of falls compared with the 24,000 IU group (mean, 0.94) (P =0.09).

▣ 핵심질문 2-2.

40세 미만 성인에서 비스포스포네이트 사용은 글루코코르티코이드 유발 골다공증 예방과 치료에 효과적인가?

▣ PICO

Patients	Intervention	Comparators	Outcomes
40세 미만 성인	비스포스포네이트		글루코코르티코이드 유발 골다공증 예방과 치료

▣ 권고비교표

	지침 1 (ACR)	지침 2 (IOF-ECTS)	지침 3 (FRENCH)	지침 4 (Canada)	지침5(NOGG)
출판년도	2017	2012	2014	2010	2017
AGREE 평가점수	89	67	56	44	67

권고문	1. For adults <40 years of age (women not of childbearing potential and men) with a history of OP fracture, or those continuing GC treatment (≥6 months at a dose of ≥7.5 mg/day) who have either a hip or spine BMD Z score <-3 or bone loss of ≥10%/year at the hip or spine as assessed by dual x-ray absorptiometry (DXA), an oral bisphosphonate should be used rather than the patient receiving no additional	1. Data on the effects of pharmacological interventions in this population are sparse, particularly with regard to fracture risk. 2.Bone-protective therapy may be appropriate in some premenopausal women and younger men, particularly in individuals with a previous history of fracture or receiving high doses of glucocorticoids. 3. Caution is advised in the use of bisphosphonates in women of childbearing age.	1. osteoporosis drug therapy should be given to patients with established bone frailty documented by a history of low-energy fracture 2. Osteoporosis drug therapy should not be given routinely to patients without a history of low-energy fracture. Instead, the treatment decision should rely on an evaluation of these verity of the underlying disease, glucocorticoid dose, expected treatment duration, and BMD values 3. When	N/A	Bone protective therapy may be appropriate in some premenopausal women and younger men, particularly in individuals with a previous history of fracture or receiving high doses of glucocorticoids

	treatment beyond calcium and vitamin D. 2. For adults 30 years of age who are receiving very high dose GC treatment (initial prednisone dose of ≥30 mg/day [or equivalent GC exposure] and a cumulative annual dose of >5 gm) (Table 3), oral bisphosphonate treatment should be initiated.		bisphosphonates are used off-label, preference should be given to a bisphosphonate with a limited carry-over effect (risedronate)		
근거수준, 권고등급	II, B	II, B	전문가 합의, B	N/A	II, B

▣ 근거 내용 정리

[지침1] ACR 2017

- **Reference**

	문헌정보	연구유형	연구대상자수 (치료군/비교군)
1	Saag KG, Emkey R, Schnitzer TJ, Brown JP, Hawkins F, Goemaere S, et al. Alendronate for the prevention and treatment of glucocorticoid induced osteoporosis. Glucocorticoid-Induced Osteoporosis Intervention Study Group. N Engl J Med. 1998;339(5):292-299 [29]	RCT	477 (318/159)
2	Wallach S, Cohen S, Reid DM, Hughes RA, Hosking DJ, Laan RF, et al. Effects of risedronate treatment on bone density and vertebral fracture in patients on corticosteroid therapy. Calcif Tissue Int. 2000;67(4):277-285 [30]	RCT	509 (339/170)
3	Adachi JD, Saag KG, Delmas PD, Liberman UA, Emkey RD, Seeman E, et al. Two-year effects of alendronate on bone mineral density and vertebral fracture in patients receiving glucocorticoids: a randomized, double-blind, placebo-controlled extension trial. Arthritis Rheum. 2001;44(1):202-211 [31]	RCT	208 (147/ 61)
4	Lems WF, Lodder MC, Lips P, Bijlsma JW, Geusens P, Schrameijer N,	RCT	

	et al. Positive effect of alendronate on bone mineral density and markers of bone turnover in patients with rheumatoid arthritis on chronic treatment with low-dose prednisone: a randomized, double-blind, placebo-controlled trial. Osteoporos Int. 2006;17(5):716-723 [32]		163 (94/69)
5	Yamada S, Takagi H, Tsuchiya H, Nakajima T, Ochiai H, Ichimura A, et al. Comparative studies on effect of risedronate and alfacalcidol against glucocorticoid-induced osteoporosis in rheumatoid arthritic patients. Yakugaku Zasshi. 2007;127(9):1491-1496 [33]	Comparative studies	1 2 (6 /6)
6	Okada Y, Nawata M, Nakayamada S, Saito K, Tanaka Y. Alendronate protects premenopausal women from bone loss and fracture associated with high-dose glucocorticoid therapy. J Rheumatol. 2008;35(11):2249-2254 [34]	prospective, open-controlled study	47 (25/22)
7	N S, R R. The effect of bisphosphonate on prevention of glucocorticoid-induced osteoporosis. IRCMJ. 2008;10(1):8-11 [35]	prospective clinical trial	72 (36/36)
8	Stoch SA, Saag KG, Greenwald M, Sebba AI, Cohen S, Verbruggen N, et al. Once-weekly oral alendronate 70 mg in patients with glucocorticoid-induced bone loss: a 12-month randomized, placebo-controlled clinical trial. J Rheumatol. 2009;36(8):1705-1714 [36]	RCT	173 (114/59)
9	Tee SI, Yosipovitch G, Chan YC, Chua SH, Koh ET, Chan YH, et al. Prevention of glucocorticoid-induced osteoporosis in immunobullous	RCT	44

	diseases with alendronate: a randomized, double-blind, placebo-controlled study. Arch Dermatol. 2012;148(3):307-314 [37]		(22/22)
10	Hakala M, Kroger H, Valleala H, Hienonen-Kempas T, Lehtonen-Veromaa M, Heikkinen J, et al. Once-monthly oral ibandronate provides significant improvement in bone mineral density in postmenopausal women treated with glucocorticoids for inflammatory rheumatic diseases: a 12-month, randomized, double-blind, placebo-controlled trial. Scand J Rheumatol. 2012;41(4):260-266 [38]	RCT	140 (68/72)
11	Wells GA, Cranney A, Peterson J, Boucher M, Shea B, Robinson V, et al. Alendronate for the primary and secondary prevention of osteoporotic fractures in postmenopausal women. Cochrane Database Syst Rev. 2008(1):CD001155 [39]	SR	
12	Wells G, Cranney A, Peterson J, Boucher M, Shea B, Robinson V, et al. Risedronate for the primary and secondary prevention of osteoporotic fractures in postmenopausal women. Cochrane Database Syst Rev. 2008(1):CD004523 [40]	SR	
13	Hopkins RB, Goeree R, Pullenayegum E, Adachi JD, Papaioannou A, Xie F, et al. The relative efficacy of nine osteoporosis medications for reducing the rate of fractures in post-menopausal women. BMC Musculoskelet Disord. 2011;12:209 [41]	SR	

14	Lyles KW, Colon-Emeric CS, Magaziner JS, Adachi JD, Pieper CF, Mautalen C, et al. Zoledronic acid and clinical fractures and mortality after hip fracture. N Engl J Med. 2007;357(18):1799-1809 [42]	RCT	2127 (1065/1062)

- **일차연구문헌 근거표**

Author, Publication year	**Saag KG et al.** **N Engl J Med. 1998 Jul 30;339(5):292-9.**
Title	Alendronate for the Prevention and Treatment of Glucocorticoid-Induced Osteoporosis
Methods	randomized, placebo-controlled studies, multicenter
Participants	**N= (중재군/비교군=318/ 159)** **▸Inclusion criteria** - Men; pre-menopausal women; post-menopausal women NOS; - steroid>7.5mg/d; prevalent steroid use at least 3 mon; - polymyalgia rheumatica; inflammatory bowel disease; asthma or COPD; rheumatoid arthritis; SLE; nephropathy/nephritis (not SLE or vasculitis); sarcodosis; Pemphigus; Inflammatory myopathy; Giant cell arteritis; Myasthenia Gravis **▸Exclusion criteria**

	- pregnancy; cardiovascular disease; renal insufficiency; - gastrointestinal disease; upper GI disease; bisphosphonates; calcitonin; fluoride; Vitamin D deficiency
Interventions	▸(중재군) - Alendronate 5mg + 800 to 1000 mg of elemental calcium + 250 to 500 IU of vitamin D daily (n=161) - Alendronate 10mg + 800 to 1000 mg of elemental calcium + 250 to 500 IU of vitamin D daily daily (n=157) ▸(비교군) - Placebo + 800 to 1000 mg of elemental calcium + 250 to 500 IU of vitamin D daily
Outcomes	▸**Primary outcome:** - the difference in the mean percent change in lumbar-spine bone density from base line to week 48 between the groups ▸**Secondary outcomes:** - changes in bone density of the hip, biochemical markers of bone turnover, and the incidence of new vertebral fractures. ▸**추적기간** - 48-week
Results	▸The mean (+/-SE) bone density of the lumbar spine increased by 2.1+/-0.3 percent and 2.9+/-0.3 percent, respectively, in the groups that received 5 and 10 mg of alendronate per day (P<0.001) and decreased by 0.4+/-0.3 percent in the placebo group

	▸The femoral-neck bone density increased by 1.2+/-0.4 percent and 1.0+/-0.4 percent in the respective alendronate groups (P<0.01) and decreased by 1.2+/-0.4 percent in the placebo group (P<0.01). The bone density of the trochanter and total body also increased significantly in the patients treated with alendronate. ▸There were proportionally fewer new vertebral fractures in the alendronate groups (overall incidence, 2.3 percent) than in the placebo group (3.7 percent) (relative risk, 0.6; 95 percent confidence interval, 0.1 to 4.4).

Author, Publication year	**Wallach S. et al.** **Calcif Tissue Int. 2000;67(4):277-285.**
Title	Effects of risedronate treatment on bone density and vertebral fracture in patients on corticosteroid therapy.
Methods	randomized, placebo-controlled studies
Participants	**N= 509 (중재군/비교군= 339/ 170)** ▸**Inclusion criteria** - ambulatory men and women, 18–85 years of age and receiving moderate-to-high doses of (equivalent to 7.5 mg prednisone daily or greater) oral corticosteroid therapy. The patients were expected to continue on corticosteroid therapy for at least 12 months

	- rheumatoid arthritis, polymyalgia rheumatica, temporal arteritis, chronic interstitial lung disease, chronic obstructive pulmonary disease, asthma, systemic lupus erythematosus, polymyositis, vasculitis, Behcet's disease, and a variety of skin diseases. ▸**Exclusion criteria** - evidence of metabolic bone disease other than CIO, recent use of HRT (within 1 year of enrollment) or other drugs known to affect bone metabolism, and any significant organic or psychiatric disease that could affect participation or interfere with the interpretation of the data.
Interventions	▸(중재군) - Risedronate 2.5mg + 500-1,000mg Calcium +400 IU Vit D daily (n=165) - Risedronate 5mg + 500-1,000mg Calcium +400 IU Vit D daily (n=174) ▸(비교군) - Placebo + 500-1,000mg Calcium +400 IU Vit D daily
Outcomes	▸**Primary outcome:** - the difference between the placebo and active groups in lumbar spine bone mineral density (BMD) at 1 year ▸**Secondary outcomes:** - changes in BMD at other sites, biochemical markers of bone turnover, and the incidence of vertebral fractures

	▸**추적기간** - 1 year
Results	▸The mean (SE) lumbar spine BMD increased 1.9 +/- 0.38% from baseline in the risedronate 5 mg group (P < 0.001) and decreased 1.0 +/- 0.4% in the placebo group (P = 0. 005). BMD at the femoral neck, trochanter, and distal radius increased or was maintained with risedronate 5 mg treatment, but decreased in the placebo group. Midshaft radius BMD did not change significantly in either treatment group. ▸The 2.5 mg dose also had a positive effect on BMD, although of a lesser magnitude than that seen with risedronate 5 mg. ▸A significant reduction of 70% in vertebral fracture risk was observed in the risedronate 5 mg group compared with the placebo group (P = 0.01).

Author, Publication year	**Adachi JD. et al.** **Arthritis Rheum. 2001;44(1):202-211.**
Title	Two-year effects of alendronate on bone mineral density and vertebral fracture in patients receiving glucocorticoids: a randomized, double-blind, placebo-controlled extension trial.
Methods	randomized, double-blind, placebo-controlled extension trial, multicenter

Participants	**N= 208 (중재군/비교군= 147/61)** ▸**Inclusion criteria** - Men; pre-menopausal women; post-menopausal women NOS; - steroid>7.5mg/d; steroid duration<1; - polymyalgia rheumatic; inflammatory bowel disease; asthma or COPD; rheumatoid arthritis; SLE; nephropathy/nephritis (not SLE or vasculitis) ▸**Exclusion criteria** - Pregnancy; metabolic bone disorder other than osteoporosis (e.g.,Paget's, renal osteodystrophy, osteomalacia); - renal insufficiency; gastrointestinal disease; upper GI; - bisphosphonates; calcitonin; fluoride
Interventions	▸(중재군) - Alendronate 5mg+ 800-1,000 mg Calcium+ 250-500 IU Vit D daily (n=63) - Alendronate 10mg +800-1,000 mg Calcium+ 250-500 IU Vit D daily (n=55) - Alendronate 2.5mg switch to 10mg + 800-1,000 mg Calcium+ 250-500 IU Vit D daily (n=29) ▸(비교군) - Placebo + 800-1,000 mg Calcium+ 250-500 IU Vit D daily
Outcomes	▸**Primary outcome:** - the mean percentage change in lumbar spine bone mineral density (BMD) from baseline to 24

	months. ▸**Secondary outcomes:** - changes in hip and total body BMD, biochemical markers of bone turnover, radiographic joint damage of the hands, and vertebral fracture incidence. ▸**추적기간** - 2 year
Results	▸The mean (+/-SEM) lumbar spine BMD increased by 2.8 +/- 0.6%, 3.9 +/- 0.7%, and 3.7 +/- 0.6%, respectively, in the groups that received 5 mg, 10 mg, and 2.5/10 mg of ALN daily (P < or = 0.001) and decreased by -0.8 +/- 0.6% in the placebo group (P not significant) over 24 months. ▸In patients receiving any dose of ALN, BMD was increased at the trochanter (P < or = 0.05) and maintained at the femoral neck. Total body BMD was increased in patients receiving 5 or 10 mg ALN (P < or = 0.01). These 2 dose levels of ALN were more effective than placebo at all sites (P < or = 0.05). ▸Bone turnover markers (N-telopeptides of type I collagen and bone-specific alkaline phosphatase) decreased 60% and 25%, respectively, during treatment with ALN (P < or = 0.05). ▸There were fewer patients with new vertebral fractures in the ALN group versus the placebo group (0.7% versus 6.8%; P = 0.026).

Author, Publication year	**Lems WF. et al.** **Osteoporos Int. 2006;17(5):716-723.**
Title	Positive effect of alendronate on bone mineral density and markers of bone turnover in patients with rheumatoid arthritis on chronic treatment with low-dose prednisone: a randomized, double-blind, placebo-controlled trial
Methods	randomized, double-blind, placebo-controlled trial
Participants	**N= 163 (중재군/비교군= 94/69)** ▸**Inclusion criteria** - Men; pre-menopauaal women; post-menopausal women NOS; - prevalent steroid use at least 3 mon; rheumatoid arthritis; ≤10mg pred; ▸**Exclusion criteria** - metabolic bone disorder other than osteoporosis (e.g. Paget's, renal osteodystrophy, osteomalacia); Upper GI; hormone use: HRT; Medications that affect bone metabolism
Interventions	▸(중재군) - Alendronate 10mg+ 500 or 1,000mg Calcium + 400 IU Vit D daily ▸(비교군) - Placebo + 500 or 1,000mg Calcium + 400 IU Vit D daily

Outcomes	▸**Primary outcome:** - the difference between the groups in percentage change from baseline to 12 months in lumbar spine BMD ▸**Secondary outcomes:** - percentage changes from baseline of total hip, femoral neck, trochanter, markers of bone turnover and the incidence of peripheral and vertebral fractures. ▸**추적기간** - 12 months
Results	▸BMD at the lumbar spine had increased by 3.7% in the alendronate-treated patients and decreased by -1.0% in the placebo-treated patients ($p<0.0001$); at the hip, the changes were +1.0% and –0.1%, respectively (not significant). ▸After 3 months, serum BAP had decreased by 16.9% in the alendronate group versus 3.3% in the placebo group ($p=0.0005$), while urinary NTX had decreased by 46.4% in the alendronate group versus 12.1% in the placebo group ($p<0.0001$). ▸After 12 months, no statistically significant difference was found between the groups with respect to number of patients with incident vertebral or non-vertebral fractures.

Author, Publication year	**Yamada S. et al.** **Yakugaku Zasshi. 2007;127(9):1491-1496**
Title	Comparative studies on effect of risedronate and alfacalcidol against glucocorticoid-induced osteoporosis in rheumatoid arthritic patients.
Methods	randomized, camparative study
Participants	**N= 12 (중재군/비교군= 6 / 6)** ▸**Inclusion criteria** - Women otherwise undefined; osteoporosis T-score<=-2.5spine; any steroid dose; steroid duration not defined; rheumatoid arthritis ▸**Exclusion criteria** - Bisphosphonates; medication that affect calcium metabolism and phosphate
Interventions	▸(중재군) - Risedronate 2.5 mg + Calcium 800mg daily ▸(비교군) - alfacalcidiol 0.5 mcg + Calcium 800mg daily
Outcomes	▸**Primary outcome:** - Bone mineral density at 12, 24 and 48 weeks after treatment ▸**Secondary outcomes:**

	- the biochemical markers of bone turnover at 12, 24 and 48 weeks after treatment **▸추적기간** - 48 weeks
Results	▸The BMD values 12, 24 and 48 weeks after treatment with risedronate increased by 3.9%, 4.1% and 5.2%, respectively, which were significantly higher than those after treatment with alfacalcidol (2.8%, 2.1% and 2.5%, respectively). ▸Urinary excretion of N-telopeptides of type I collagen and deoxypyridinoline after risedronate treatment were more significantly decrease than that after alfacalcidol treatment.

Author, Publication year	**YOSUKE OKADA. et al.** **J Rheumatol. 2008;35(11):2249-2254.**
Title	Alendronate Protects Premenopausal Women from Bone Loss and Fracture Associated with High-dose Glucocorticoid Therapy
Methods	single center, prospective, open-controlled study
Participants	**N= 45 (중재군/비교군= 25/22)**

	▸**Inclusion criteria** - premenopausal women (aged 17–47 yrs) must be GC-naive and have a systemic autoimmune disease requiring treatment with high-dose GC (starting dose of prednisolone ≥ 1 mg/kg/day), and that this treatment was expected to continue for at least 12 months with the daily dose after 6 months being not less than 7.5 mg/day. ▸**Exclusion criteria** - Patients with rheumatoid arthritis, renal dysfunction, pregnancy, lactation, or of childbearing potential or those who were taking medications known to affect bone metabolism were excluded
Interventions	▸(중재군) - alfacalcidol (1 mg/day) and alendronate (5 mg/day) ▸(비교군) - alfacalcidol (1 mg/day)
Outcomes	▸**Primary outcome:** the percentage change in BMD after 6, 12, and 18 months of therapy compared with the baseline ▸**Secondary outcomes:** metabolic bone markers after 6, 12, and 18 months of therapy compared with the baseline ▸**추적기간**

	- 18 months
Results	▸The percentage changes in lumbar spine bone mineral density (BMD) after 6 months of the therapy were –10.5% ± 0.8% in the alfacalcidol group, but only –2.1% ± 1.2% in the combined group. ▸The rate of bone loss in the lumbar spine was significantly lower in the combined group than in the alfacalcidol group at 6 months. At 12 months of treatment, the percentage change in lumbar spine BMD was increased by 1.7% ± 1.4% in the combined group, but decreased by 9.9% ± 1.9% in the alfacalcidol group; the difference was significant. ▸Bone fracture occurred at 12 months or later in 4 patients of the alfacalcidol groups, but not in the combined group, even at up to 18 months.

Author, Publication year	**N Saadati and R Rajabian** **IRCMJ. 2008;10(1):8-11.**
Title	The effect of bisphosphonate on prevention of glucocorticoid-induced osteoporosis.
Methods	prospective clinical trial
Participants	**N= 72 (중재군/비교군= 36/36)**

	Inclusion criteria - high dose of glucocorticoid (30-80 mg/day) - autoimmune disease such as SLE, Polymyositis, or Dermatomyositis **Exclusion criteria** - NA
Interventions	▸(중재군) oral vitamin-D, 50000 IU twice weekly, calcium, 500 mg twice daily, and alendronate, 10 mg per day. (group2) ▸(비교군) oral vitamin-D, 50000 IU twice weekly and calcium, 500 mg twice daily. (group1)
Outcomes	▸**Primary outcome:** Change of BMD in the lumbar spine after 18 month ▸**Secondary outcomes:** Change in femoral neck BMD after 18 month ▸**추적기간** - 18 months
Results	▸Change of BMD in the lumbar spine after 18 months of therapy was -1/67% and +2.4% in groups 1 and 2, respectively. ▸Change in femoral neck BMD was -2.1% in group 1 and +1.8% in group 2.

Author, Publication year	**Stoch SA. et al.** **J Rheumatol. 2009;36(8):1705-1714.**
Title	Once-weekly oral alendronate 70 mg in patients with glucocorticoid-induced bone loss: a 12-month randomized, placebo-controlled clinical trial.
Methods	multicenter, randomized, placebo-controlled clinical trial.
Participants	**N= 173 (중재군/비교군= 114/59)** **▸Inclusion criteria** - Adults ≤ 80 years of age who were taking a mean of ≥ 7.5 mg/day of oral prednisone (or equivalent) and were considered by the site investigator to be highly likely to require oral glucocorticoid treatment for ≥ 12 consecutive months were eligible to participate. - serum 25-hydroxyvitamin D [25(OH)D] levels > 15 ng/ml (37.4 nmol/l). - lumbar spine anatomy suitable for dual-energy x-ray absorptiometry (DEXA), and hip and lumbar spine BMD T-score more than 2.5 SD below the sex-matched, young adult reference mean (T-score < –2.5). **▸Exclusion criteria** - prior vertebral or osteoporotic fractures with certain - malignancies, recent major upper gastrointestinal (GI) disease (e.g., significant upper GI bleeding,

	recurrent ulcer disease, esophageal or gastric varices, esophageal stricture, achalasia, or severe esophageal motor dysfunction), myocardial infarction, or pregnancy. - unwilling to take either calcium or vitamin D supplements - those with a history of alcohol or drug abuse
Interventions	▸(중재군) - alendronate 70 mg once weekly + calcium (1000 mg) daily + 400 IU vitamin D daily ▸(비교군) - Placebo + calcium (1000 mg) daily + 400 IU vitamin D daily
Outcomes	▸**Primary outcome:** - the percentage change from baseline in posterior-anterior BMD of the lumbar spine at Month 12, and the safety and tolerability profile of ALN OW through 12 months. ▸**Secondary outcomes:** - percentage change from baseline in hip, femoral neck, trochanter, total hip, and total body BMD at 12 months, and the effects of ALN OW after 12 months on biochemical markers of boneturnover (NTX, BSAP). ▸**추적기간** - 12 months

Results	▸At 12 months, there was a significant mean percentage increase from baseline in the ALN OW group for lumbar spine (2.45%), trochanter (1.27%), total hip (0.75%), and total body (1.70%) bone mineral density (BMD). ▸Comparing ALN OW versus placebo at 12 months, a significant treatment difference for the mean percentage change from baseline was observed for lumbar spine (treatment difference of 2.92%; p </= 0.001), trochanter (treatment difference 1.66%; p = 0.007), and total hip (treatment difference 1.19; p = 0.008) BMD. ▸Biochemical markers of bone remodeling also showed significant mean percentage decreases from baseline.

Author, Publication year	**Tee SI. et al.** **Arch Dermatol. 2012;148(3):307-314.**
Title	Prevention of glucocorticoid-induced osteoporosis in immunobullous diseases with alendronate: a randomized, double-blind, placebo-controlled study.
Methods	randomized, double-blind, placebo-controlled trial
Participants	**N= 44 (중재군/비교군= 22/22)** ▸**Inclusion criteria**

	- Patients who were newly diagnosed as having an immunobullous disease, including bullous pemphigoid and pemphigus, were eligible for participation if they were considered by study investigators to be highly likely to require long-term systemic glucocorticoid therapy (>6 months) ▸**Exclusion criteria** -concurrent treatment with medications known to have an effect on osteoporosis (eg, hormone replacement, oral contraceptives, selective estrogen receptor modulators, cyclosporine, warfarin, and antiepileptic drugs); -a history of allergy or an absolute contraindication to alendronate (eg, pregnant patients); -a contraindication to use of calcium plus vitamin D (eg, a history of renal calculi or hypercalcemia); -a history of upper gastrointestinal tract disorders (eg, dysphagia, peptic ulcer disease); -a low testosterone state (eg, chronic alcoholism, Klinefelter syndrome); -an active endocrine disorder that can induce osteoporosis (eg, thyrotoxicosis); -prior vertebral or osteoporotic fractures; -a history of alcohol or drug abuse.
Interventions	▸(중재군) - alendronate (10mg/day) + Calcium + Vit D ▸(비교군) - Placebo + Calcium + Vit D
Outcomes	▸**Primary outcome:**

	- the percent change in both lumbar spine and femoral neck bone densities at 12 months compared with baseline. ▸**Secondary outcomes:** - the change in hl-ALP levels at 12 months, the presence of new clinical or radiologic fractures, and any significant adverse events encountered during the study. ▸**추적기간** - 12 months
Results	▸The percent change in BMD in the alendronate group was +3.7% and +3.5% at the lumbar spine and the femoral neck, respectively, whereas in the placebo group, it was -1.4% and -0.7% at the lumbar spine and the femoral neck, respectively. ▸The increase in BMD observed in the alendronate group compared with the placebo group was statistically significant at both the lumbar spine (P = .01) and the femoral neck (P = .01). ▸There was also a statistically significant decrease in serum heat-labile alkaline phosphatase levels after 12 months (-32.6%, P < .01) in the alendronate group but not in the placebo group.

Author, Publication year	**Hakala M. et al.** **Scand J Rheumatol. 2012;41(4):260-266.**
Title	Once-monthly oral ibandronate provides significant improvement in bone mineral density in

	postmenopausal women treated with glucocorticoids for inflammatory rheumatic diseases: a 12-month, randomized, double-blind, placebo-controlled trial.
Methods	randomized, double-blind, placebo-controlled, parallel-group study
Participants	**N= 140 (중재군/비교군= 68/72)** ▸**Inclusion criteria** -Women aged 50–85 years, ≥ 1 year since menopause, with a normal or osteopaenic mean lumbar spine (LS; L1–L4) bone mineral density (BMD; T-score ≥ –2.0) and receiving treatment with 5–15 mg/day of prednisone equivalent -The other therapies for the rheumatic disease had to have been stable for 3 months prior to screening. ▸**Exclusion criteria** - clinical osteoporotic fractures (qualitative assessment of prevalent vertebral fractures) - conditions that may interfere with the evaluation of spinal or hip osteoporosis by dual-energy X-ray absorptiometry (DXA) such as two or more vertebral (L1–L4) fractures or other vertebral deformities - treatment with other drugs affecting bone metabolism within the past 6 months - previous treatment with an oral bisphosphonate within the past 6 months or previous treatment with intravenous - bisphosphonates at any time.
Interventions	▸(중재군)

	- oral ibandronate 150 mg monthly + 1,000mg Calcium daily + 800 IU Vit D daily ▸(비교군) - Placebo + 1,000mg Calcium daily + 800 IU Vit D daily
Outcomes	▸**Primary outcome** - the relative change (%) in mean LS BMD from baseline to 12 months ▸**Secondary outcomes** - change (%) in mean LS BMD from baseline to 6 months - change (%) in total hip BMD from baseline to 6 and 12 months - changes (%) in serum levels of bone turnover markers C-terminal telopeptide of type I collagen (sCTX), N-terminal propeptide of type I procollagen (P1NP) and tartrate-resistant acid phosphatase (TRACP) from baseline to 1, 6, and 12 months. Blood samples for bone turnover markers were collected in fasting patients before study drug intake. - Difference in withdrawal rate due to worsening in BMD (BMD T-score at any site≤ –2.5 SD) at 6 months and/or worsening in BMD of at least 7% at any site at 6 months. ▸**추적기간** - 12 months
Results	▸Mean LS BMD increased significantly by 2.6% and 3.2% from baseline to 6 and 12 months with ibandronate compared to 0.3% and -0.1% with placebo, respectively ($p < 0.001$). Comparable significant mean increases were also found in trochanter, femoral neck and total hip BMDs at 12

	months. ▸Reductions in the serum levels of bone turnover markers C-terminal telopeptide of type I collagen (sCTX), N-terminal propeptide of type I procollagen (P1NP), and tartrate-resistant acid phosphatase (TRACP) were significantly more marked in the ibandronate group than in the placebo group at 1, 6, and 12 months.

Author, Publication year	**Lyles KW et al.** **N Engl J Med. 2007;357(18):1799-1809.**
Title	Zoledronic acid and clinical fractures and mortality after hip fracture.
Methods	multicenter, randomized, double-blind, placebo-controlled trial,
Participants	**N= 2127 (중재군/비교군= 1065 / 1062)** ▸**Inclusion criteria** - Men and women 50 years of age or older were eligible for inclusion within 90 days after surgical repair of a hip fracture sustained with minimal trauma (i.e., a fall from standing height or a lower height). Additional enrollment criteria included being ambulatory before the hip fracture and having both legs. ▸**Exclusion criteria** - previous hypersensitivity to a bisphosphonate, a potential for pregnancy, a calculated creatinine clearance of less than 30 ml per minute, a corrected serum calcium level of more than 11.0 mg per

	deciliter (2.8 mmol per liter) or less than 8.0 mg per deciliter (2.0 mmol per liter), active cancer, metabolic bone disease other than osteoporosis, and a life expectancy of less than 6 months in the investigator's judgment.
Interventions	▸(중재군) - zoledronic acid 5mg iv yealy + 1,000-1,500mg calcium daily +800-1,200 IU Vit D daily ▸(비교군) - Placebo + Calcium + Vit D
Outcomes	▸**Primary outcome:** - a new clinical fracture, excluding facial and digital fractures and fractures in abnormal bone (e.g., bone containing metastases) ▸**Secondary outcomes:** - the change in bone mineral density in the nonfractured hip, as measured annually with dual-energy x-ray absorptiometry; new vertebral, nonvertebral, and hip fractures; and prespecified safety end points, including death. ▸**추적기간** - 5 years
Results	▸The rates of any new clinical fracture were 8.6% in the zoledronic acid group and 13.9% in the placebo group, a 35% risk reduction with zoledronic acid (P=0.001); the respective rates of a new

	clinical vertebral fracture were 1.7% and 3.8% (P=0.02), and the respective rates of new nonvertebral fractures were 7.6% and 10.7% (P=0.03).

[지침2] 2012 IOF-ECTS

- **Reference**

	문헌정보	연구유형	연구대상자수 (치료군/비교군)
1	Saag KG, Emkey R, Schnitzer TJ, Brown JP, Hawkins F, Goemaere S, Thamsborg G, Liberman UA, Delmas PD, Malice MP, Czachur M, Daifotis AG (1998) Alendronate for the prevention and treatment of glucocorticoid-induced osteoporosis. Glucocorticoid Induced Osteoporosis Intervention Study Group. N Engl J Med 339:292–299 [29]	RCT	477 (318/159)
2	Adachi JD, Bensen WG, Brown J, Hanley D, Hodsman A, Josse R, Kendler DL, Lentle B, Olszynski W, Ste-Marie LG, Tenenhouse A, Chines AA (1997) Intermittent etidronate therapy to prevent corticosteroid-induced osteoporosis.	RCT	141 (67/74)

	N Engl J Med 337:382–387 [43]		
3	Cohen S, Levy RM, Keller M, Boling E, Emkey RD, Greenwald M, Zizic TM, Wallach S, Sewell KL, Lukert BP, Axelrod DW, Chines AA (1999) Risedronate therapy prevents corticosteroid induced bone loss: a twelve month, multicenter, randomized, double-blind, placebo-controlled, parallel-group study. Arthritis Rheum 42:2309–2318 [44]	RCT	228 (151/77)
4	Saag KG, Shane E, Boonen S, Marín F, Donley DW, Taylor KA, Dalsky GP, Marcus R (2007) Teriparatide or alendronate in glucocorticoid-induced osteoporosis. N Engl J Med 357:2028– 2039 [45]	RCT	428 (214/214)
5	Sambrook PN, Kotowicz M, Nash P, Styles CB, Naganathan V, Henderson-Briffa KN, Eisman JA, Nicholson GC (2003) Prevention and treatment of glucocorticoid-induced osteoporosis: a comparison of calcitriol, vitamin D plus calcium, and alendronate plus calcium. J Bone Miner Res 18:919–924 [46]	randomized, open-label, parallel group study	195 (131/67)
6	Roux C, Reid DM, Devogelaer JP, Saag K, Lau CS, Reginster JY, Papanastasiou P, Bucci-Rechtweg C, Su G, Sambrook PN (2011) Post hoc analysis of a single IV infusion of zoledronic acid versus daily oral risedronate on lumbar spine bone mineral density in different subgroups with glucocorticoid-induced osteoporosis. Osteoporos Int (2012) 23:1083–1090 [47]	RCT	833 (416/417)

- **일차연구문헌 근거표**

Author, Publication year	**Saag KG et al.** **N Engl J Med. 1998 Jul 30;339(5):292-9.**
Title	Alendronate for the Prevention and Treatment of Glucocorticoid-Induced Osteoporosis
Methods	randomized, placebo-controlled studies, multicenter
Participants	**N= (중재군/비교군=318/ 159)** **▸Inclusion criteria** - Men; pre-menopausal women; post-menopausal women NOS; - steroid>7.5mg/d; prevalent steroid use at least 3 mon; - polymyalgia rheumatica; inflammatory bowel disease; asthma or COPD; rheumatoid arthritis; SLE; nephropathy/nephritis (not SLE or vasculitis); sarcodosis; Pemphigus; Inflammatory myopathy; Giant cell arteritis; Myasthenia Gravis **▸Exclusion criteria** - pregnancy; cardiovascular disease; renal insufficiency;

	- gastrointestinal disease; upper GI disease; bisphosphonates; calcitonin; fluoride; Vitamin D deficiency
Interventions	▸(중재군) - Alendronate 5mg + 800 to 1000 mg of elemental calcium + 250 to 500 IU of vitamin D daily (n=161) - Alendronate 10mg + 800 to 1000 mg of elemental calcium + 250 to 500 IU of vitamin D daily daily (n=157) ▸(비교군) - Placebo + 800 to 1000 mg of elemental calcium + 250 to 500 IU of vitamin D daily
Outcomes	▸**Primary outcome:** - the difference in the mean percent change in lumbar-spine bone density from base line to week 48 between the groups ▸**Secondary outcomes:** - changes in bone density of the hip, biochemical markers of bone turnover, and the incidence of new vertebral fractures. ▸**추적기간** - 48-week
Results	▸The mean (+/-SE) bone density of the lumbar spine increased by 2.1+/-0.3 percent and 2.9+/-0.3 percent, respectively, in the groups that received 5 and 10 mg of alendronate per day (P<0.001) and decreased by 0.4+/-0.3 percent in the placebo group ▸The femoral-neck bone density increased by 1.2+/-0.4 percent and 1.0+/-0.4 percent in the respective

	alendronate groups (P<0.01) and decreased by 1.2+/-0.4 percent in the placebo group (P<0.01). The bone density of the trochanter and total body also increased significantly in the patients treated with alendronate. ▸There were proportionally fewer new vertebral fractures in the alendronate groups (overall incidence, 2.3 percent) than in the placebo group (3.7 percent) (relative risk, 0.6; 95 percent confidence interval, 0.1 to 4.4).

Author, Publication year	**Adachi JD et al.** **N Engl J Med 337:382–387**
Title	Intermittent etidronate therapy to prevent corticosteroid-induced osteoporosis.
Methods	randomized, placebo-controlled study
Participants	**N=141 (중재군/비교군= 67 /74)** ▸**Inclusion criteria** - Ambulatory patients, 18 to 90 years of age, with a variety of diseases were eligible for the study if they had started high-dose therapy with prednisone or its equivalent within the previous 100 days and were expected to continue treatment for at least 1 year at a mean daily dose of 7.5 mg

	or greater for 90 days, with subsequent ongoing treatment at a mean daily dose of 2.5 mg or greater. ▸**Exclusion criteria** - Patients were excluded if they had abnormalities on spinal radiographs that precluded accurate measurements of the lumbar spine with dual-energy x-ray absorptiometry, or if they had diseases or had taken medications known to affect bone metabolism within the preceding year. Patients were excluded if they had taken corticosteroids in the past.
Interventions	▸(중재군) - intermittent etidronate (400 mg per day for 14 days) followed by calcium (500 mg per day for 76 days), given for four cycles ▸(비교군) - intermittent etidronate (400 mg per day for 14 days) followed by calcium (500 mg per day for 76 days), given for four cycles
Outcomes	▸**Primary outcome:** - the difference in the change in the bone density of the lumbar spine between the groups from base line to week 52. ▸**Secondary outcomes:**

	- changes in the bone density of the femoral neck, trochanter, and radius and the rate of new vertebral fractures. **▸추적기간** - 12 month
Results	▸The mean (±SE) bone density of the lumbar spine and trochanter in the etidronate group increased 0.61±0.54 and 1.46±0.67 percent, respectively, as compared with decreases of 3.23±0.60 and 2.74±0.66 percent, respectively, in the placebo group. ▸The mean differences between the groups after one year were 3.72±0.88 percentage points for the lumbar spine (P=0.02) and 4.14±0.94 percentage points for the trochanter (P=0.02). ▸The changes in the femoral neck and the radius were not significantly different between the groups. ▸There was an 85 percent reduction in the proportion of postmenopausal women with new vertebral fractures in the etidronate group as compared with the placebo group (1 of 31 patients vs. 7 of 32 patients, P=0.05), and the etidronate-treated postmenopausal women also had significantly fewer vertebral fractures per patient (P=0.04).

Author, Publication year	**Cohen S. et al.** **Arthritis Rheum 42:2309–2318 (1999)**

Title	Risedronate therapy prevents corticosteroidinduced bone loss: a twelve month, multicenter, randomized, double-blind, placebo-controlled, parallel-group study.
Methods	multicenter, double-blind, placebo-controlled parallel-group study.
Participants	**N= 428 (중재군/비교군= 214/214)** ▸**Inclusion criteria** - Inception cohort: Men; pre and post menopausal women; steroid>7.5mg/d; steroid duration 0-3mon, "various rheumatic diseases" ▸**Exclusion criteria** - hyperparathyroidism; bisphosphonates; hormone use: estrogen antagonists; vitamin D; Conditions interfering with spinal DEXA
Interventions	▸**(중재군)** - risedronate 2.5mg daily + 500mg calcium daily (n=75) - risedronate 5mg daily + 500mg calcium daily (n=76) ▸**(비교군)** - placebo + 500mg clacium daily (n=77)
Outcomes	▸**Primary outcome:** - the percentage of change in lumbar spine bone mineral density (BMD).

	▸**Secondary outcomes:** - proximal femur BMD and incidence of vertebral fractures ▸**추적기간** - 12 months
Results	▸After 12 months, the lumbar spine BMD (mean +/- SEM) did not change significantly compared with baseline in the 5-mg (0.6 +/- 0.5%) or the 2.5-mg (-0.1 +/- 0.7%) risedronate groups, while it decreased in the placebo group (-2.8 +/- 0.5%; P < 0.05). ▸The mean differences in BMD between the 5-mg risedronate and the placebo groups were 3.8 +/- 0.8% at the lumbar spine (P < 0.001), 4.1 +/- 1.0% at the femoral neck (P < 0.001), and 4.6 +/- 0.8% at the femoral trochanter (P < 0.001). ▸A trend toward a decrease in the incidence of vertebral fracture was observed in the 5-mg risedronate group compared with the placebo group (5.7% versus 17.3%; P = 0.072). Risedronate was well tolerated, and the incidence of upper gastrointestinal adverse events was comparable among the 3 groups.

Author, Publication year	**Kenneth G. Saag et al.** **N Engl J Med 2007;357:2028-39.**

Title	Teriparatide or alendronate in glucocorticoid-induced osteoporosis.
Methods	randomized, double-blind, controlled trial
Participants	**N= (중재군/비교군=318/ 159)** **▸Inclusion criteria** - an age of 21 years or more, a history of sustained glucocorticoid therapy, and a T score (the number of standard deviations above or below the mean value in normal adults) for bone mineral density at the lumbar spine or total hip of either −2.0 or less or −1.0 or less in addition to at least one fragility fracture during treatment with glucocorticoids. **▸Exclusion criteria** - Patients were excluded if they had fewer than three lumbar vertebrae that could be evaluated on dual energy x-ray absorptiometry, abnormal laboratory values, unresolved skeletal diseases other than glucocorticoid-induced osteoporosis, a history of cancer within 5 years before screening (with the exception of superficial basal-cell or squamous cell carcinomas of the skin that had been definitively treated), an increased risk of osteosarcoma, gastrointestinal disorders that would be likely to reduce tolerance of oral alendronate, or substantial renal impairment (on the basis of the Cockcroft–Gault formula). - Patients were excluded if they had received a bisphosphonate for more than 2 weeks within 6 months before enrollment or for more than 2 years within the previous 3 years and for nontrivial exposure to other osteoporosis therapies.

Interventions	▸(중재군) - 20 μg of teriparatide once daily ▸(비교군) - 10 mg of alendronate once daily
Outcomes	▸**Primary outcome:** - the change in bone mineral density at the lumbar spine. ▸**Secondary outcomes:** - changes in bone mineral density at the total hip and in markers of bone turnover, the time to changes in bone mineral density, the incidence of fractures, and safety. ▸**추적기간** - 18 months
Results	▸the mean (±SE) bone mineral density at the lumbar spine had increased more in the teriparatide group than in the alendronate group (7.2±0.7% vs. 3.4±0.7%, P<0.001).A significant difference between the groups was reached by 6 months (P<0.001). ▸At 12 months, bone mineral density at the total hip had increased more in the teriparatide group ▸Fewer new vertebral fractures occurred in the teriparatide group than in the alendronate group (0.6% vs. 6.1%, P = 0.004); the incidence of nonvertebral fractures was similar in the two groups (5.6% vs.

	3.7%, P = 0.36). ▸Significantly more patients in the teriparatide group had at least one elevated measure of serum calcium.

Author, Publication year	**Sambrook PN. et al.** **JOURNAL OF BONE AND MINERAL RESEARCH, Volume 18, Number 5, 2003**
Title	Prevention and Treatment of Glucocorticoid-Induced Osteoporosis: A Comparison of Calcitriol, Vitamin D Plus Calcium, and Alendronate Plus Calcium.
Methods	multicenter, randomized, open-label, parallel group study
Participants	**N= 195 (중재군/비교군=131/ 64)** ▸**Inclusion criteria** - Patients of either sex ages 20–80 years receiving or starting glucocorticoids (5 mg prednisone) were recruited. ▸**Exclusion criteria** - Exclusion criteria included medical conditions known to affect bone metabolism or treatment with medications known to affect bone metabolism (apart from glucocorticoids).

Interventions	▸(중재군) - calcitriol, 0.5 to 0.75 g/day (n=67) - alendronate, 10 mg/day plus calcium carbonate (600 mg daily). (n=64) ▸(비교군) - simple vitamin D (ergocalciferol, 30,000 IU weekly) plus calcium carbonate (600 mg daily) (n=64)
Outcomes	▸**Primary outcome:** - bone mineral density (BMD), measured by DXA of the lumbar spine at 0, 6, 12, 18, and 24 months ▸**Secondary outcomes:** - Secondary endpoints were BMD of the femoral neck and total body, at 0, 6, 12, 18, and 24 months ▸**추적기간** - 2 years
Results	▸Over 2 years, mean lumbar bone mineral density change was 5.9% with alendronate, 0.5% with ergocalciferol, and –0.7% with calcitriol ($p < 0.001$). At the femoral neck, there was no significant difference in bone mineral density change between the treatments over 2 years: alendronate (0.9%), ergocalciferol (3.2%), and calcitriol (2.2%). ▸Lumbar bone loss varied according to whether patients were starting or receiving chronic glucocorticoids, and there was a significant treatment prior glucocorticoid use interaction effect. Six of 66 calcitriol subjects, 1 of 61 ergocalciferol subjects, and 0 of 64 alendronate subjects sustained new

	vertebral fractures.

Author, Publication year	**C. Roux. et al.** **Osteoporos Int (2012) 23:1083–1090**
Title	Post hoc analysis of a single IV infusion of zoledronic acid versus daily oral risedronate on lumbar spine bone mineral density in different subgroups with glucocorticoid-induced osteoporosis
Methods	randomized, double-blind trial
Participants	**N= 833 (중재군/비교군=416/ 417)** **▸Inclusion criteria** - Men; pre-menopausal women; post-menopausal women NOS; steroid>7.5mg/d; steroid duration<1mon; steroid duration 1-3mon; prevalent steroid use at least 3mon; polymyalgia rheumatica; asthma or COPD; rheumatoid arthritis; SLE **▸Exclusion criteria** - age>85; pregnancy; carcinoma or suspected carcinoma; hyperparathyroidism; hypoparathyroidism;

	renal insufficiency; bisphosphonates; Medications that affect bone metabolism; serum 25-hydroxy-Vitamin D concentration <30 nmol/L
Interventions	▸(중재군) - zoledronic acid 5mg iv once a year + 1,000mg calcium daily + 400-1,200 IU Vit D daily (treatment arm, n=272) - zoledronic acid 5mg iv once a year + 1,000mg calcium daily + 400-1,200 IU Vit D daily (prevention arm, n=144) ▸(비교군) - Risedronate 5mg daily + 1,000mg calcium daily + 400-1,200 IU Vit D daily (treatment arm, n=273) - Risedronate 5mg daily + 1,000mg calcium daily + 400-1,200 IU Vit D daily (prevention arm, n=144)
Outcomes	▸**Primary outcome:** - percentage change from baseline in lumbar spine bone mineral density ▸**Secondary outcomes:** - Changes in bone turnover biomarker concentrations ▸**추적기간** - 1 year
Results	▸At month 12, zoledronic acid significantly increased LS BMD versus risedronate in patients≤74 years (P<0.05) in the treatment and 65–74 years (P=0.0008) in the prevention subpopulation. ▸At month 12, zoledronic acid significantly increased LS BMD versus risedronate in both subpopulations irrespective of gender (all P<0.05), cumulative prednisone dose (all P<0.01), and postmenopausal status

	(all P<0.05). ▸In premenopausal women, in both subpopulations, zoledronic acid significantly increased total hip BMD (all P<0.05) versus risedronate at month 12 but not LS BMD. ▸Osteoporotic patients in the prevention (P=0.0189) and osteopenic patients in the treatment subpopulation (P=0.0305) showed significant LS BMD increases with zoledronic acid versus risedronate at month 12.

지침3] 2014 FRENCH

- **Reference : 없음**

- 일차연구문헌 근거표 : 없음.

지침4] 2010 CANADA

- **Reference : 없음**

- 일차연구문헌 근거표 : 없음.

[지침5] 2017 NOGG

- **Reference**

	문헌정보	연구유형	연구대상자수 (치료군/비교군)
1	Lekamwasam S, Adachi JD, Agnusdei D et al. A framework for the development of guidelines for the management of glucocorticoid induced osteoporosis. Osteoporos Int 2012a;23:2257-76 [48]	clinical practical guidelines	
2	Grossman JM, Gordon R, Ranganath VK et al. American College of Rheumatology 2010 recommendations for the prevention and treatment of glucocorticoid-induced osteoporosis. Arthritis Care Res (Hoboken) 2010;62:1515-26 [49]	clinical practical guidelines	

- 일차연구문헌 근거표 : 없음

▣ 핵심질문 2-3.

40세 미만 성인에서 테리파라티드 사용은 글루코코르티코이드 유발 골다공증 예방과 치료에 효과적인가?

▣ PICO

Patients	Intervention	Comparators	Outcomes
40세 미만 성인	테리파라티드		글루코코르티코이드 유발 골다공증예방과 치료 효과

▣ 권고비교표

	지침 1 (ACR)	지침 2 (IOF-ECTS)	지침 3 (FRENCH)	지침 4 (CANADA)	지침 5 (NOGG)
출판년도	2017	2012	2014	2010	2017
AGREE 평가점수	89	67	56	44	67

권고문	1. For adults <40 years of age (women not of childbearing potential and men) with a history of OP fracture, or those continuing GC treatment (≥6 months at a dose of ≥7.5 mg/day) who have either a hip or spine BMD Z score <-3 or bone loss of ≥10%/year at the hip or spine as assessed by dual x-ray absorptiometry (DXA), If treatment with an oral bisphosphonate is not appropriate, the same alternative medications listed for	1. Data on the effects of pharmacological interventions in this population are sparse, particularly with regard to fracture risk. 2.Bone-protective therapy may be appropriate in some premenopausal women and younger men, particularly in individuals with a previous history of fracture or receiving high doses of glucocorticoids. 3. Caution is advised in the use of bisphosphonates in women of	NA	NA	Bone protective therapy may be appropriate in some premenopausal women and younger men, particularly in individuals with a previous history of fracture or receiving high doses of glucocorticoids

	adults <40 years of age are recommended with the exception of raloxifene, which is not used in men and premenopausal women 2. For adults 30 years of age who are receiving very highdose GC treatment (initial prednisone dose of ≥30 mg/day [or equivalent GC exposure] and a cumulative annual dose of >5 gm) (Table 3), oral bisphosphonate treatment should be	childbearing age.			

	initiated. If treatment with an oral bisphosphonate is not appropriate, the age-related recommendations for secondline therapy (Table 2) should be followed (with adjustments for women of childbearing potential as outlined in these guidelines).				
근거수준,권고등급	II / B	II / B	NA	NA	II / A

▣ 근거 내용 정리

[지침1] 2017 ACR

- **reference** : 없음

- **일차연구문헌 근거표** : 없음

[지침2] 2010 IOF-ECTS

- **reference** : 없음

	문헌정보	연구유형	연구대상자수 (치료군/비교군)
1	Saag KG, Zanchetta JR, Devogelaer JP. et al. Effects of Teriparatide Versus Alendronate for Treating Glucocorticoid-Induced Osteoporosis Thirty-Six–Month Results of a Randomized, Double-Blind, Controlled Trial Arthritis Rheum. 2009 Nov;60(11):3346-55 [50]	RCT	428 (214/214)
2	Langdahl BL, Marin F, Shane E, Dobnig H, Zanchetta JR, Maricic M, Krohn K, See K, Warner MR (2009) Teriparatide versus alendronate for treating glucocorticoid-induced osteoporosis: an analysis by gender and menopausal status. Osteoporos Int 20:2095–2104 [51]	randomized, double-blind study	277 (143/134)

- **일차연구문헌 근거표**

Author, Publication year	**Saag KG et al.** **Arthritis Rheum. 2009 Nov;60(11):3346-55**
Title	Effects of Teriparatide Versus Alendronate for Treating Glucocorticoid-Induced Osteoporosis Thirty-Six–Month Results of a Randomized, Double-Blind, Controlled Trial Arthritis Rheum.
Methods	a Randomized, Double-Blind, Controlled Tria
Participants	**N= 428 (중재군/비교군= 214/214)** **▸Inclusion criteria** - Ambulatory patients were eligible for enrollment - if they met the following criteria: - an age of 21 years or more, - a history of sustained glucocorticoid therapy, - and a T score (the number of standard deviations above or below the mean value in normal adults) for bone mineral density at the lumbar spine or total hip of either −2.0 or less or −1.0 or less in addition to at least one fragility fracture during treatment with glucocorticoids. - Sustained glucocorticoid therapy was defined as a mean daily dose of 5 mg or more of prednisone or its equivalent for 3 or more consecutive months immediately preceding the screening visit.

	▸**Exclusion criteria** - Patients were excluded if they had fewer than three lumbar vertebrae that could be evaluated on dual energy x-ray absorptiometry, abnormal laboratory values, unresolved skeletal diseases other than glucocorticoid-induced osteoporosis, - a history of cancer within 5 years before screening (with the exception of superficial basal-cell or squamous-cell carcinomas of the skin that had been definitively treated), - an increased risk of osteosarcoma - gastrointestinal disorders that would be likely to reduce tolerance of oral alendronate, or substantial renal impairment (on the basis of the Cockcroft–Gault formula). - Patients were excluded if they had received a bisphosphonate for more than 2 weeks within 6 months before enrollment or for more than 2 years within the previous 3 years and for nontrivial exposure to other osteoporosis therapies.
Interventions	▸(중재군) - teriparatide 20 μg/day ▸(비교군) - alendronate 10 mg/day
Outcomes	▸**Primary outcome:** - BMD change at 18months ▸**Secondary outcomes:** - Fracture

	▸**추적기간** - 36 months
Results	▸Increases in BMD from baseline were significantly greater in the teriparatide group than in the alendronate group, and at 36 months were 11.0% versus 5.3% for lumbar spine, 5.2% versus 2.7% for total hip, and 6.3% versus 3.4% for femoral neck (*P* < 0.001 for all). ▸Fewer subjects had vertebral fractures in the teriparatide group than in the alendronate group (3 [1.7%] of 173 versus 13 [7.7%] of 169; *P* 0.007), with most occurring during the first 18 months. There was no significant difference between groups in the incidence of nonvertebral fractures (16 [7.5%] of 214 subjects taking teriparatide versus 15 [7.0%] of 214 subjects taking alendronate; *P* 0.843).

Author, Publication year	**Langdahl et al.** **Osteoporos Int 20:2095–2104**
Title	Teriparatide versus alendronate for treating glucocorticoid-induced osteoporosis: an analysis by gender and menopausal status.
Methods	a multicenter, randomized, double-blind study

Participants	**N= 277 (중재군/비교군= 134/143)** ▸**Inclusion criteria:** - patients on ≥5 mg/day of prednisolone or equivalent for ≥3 months, either T score ≤−2.0 (LS or TH) or T score of ≤1.0 plus at least one fragility fracture ▸**Exclusion criteria:** - skeletal diseases other than GIO, malignancies, Paget's disease, impaired renal functions, untreated thyroid diseases, heparin therapy, excess alcohol
Interventions	▸(중재군) - teriparatide 20 μg/day ▸(비교군) - alendronate 10 mg/day
Outcomes	▸**Primary outcome:** **-** change in lumbar spine BMD ▸**Secondary outcomes:** - change in hip BMD, change in bone biomarkers, fracture incidence, and safety. ▸ 추적기간 - 18 months

Results	▸At 18 months, mean percent increases from baseline in lumbar spine BMD were significantly greater in the teriparatide versus alendronate group in postmenopausal women (7.8% versus 3.7%, p<0.001), premenopausal women (7.0% versus 0.7%, p<0.001), and men (7.3% versus 3.7%, p=0.03). ▸Radiographic vertebral fractures occurred in one teriparatide (one postmenopausal) and ten alendronate patients (six postmenopausal, four men), and nonvertebral fractures occurred in 12 teriparatide (nine postmenopausal, two premenopausal, one man) and eight alendronate patients (six postmenopausal, two men). The proportion of patients reporting adverse events in teriparatide versus alendronate groups was consistent across subgroups.

[지침3] 2014 FRENCH

- **reference** : 없음

- **일차연구문헌 근거표 : 없음.**

[지침4] 2010 CANADA

- **reference** : 없음

- **일차연구문헌 근거표 : 없음.**

[지침5] 2017 NOGG

- **reference**

	문헌정보	연구유형	연구대상자수 (치료군/비교군)
1	Albaum JM, Youn S, Levesque LE, Gershon AS, Cadarette SM. Osteoporosis management among chronic glucocorticoid users: a systematic review. J Popul Ther Clin Pharmacol. 2014;21(3):e486-504 [52]	SR	
2	Amiche MA, Albaum JM, Tadrous M et al. Efficacy of osteoporosis pharmacotherapies in preventing fracture among oral glucocorticoid users: a network meta-analysis. Osteoporos Int 2016;27:1989-98 [53]	meta-analysis	
3	Lekamwasam S, Adachi JD, Agnusdei D et al. A framework for the	clinical practice guideline	

	development of guidelines for the management of glucocorticoid-induced osteoporosis. Osteoporos Int 2012a;23:2257-76 [48]		
4	Grossman JM, Gordon R, Ranganath VK et al. American College of Rheumatology 2010 recommendations for the prevention and treatment of glucocorticoid-induced osteoporosis. Arthritis Care Res (Hoboken) 2010;62:1515-26 [49]	clinical practice guideline	

- **일차연구문헌 근거표 : 없음.**

▣ 핵심질문 2-4.

40세 미만 성인에서 데노수맙 사용은 글루코코르티코이드 유발 골다공증 예방과 치료에 효과적인가?

▣ PICO

Patients	Intervention	Comparators	Outcomes
40세 미만 성인	데노수맙		글루코코르티코이드 유발 골다공증 예방과 치료 효과

▣ 권고비교표

	지침 1 (ACR)	지침 2 (IOF-ECTS)	지침 3 (FRENCH)	지침 4 (CANCDA)	지침 5 (NOGG)
출판년도	2017	2012	2014	2010	2017
AGREE 평가점수	89	67	56	44	67

권고문	If treatment with an oral bisphosphonate is not appropriate, the same alternative medications listed for adults≥40 years of age are recommended with the exception of raloxifene, which is not used in men and premenopausal women.				
근거수준, 권고등급	II / B				

▣ 근거 내용 정리

[지침1] 2017 ACR

- **Reference** - 없음

- **일차연구문헌 근거표** – 없음

[지침 2] 2012 IOF-ECTS

- **Reference** - 없음

- **일차연구문헌 근거표** – 없음

[지침3] 2014 FRENCH

- **Reference** - 없음

- **일차연구문헌 근거표** – 없음

[지침4] 2010 CANADA

- **Reference** - 없음

- **일차연구문헌 근거표** – 없음

[지침5] 2017 NOGG

- **Reference** - 없음

- **일차연구문헌 근거표** – 없음

▣ 핵심질문 3.

40세 이상 성인에서 어떤 약물 치료가 글루코코르티코이드 유발 골다공증 예방과 치료에 효과적인가?

▣ 핵심질문 3-1.

40세 이상 성인에서 칼슘과 비타민 D 보충은 글루코코르티코이드 유발 골다공증 예방과 치료에 효과적인가?

▣ PICO

Patients	Intervention	Comparators	Outcomes
40세 이상 성인	칼슘과 비타민 D 보충		글루코코르티코이드 유발 골다공

			증 예방과 치료 효과

▣ 권고비교표

	지침1 (ACR)	지침2 (IOF-ECTS)	지침3 (FRENCH)	지침4 (CANADA)	지침5 (NOGG)
출판년도	2017	2012	2014	2010	2017
AGREE 평가점수	89	67	56	44	67
권고문	All adults taking prednisone at a dose of ≥2.5 mg/day for ≥3 months Optimize calcium intake (800–1,000 mg/day) and vitamin D intake (600–800 IU/day) and lifestyle modifications	1. Advise good nutrition especially with calcium and vitamin D 2. Adequate calcium intake should be achieved through dietary intake if possible, with the use of supplements if necessary.	1. Ensure adequate intakes of calcium (preferably via a balanced diet) and vitamin D 2. Routine prescription of calcium supplements is not recommended 3. The serum levelof 25-OH vitamin D	NOT GIOP 1. The total daily intake of elemental calcium (through diet and supplements) for individuals over age 50 should be 1200 mg [grade B]. 2. For healthy adults at low risk of vitamin D	NOT GIOP, General 1. A daily calcium intake of between 700 and 1200mg should be advised, if possible achieved through dietary intake, with use of supplements if

	(balanced diet, maintaining weight in the recommended range, smoking cessation, regular weight-bearing or resistance training exercise, limiting alcohol intake to 1–2 alcoholic beverages/day) over no treatment or over any of these treatments alone.	3. An adequate vitamin D status should be maintained, using supplements if required	should be maintained at the optimal value,which has been set at 30 ng/mL (75 nmoL/L) [52] based on findingsfrom biological and clinical studies that did not focus specificallyon glucocorticoid-induced osteoporosis 4. In patients with vitamin D insufficiency or deficiency, a loading dose of vitamin D should be given to elevate the serum 25-OH vita-min D level above the target of 30 ng/mL 5. The maintenance dose is 800 to 1200	deficiency, routine supplementation with 400–1000 IU (10–25 µg) vitamin D 3 daily is recommended [grade D]. 3. For adults over age 50 at moderate risk of vitamin D defi-ciency, supplementation with 800–1000 IU (20–25 µg) vitamin D 3 daily is recommended. To achieve optimal vitamin D status, daily supplementation with more than 1000 IU (25 µg) may be required. Daily doses up to 2000 IU (50 µg) are safe and do not necessitate monitoring [grade C].	necessary. 2. In postmenopausal women and older men (≥50 ears) at increased risk of fracture a daily dose of 800IU cholecalciferol should be advised. 3. In postmenopausal women and older men receiving bone protective therapy for osteoporosis, calcium supplementation should be given if the dietary intake is below 700 mg/day, and vitamin D supplementation considered in those at risk of, or with evidence of, vitamin D

			IU/day (or the equivalent of 100,000 IU every 2–3 months). The currently available data do not support the use of high-dose vitamin D supplementation (500,000 or 600,000 IU once or twice every year)	4. For individuals receiving pharmacologic therapy for osteo-porosis, measurement of serum 25-hydroxyvitamin D should follow three to four months of adequate supplementation and should not be repeated if an optimal level (≥ 75 nmol/L) is achieved [grade D].	insufficiency.
근거수준,권고등급	II / B	II / B	II / B	II / B	II / B

▣ 근거 내용 정리

[지침1] 2017 ACR

	문헌정보	연구유형	연구대상자수 (치료군/비교군)
1	Braun JJ, Birkenhager-Frenkel DH, Rietveld AH, Juttmann JR, Visser TJ, Birkenhager JC. Influence of 1 alpha-(OH)D3 administration on bone and bone mineral metabolism in patients on chronic glucocorticoid treatment; a double blind controlled study. Clin Endocrinol (Oxf). 1983;19(2):265-273 [7]	RCT	14 (7/7)
2	Adachi JD, Bensen WG, Bianchi F, Cividino A, Pillersdorf S, Sebaldt RJ, et al. Vitamin D and calcium in the prevention of corticosteroid induced osteoporosis: a 3 year followup. J Rheumatol. 1996;23(6):995-1000 [8]	RCT	62
3	Grant AM, Avenell A, Campbell MK, McDonald AM, MacLennan GS, McPherson GC, et al. Oral vitamin D3 and calcium for secondary prevention of low-trauma fractures in elderly people (Randomised Evaluation of Calcium Or vitamin D, RECORD): a randomised placebo-controlled trial. Lancet. 2005;365(9471):1621-1628 [9]	RCT	5292 (3940/1332)

4	Porthouse J, Cockayne S, King C, Saxon L, Steele E, Aspray T, et al. Randomised controlled trial of calcium and supplementation with cholecalciferol (vitamin D3) for prevention of fractures in primary care. BMJ. 2005;330(7498):1003 [10]	RCT	4133 (1321/ 1993)
5	Jackson RD, LaCroix AZ, Gass M, Wallace RB, Robbins J, Lewis CE, et al. Calcium plus vitamin D supplementation and the risk of fractures. N Engl J Med. 2006;354(7)669 -683 [11]	RCT	36,282 (18,176/18,106)
6	Salovaara K, Tuppurainen M, Karkkainen M, Rikkonen T, Sandini L, Sirola J, et al. Effect of vitamin D(3) and calcium on fracture risk in 65- to 71-year-old women: a population-based 3-year randomized, controlled trial—the OSTPRE-FPS. J Bone Miner Res. 2010;25(7):1487-1495 [12]	observational cohort study	3195 (1586/1609)

- **일차연구문헌 근거표**

Author, Publication year	**J. J. BRAUN et al.** **Clinical Endocrinology (1983) 18,265-273**
Title	INFLUENCE OF 1α-(OH)D3 ADMINISTRATION ON BONE AND BONE MINERAL METABOLISM IN PATIENTS ON CHRONIC GLUCOCORTICOID TREATMENT; A DOUBLE BLIND CONTROLLED STUDY
Methods	a double-blind placebo controlled study
Participants	**N= 14 (중재군/비교군= 7/7)** ▸**Inclusion criteria** - No medication with known influence on bone metabolism was used. - All patients with chronic obstructive lung disease used a P-adrenergic drug and a xanthine-derivative. - - - - Patients were not immobilized. ▸**Exclusion criteria** - Renal disease
Interventions	▸(중재군) - a daily dose of 2 pg l a-(OH)D3 ▸(비교군) - placebo
Outcomes	▸**Primary outcome:**

	- Biochemistrical change ▸**Secondary outcomes:** - the changes of Bone histontorphometry and Bone mineral content ▸추적기간 - 6 month
Results	▸Two of the 14 patients showed an increased serum immunoreactive parathyroid hormone (iPTH) concentration. ▸Serum 25-hydroxyvitamin D and 1,25-dihydroxyvitamin D (1,25-$(0H)_3$D) were normal but the average 24,25-dihydroxyvitamin D (24,25-(OH)2D) was low. ▸The histomorphometrically determined trabecular bone volume of an iliac crest biopsy appeared to be low in 6 patients ▸The average active bone resorption and osteoid seams were increased, while the average osteoblast seams were within the normal range. ▸Treatment with 1 a-(OH)D3 raised 47Ca2+ intestinal absorption and 24 h urinary Ca2+ excretion significantly at 3 and 6 months and at 6 months serum iPTH concentration and 24 h urinary hydroxyproline excretion had fallen significantly in the treated group. During treatment with 1 a-(OH)D3 the serum 1,25-(OH)2D and 24,25-(OH)2D levels increased significantly ▸trabecular bone volume remained constant or even increased in the la-(OH)D3-group ▸In both groups osteoid seams and osteoblast seams did not change significantly

Author, Publication year	**Adachi JD et al.** **J Rheumatol. 1996 Jun;23(6):995-1000.**
Title	Vitamin D and calcium in the prevention of corticosteroid induced osteoporosis: a 3 year followup.
Methods	a minimized double blind, placebo controlled trial
Participants	**N= 62 (중재군/비교군=)** ▸**Inclusion criteria** - subjects with polymyalgia rheumatica, temporal arteritis, asthma, vasculitis, or systemic lupus erythematosus ▸**Exclusion criteria** - NA
Interventions	▸(중재군) - vitamin D 50,000 units/week and calcium 1,000 mg/day ▸(비교군) - placebo
Outcomes	▸**Primary outcome:** - the percentage change in bone mineral density (BMD) of the lumbar spine in the 2 treatment groups from baseline to 36 months follow-up.

	▸**Secondary outcomes:** - NA ▸추적기간 - 3 years
Results	▸BMD of the lumbar spine in the vitamin D and calcium treated group decreased by a mean (SD) of 2.6% (4.1%) at 12 mo, 3.7% (4.5%) at 24 mo, and 2.2% (5.8%) at 36 mo. ▸In the placebo group there was a decrease of 4.1% (4.1%) at 12 mo, 3.8% (5.6%) at 24 mo, and 1.5% (8.8%) at 36 mo. ▸The observed differences between groups were not statistically significant. The difference at 36 mo was-0.693% (95% CI -5.34, 3.95).

Author, Publication year	**Grant AM. et al.** **Lancet. 2005;365(9471):1621-1628.**
Title	Oral vitamin D3 and calcium for secondary prevention of low-trauma fractures in elderly people (Randomised Evaluation of Calcium Or vitamin D, RECORD): a randomised placebo-controlled trial.
Methods	a randomised placebo-controlled trial

Participants	**N= 5292(중재군/비교군= 3940/1332)** **▸Inclusion criteria** - age 70 years or older who had had a low-trauma, osteoporotic fracture in the previous 10 years were assessed between Feb 1, 1999, and March 31, 2002 **▸Exclusion criteria** **-** bed or chair bound before fracture - cognitive impairment indicated by an abbreviated mental test score8 of less than seven - cancer in the past 10 years that was likely to metastasise to bone - fracture associated with pre-existing local bone abnormality - those known to have hypercalcaemia; renal stone in the past 10 years - life expectancy of less than 6 months; individuals known to be leaving the UK - daily intake of more than 200 IU vitamin D or more than 500 mg calcium supplements - intake in the past 5 years of fluoride, bisphosphonates, calcitonin, tibolone, hormone-replacement therapy, selective oestrogen-receptor modulators, or any vitamin D metabolite (eg, calcitriol); and vitamin D by injection in the past year
Interventions	▸(중재군) - oral vitamin D3 (800 IU per day) (n=1343) - oral calcium (1000 mg per day) (n=1311) - oral vitamin D3 (800 IU per day) combined with calcium (1000 mg per day) (n=1306) ▸(비교군)

	- placebo (n=1332)
Outcomes	▸**Primary outcome:** - new low-energy fractures ▸**Secondary outcomes:** - quality of life ▸추적기간 - between 24 months and 62 months
Results	▸The incidence of new, low-trauma fractures did not differ significantly between participants allocated calcium and those who were not (331 [12.6%] of 2617 vs 367 [13.7%] of 2675; hazard ratio (HR) 0.94 [95% CI 0.81-1.09]); between participants allocated vitamin D3 and those who were not (353 [13.3%] of 2649 vs 345 [13.1%] of 2643; 1.02 [0.88-1.19]); or between those allocated combination treatment and those assigned placebo (165 [12.6%] of 1306 vs 179 [13.4%] of 1332; HR for interaction term 1.01 [0.75-1.36]). ▸The groups did not differ in the incidence of all-new fractures, fractures confirmed by radiography, hip fractures, death, number of falls, or quality of life. ▸By 24 months, 2886 (54.5%) of 5292 were still taking tablets, 451 (8.5%) had died, 58 (1.1%) had withdrawn, and 1897 (35.8%) had stopped taking tablets but were still providing data for at least the main outcomes. ▸Compliance with tablets containing calcium was significantly lower (difference: 9.4% [95% CI 6.6-12.2]), partly because of gastrointestinal symptoms. However, potentially serious adverse events were rare and did

	not differ between groups.

Author, Publication year	**Porthouse J et al.** **BMJ. 2005;330(7498):1003.**
Title	Randomised controlled trial of calcium and supplementation with cholecalciferol (vitamin D3) for prevention of fractures in primary care.
Methods	randomised controlled trial
Participants	**N= 4133 (중재군/비교군= 1321/ 1993)** **▸Inclusion criteria** - We identified women aged 70 and over who had at least one self reported risk factor for hip fracture: low bodyweight (< 58 kg), any previous fracture, maternal history of hip fracture, smoker, and poor or fair health. **▸Exclusion criteria** - Women were excluded from the study if they could not give written consent or were receiving any calcium supplementation of more than 500 mg a day. - We also excluded women with a history of kidney or bladder stones, renal failure, or hypercalcaemia**.**

Interventions	▸(중재군) - daily oral supplementation using 1000 mg calcium with 800 IU cholecaliferol ▸(비교군) - information leaflet on dietary calcium intake and prevention of falls, or leaflet only
Outcomes	▸**Primary outcome:** -all clinical fractures ▸**Secondary outcomes:** -adherence to treatment, falls, and quality of life (measured with the SF-12). ▸추적기간 - median follow-up of 25 months (range 18 to 42 months)
Results	▸69% of the women who completed the follow-up questionnaire at 24 months were still taking supplements (55% with inclusion of randomised participants known to be alive). ▸After a median follow-up of 25 months (range 18 to 42 months), clinical fracture rates were lower than expected in both groups but did not significantly differ for all clinical fractures (odds ratio for fracture in supplemented group 1.01, 95% confidence interval 0.71 to 1.43). ▸The odds ratio for hip fracture was 0.75 (0.31 to 1.78). ▸The odds of a woman having a fall at six and 12 months was 0.99 and 0.98, respectively. ▸Quality of life did not significantly differ between the groups.

Author, Publication year	**Jackson RD et al.** **N Engl J Med. 2006;354(7)669-683**
Title	Calcium plus vitamin D supplementation and the risk of fractures.
Methods	randomised controlled trial
Participants	**N= 36,282 (중재군/비교군= 18,176/18,106)** ▸**Inclusion criteria** - Eligible women were 50 to 79 years of age at the initial screening and had no evidence of a medical condition associated with a predicted survival of less than three years and no safety, adherence, or retention risks ▸**Exclusion criteria** - hypercalcemia, renal calculi, corticosteroid use, and calcitriol use.
Interventions	▸(중재군) - 1000 mg of elemental calcium + 400 IU of vitamin D3 daily ▸(비교군) - 1000 mg of elemental calcium + placebo

Outcomes	▸**Primary outcome:** - Hip bone density ▸**Secondary outcomes:** - spine, whole body bone density - fraciture ▸추적기간 - 9 years
Results	▸Hip bone density was 1.06 percent higher in the calcium plus vitamin D group than in the placebo group (P<0.01). ▸Intention-to-treat analysis indicated that participants receiving calcium plus vitamin D supplementation had a hazard ratio of 0.88 for hip fracture (95 percent confidence interval, 0.72 to 1.08), 0.90 for clinical spine fracture (0.74 to 1.10), and 0.96 for total fractures (0.91 to 1.02). ▸The risk of renal calculi increased with calcium plus vitamin D (hazard ratio, 1.17; 95 percent confidence interval, 1.02 to 1.34). ▸Censoring data from women when they ceased to adhere to the study medication reduced the hazard ratio for hip fracture to 0.71 (95 percent confidence interval, 0.52 to 0.97 ▸Effects did not vary significantly according to prerandomization serum vitamin D levels.

Author, Publication year	**Salovaara K. et al.** **J Bone Miner Res. 2010;25(7):1487-1495.**
Title	Effect of vitamin D(3) and calcium on fracture risk in 65- to 71-year-old women: a population-based 3-year randomized, controlled trial—the OSTPRE-FPS.
Methods	observational cohort study.
Participants	**N= 3195 (중재군/비교군= 1586/1609)** ▸**Inclusion criteria** - all women living in the region of northern Savonia, previous Kuopio Province (latitude 628 to 648N), born between 1932 and 1941 ▸**Exclusion criteria** **-** no exclusion criteria
Interventions	▸(중재군) - 800 IU of cholecalciferol + 1000 mg of calcium ▸(비교군) - placebo
Outcomes	▸**Primary outcome:** - incident fractures ▸**Secondary outcomes:**

	- serum vitamin D levels during follow-up. ▸추적기간 - 36 months
Results	▸In adjusted Cox proportional hazards models, the risk of any fracture decreased in the vitamin D and calcium group by 17% [adjusted hazard ratio (aHR) ¼ 0.83; 95% confidence interval (CI) 0.61–1.12], and the risk of any nonvertebral fracture decreased by 13% (aHR ¼ 0.87; 95% CI 0.63–1.19). ▸The risk of distal forearm fractures decreased by 30% (aHR ¼ 0.70; 95% CI 0.41–1.20), and the risk of any upper extremity fractures decreased by 25% (aHR ¼ 0.75; 95% CI 0.49–1.16), whereas the risk of lower extremity fractures remained essentially equal (aHR ¼ 1.02; 95% CI 0.58–1.80). None of these effects reached statistical significance.

[지침2] 2012 IOF-ECTS

- **Reference**

	문헌정보	연구유형	연구대상자수 (치료군/비교군)
	Amin S, LaValley MP, Simms RW, Felson DT (1999) The role	meta-analysis	

1	of vitamin D in corticosteroid-induced osteoporosis: a meta-analytic approach. Arthritis Rheum 42:1740–1751 [5]		
2	Reginster JY, Kuntz D, Verdickt W, Wouters M, Guillevin L, Menkes CJ, Nielsen K (1999) Prophylactic use of alfacalcidol in corticosteroid-induced osteoporosis. Osteoporos Int 9:75–81 [13]	RCT	145 (74/71)
3	Corticosteroid osteoporosis: practical implications of recent trials. J Bone Miner Res 15:1645–1649 [14]	review	
4	Holick MF (2007) Optimal vitamin d status for the prevention and treatment of osteoporosis. Drugs Aging 24:1017–1029 [15]	review	
5	Buckley LM, Leib ES, Cartularo KS, Vacek PM, Cooper SM (1996) Calcium and vitamin D3 supplementation prevents bone loss in the spine secondary to low-dose corticosteroids in patients with rheumatoid arthritis. A randomized, double-blind, placebo-controlled trial. Ann Intern Med 125:961–968 [16]	RCT	66 (31/35)

6	Homik J, Suarez-Almazor ME, Shea B, Cranney A, Wells G, Tugwell P (2000) Calcium and vitamin D for corticosteroid induced osteoporosis. Cochrane Database Syst Rev 2:CD000952 [17]	meta-analysis	

- **일차연구문헌 근거표**

Author, Publication year	**Reginster JY. et al.** **Osteoporos Int. 1999;9(1):75-81.**
Title	Prophylactic use of alfacalcidol in corticosteroid-induced osteoporosis.
Methods	randomized placebo-controlled trial
Participants	**N= 145 (중재군/비교군= 74/71)** **▸Inclusion criteria** - One hundred and forty-five patients suffering from diseases requiring long-term treatment with high doses of corticosteroids (30 mg/day or greater of prednisolone) were recruited to the study. - Patients had to be steroid naive on entry to the study (not more than 15 days of treatment with a

	corticosteroid within the previous 24 months). ▸**Exclusion criteria** **-** no exclusion criteria
Interventions	▸(중재군) - 1 microgram/day alfacalcidol ▸(비교군) - placebo
Outcomes	▸**Primary outcome:** - Bone mineral density (BMD) of the lumbar spine ▸**Secondary outcomes:** - Safety, serum calcium ▸추적기간 - 12 months
Results	▸The percentage change in BMD after 6 months' treatment was -2.11% in the alfacalcidol group and –4.00% in the placebo group (p = 0.39). ▸After 12 months the percentage change in BMD was +0.39% (CI: -4.28 to 4.81) in the alfacalcidol group and -5.67% (CI: -8.13 to -3.21) in the placebo group, this difference (6.06%, CI: 0.88 to 11.24) being statistically significant (p = 0.02). ▸An intention to treat analysis also showed a significant difference between the two treatment groups in

	alfacalcidol's favor (3.81%, p = 0.01; CI: 0.92 to 6.70). ▸There was no significant difference between the two treatment groups in the corticosteroid dose at any time point during the study. ▸Serum calcium was measured throughout and there were no significant differences between the two treatment groups at any visit.

Author, Publication year	**Buckley LM et al** **Ann Intern Med. 1996 Dec 15;125(12):961-8.**
Title	Calcium and vitamin D3 supplementation prevents bone loss in the spine secondary to low-dose corticosteroids in patients with rheumatoid arthritis. A randomized, double-blind, placebo-controlled trial.
Methods	A randomized, double-blind, placebo-controlled trial.
Participants	**N= 66 (중재군/비교군= 31/35)** ▸**Inclusion criteria** - Patients were eligible if they were between 18 and 65 years of age and had a diagnosis of rheumatoid arthritis as defined by the revised American College of Rheumatology criteria, serum creatinine level less than 176.8 µmol/L, and normal liver function. ▸**Exclusion criteria**

	- Patients were excluded if they were receiving an anticonvulsant medication, hydrochlorothiazide, bisphosphonates, fluoride, calcitonin, or calcitriol or if they had a history of malabsorption, hyperparathyroidism, immobilization, metabolic bone disease, or thyroid disease with an abnormal thyroid-stimulating hormone
Interventions	▸(중재군) - Calcium carbonate (1000 mg/d) and vitamin D3 (500 IU/d) ▸(비교군) - placebo
Outcomes	▸**Primary outcome:** - Bone Densitometry of the Lumbar Spine ▸**Secondary outcomes:** - Bone Densitometry of the femur ▸추적기간 - 24 months
Results	▸Patients receiving prednisone therapy who were given placebo lost bone mineral density in the lumbar spine and trochanter at a rate of 2.0% and 0.9% per year, respectively. ▸Patients receiving prednisone therapy who were given calcium and vitamin D3 gained bone mineral density in the lumbar spine and trochanter at a rate of 0.72% (P = 0.005) and 0.85% (P = 0.024) per year, respectively. ▸In patients receiving prednisone therapy, bone mineral densities of the femoral neck and the Ward triangle

	did not increase significantly with calcium and vitamin D3. Calcium and vitamin D3 did not improve bone mineral density at any site in patients who were not receiving corticosteroids

[지침3] 2014 FRENCH

- **Reference**

	문헌정보	연구유형	연구대상자수 (치료군/비교군)
1	Sanders KM, Stuart AL, Williamson EJ, et al. Annual high-dose oral vitamin D and falls and fractures in older women: a randomized controlled trial. JAMA 2010;303:1815–22 [18]	RCT	2256 (1131/1125)

- **일차연구문헌 근거표**

Author, Publication year	**Sanders KM, et al.** **JAMA 2010;303:1815–22.**
Title	Annual high-dose oral vitamin D and falls and fractures in older women: a randomized controlled trial.
Methods	A double-blind, placebo-controlled trial
Participants	**N= 2256 (중재군/비교군= 1131/1125)** ▸**Inclusion criteria** - Patients were eligible if they were between 18 and 65 years of age and had a diagnosis of rheumatoid arthritis as defined by the revised American College of Rheumatology criteria, serum creatinine level less than 176.8 µmol/L, and normal liver function. ▸**Exclusion criteria** - Patients were excluded if they were receiving an anticonvulsant medication, hydrochlorothiazide, bisphosphonates, fluoride, calcitonin, or calcitriol or if they had a history of malabsorption, hyperparathyroidism, immobilization, metabolic bone disease, or thyroid disease with an abnormal thyroid-stimulating hormone
Interventions	▸(중재군) - 500,000 IU of cholecalciferol orally once a year ▸(비교군) - placebo
Outcomes	▸**Primary outcome:**

	- fall and fractures ▸**Secondary outcomes:** - serum 25-hydroxycholecalciferol and parathyroid hormone levels ▸추적기간 - 12 months
Results	▸Women in the cholecalciferol (vitamin D) group had 171 fractures vs 135 in the placebo group ▸837 women in the vitamin D group fell 2892 times (rate, 83.4 per 100 person-years) while 769 women in the placebo group fell 2512 times (rate, 72.7 per 100 person-years; incidence rate ratio [RR], 1.15; 95% confidence interval [CI], 1.02-1.30; P = .03). ▸The incidence RR for fracture in the vitamin D group was 1.26 (95% CI, 1.00-1.59; P = 0.047) vs the placebo group (rates per 100 person-years, 4.9 vitamin D vs 3.9 placebo). A temporal pattern was observed in a post hoc analysis of falls. ▸The incidence RR of falling in the vitamin D group vs the placebo group was 1.31 in the first 3 months after dosing and 1.13 during the following 9 months (test for homogeneity; P = .02). ▸In the substudy, the median baseline serum 25-hydroxycholecalciferol was 49 nmol/L. Less than 3% of the substudy participants had 25-hydroxycholecalciferol levels lower than 25 nmol/L. In the vitamin D group, 25-hydroxycholecalciferol levels increased at 1 month after dosing to approximately 120 nmol/L, were approximately 90 nmol/L at 3 months, and remained higher than the placebo group 12 months after dosing.

[지침4] 2010 CANADA

- **Reference**

	문헌정보	연구유형	연구대상자수 (치료군/비교군)
1	Tang BM, Eslick GD, Nowson C, et al. Use of calcium or calcium in combination with vitamin D supplementation to prevent fractures and bone loss in people aged 50 years and older: a meta-analysis. *Lancet* 2007;370:657-66 [19]	meta-analysis	
2	Reid IR, Bolland MJ, Grey A. Effect of calcium supplementation on hip fractures. Osteoporos Int 2008;19:1119-23 [20]	meta-analysis	
4	Hanley DA, Cranney A, Jones G, et al.; Guidelines Committee of the Scientific Advisory Council of Osteoporosis Canada. Vitamin D in adult health and disease: a review and guideline [21]	review	

- **일차연구문헌 근거표** – 없음

[지침5] 2017 NOGG

- **Reference**

	문헌정보	연구유형	연구대상자수 (치료군/비교군)
1	Tai V, Leung W, Grey A, Reid IR, Bolland MJ. Calcium intake and bone mineral density: systematic review and meta-analysis. BMJ 2015 Sep 29;351:h4183 [22]	systematic review and meta-analysis.	
2	Shea B, Wells G, Cranney A et al. Meta-analyses of therapies for postmenopausal osteoporosis. VII. Meta-analysis of calcium supplementation for the prevention of postmenopausal osteoporosis. Endocr Rev 2002; 23, 552-9 [23]	meta-analysis	
3	Bolland MJ, Leung W, Tai V et al. Calcium intake and risk of fracture: systematic review. BMJ 2015 Sep 29;351:h4580. doi: 10.1136/bmj.h4580 [24]	systematic review	

4	Tang BM, Eslick GD, Nowson C, Smith C, Bensoussan A. Use of calcium or calcium in combination with vitamin D supplementation to prevent fractures and bone loss in people aged 50 years and older: a meta-analysis. Lancet 2007 Aug 25;370(9588):657-66 [19]	meta-analysis	
5	Avenell A, Mak JCS, O'Connell D. Vitamin D and vitamin D analogues for preventing fractures in post-menopausal women and older men. The Cochrane database of systematic reviews 2014;4, CD000227-CD000227 [25]	systematic review	
6	Bischoff-Ferrari HA, Willett WC, Wong JB et al. Prevention of nonvertebral fractures with oral vitamin D and dose dependency: a meta-analysis of randomized controlled trials. Arch Intern Med 2009a;169:551-61 [26]	meta-analysis	
7	Bischoff-Ferrari HA, Dawson-Hughes B, Staehelin HB et al. Fall prevention with supplemental and active forms of vitamin D: a meta-analysis of randomised controlled trials. BMJ 2009b; 339, b3692-b3692 [27]	meta-analysis	
8	Sanders KM, Stuart AL, Williamson EJ et al. Annual high-dose oral vitamin D and falls and fractures in older women: a	RCT	2256 (1131/1125)

	randomized controlled trial. JAMA 2010; 303:1815-22 [18]		
9	Bischoff-Ferrari HA, Dawson-Hughes B, Orav EJ et al. Monthly high-dose vitamin D treatment for the prevention of functional decline: a randomized clinical trial. JAMA Intern Med 2016;176:175-83 [28]	RCT	200 (67/133)

- **일차연구문헌 근거표**

Author, Publication year	**Sanders KM, et al.** **JAMA 2010;303:1815–22.**
Title	Annual high-dose oral vitamin D and falls and fractures in older women: a randomized controlled trial.
Methods	A double-blind, placebo-controlled trial
Participants	**N= 2256 (중재군/비교군= 1131/1125)** ▸**Inclusion criteria** - Patients were eligible if they were between 18 and 65 years of age and had a diagnosis of rheumatoid arthritis as

	defined by the revised American College of Rheumatology criteria, serum creatinine level less than 176.8 μmol/L, and normal liver function. ▸**Exclusion criteria** - Patients were excluded if they were receiving an anticonvulsant medication, hydrochlorothiazide, bisphosphonates, fluoride, calcitonin, or calcitriol or if they had a history of malabsorption, hyperparathyroidism, immobilization, metabolic bone disease, or thyroid disease with an abnormal thyroid-stimulating hormone
Interventions	▸(중재군) - 500,000 IU of cholecalciferol orally once a year ▸(비교군) - placebo
Outcomes	▸**Primary outcome:** - fall and fractures ▸**Secondary outcomes:** - serum 25-hydroxycholecalciferol and parathyroid hormone levels ▸추적기간 - 12 months
Results	▸Women in the cholecalciferol (vitamin D) group had 171 fractures vs 135 in the placebo group ▸837 women in the vitamin D group fell 2892 times (rate, 83.4 per 100 person-years) while 769 women in the placebo group fell 2512 times (rate, 72.7 per 100 person-years; incidence rate ratio [RR], 1.15; 95%

	confidence interval [CI], 1.02-1.30; P = .03). ▸The incidence RR for fracture in the vitamin D group was 1.26 (95% CI, 1.00-1.59; P = 0.047) vs the placebo group (rates per 100 person-years, 4.9 vitamin D vs 3.9 placebo). A temporal pattern was observed in a post hoc analysis of falls. ▸The incidence RR of falling in the vitamin D group vs the placebo group was 1.31 in the first 3 months after dosing and 1.13 during the following 9 months (test for homogeneity; P = .02). ▸In the substudy, the median baseline serum 25-hydroxycholecalciferol was 49 nmol/L. Less than 3% of the substudy participants had 25-hydroxycholecalciferol levels lower than 25 nmol/L. In the vitamin D group, 25-hydroxycholecalciferol levels increased at 1 month after dosing to approximately 120 nmol/L, were approximately 90 nmol/L at 3 months, and remained higher than the placebo group 12 months after dosing.

Author, Publication year	**Bischoff-Ferrari HA, et al.** **JAMA Intern Med 2016;176:175-83.**
Title	Monthly high-dose vitamin D treatment for the prevention of functional decline: a randomized clinical trial.
Methods	double-blind, randomized clinical trial

Participants	**N= 200 (중재군/비교군= 133/67)** ▸**Inclusion criteria** - maintaining mobility with or without a walking aid, having the ability to use public transportation to attend the clinic visits, and scoring at least 27 on the Mini-Mental State Examination to ensure that participants understood the study procedures and voluntarily agreed to participate by providing written informed consent. ▸**Exclusion criteria** - supplemental vitamin D use exceeding 800 IU/d and unwillingness to discontinue additional calciumandvitaminDsupplementation
Interventions	▸(중재군) - receiving 60,000 IU of vitamin D3 (60,000 IU group) monthly (n=67) - receiving 24,000 IU of vitamin D3 plus 300 μg of calcifediol (24,000 IU plus calcifediol group) monthly (n=66) ▸(비교군) - 24,000 IU of vitamin D3 (24,000 IU group) monthly (n=67)
Outcomes	▸**Primary outcome:** - improving lower extremity function (on the Short Physical Performance Battery) and achieving 25-hydroxyvitamin D levels of at least 30 ng/mL at 6 and 12 months ▸**Secondary outcomes:** - monthly reported falls. Analyses were adjusted for age, sex, and body mass index.

	▸추적기간 - 12 months
Results	▸Intent-to-treat analyses showed that, while 60,000 IU and 24,000 IU plus calcifediol were more likely than 24,000 IU to result in 25-hydroxyvitamin D levels of at least 30 ng/mL (P = .001), they were not more effective in improving lower extremity function, which did not differ among the treatment groups (P=0.26). ▸However, over the 12-month follow-up, the incidence of falls differed significantly among the treatment groups, with higher incidences in the 60,000 IU group (66.9%; 95% CI, 54.4% to 77.5%) and the 24,000 IU plus calcifediol group (66.1%; 95% CI, 53.5%-76.8%) group compared with the 24,000 IU group (47.9%; 95% CI, 35.8%-60.3%) (P = .048). ▸Consistent with the incidence of falls, the mean number of falls differed marginally by treatment group. ▸The 60,000 IU group (mean, 1.47) and the 24,000 IU plus calcifediol group (mean, 1.24) had higher mean numbers of falls compared with the 24,000 IU group (mean, 0.94) (P =0.09).

▣ 핵심질문 3-2.

40세 이상 성인에서 비스포스포네이트 사용은 글루코코르티코이드 유발 골다공증 예방과 치료에 효과적인가?

▣ PICO

Patients	Intervention	Comparators	Outcomes
40세 이상 성인	비스포스포네이트		글루코코르티코이드 유발 골다공증 예방과 치료효과

▣ 권고비교표

	지침 1 (ACR)	지침 2 (IOF-ECTS)	지침 3 (Canada)	지침 4 (Canada)	지침5(NOGG)
출판년도	2017	2012	2014	2010	2017
AGREE 평가점수	89	67	56	44	67
권고문	1) Women ≥40 years of age and not of	1) Bone-protective treatment should be	1) Postmenopausal women and men older	1) For individuals over age 50 who are on	1) Women and men age ≥70 years with a

	childbearing potential and men ≥40 years of age (Figure 3) who are at moderate to high risk of fracture should be treated with an oral bisphosphonate. 2) For patients in whom oral bisphosphonates are not appropriate (for example, due to comorbidities, patient preference, or concerns about adherence with an oral medication regimen), IV bisphosphonates should be used rather than the patient receiving no additional treatment beyond	started at the onset of glucocorticoid therapy in patients at increased risk of fracture. 2) Alendronate, etidronate, risedronate, zoledronic acid and teriparatide are the front-line therapeutic options for the majority of patients.	than 50 years of ages hould be considered at high risk for fractures and therefore eligiblefor osteoporosis drug therapy if they meet the following criteria - history of bone frailty fracture after 50 years of age - T-score ≤ −2.5 at the lumbar spine and/or femur - age ≥ 70 years, since in this age group FRAX® scores evaluating the fracture risk are similar in women starting glucocorticoid	long-term glucocorticoid therapy (≥ three months cumulative therapy during the preceding year at a prednisone equivalent dose ≥ 7.5 mg daily), a bisphosphonate (alendronate,risedronate, zoledronic acid) should be initiated at the outset and should be continued for at least the duration of the glucocorticoid therapy 2) For long-term glucocorticoid users who are intolerant of first line therapies, calcitonin or etidronate	previous fragility fracture, or taking high doses of glucocorticoids (≥7.5 mg/day prednisolone), should be considered for bone protective therapy. 2) Bone-protective treatment should be started at the onset of glucocorticoid therapy in individuals at high risk of racture. 3) Alendronate and risedronate are first line treatment options. Where these are contraindicated or not tolerated, zoledronic acid or

	calcium and vitamin D.		therapy and in women with a history of fracture - long-term high dose glucocorticoid therapy (≥7.5mg/d prednisone equivalent for longer than 3 months); selection of this dose cutoff is based on its use in most clinical trials as aninclusion criterion and on epidemiological data showing that the relative risk of vertebral fracture increases from 2.6 with dosesof 2.5 to 7.5 mg/d to 5.2	may be considered for preventing loss of bone mineral density	teriparatide are alternative options

			with doses > 7.5 mg/d 2) Among bisphosphonates, zoledronic acid or risedronate is always an appropriate choice		
근거수준, 권고등급	I, A	I, A	I, A	I, A	I, A

▣ 근거 내용 정리

[지침1] ACR 2017

- **Reference**

	문헌정보	연구유형	연구대상자수 (치료군/비교군)
1	Saag KG, Emkey R, Schnitzer TJ, Brown JP, Hawkins F, Goemaere S, et al.	RCT	

	Alendronate for the prevention and treatment of glucocorticoid-induced osteoporosis. Glucocorticoid-Induced Osteoporosis Intervention Study Group. N Engl J Med. 1998;339(5):292-299 [29]		477 (318/159)
2	Wallach S, Cohen S, Reid DM, Hughes RA, Hosking DJ, Laan RF, et al. Effects of risedronate treatment on bone density and vertebral fracture in patients on corticosteroid therapy. Calcif Tissue Int. 2000;67(4):277-285 [30]	RCT	509 (339/170)
3	Adachi JD, Saag KG, Delmas PD, Liberman UA, Emkey RD, Seeman E, et al. Two-year effects of alendronate on bone mineral density and vertebral fracture in patients receiving glucocorticoids: a randomized, double-blind, placebo-controlled extension trial. Arthritis Rheum. 2001;44(1):202-211 [31]	RCT	208 (147/ 61)
4	Lems WF, Lodder MC, Lips P, Bijlsma JW, Geusens P, Schrameijer N, et al. Positive effect of alendronate on bone mineral density and markers of bone turnover in patients with rheumatoid arthritis on chronic treatment with low-dose prednisone: a randomized, double-blind, placebo-controlled trial. Osteoporos Int. 2006;17(5):716-723 [32]	RCT	163 (94/69)
5	Yamada S, Takagi H, Tsuchiya H, Nakajima T, Ochiai H, Ichimura A, et al. Comparative studies on effect of risedronate and alfacalcidol against glucocorticoid-induced osteoporosis in rheumatoid arthritic patients. Yakugaku Zasshi. 2007;127(9):1491-1496 [33]	Comparative studies	1 2 (6 /6)

6	N S, R R. The effect of bisphosphonate on prevention of glucocorticoid-induced osteoporosis. IRCMJ. 2008;10(1):8-11 [35]	prospective clinical trial	72 (36/36)
7	Stoch SA, Saag KG, Greenwald M, Sebba AI, Cohen S, Verbruggen N, et al. Once-weekly oral alendronate 70 mg in patients with glucocorticoid-induced bone loss: a 12-month randomized, placebo-controlled clinical trial. J Rheumatol. 2009;36(8):1705-1714 [36]	RCT	173 (114/59)
8	Tee SI, Yosipovitch G, Chan YC, Chua SH, Koh ET, Chan YH, et al. Prevention of glucocorticoid-induced osteoporosis in immunobullous diseases with alendronate: a randomized, double-blind, placebo-controlled study. Arch Dermatol. 2012;148(3):307-314 [37]	RCT	44 (22/22)
9	Hakala M, Kroger H, Valleala H, Hienonen-Kempas T, Lehtonen-Veromaa M, Heikkinen J, et al. Once-monthly oral ibandronate provides significant improvement in bone mineral density in postmenopausal women treated with glucocorticoids for inflammatory rheumatic diseases: a 12-month, randomized, double-blind, placebo-controlled trial. Scand J Rheumatol. 2012;41(4):260-266 [38]	RCT	140 (68/72)
10	Wells GA, Cranney A, Peterson J, Boucher M, Shea B, Robinson V, et al. Alendronate for the primary and secondary prevention of osteoporotic fractures in postmenopausal women. Cochrane Database Syst Rev. 2008(1):CD001155 [39]	SR	

11	Wells G, Cranney A, Peterson J, Boucher M, Shea B, Robinson V, et al. Risedronate for the primary and secondary prevention of osteoporotic fractures in postmenopausal women. Cochrane Database Syst Rev. 2008(1):CD004523 [40]	SR	
12	Hopkins RB, Goeree R, Pullenayegum E, Adachi JD, Papaioannou A, Xie F, et al. The relative efficacy of nine osteoporosis medications for reducing the rate of fractures in post-menopausal women. BMC Musculoskelet Disord. 2011;12:209 [41]	SR	
13	Reid DM, Devogelaer JP, Saag K, Roux C, Lau CS, Reginster JY, et al. Zoledronic acid and risedronate in the prevention and treatment of glucocorticoid-induced osteoporosis (HORIZON): a multicentre, double-blind, double-dummy, randomised controlled trial. Lancet. 2009;373(9671):1253-1263 [54]	RCT	833 (416 / 417)

- **일차연구문헌 근거표**

Author, Publication year	**Saag KG et al.** **N Engl J Med. 1998 Jul 30;339(5):292-9.**

Title	Alendronate for the Prevention and Treatment of Glucocorticoid-Induced Osteoporosis
Methods	randomized, placebo-controlled studies, multicenter
Participants	**N= (중재군/비교군=318/ 159)** ▸**Inclusion criteria** - Men; pre-menopausal women; post-menopausal women NOS; - steroid>7.5mg/d; prevalent steroid use at least 3 mon; - polymyalgia rheumatica; inflammatory bowel disease; asthma or COPD; rheumatoid arthritis; SLE; nephropathy/nephritis (not SLE or vasculitis); sarcodosis; Pemphigus; Inflammatory myopathy; Giant cell arteritis; Myasthenia Gravis ▸**Exclusion criteria** - pregnancy; cardiovascular disease; renal insufficiency; - gastrointestinal disease; upper GI disease; bisphosphonates; calcitonin; fluoride; Vitamin D deficiency
Interventions	▸(중재군) Alendronate 5mg daily + 800 to 1000 mg of elemental calcium daily + 250 to 500 IU of vitamin D daily. (n=161) Alendronate 10mg daily + 800 to 1000 mg of elemental calcium daily + 250 to 500 IU of vitamin D daily. (n=157) ▸(비교군) Placebo + 800 to 1000 mg of elemental calcium daily + 250 to 500 IU of vitamin D daily.

Outcomes	▸**Primary outcome:** the difference in the mean percent change in lumbar-spine bone density from base line to week 48 between the groups ▸**Secondary outcomes:** changes in bone density of the hip, biochemical markers of bone turnover, and the incidence of new vertebral fractures. ▸**추적기간** - 48-week
Results	▸The mean (+/-SE) bone density of the lumbar spine increased by 2.1+/-0.3 percent and 2.9+/-0.3 percent, respectively, in the groups that received 5 and 10 mg of alendronate per day (P<0.001) and decreased by 0.4+/-0.3 percent in the placebo group ▸The femoral-neck bone density increased by 1.2+/-0.4 percent and 1.0+/-0.4 percent in the respective alendronate groups (P<0.01) and decreased by 1.2+/-0.4 percent in the placebo group (P<0.01). The bone density of the trochanter and total body also increased significantly in the patients treated with alendronate. ▸There were proportionally fewer new vertebral fractures in the alendronate groups (overall incidence, 2.3 percent) than in the placebo group (3.7 percent) (relative risk, 0.6; 95 percent confidence interval, 0.1 to 4.4).

Author, Publication year	**Wallach S. et al.** **Calcif Tissue Int. 2000;67(4):277-285.**
Title	Effects of risedronate treatment on bone density and vertebral fracture in patients on corticosteroid therapy.
Methods	randomized, placebo-controlled studies
Participants	**N= 509 (중재군/비교군= 339/ 170)** ▸**Inclusion criteria** - ambulatory men and women, 18–85 years of age and receiving moderate-to-high doses of (equivalent to 7.5 mg prednisone daily or greater) oral corticosteroid therapy. The patients were expected to continue on corticosteroid therapy for at least 12 months - rheumatoid arthritis, polymyalgia rheumatica, temporal arteritis, chronic interstitial lung disease, chronic obstructive pulmonary disease, asthma, systemic lupus erythematosus, polymyositis, vasculitis, Behcet's disease, and a variety of skin diseases. ▸**Exclusion criteria** - evidence of metabolic bone disease other than CIO, recent use of HRT (within 1 year of enrollment) or other drugs known to affect bone metabolism, and any significant organic or psychiatric disease that could affect participation or interfere with the interpretation of the data.
Interventions	▸(중재군) - Risedronate 2.5mg + 500-1,000mg Calcium daily + 400 IU Vit D daily (n=165)

	- Risedronate 5mg + 500-1,000mg Calcium daily + 400 IU Vit D daily (n=174) ▸(비교군) - Placebo + 500-1,000mg Calcium daily + 400 IU Vit D daily
Outcomes	▸**Primary outcome:** - the difference between the placebo and active groups in lumbar spine bone mineral density (BMD) at 1 year ▸**Secondary outcomes:** - changes in BMD at other sites, biochemical markers of bone turnover, and the incidence of vertebral fractures ▸**추적기간** - 1 year
Results	▸The mean (SE) lumbar spine BMD increased 1.9 +/- 0.38% from baseline in the risedronate 5 mg group ($P < 0.001$) and decreased 1.0 +/- 0.4% in the placebo group ($P = 0.005$). BMD at the femoral neck, trochanter, and distal radius increased or was maintained with risedronate 5 mg treatment, but decreased in the placebo group. Midshaft radius BMD did not change significantly in either treatment group. ▸The 2.5 mg dose also had a positive effect on BMD, although of a lesser magnitude than that seen with risedronate 5 mg. ▸A significant reduction of 70% in vertebral fracture risk was observed in the risedronate 5 mg group compared with the placebo group ($P = 0.01$).

Author, Publication year	**Adachi JD. et al.** **Arthritis Rheum. 2001;44(1):202-211.**
Title	Two-year effects of alendronate on bone mineral density and vertebral fracture in patients receiving glucocorticoids: a randomized, double-blind, placebo-controlled extension trial.
Methods	randomized, double-blind, placebo-controlled extension trial, multicenter
Participants	**N= 208 (중재군/비교군= 147/61)** ▸**Inclusion criteria** - Men; pre-menopausal women; post-menopausal women NOS; - steroid>7.5mg/d; steroid duration<1; - polymyalgia rheumatic; inflammatory bowel disease; asthma or COPD; rheumatoid arthritis; SLE; nephropathy/nephritis (not SLE or vasculitis) ▸**Exclusion criteria** - Pregnancy; metabolic bone disorder other than osteoporosis (e.g.,Paget's, renal osteodystrophy, osteomalacia); - renal insufficiency; gastrointestinal disease; upper GI; - bisphosphonates; calcitonin; fluoride

Interventions	▸(중재군) - Alendronate 5mg daily + 800-1,000 mg Calcium daily +250-500 IU Vit D daily (n=63) - Alendronate 10mg daily + 800-1,000 mg Calcium daily +250-500 IU Vit D daily (n=55) - Alendronate 2.5mg daily switch to10mg daily + 800-1,000 mg Calcium daily +250-500 IU Vit D daily (n=29) ▸(비교군) - Placebo + 800-1,000 mg Calcium daily +250-500 IU Vit D daily
Outcomes	▸**Primary outcome:** - the mean percentage change in lumbar spine bone mineral density (BMD) from baseline to 24 months. ▸**Secondary outcomes:** - changes in hip and total body BMD, biochemical markers of bone turnover, radiographic joint damage of the hands, and vertebral fracture incidence. ▸**추적기간** - 2 year
Results	▸The mean (+/-SEM) lumbar spine BMD increased by 2.8 +/- 0.6%, 3.9 +/- 0.7%, and 3.7 +/- 0.6%, respectively, in the groups that received 5 mg, 10 mg, and 2.5/10 mg of ALN daily (P < or = 0.001) and decreased by -0.8 +/- 0.6% in the placebo group (P not significant) over 24 months. ▸In patients receiving any dose of ALN, BMD was increased at the trochanter (P < or = 0.05) and maintained at the femoral neck. Total body BMD was increased in patients receiving 5 or 10 mg

	ALN (P < or = 0.01). These 2 dose levels of ALN were more effective than placebo at all sites (P < or = 0.05). ▸Bone turnover markers (N-telopeptides of type I collagen and bone-specific alkaline phosphatase) decreased 60% and 25%, respectively, during treatment with ALN (P < or = 0.05). ▸There were fewer patients with new vertebral fractures in the ALN group versus the placebo group (0.7% versus 6.8%; P = 0.026).

Author, Publication year	**Lems WF. et al.** **Osteoporos Int. 2006;17(5):716-723.**
Title	Positive effect of alendronate on bone mineral density and markers of bone turnover in patients with rheumatoid arthritis on chronic treatment with low-dose prednisone: a randomized, double-blind, placebo-controlled trial
Methods	randomized, double-blind, placebo-controlled trial
Participants	**N= 163 (중재군/비교군= 94/69)** ▸**Inclusion criteria** - Men; pre-menopauaal women; post-menopausal women NOS; - prevalent steroid use at least 3 mon; rheumatoid arthritis; ≤10mg pred; ▸**Exclusion criteria**

	- metabolic bone disorder other than osteoporosis (e.g. Paget's, renal osteodystrophy, osteomalacia); Upper GI; hormone use: HRT; Medications that affect bone metabolism
Interventions	▸(중재군) - Alendronate 10mg daily + 500mg or 1,000mg Calcium daily + 400 IU Vit D daily ▸(비교군) - Placebo + 500mg or 1,000mg Calcium daily + 400 IU Vit D daily
Outcomes	▸**Primary outcome:** - the difference between the groups in percentage change from baseline to 12 months in lumbar spine BMD ▸**Secondary outcomes:** - percentage changes from baseline of total hip, femoral neck, trochanter, markers of bone turnover and the incidence of peripheral and vertebral fractures. ▸**추적기간** - 12 months
Results	▸BMD at the lumbar spine had increased by 3.7% in the alendronate-treated patients and decreased by -1.0% in the placebo-treated patients ($p<0.0001$); at the hip, the changes were +1.0% and –0.1%, respectively (not significant).

	▸After 3 months, serum BAP had decreased by 16.9% in the alendronate group versus 3.3% in the placebo group (p=0.0005), while urinary NTX had decreased by 46.4% in the alendronate group versus 12.1% in the placebo group (p<0.0001). ▸After 12 months, no statistically significant difference was found between the groups with respect to number of patients with incident vertebral or non-vertebral fractures.

Author, Publication year	**Yamada S. et al.** **Yakugaku Zasshi. 2007;127(9):1491-1496**
Title	Comparative studies on effect of risedronate and alfacalcidol against glucocorticoid-induced osteoporosis in rheumatoid arthritic patients.
Methods	randomized, camparative study
Participants	**N= 12 (중재군/비교군= 6 / 6)** ▸**Inclusion criteria** - Women otherwise undefined; osteoporosis T-score<=-2.5spine; any steroid dose; steroid duration not defined; rheumatoid arthritis ▸**Exclusion criteria** - Bisphosphonates; medication that affect calcium metabolism and phosphate

Interventions	▸(중재군) - Risedronate 2.5 mg/day+ Calcium 800mg/day ▸(비교군) - alfacalcidiol 0.5 mcg/day + Calcium 800mg/day
Outcomes	▸**Primary outcome:** - Bone mineral density at 12, 24 and 48 weeks after treatment ▸**Secondary outcomes:** - the biochemical markers of bone turnover at 12, 24 and 48 weeks after treatment ▸**추적기간** - 48 weeks
Results	▸The BMD values 12, 24 and 48 weeks after treatment with risedronate increased by 3.9%, 4.1% and 5.2%, respectively, which were significantly higher than those after treatment with alfacalcidol (2.8%, 2.1% and 2.5%, respectively). ▸Urinary excretion of N-telopeptides of type I collagen and deoxypyridinoline after risedronate treatment were more significantly decrease than that after alfacalcidol treatment.

Author, Publication year	**N Saadati and R Rajabian** **IRCMJ. 2008;10(1):8-11.**
Title	The effect of bisphosphonate on prevention of glucocorticoid-induced osteoporosis.
Methods	prospective clinical trial
Participants	**N= 72 (중재군/비교군= 36/36)** ▸**Inclusion criteria** - high dose of glucocorticoid (30-80 mg/day) - autoimmune disease such as SLE, Polymyositis, or Dermatomyositis ▸**Exclusion criteria** - NA
Interventions	▸(중재군) - oral vitamin-D, 50000 IU twice weekly, calcium, 500 mg twice daily, and alendronate, 10 mg per day. (group2) ▸(비교군) - oral vitamin-D, 50000 IU twice weekly and calcium 500 mg twice daily. (group1)
Outcomes	▸**Primary outcome:** - Change of BMD in the lumbar spine after 18 month ▸**Secondary outcomes:** - Change in femoral neck BMD after 18 month

	▸**추적기간** - 18 months
Results	▸Change of BMD in the lumbar spine after 18 months of therapy was -1/67% and +2.4% in groups 1 and 2, respectively. ▸Change in femoral neck BMD was -2.1% in group 1 and +1.8% in group 2.

Author, Publication year	**Stoch SA. et al.** **J Rheumatol. 2009;36(8):1705-1714.**
Title	Once-weekly oral alendronate 70 mg in patients with glucocorticoid-induced bone loss: a 12-month randomized, placebo-controlled clinical trial.
Methods	multicenter, randomized, placebo-controlled clinical trial.
Participants	**N= 173 (중재군/비교군= 114/59)** ▸**Inclusion criteria** - Adults ≤ 80 years of age who were taking a mean of ≥ 7.5 mg/day of oral prednisone (or equivalent) and were considered by the site investigator to be highly likely to require oral glucocorticoid treatment for≥ 12 consecutive months were eligible to participate.

	- serum 25-hydroxyvitamin D [25(OH)D] levels > 15 ng/ml (37.4 nmol/l). - lumbar spine anatomy suitable for dual-energy x-ray absorptiometry (DEXA), and hip and lumbar spine BMD T-score more than 2.5 SD below the sex-matched, young adult reference mean (T-score < –2.5). ▸**Exclusion criteria** - prior vertebral or osteoporotic fractures with certain - malignancies, recent major upper gastrointestinal (GI) disease (e.g., significant upper GI bleeding, recurrent ulcer disease, esophageal or gastric varices, esophageal stricture, achalasia, or severe esophageal motor dysfunction), myocardial infarction, or pregnancy. - unwilling to take either calcium or vitamin D supplements - those with a history of alcohol or drug abuse
Interventions	▸(중재군) - alendronate 70 mg once weekly + 1,000mg Calcium daily + 400 IU Vit D daily ▸(비교군) - Placebo + 1,000mg Calcium daily + 400 IU Vit D daily
Outcomes	▸**Primary outcome:** - the percentage change from baseline in posterior-anterior BMD of the lumbar spine at Month 12, and the safety and tolerability profile of ALN OW through 12 months.

	▸**Secondary outcomes:** - percentage change from baseline in hip, femoral neck, trochanter, total hip, and total body BMD at 12 months, and the effects of ALN OW after 12 months on biochemical markers of boneturnover (NTX, BSAP). ▸**추적기간** - 12 months
Results	▸At 12 months, there was a significant mean percentage increase from baseline in the ALN OW group for lumbar spine (2.45%), trochanter (1.27%), total hip (0.75%), and total body (1.70%) bone mineral density (BMD). ▸Comparing ALN OW versus placebo at 12 months, a significant treatment difference for the mean percentage change from baseline was observed for lumbar spine (treatment difference of 2.92%; p </= 0.001), trochanter (treatment difference 1.66%; p = 0.007), and total hip (treatment difference 1.19; p = 0.008) BMD. ▸Biochemical markers of bone remodeling also showed significant mean percentage decreases from baseline.

Author, Publication year	**Tee SI. et al.**

	Arch Dermatol. 2012;148(3):307-314.
Title	Prevention of glucocorticoid-induced osteoporosis in immunobullous diseases with alendronate: a randomized, double-blind, placebo-controlled study.
Methods	randomized, double-blind, placebo-controlled trial
Participants	**N= 44 (중재군/비교군= 22/22)** **▸Inclusion criteria** - Patients who were newly diagnosed as having an immunobullous disease, including bullous pemphigoid and pemphigus, were eligible for participation if they were considered by study investigators to be highly likely to require long-term systemic glucocorticoid therapy (>6 months) **▸Exclusion criteria** - concurrent treatment with medications known to have an effect on osteoporosis (eg, hormone replacement, oral contraceptives, selective estrogen receptor modulators, cyclosporine, warfarin, and antiepileptic drugs); - a history of allergy or an absolute contraindication to alendronate (eg, pregnant patients); - a contraindication to use of calcium plus vitamin D (eg, a history of renal calculi or hypercalcemia); - a history of upper gastrointestinal tract disorders (eg, dysphagia, peptic ulcer disease); - a low testosterone state (eg, chronic alcoholism, Klinefelter syndrome); - an active endocrine disorder that can induce osteoporosis (eg, thyrotoxicosis); - prior vertebral or osteoporotic fractures; -a history of alcohol or drug abuse.

Interventions	▸(중재군) - alendronate (10mg/day) + Calcium + Vit D ▸(비교군) - Placebo + Calcium + Vit D
Outcomes	▸**Primary outcome:** - the percent change in both lumbar spine and femoral neck bone densities at 12 months compared with baseline. ▸**Secondary outcomes:** - the change in hl-ALP levels at 12 months, the presence of new clinical or radiologic fractures, and any significant adverse events encountered during the study. ▸**추적기간** - 12 months
Results	▸The percent change in BMD in the alendronate group was +3.7% and +3.5% at the lumbar spine and the femoral neck, respectively, whereas in the placebo group, it was -1.4% and -0.7% at the lumbar spine and the femoral neck, respectively. ▸The increase in BMD observed in the alendronate group compared with the placebo group was statistically significant at both the lumbar spine (P = .01) and the femoral neck (P = .01). ▸There was also a statistically significant decrease in serum heat-labile alkaline phosphatase levels

	after 12 months (-32.6%, P < .01) in the alendronate group but not in the placebo group.

Author, Publication year	**Hakala M. et al.** **Scand J Rheumatol. 2012;41(4):260-266.**
Title	Once-monthly oral ibandronate provides significant improvement in bone mineral density in postmenopausal women treated with glucocorticoids for inflammatory rheumatic diseases: a 12-month, randomized, double-blind, placebo-controlled trial.
Methods	randomized, double-blind, placebo-controlled, parallel-group study
Participants	**N= 140 (중재군/비교군= 68/72)** ▸**Inclusion criteria** -Women aged 50–85 years, ≥ 1 year since menopause, with a normal or osteopaenic mean lumbar spine (LS; L1–L4) bone mineral density (BMD; T-score ≥ –2.0) and receiving treatment with 5–15 mg/day of prednisone equivalent -The other therapies for the rheumatic disease had to have been stable for 3 months prior to screening. ▸**Exclusion criteria** - clinical osteoporotic fractures (qualitative assessment of prevalent vertebral fractures)

	- conditions that may interfere with the evaluation of spinal or hip osteoporosis by dual-energy X-ray absorptiometry (DXA) such as two or more vertebral (L1–L4) fractures or other vertebral deformities - treatment with other drugs affecting bone metabolism within the past 6 months - previous treatment with an oral bisphosphonate within the past 6 months or previous treatment with intravenous - bisphosphonates at any time.
Interventions	▸(중재군) - oral ibandronate 150 mg monthly + 1,000mg Calcium daily + 800 IU Vit D daily ▸(비교군) Placebo + 1,000mg Calcium daily + 800 IU Vit D daily
Outcomes	▸**Primary outcome** - the relative change (%) in mean LS BMD from baseline to 12 months ▸**Secondary outcomes** - change (%) in mean LS BMD from baseline to 6 months - change (%) in total hip BMD from baseline to 6 and 12 months - changes (%) in serum levels of bone turnover markers C-terminal telopeptide of type I collagen (sCTX), N-terminal propeptide of type I procollagen (P1NP) and tartrate-resistant acid phosphatase (TRACP) from baseline to 1, 6, and 12 months. Blood samples for bone turnover markers were collected in fasting patients before study drug intake.

	- Difference in withdrawal rate due to worsening in BMD (BMD T-score at any site≤ –2.5 SD) at 6 months and/or worsening in BMD of at least 7% at any site at 6 months. **▸추적기간** - 12 months
Results	▸Mean LS BMD increased significantly by 2.6% and 3.2% from baseline to 6 and 12 months with ibandronate compared to 0.3% and -0.1% with placebo, respectively ($p < 0.001$). Comparable significant mean increases were also found in trochanter, femoral neck and total hip BMDs at 12 months. ▸Reductions in the serum levels of bone turnover markers C-terminal telopeptide of type I collagen (sCTX), N-terminal propeptide of type I procollagen (P1NP), and tartrate-resistant acid phosphatase (TRACP) were significantly more marked in the ibandronate group than in the placebo group at 1, 6, and 12 months.

Author, Publication year	**Lyles KW et al.** **N Engl J Med. 2007;357(18):1799-1809.**
Title	Zoledronic acid and clinical fractures and mortality after hip fracture.
Methods	multicenter, randomized, double-blind, placebo-controlled trial,

Participants	**N= 2127 (중재군/비교군= 1065 / 1062)** ▸**Inclusion criteria** - Men and women 50 years of age or older were eligible for inclusion within 90 days after surgical repair of a hip fracture sustained with minimal trauma (i.e., a fall from standing height or a lower height). Additional enrollment criteria included being ambulatory before the hip fracture and having both legs. ▸**Exclusion criteria** - previous hypersensitivity to a bisphosphonate, a potential for pregnancy, a calculated creatinine clearance of less than 30 ml per minute, a corrected serum calcium level of more than 11.0 mg per deciliter (2.8 mmol per liter) or less than 8.0 mg per deciliter (2.0 mmol per liter), active cancer, metabolic bone disease other than osteoporosis, and a life expectancy of less than 6 months in the investigator's judgment.
Interventions	▸(중재군) - zoledronic acid 5mg iv once a year + 1,000-1,500mg calcium + 800-1,200 IU Vit D ▸(비교군) - Placebo + 1,000-1,500mg calcium + 800-1,200 IU Vit D
Outcomes	▸**Primary outcome:** - a new clinical fracture, excluding facial and digital fractures and fractures in abnormal bone (e.g., bone containing metastases)

	▸**Secondary outcomes:** - the change in bone mineral density in the nonfractured hip, as measured annually with dual-energy x-ray absorptiometry; new vertebral, nonvertebral, and hip fractures; and prespecified safety end points, including death. ▸**추적기간** - 5 years
Results	▸The rates of any new clinical fracture were 8.6% in the zoledronic acid group and 13.9% in the placebo group, a 35% risk reduction with zoledronic acid (P=0.001); the respective rates of a new clinical vertebral fracture were 1.7% and 3.8% (P=0.02), and the respective rates of new nonvertebral fractures were 7.6% and 10.7% (P=0.03).

Author, Publication year	**Reid DM. et al.** **Lancet, 2009;373(9671):1253-1263.**
Title	Zoledronic acid and risedronate in the prevention and treatment of glucocorticoid-induced osteoporosis (HORIZON): a multicentre, double-blind, double-dummy, randomised controlled trial.
Methods	multicentre, double-blind, double-dummy, randomised controlled trial.
Participants	**N= 833 (중재군/비교군= 416 / 417)** ▸**Inclusion criteria**

	- Men; pre-menopausal women; post-menopausal women NOS; steroid>7.5mg/d; steroid duration<1mon; steroid duration 1-3mon; prevalent steroid use at least 3mon; polymyalgia rheumatica; asthma or COPD; rheumatoid arthritis; SLE ▸**Exclusion criteria** - age>85; pregnancy; carcinoma or suspected carcinoma; hyperparathyroidism; hypoparathyroidism; renal insufficiency; bisphosphonates; Medications that affect bone metabolism; serum 25-hydroxy-Vitamin D concentration <30 nmol/L
Interventions	▸(중재군) - zoledronic acid 5mg iv yearly + 1,000mg calcium daily + 400-1,200 IU Vit D daily (treatment arm, n=272) - zoledronic acid 5mg iv yearly + 1,000mg calcium daily + 400-1,200 IU Vit D daily (prevention arm, n=144) ▸(비교군) - Risedronate 5mg daily + 1,000mg calcium daily + 400-1,200 IU Vit D daily (treatment arm, n=273) - Risedronate 5mg daily + 1,000mg calcium daily + 400-1,200 IU Vit D daily (prevention arm, n=144)
Outcomes	▸**Primary outcome:** - percentage change from baseline in lumbar spine bone mineral density ▸**Secondary outcomes:** - Changes in bone turnover biomarker concentrations ▸**추적기간**

	- 1 year
Results	▸Zoledronic acid was non-inferior and superior to risedronate for increase of lumbar spine bone mineral density in both the treatment (least-squares mean 4.06% [SE 0.28] vs 2.71% [SE 0.28], mean difference 1.36% [95% CI 0.67-2.05], p=0.0001) and prevention (2.60% [0.45] vs 0.64% [0.46], 1.96% [1.04-2.88], p<0.0001) subgroups at 12 months.

[지침2] 2012 IOF-ECTS

- **Reference**

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1	Adachi JD, Saag KG, Delmas PD, Liberman UA, Emkey RD, Seeman E, Lane NE, Kaufman JM, Poubelle PE, Hawkins F, Correa-Rotter R, Menkes CJ, Rodriguez-Portales JA, Schnitzer TJ, Block JA, Wing J, McIlwain HH, Westhovens R, Brown J, Melo-Gomes JA, Gruber BL, Yanover MJ, Leite MO, Siminoski KG, Nevitt MC, Sharp JT, Malice MP, Dumortier T, Czachur M, Carofano W, Daifotis AG (2001) Two-year effects of alendronate on bone mineral density and vertebral fracture in patients receiving glucocorticoids: a randomized, double-	RCT	208 (147/61)

	blind, placebo-controlled extension trial. Arthritis Rheum 44:202–211 [31]		
2	de Nijs RN, Jacobs JW, Lems WF, Laan RF, Algra A, Huisman AM, Buskens E, de Laet CE, Oostveen AC, Geusens PP, Bruyn GA, Dijkmans BA, Bijlsma JW, Investigators STOP (2006) Alendronate or alfacalcidol in glucocorticoid-induced osteoporosis. N Engl J Med 355:675–684 [55]	RCT	201 (100/101)
3	Saag KG, Emkey R, Schnitzer TJ, Brown JP, Hawkins F, Goemaere S, Thamsborg G, Liberman UA, Delmas PD, Malice MP, Czachur M, Daifotis AG (1998) Alendronate for the prevention and treatment of glucocorticoid-induced osteoporosis. Glucocorticoid-Induced Osteoporosis Intervention Study Group. N Engl J Med 339:292–299 [29]	RCT	477 (318/159)
4	Stoch SA, Saag KG,Greenwald M, SebbaAI, Cohen S,Verbruggen N, Giezek H,West J, Schnitzer TJ (2009) Once-weekly oral alendronate 70mg in patients with glucocorticoid induced bone loss: a 12- month randomized, placebo-controlled clinical trial. J Rheumatol 36:1705–1714 [36]	RCT	173 (114/59)
5	Yilmaz L, Ozpran K, Gündüz OH, Ucan H, Yücel M (2001) Alendronate in rheumatoid arthritis patients treated with methotrexate and glucocorticoids. Rheumatol Int 20:65–69 [56]	RCT	70 (50/20)
6	Adachi JD, Bensen WG, Brown J, Hanley D, Hodsman A, Josse R, Kendler DL, Lentle B, Olszynski W, Ste-Marie LG, Tenenhouse A, Chines AA (1997) Intermittent etidronate therapy	RCT	141 (67/74)

	to prevent corticosteroid-induced osteoporosis. N Engl J Med 337:382–387 [43]		
7	Cortet B, Hachulla E, Barton I, Bonvoisin B, Roux C (1999) Evaluation of the efficacy of etidronate therapy in preventing glucocorticoid-induced bone loss in patients with inflammatory rheumatic diseases. Rev Rheumatol 66:214–219 [57]	RCT	83
8	Geusens P, Dequecker J, Vanhoof J, Stalmans R, Boonen S, Joly J, Nijs J, Raus J (1998) Cyclical etidronate increases bone density in the spine and hip of postmenopausal women receiving long term corticosteroid treatment. A double blind, randomised placebo controlled study. Ann Rheum Dis 57:724–727 [58]	RCT	37 (19/18)
9	Jenkins EA, Walker-Bone KE, Wood A, McCrae FC, Cooper C, Cawley MI (1999) The prevention of corticosteroid-induced bone loss with intermittent cyclical etidronate. Scand J Rheumatol 28:152–156 [59]	prospective study	28 (15/13)
10	Jinnouchi Y (2000) Efficacy of intermittent etidronate therapy for corticosteroid-induced osteoporosis in patients with diffuse connective tissue disease. Kurume Med J 47:219–224 [60]	comparative study	25 (16/9)
11	Mulder H, Struys A (1994) Intermittent cyclical etidronate in the prevention of corticosteroid induced bone loss. Br J Rheumatol 33:348–350 [61]	prospective study	2 0 (10/10)
12	Pitt P, Li F, Todd P, Webber D, Pack S, Moniz C (1998) A double blind placebo controlled study to determine the effects of intermittent cyclical etidronate on bone mineral density in	RCT	49 (26/23)

	patients on long term oral corticosteroid treatment. Thorax 53:351–356 [62]		
13	Roux C, Oriente P, Laan R, Hughes RA, Ittner J, Goemaere S, Di Munno O, Pouillès JM, Horlait S, Cortet B (1998) Randomized trial of effect of cyclical etidronate in the prevention of corticosteroid-induced bone loss. J Clin Endocrinol Metab 83:1128–1133 [63]	RCT	117 (59/58)
14	Skingle SJ, Crisp AJ (1994) Increased bone density in patients on steroids with etidronate. Lancet Infect Dis 344:543–544 [64]	RCT	38 (20/18)
15	Struys A, Snelder AA, Mulder H (1995) Cyclical etidronate reverses bone loss of the spine and proximal femur in patients with established corticosteroid-induced osteoporosis. Am J Med 99:235–242 [65]	RCT	25 (16/9)
16	Cohen S, Levy RM, Keller M, Boling E, Emkey RD, Greenwald M, Zizic TM, Wallach S, Sewell KL, Lukert BP, Axelrod DW, Chines AA (1999) Risedronate therapy prevents corticosteroidinduced bone loss: a twelve month, multicenter, randomized, double-blind, placebo-controlled, parallel-group study. Arthritis Rheum 42:2309–2318 [44]	RCT	228 (151/77)
17	Eastell R, Devogelaer J-P, Peel NFA, Chines AA, Bax DE, Sacco-Gibson N, Nagant de Deuxchaisnes C, Russell RG (2000) Prevention of bone loss with risedronate in glucocorticoid-treated rheumatoid arthritis patients. Osteoporos Int 11:331–337 [66]	RCT	120 (80/40)
18	Reid DM, Adami S, Devogelaer JP, Chines AA (2001) Risedronate increases bone density and reduces vertebral fracture risk within one year in men on corticosteroid therapy. Calcif	RCT	184 (124/ 60)

	Tissue Int 69:242–247 [67]		
19	Reid DM, Hughes RA, Laan RF, Sacco-Gibson NA, Wenderoth DH, Adami S, Eusebio RA, Devogelaer JP (2000) Efficacy and safety of daily risedronate in the treatment of corticosteroidinduced osteoporosis in men and women: a randomized trial. European Corticosteroid-Induced Osteoporosis Treatment Study. J Bone Miner Res 15:1006–1013 [68]	RCT	290 (194 /96)
20	Wallach S, Cohen S, Reid DM, Hughes RA, Hosking DJ, Laan RF, Doherty SM, Maricic M, Rosen C, Brown J, Barton I, Chines AA (2000) Effects of risedronate treatment on bone density and vertebral fracture in patients on corticosteroid therapy. Calcif Tissue Int 67:277–285 [30]	RCT	509 (339/170)
21	Reid DM, Devogelaer JP, Saag K, Roux C, Lau CS, Reginster JY, Papanastasiou P, Ferreira A, Hartl F, Fashola T, Mesenbrink P, Sambrook PN, HORIZON investigators (2009) Zoledronic acid and risedronate in the prevention and treatment of glucocorticoidinduced osteoporosis (HORIZON): a multicentre, double-blind, double-dummy, randomised controlled trial. Lancet 373:1253– 1263 [54]	RCT	833 (416/417)

- **일차연구문헌 근거표**

Author, Publication year	**Adachi JD. et al.** **Arthritis Rheum. 2001;44(1):202-211.**
Title	Two-year effects of alendronate on bone mineral density and vertebral fracture in patients receiving glucocorticoids: a randomized, double-blind, placebo-controlled extension trial.
Methods	randomized, double-blind, placebo-controlled extension trial, multicenter
Participants	**N= 208 (중재군/비교군= 147/61)** ▸**Inclusion criteria** - Men; pre-menopausal women; post-menopausal women NOS; - steroid>7.5mg/d; steroid duration<1; - polymyalgia rheumatic; inflammatory bowel disease; asthma or COPD; rheumatoid arthritis; SLE; nephropathy/nephritis (not SLE or vasculitis) ▸**Exclusion criteria** - Pregnancy; metabolic bone disorder other than osteoporosis (e.g.,Paget's, renal osteodystrophy, osteomalacia); - renal insufficiency; gastrointestinal disease; upper GI; - bisphosphonates; calcitonin; fluoride
Interventions	▸(중재군) - Alendronate 5mg daily + 800-1,000 mg Calcium daily + 250-500 IU Vit D daily (n=63) - Alendronate 10mg daily +800-1,000 mg Calcium daily + 250-500 IU Vit D daily (n=55)

	- Alendronate 2.5mg daily switch to 10mg daily + 800-1,000 mg Calcium daily + 250-500 IU Vit D daily (n=29) ▸(비교군) - Placebo + 800-1,000 mg Calcium daily + 250-500 IU Vit D daily
Outcomes	▸**Primary outcome:** - the mean percentage change in lumbar spine bone mineral density (BMD) from baseline to 24 months. ▸**Secondary outcomes:** - changes in hip and total body BMD, biochemical markers of bone turnover, radiographic joint damage of the hands, and vertebral fracture incidence. ▸**추적기간** - 2 year
Results	▸The mean (+/-SEM) lumbar spine BMD increased by 2.8 +/- 0.6%, 3.9 +/- 0.7%, and 3.7 +/- 0.6%, respectively, in the groups that received 5 mg, 10 mg, and 2.5/10 mg of ALN daily (P < or = 0.001) and decreased by -0.8 +/- 0.6% in the placebo group (P not significant) over 24 months. ▸In patients receiving any dose of ALN, BMD was increased at the trochanter (P < or = 0.05) and maintained at the femoral neck. Total body BMD was increased in patients receiving 5 or 10 mg ALN (P < or = 0.01). These 2 dose levels of ALN were more effective than placebo at all sites (P < or = 0.05).

	▸Bone turnover markers (N-telopeptides of type I collagen and bone-specific alkaline phosphatase) decreased 60% and 25%, respectively, during treatment with ALN (P < or = 0.05). ▸There were fewer patients with new vertebral fractures in the ALN group versus the placebo group (0.7% versus 6.8%; P = 0.026).

Author, Publication year	**de Nijs RN. et al.** **N Engl J Med. 2006 Aug 17;355(7):675-84**
Title	Alendronate or alfacalcidol in glucocorticoid-induced osteoporosis.
Methods	randomized, double-placebo, double-blind clinical trial
Participants	**N= 201 (중재군/비교군= 100/101)** **▸Inclusion criteria** - all racial and ethnic groups between the ages of 18 and 90 years who had a rheumatic disease and either were starting glucocorticoid therapy or had begun glucocorticoid therapy within the previous 12 weeks at a daily dose of at least 7.5 mg of prednisone or its equivalent. - The anticipated duration of glucocorticoid treatment was six months or more for all patients. **▸Exclusion criteria**

	- glucocorticoid treatment for longer than the previous 12 weeks; - therapy with hormone-replacement agents, anabolic steroids, calcitonin, active vitamin D3 analogues, fluoride, or bisphosphonates during the previous 12 months; - the presence of primary hyperparathyroidism, hyperthyroidism, or hypothyroidism in the year before the study began. - Patients who were pregnant or breast-feeding were excluded, as were patients with metabolic bone diseases, documented hypocalcemia or hypercalciuria, a creatinine clearance of less than 50 ml per minute, or a history of nephrolithiasis during the previous five years.
Interventions	▸(중재군) - alendronate (10 mg) + a placebo capsule of alfacalcidol daily ▸(비교군) - alfacalcidol (1 microg) + a placebo tablet of alendronate daily
Outcomes	▸**Primary outcome:** - the change in bone mineral density of the lumbar spine in 18 months ▸**Secondary outcomes:** - the incidence of morphometric vertebral deformities ▸**추적기간** - 18 months

Results	▸The bone mineral density of the lumbar spine increased by 2.1 percent in the alendronate group (95 percent confidence interval, 1.1 to 3.1 percent) and decreased by 1.9 percent in the alfacalcidol group (95 percent confidence interval, -3.1 to -0.7 percent). ▸At 18 months, the mean difference of change in bone mineral density between the two groups was 4.0 percent (95 percent confidence interval, 2.4 to 5.5 percent) ▸Three patients in the alendronate group had a new vertebral deformity, as compared with eight patients in the alfacalcidol group (of whom three had symptomatic vertebral fractures) (hazard ratio, 0.4; 95 percent confidence interval, 0.1 to 1.4).

Author, Publication year	**Saag KG et al.** **N Engl J Med. 1998 Jul 30;339(5):292-9.**
Title	Alendronate for the Prevention and Treatment of Glucocorticoid-Induced Osteoporosis
Methods	randomized, placebo-controlled studies, multicenter
Participants	**N= (중재군/비교군=318/ 159)** ▸**Inclusion criteria** - Men; pre-menopausal women; post-menopausal women NOS;

	- steroid>7.5mg/d; prevalent steroid use at least 3 mon; - polymyalgia rheumatica; inflammatory bowel disease; asthma or COPD; rheumatoid arthritis; SLE; nephropathy/nephritis (not SLE or vasculitis); sarcodosis; Pemphigus; Inflammatory myopathy; Giant cell arteritis; Myasthenia Gravis ▸**Exclusion criteria** - pregnancy; cardiovascular disease; renal insufficiency; - gastrointestinal disease; upper GI disease; bisphosphonates; calcitonin; fluoride; Vitamin D deficiency
Interventions	▸(중재군) - Alendronate 5mg daily + 800-1,000mg Calcium daily +250-500 IU Vit D daily (n=161) - Alendronate 10mg daily + 800-1,000mg Calcium daily +250-500 IU Vit D daily (n=157) ▸(비교군) - Placebo + 800-1,000mg Calcium daily +250-500 IU Vit D daily
Outcomes	▸**Primary outcome:** - the difference in the mean percent change in lumbar-spine bone density from base line to week 48 between the groups ▸**Secondary outcomes:** - changes in bone density of the hip, biochemical markers of bone turnover, and the incidence of new vertebral fractures.

	▸**추적기간** - 48-week
Results	▸The mean (+/-SE) bone density of the lumbar spine increased by 2.1+/-0.3 percent and 2.9+/-0.3 percent, respectively, in the groups that received 5 and 10 mg of alendronate per day (P<0.001) and decreased by 0.4+/-0.3 percent in the placebo group ▸The femoral-neck bone density increased by 1.2+/-0.4 percent and 1.0+/-0.4 percent in the respective alendronate groups (P<0.01) and decreased by 1.2+/-0.4 percent in the placebo group (P<0.01). The bone density of the trochanter and total body also increased significantly in the patients treated with alendronate. ▸There were proportionally fewer new vertebral fractures in the alendronate groups (overall incidence, 2.3 percent) than in the placebo group (3.7 percent) (relative risk, 0.6; 95 percent confidence interval, 0.1 to 4.4).

Author, Publication year	**Stoch SA. et al.** **J Rheumatol. 2009;36(8):1705-1714.**
Title	Once-weekly oral alendronate 70 mg in patients with glucocorticoid-induced bone loss: a 12-month randomized, placebo-controlled clinical trial.

Methods	multicenter, randomized, placebo-controlled clinical trial.
Participants	**N= 173 (중재군/비교군= 114/59)** ▸**Inclusion criteria** - Adults ≤ 80 years of age who were taking a mean of ≥ 7.5 mg/day of oral prednisone (or equivalent) and were considered by the site investigator to be highly likely to require oral glucocorticoid treatment for ≥ 12 consecutive months were eligible to participate. - serum 25-hydroxyvitamin D [25(OH)D] levels > 15 ng/ml (37.4 nmol/l). - lumbar spine anatomy suitable for dual-energy x-ray absorptiometry (DEXA), and hip and lumbar spine BMD T-score more than 2.5 SD below the sex-matched, young adult reference mean (T-score < –2.5). ▸**Exclusion criteria** - prior vertebral or osteoporotic fractures with certain - malignancies, recent major upper gastrointestinal (GI) disease (e.g., significant upper GI bleeding, recurrent ulcer disease, esophageal or gastric varices, esophageal stricture, achalasia, or severe esophageal motor dysfunction), myocardial infarction, or pregnancy. - unwilling to take either calcium or vitamin D supplements - those with a history of alcohol or drug abuse
Interventions	▸(중재군) - alendronate 70 mg once weekly + 1,000mg Calcium daily + 400 IU Vit D daily

	▸(비교군) - Placebo + 1,000mg Calcium daily + 400 IU Vit D daily
Outcomes	▸**Primary outcome:** - the percentage change from baseline in posterior-anterior BMD of the lumbar spine at Month 12, and the safety and tolerability profile of ALN OW through 12 months. ▸**Secondary outcomes:** - percentage change from baseline in hip, femoral neck, trochanter, total hip, and total body BMD at 12 months, and the effects of ALN OW after 12 months on biochemical markers of boneturnover (NTX, BSAP). ▸**추적기간** - 12 months
Results	▸At 12 months, there was a significant mean percentage increase from baseline in the ALN OW group for lumbar spine (2.45%), trochanter (1.27%), total hip (0.75%), and total body (1.70%) bone mineral density (BMD). ▸Comparing ALN OW versus placebo at 12 months, a significant treatment difference for the mean percentage change from baseline was observed for lumbar spine (treatment difference of 2.92%; p </= 0.001), trochanter (treatment difference 1.66%; p = 0.007), and total hip (treatment difference 1.19; p = 0.008) BMD. ▸Biochemical markers of bone remodeling also showed significant mean percentage decreases from

	baseline.

Author, Publication year	**Yilmaz L. et al.** **Rheumatol Int 20:65–69**
Title	Alendronate in rheumatoid arthritis patients treated with methotrexate and glucocorticoids.
Methods	multicenter, randomized, placebo-controlled clinical trial.
Participants	**N= 70 (중재군/비교군= 50/20)** **▸Inclusion criteria** - fifty RA patients classified according to ARA criteria were included. - the control group consisted of 20 postmenopausal osteoporotic patients. **▸Exclusion criteria** - history of anticonvulsant, thiazide diuretic, fluoridem calcitriol, or calcitonin treatment - history or presence of malabsorption, metabolic bone disease, and thyroid disease - immobilization

Interventions	▸(중재군) - all RA patients were started on MTX 7.5mg/week, 2.5mg daily folic acid, and 7.5mg daily prednisolone. - the first group: 25 femles - 10mg daily alendronate and 1000mg daily Ca - the second group : 25 females - 1000mg daily Ca ▸(비교군) - 20 female postmenopausal osteoporosis patients 10mg daily alendronate and 1000mg daily Ca
Outcomes	▸**Primary outcome:** - the BMD changes after 6 months ▸**Secondary outcomes:** - the changes of ALP, ASO, CRP, ESR, RF ▸**추적기간** - 6 months
Results	▸RA patients given only calcium had reduced mean BMD, and patients treated with alendronate and calcium showed incerased mean BMD almost in all regions. This increase was significant in the L2 and L1-4 total regions. ▸In postmenopausal osteoporotic patients, we saw statistically significant increases in BMD in all regions.

	▸The increase in BMD values in RA patients treated with aldendronate was smaller than in those of the control group of postmenopausal osteoporosis patients.

Author, Publication year	**Adachi JD et al.** **N Engl J Med 337:382–387**
Title	Intermittent etidronate therapy to prevent corticosteroid-induced osteoporosis.
Methods	randomized, placebo-controlled study
Participants	**N=141 (중재군/비교군= 67 /74)** **▸Inclusion criteria** - Ambulatory patients, 18 to 90 years of age, with a variety of diseases were eligible for the study if they had started high-dose therapy with prednisone or its equivalent within the previous 100 days and were expected to continue treatment for at least 1 year at a mean daily dose of 7.5 mg or greater for 90 days, with subsequent ongoing treatment at a mean daily dose of 2.5 mg or greater. **▸Exclusion criteria**

	- Patients were excluded if they had abnormalities on spinal radiographs that precluded accurate measurements of the lumbar spine with dual-energy x-ray absorptiometry, or if they had diseases or had taken medications known to affect bone metabolism within the preceding year. Patients were excluded if they had taken corticosteroids in the past.
Interventions	▸(중재군) - intermittent etidronate (400 mg per day for 14 days) followed by calcium (500 mg per day for 76 days), given for four cycles ▸(비교군) - intermittent etidronate (400 mg per day for 14 days) followed by calcium (500 mg per day for 76 days), given for four cycles
Outcomes	▸**Primary outcome:** - the difference in the change in the bone density of the lumbar spine between the groups from base line to week 52. ▸**Secondary outcomes:** - changes in the bone density of the femoral neck, trochanter, and radius and the rate of new vertebral fractures. ▸**추적기간** - 12 month

Results	▸The mean (±SE) bone density of the lumbar spine and trochanter in the etidronate group increased 0.61±0.54 and 1.46±0.67 percent, respectively, as compared with decreases of 3.23±0.60 and 2.74±0.66 percent, respectively, in the placebo group. ▸The mean differences between the groups after one year were 3.72±0.88 percentage points for the lumbar spine (P=0.02) and 4.14±0.94 percentage points for the trochanter (P=0.02). ▸The changes in the femoral neck and the radius were not significantly different between the groups. ▸There was an 85 percent reduction in the proportion of postmenopausal women with new vertebral fractures in the etidronate group as compared with the placebo group (1 of 31 patients vs. 7 of 32 patients, P=0.05), and the etidronate-treated postmenopausal women also had significantly fewer vertebral fractures per patient (P=0.04).

Author, Publication year	**Cortet B et al.** **Rev Rhum Engl Ed. 1999 Apr;66(4):214-9.**
Title	Evaluation of the efficacy of etidronate therapy in preventing glucocorticoid-induced bone loss in patients with inflammatory rheumatic diseases.

Methods	randomized placebo-controlled design
Participants	**N= 83** ▸**Inclusion criteria** - Men; women otherwise undefined; T-score<-1.0spine; - steroid>2.5mg/d; steroid>7.5mg/d; steroid duration <3mon; - polymyalgia rheumatica; rheumatoid arthritis; ▸**Exclusion criteria** - pregnancy; bisphosphonates; calcitonin; calcium (including antacids); fluoride; hormone use: estrogen agonists (including estrogen); hormone use: progestin; vitamin D; medications that affect calcium metabolism and phosphate
Interventions	▸(중재군) -Etidronate 400 mg/d for periods of 14 days separated by 76-day intervals during which patients took 500 mg of supplemental calcium per day. ▸(비교군) - Placebo + 500 mg Calcium daily
Outcomes	▸**Primary outcome:** - the change in lumbar spine bone mineral density after one year of etidronate therapy

	▸**Secondary outcomes:** **-** the change in femoral neck bone mineral density after one year of etidronate therapy - fracture ▸**추적기간** - 12 months
Results	▸Bone mineral density decreased by 1.94 +/- 0.61% in the placebo group and increased by 0.86 +/- 0.6% in the etidronate group, yielding a between-group difference of 2.8 +/- 0.86% (P = 0.002). ▸The difference was largest in postmenopausal women (3.38 +/- 1.11%; P = 0.004). At the femoral neck, there was a smaller bone mineral density decrease in the etidronate than in the placebo group, but the difference (1.11 +/- 1.13%) was not statistically significant ▸Four fractures (including one vertebral fracture) occurred in the placebo group versus two (including one vertebral) in the etidronate group

Author, Publication year	**Geusens P et al.** **Ann Rheum Dis 57:724–727**
Title	Cyclical etidronate increases bone density in the spine and hip of postmenopausal women receiving long term

	corticosteroid treatment. A double blind, randomised placebo controlled study.
Methods	double blind, randomised placebo controlled study
Participants	**N= 37 (중재군/비교군= 19 / 18)** ▸**Inclusion criteria** - Post-menopausal women NOS; post-menopausal women>5 yrs; Steroid >5mg/d; Steroid >10mg/d; Steroid duration ≥3; Prevalent steroid use at least 3 months; polymyalgia rheumatica, RA, sarcoid, inflammatory GI disease ▸**Exclusion criteria** - Hormone use
Interventions	▸**(중재군)** - intermittent etidronate 400mg/day for 14 days + 500mg Calcium daily ▸**(비교군)** - Placebo + 500mg Calcium daily
Outcomes	▸**Primary outcome:** - comparison between the treatment groups by an analysis of covariance of the spinal bone density percent change from baseline at two years for the intent to treat population ▸**Secondary outcomes:**

	- comparison between the treatment groups by an analysis of covariance of the hip bone density percent change from baseline at two years for the intent to treat population ▸**추적기간** - 24 months
Results	▸After two years of treatment there was a significant difference between the groups in mean per cent change from baseline in bone density in the spine in favour of etidronate (p = 0.003). The estimated treatment difference (mean (SD)) was 9.3 (2.1)%. Etidronate increased bone density in the spine (4.9 (2.1)%, p < 0.05) whereas the placebo group lost bone (-2.4 (1.6)%). ▸At the femoral neck there was an estimated difference of 5.3 (2.6)% between the groups (etidronate: 3.6% (1.4)%, p < 0.05, placebo: -2.4 (2.1)%). The estimated difference at the trochanter was 8.2 (3.0) (etidronate: 9.0 (1.5)%, p < 0.0001, placebo: 0.5 (2.3)%). No significant bone loss occurred in the hip in placebo treated patients.

Author, Publication year	**Jenkins EA et al.** **Scand J Rheumatol 28:152–156(1999)**
Title	The prevention of corticosteroid-induced bone loss with intermittent cyclical etidronate.

Methods	prospective, randomised, double-blind, placebo controlled study
Participants	**N= 28 (중재군/비교군= 15 / 13)** **▸Inclusion criteria** - Men; women otherwise undefined; steroid >10mg/d; Steroid duration <1mon; polymyalgia rheumatica; rheumatoid arthritis **▸Exclusion criteria** - Medications that affect bone metabolism
Interventions	**▸(중재군)** - intermittent cyclical etidronate (400 mg daily for 2 weeks) + calcium (500 mg daily for 11 weeks) **▸(비교군)** - placebo + calcium (500 mg daily for 11 weeks)
Outcomes	**▸Primary outcome:** - changes in bone mineral density at the lumbar spine and proximal femur **▸Secondary outcomes:** - incident clinically diagnosed fractures - changes in calcium metabolism in the blood and urine.

	▸**추적기간** - 12 months
Results	▸After 52 weeks of treatment, lumbar spine BMD increased by 1.8% in the etidronate group, while it decreased by 3.7% in the placebo group. The differences in bone loss rate were statistically significant ($p<0.01$) at both 6 and 12 months ▸ Similar trends were observed at the proximal femur, but differences were not statistically significant.

Author, Publication year	**Jinnouchi Y (2000)** **Kurume Med J 47:219–224**
Title	Efficacy of intermittent etidronate therapy for corticosteroid-induced osteoporosis in patients with diffuse connective tissue disease.
Methods	comparative study
Participants	**N= (중재군/비교군= 16 / 9)** ▸**Inclusion criteria** - Men; women otherwise undefined; steroid>5mg/d; prevalent steroid use at least 3 mon; “diffuse

	connective tissue disease” ▸**Exclusion criteria** - pregnancy
Interventions	▸**(중재군)** - Etidronate, 200mg/day for 14 consecutive days every 3 months for a year + vitD3 1 mcg/day ▸**(비교군)** - vitD3 1 mcg/day
Outcomes	▸**Primary outcome:** - the changes of serum alkaline phosphatase (ALP), urinary deoxypyridinoline (DPD), young adult mean (YAM) ▸**Secondary outcomes:** - bone fracture ratio. ▸**추적기간** - 12 months
Results	▸ ALP decreased in both groups with no significant difference between groups ▸ DPD increased significantly from baseline ($p < 0.05$) in group with active vitamin D3 monotherapy, but it decreased significantly from baseline ($p < 0.05$) in group with combination therapy with V.D3

	and etidronate, but again without a significant difference between groups. ▸ YAM resulted in no significant improvement in group with active vitamin D3 monotherapy, but a significant improvement from baseline ($p < 0.01$) was shown in group with combination therapy with V.D3, with a significant difference between groups ($p < 0.05$); and a new spinal compression fracture ratio was extremely lower in group ith active vitamin D3 monotherapy than in group with combination therapy with V.D3

Author, Publication year	**Mulder H. et al. (1994)** **Br J Rheumatol 33:348–350**
Title	Intermittent cyclical etidronate in the prevention of corticosteroid-induced bone loss.
Methods	prospective study
Participants	**N= 20 (중재군/비교군= 10 / 10)** **▸Inclusion criteria** - postmenopausal women with a biopsy-confirmed diagnosis of temporal arteritis for whom high-dose prednisone therapy was indicated. **▸Exclusion criteria**

	- if they had any disease or were receiving any medication, with the exception of the study drugs, that would interfere with calcium or bone metabolism.
Interventions	▸**(중재군): group A** - etidronate (400 mg/day for 2 weeks, then 11 weeks off etidronate; four cycles total) and prednisone ▸**(비교군): group B** - received only prednisone
Outcomes	▸**Primary outcome:** - the changes of vertebral BMD ▸**Secondary outcomes:** - the changes of serum alkaline phosphatase (a biochemical marker of bone turnover) - adverse events ▸**추적기간** - 12 months
Results	▸ At 3, 6 and 12 months, vertebral BMD was significantly ($P < 0.01$) increased in Group A and decreased in Group B, based on mean actual and percent changes in BMD and mean changes in BMD Z-score from baseline. Between-group comparisons were also significant ($P < 0.002$) at each time point. ▸No adverse events related to etidronate treatment were reported.

Author, Publication year	**Pitt P. et al.** **Thorax 53:351–356 (1998)**
Title	A double blind placebo controlled study to determine the effects of intermittent cyclical etidronate on bone mineral density in patients on long term oral corticosteroid treatment.
Methods	double blind, placebo controlled study
Participants	**N= 49 (중재군/비교군= 26 / 23)** **▸Inclusion criteria** - Pre-menopausal women; Post-menopausal women NOS; - steroid>5mg/d; steroid duration>=3; prevalent steroid use at least 3 mon; - polymyalgia rheumatica; vasculitis other than GCA; asthma or COPD; SLE; Fasciitis; Bronchiectasis; Fibrosing alveolitis **▸Exclusion criteria** - hypothyrodism; hyperthyroidism; metabolic bone disorder other than osteoporosis (e.g. Paget's, renal osteodystrophy, osteomalacia); renal insufficiency; gastrointestinal disease; Pre-menopausal without hysterectomy;Medications that affect bone metabolism

Interventions	▸**(중재군)** - 400 mg/day etidronate for 14 days followed in both groups by calcium (equivalent to 97 mg elemental Ca/day) with vitamin D (400 IU) for 76 days ▸**(비교군)** - Placebo for 14 days followed in both groups by calcium (equivalent to 97 mg elemental Ca/day) with vitamin D (400 IU) for 76 days
Outcomes	▸**Primary outcome:** - percentage change from baseline in bone mineral density (BMD) of the lumbar spine at week 104 ▸**Secondary outcomes:** - percentage change from baseline in BMD of the lumbar spine at weeks 26, 52, and 78. In addition, percentage change from baseline in BMD of the femoral neck, BMD of the trochanter, and serum and urine markers of bone metabolism were also compared at each time point. ▸**추적기간** - 104 weeks
Results	▸All had a low BMD at entry and with treatment a significant difference was observed between groups in the mean (SE) percentage change from baseline in lumbar spine BMD at week 104 of 4.5 (1.65)% (p = 0.007) with a 95% confidence interval (CI) of 1.12 to 7.87%. ▸No clinically or statistically significant treatment differences were observed at the hip or with bone

	markers. ▸The incidence of adverse events was similar in the two groups.

Author, Publication year	**Roux C. et al.** **J Clin Endocrinol Metab 83:1128–1133 (1998)**
Title	Randomized trial of effect of cyclical etidronate in the prevention of corticosteroid-induced bone loss.
Methods	double-blind, randomized, multicenter, and parallelgroup
Participants	**N= 117 (중재군/비교군= 59 / 58)** **▸Inclusion criteria** - Men; pre-menopausal women; post-menopausal women NOS: - steroid >2.5mg/d ; prevention trial with steroid use≤ 3 mon; - polymyalgia rheumatica; vasculitis other than GCA; rheumatoid arthritis; SLE **▸Exclusion criteria** - Pregnancy; bisphosphonates; calcitonin; fluoride; Hormone use: HRT; Hormone use: Estrogen agonists (including estrogen); hormone use: progestin

Interventions	▸**(중재군)** - oral etidronate 400 mg/day for 14 days, followed by 76 days of oral calcium carbonate (500 mg elemental calcium), cycled over 12 months ▸**(비교군)** - placebo for 14 days, followed by 76 days of oral calcium carbonate (500 mg elemental calcium), cycled over 12 months
Outcomes	▸**Primary outcome:** - the difference in percent change from baseline in bone mineral density of the lumbar spine between the groups at the end of year 1. ▸**Secondary outcomes:** - changes in femur bone density and in biochemical markers of bone remodeling. ▸**추적기간** - 12 months
Results	▸ The mean (6SEM) lumbar spine bone density changed 0.30 ± 0.61% and –2.79 ± 0.63% in the etidronate and placebo groups, respectively. The mean difference between groups after 1 yr was 3.0 ± 0.84% (*P* = 0.004). ▸ The changes in the femoral neck and great trochanter were not different between the groups. ▸ There was a decrease in pyridinium crosslinks, significant from baseline at both 6 and 12 months,

	in the etidronate group. Osteocalcin increased in the placebo group, and difference between groups was -25.07 ± 14.89% (*P* = 0.032) and -34.68 ± 19.77% (*P* = 0.051), at 6 and 12 months respectively. ▸ There was no significant difference between the groups in number of adverse experiences, including gastrointestinal disorders.

Author, Publication year	**Skingle SJ. et al.** **Lancet Infect Dis 344:543–544 (1994)**
Title	Increased bone density in patients on steroids with etidronate.
Methods	randomised controlled study
Participants	**N= 38 (중재군/비교군= 20 / 18)** **▸Inclusion criteria** - polymyalgia rheumatica, temporal arteritis, or chronic obstructive airways minimum daily equivalent of 5 mg oral prednisolone **▸Exclusion criteria** - medication interfering with bone metabolism

Interventions	▸**(중재군)** - etidronate 400 mg for 2 weeks out of 15 + calcium 1g daily ▸**(비교군)** - palcebo + calcium 1g daily
Outcomes	▸**Primary outcome:** - Changes in mean spinal BMD ▸**Secondary outcomes:** - Changes in mean hip BMD ▸**추적기간** - 24 months
Results	▸Mean spinal BMD in the etidronate group rose by 4-1% after 1 year ($p<0.01$) and by 4-8% after 2 years ($p<0.05$). Mean spinal BMD of the calcium alone group decreased from baseline by 0-8% at year one ($p=0.429$) and by 0-7% ($p=0.612$) at year two. Most patients who took etidronate showed an increase in BMD, whereas most on calcium alone showed a decrease. A comparison of the spinal changes between the groups was significant at year one ($p<0.01$) and year 2 ($p<0.05$). ▸In the hip, none of the changes was statistically significant. Both groups showed a decrease of about 1% between baseline and year one. The etidronate group showed an increase of 3% after two years which was not significant.

Author, Publication year	**Struys A. et al.** **Am J Med 99:235–242 (1995)**
Title	Cyclical etidronate reverses bone loss of the spine and proximal femur in patients with established corticosteroid-induced osteoporosis.
Methods	open label study
Participants	**N= 25 (중재군/비교군= 16 / 9)** **▸nclusion criteria** - Men; Pre-menopausal women; Post-menopausal women NOS; - Osteopenia NOS, - Prevalent steroid use at least 3 mon; - inflammatory bowel disease; asthma or COPD; GCA; hemolytic anemia; thrombocytopenia; heptatitis; Relapsing polychondritis **▸Exclusion criteria** - Metabolic bone disorder other than osteoporosis (e.g. Paget's, renal osteodystrophy, osteomalacia); - Bisphosphonates; Calcitonin; Calcium (includes antacids); Hormone use: Estrogen agonists (including

	estrogen); Vitamin D
Interventions	▸**(중재군)** - etidronate 400 mg/d for 14 days followed by calcium 500 mg/d for 76 days, 4 cycles ▸**(비교군)** - placebo for 14 days followed by calcium 500 mg/d for 76 days, 4 cycles
Outcomes	▸**Primary outcome:** - Changes in spinal BMD ▸**Secondary outcomes:** - Changes in proximal femur (total hip) ▸**추적기간** - 12 months
Results	▸Treatment with intermittent cyclic etidronate for 12 months resulted in significant increases of 5.7% and 6.8% in BMD of the spine and proximal femur (total hip), respectively (P<0.02 versus baseline; P<0.001 versus calcium group). ▸Calcium supplementation alone did not prevent significant losses of 3.4% and 4.1% in BMD at the respective sites (P < 0.02 versus baseline). ▸At the end of the study Z scores reflected proximal femur (all regions) in the etidronate group

	(P<0.01), and significant decreases at the spine, proximal femur, and trochanter in the calcium group (P<0.01). ▸After 12 months, the difference between the groups was 9.1% (P ~0.01; 95% Cl 6.3% to 11.9%) at the spine and 10.9%(P ~0.01; 95% Cl 7.8% to 14.1%) at the proximal femur.

Author, Publication year	**Cohen S. et al.** **Arthritis Rheum 42:2309–2318 (1999)**
Title	Risedronate therapy prevents corticosteroidinduced bone loss: a twelve month, multicenter, randomized, double-blind, placebo-controlled, parallel-group study.
Methods	multicenter, double-blind, placebo-controlled parallel-group study.
Participants	**N= 228 (중재군/비교군= 151/77)** ▸**Inclusion criteria** - Inception cohort: Men; pre and post menopausal women; steroid>7.5mg/d; steroid duration 0-3mon, "various rheumatic diseases" ▸**Exclusion criteria** - hyperparathyroidism; bisphosphonates; hormone use: estrogen antagonists; vitamin D; Conditions

	interfering with spinal DEXA
Interventions	▸**(중재군)** - risedronate 2.5mg daily + 500mg calcium daily (n=75) - risedronate 5mg daily + 500mg calcium daily (n=76) ▸**(비교군)** - placebo + 500mg calcium daily (n=77)
Outcomes	▸**Primary outcome:** - the percentage of change in lumbar spine bone mineral density (BMD). ▸**Secondary outcomes:** - proximal femur BMD and incidence of vertebral fractures ▸**추적기간** - 12 months
Results	▸After 12 months, the lumbar spine BMD (mean +/- SEM) did not change significantly compared with baseline in the 5-mg (0.6 +/- 0.5%) or the 2.5-mg (-0.1 +/- 0.7%) risedronate groups, while it decreased in the placebo group (-2.8 +/- 0.5%; P < 0.05). ▸The mean differences in BMD between the 5-mg risedronate and the placebo groups were 3.8 +/- 0.8% at the lumbar spine (P < 0.001), 4.1 +/- 1.0% at the femoral neck (P < 0.001), and 4.6 +/- 0.8% at the femoral trochanter (P < 0.001).

	▸A trend toward a decrease in the incidence of vertebral fracture was observed in the 5-mg risedronate group compared with the placebo group (5.7% versus 17.3%; P = 0.072). Risedronate was well tolerated, and the incidence of upper gastrointestinal adverse events was comparable among the 3 groups.

Author, Publication year	**Eastell R. et al. (2000)** **Osteoporos Int 11:331–337**
Title	Prevention of bone loss with risedronate in glucocorticoid-treated rheumatoid arthritis patients.
Methods	double-masked, placebo-controlled trial with a third year of nontreatment follow-up
Participants	**N= 120 (중재군/비교군= 80/ 40)** ▸**Inclusion criteria** - postmenopausal women with rheumatoid arthritis who required long-term (46 months) treatment with oral glucocorticoids at an average daily dose of at least 2.5 mg prednisolone ▸**Exclusion criteria** - metabolic bone disease other than glucocorticoids induced osteoporosis, and any significant organic disease that could affect participation or interfere with the interpretation of the data. Patients who

	had been treated with androgens, estrogens or calcitonin for 43 months, or with vitamin D (at doses 4800 IU/day) or fluoride for 5 1 month, within 6 months of enrollment were also excluded
Interventions	▸**(중재군)** - 2.5 mg risedronate daily - cyclical 15 mg risedronate (2 out of 12 weeks) ▸**(비교군)** - placebo
Outcomes	▸**Primary outcome:** - the mean percent change from baseline at week 97 in bone mineral density at the lumbar spine. ▸**Secondary outcomes:** - mean percent changes from baseline at week 97 in bone mineral density at the femoral neck and trochanter. ▸**추적기간** - 24 months
Results	▸ At 97 weeks, bone mineral density was maintained at the lumbar spine (+1.4%) and trochanter (+0.4%) in the daily 2.5 mg risedronate group, while significant bone loss occurred in the placebo group (-1.6%, $p = 0.03$; and 4.0%, $p < 0.005$, respectively). ▸At the femoral neck, there was a nonsignificant bone loss in the daily 2.5 mg risedronate group

	(-1.0%) while in the placebo group bone mass decreased significantly (-3.6%, p < 0.001).

Author, Publication year	**Reid DM. et al.** **Calcif Tissue Int 69:242–247 (2001)**
Title	Risedronate increases bone density and reduces vertebral fracture risk within one year in men on corticosteroid therapy
Methods	double-blind, placebo-controlled study
Participants	**N= 184 (중재군/비교군= 124/60)** **▸Inclusion criteria** - patients beginning corticosteroid treatment at a dose of at least 7.5 mg per day of prednisone or equivalent (prevention study) or continuing long-term treatment of corticosteroid at that dose (treatment study). - The underlying diseases requiring corticosteroid treatment included rheumatoid arthritis, lung disease, polymyositis, polymyalgia rheumatica, temporal arteritis, and vasculitis. **▸Exclusion criteria**

	- evidence of metabolic bone disease other than CIO, recent use of drugs known to affect bone metabolism, and any significant organic or psychiatric disease that could affect participation or interfere with the interpretation of the data.
Interventions	▸**(중재군)** - risedronate (2.5 mg) daily + calcium 1000 mg + 400 IU vitamin D (n=61) - risedronate (5 mg) daily + calcium 1000 mg + 400 IU vitamin D (n=63) ▸**(비교군)** - placebo + calcium 1000 mg + 400 IU vitamin D (n=60)
Outcomes	▸**Primary outcome:** - differences in bone mineral density (BMD) at the lumbar spine, femoral neck, and femoral trochanter ▸**Secondary outcomes:** - vertebral fractures, changes in biochemical markers of bone turnover, and overall safety ▸**추적기간** - 12 months
Results	▸risedronate 5 mg significantly ($P < 0.01$) increased lumbar spine BMD by 4.8% at the lumbar spine, 2.1% at the femoral neck, and 2.6% at the femoral trochanter compared with baseline values. ▸In the prevention study, bone loss was prevented with risedronate 5 mg; in the placebo group, BMD decreased significantly ($P < 0.01$) by 3.4%, 3.3%, and 3.4% in the lumbar spine, femoral neck,

	and trochanter, respectively, at 1 year. The differences between risedronate 5 mg and placebo groups were significant at all skeletal sites in the prevention study (P < 0.01) and at the lumbar spine in the treatment study (P < 0.001). ▸The 2.5 mg dose also had a positive effect on BMD, although of a lesser magnitude than the 5 mg dose. ▸When the data from the two studies were combined, the incidence of vertebral fractures decreased 82.4% (95% confidence interval, 36.6%–-95.1%) in the pooled risedronate groups compared with placebo (P = 0.008). ▸Risedronate was well tolerated in men, with a similar incidence of upper gastrointestinal adverse events in the placebo and treatment groups.

Author, Publication year	**Reid DM. et al.** **J Bone Miner Res 15:1006–1013 (2000)**
Title	Efficacy and safety of daily risedronate in the treatment of corticosteroidinduced osteoporosis in men and women: a randomized trial. European Corticosteroid-Induced Osteoporosis Treatment Study.
Methods	multicenter, randomized double-blind study

Participants	**N= 290 (중재군/비교군= 194/ 96)** **▸Inclusion criteria** - ambulatory men and women receiving high-dose oral corticosteroid therapy (prednisone > or = 7.5 mg/day or equivalent) for 6 or more months **▸Exclusion criteria** - conditions that might interfere with the evaluation of spinal osteoporosis; - history of hyperparathyroidism, hyperthyroidism, or osteomalacia within a year before the study; - history of sarcoidosis or cancer. - Patients were also excluded if they had taken (within 6–12 months, depending on the medication) or were still taking medication known to affect bone metabolism, including hormone replacement therapy.
Interventions	**▸(중재군)** - risedronate 2.5 mg/day + calcium 1 g/d+ vitamin D 400 IU/d (n=94) - risedronate 5 mg/day + calcium 1 g/d + vitamin D 400 IU /d(n=100) **▸(비교군)** - placebo + calcium 1 g/d + vitamin D 400 IU/d
Outcomes	**▸Primary outcome:** - lumbar spine bone mineral density (BMD) at month 12

	▸**Secondary outcomes:** - BMD at the femoral neck and trochanter and the incidence of vertebral fractures. ▸**추적기간** - 12 months
Results	▸There were statistically significant treatment effects on BMD at 12 months at the lumbar spine ($p < 0.001$), femoral neck ($p = 0.004$), and trochanter ($p = 0.010$). Risedronate 5 mg increased BMD at 12 months by a mean (SEM) of 2.9% (0.49%) at the lumbar spine, 1.8% (0.46%) at the femoral neck, and 2.4% (0.54%) at the trochanter, whereas BMD was maintained only in the control group ▸Although not powered to show fracture efficacy, we observed a reduction in the incidence of vertebral fractures of 70% in the combined risedronate treatment groups, relative to placebo ($p = 0.042$).

Author, Publication year	**Wallach S et al.** **Calcif Tissue Int 67:277–285 (2002)**
Title	Effects of risedronate treatment on bone density and vertebral fracture in patients on corticosteroid therapy
Methods	randomized, double-blind, placebo-controlled,

Participants	**N= 509(중재군/비교군= 339/170)** **▸Inclusion criteria** - ambulatory men and women, 18–85 years of age and receiving moderate-to-high doses of (equivalent to 7.5 mg prednisone daily or greater) oral corticosteroid therapy were enrolled in two parallel studies. - The patients were expected to continue on corticosteroid therapy for at least 12 months. - The diseases being treated included rheumatoid arthritis, polymyalgia rheumatica, temporal arteritis, chronic interstitial lung disease, chronic obstructive pulmonary disease, asthma, systemic lupus erythematosus, polymyositis, vasculitis, Behcet's disease, and a variety of skin diseases **▸Exclusion criteria** - evidence of metabolic bone disease other than CIO, recent use of HRT (within 1 year of enrollment) or other drugs known to affect bone metabolism, and any significant organic or psychiatric disease that could affect participation or interfere with the interpretation of the data.
Interventions	**▸(중재군)** - risedronate 2.5 mg/day + calcium 1 g/d + vitamin D 400 IU/d (n=165) - risedronate 5 mg/day + calcium 1 g/d + vitamin D 400 IU/d (n=174) **▸(비교군)** placebo + calcium 1 g/d + vitamin D 400 IU/d

Outcomes	▸**Primary outcome:** - the difference between the placebo and active groups in lumbar spine bone mineral density (BMD) at 1 year ▸**Secondary outcomes:** - changes in BMD at other sites, biochemical markers of bone turnover, and the incidence of vertebral fractures ▸**추적기간** - 12 months
Results	▸the mean (SE) lumbar spine BMD increased 1.9 ± 0.38% from baseline in the risedronate 5 mg group (P < 0.001) and decreased 1.0 ± 0.4% in the placebo group (P=0.005). ▸BMD at the femoral neck, trochanter, and distal radius increased or was maintained with risedronate 5 mg treatment, but decreased in the placebo group. Midshaft radius BMD did not change significantly in either treatment group. The difference in BMD between the risedronate 5 mg and placebo groups was significant at all skeletal sites (P <0.05) except the midshaft radius at 1 year. ▸The 2.5 mg dose also had a positive effect on BMD, although of a lesser magnitude than that seen with risedronate 5 mg. ▸A significant reduction of 70% in vertebral fracture risk was observed in the risedronate 5 mg group compared with the placebo group (P = 0.01).

Author, Publication year	**Reid DM, et al.** **Lancet 373:1253–1263 (2009)**
Title	Zoledronic acid and risedronate in the prevention and treatment of glucocorticoidinduced osteoporosis (HORIZON): a multicentre, double-blind, double-dummy, randomised controlled trial.
Methods	a multicentre, double-blind, double-dummy, randomised controlled trial.
Participants	**N= 833 (중재군/비교군= 416 / 417)** ▸**Inclusion criteria** - Men; pre-menopausal women; post-menopausal women NOS; - steroid>7.5mg/d; steroid duration<1mon; steroid duration 1-3mon; prevalent steroid use at least 3mon; - polymyalgia rheumatica; asthma or COPD; rheumatoid arthritis; SLE ▸**Exclusion criteria** - age>85; pregnancy; carcinoma or suspected carcinoma; hyperparathyroidism; hypoparathyroidism; renal insufficiency; bisphosphonates; Medications that affect bone metabolism; serum 25-hydroxy-Vitamin D concentration <30 nmol/L
Interventions	▸(중재군)

	- zoledronic acid 5mg yearly + 1g calcium daily + 400-1,200 IU Vit D daily (treatment arm, n=272) - zoledronic acid 5mg yealy + 1g calcium daily + 400-1,200 IU Vit D daily (prevention arm, n=144) ▸(비교군) - Risedronate 5mg daily + 1g calcium daily + 400-1,200 IU Vit D daily (treatment arm, n=273) - Risedronate 5mg daily + 1g calcium daily + 400-1,200 IU Vit D daily (prevention arm, n=144)
Outcomes	▸**Primary outcome:** - percentage change from baseline in lumbar spine bone mineral density ▸**Secondary outcomes:** - Changes in bone turnover biomarker concentrations ▸**추적기간** - 1 year
Results	▸Zoledronic acid was non-inferior and superior to risedronate for increase of lumbar spine bone mineral density in both the treatment (least-squares mean 4.06% [SE 0.28] vs 2.71% [SE 0.28], mean difference 1.36% [95% CI 0.67-2.05], p=0.0001) and prevention (2.60% [0.45] vs 0.64% [0.46], 1.96% [1.04-2.88], p<0.0001) subgroups at 12 months.

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- **Reference**

	문헌정보	연구유형	연구대상자수 (치료군/비교군)
1	Roux C, Oriente P, Laan R, et al. Randomized trial of effect of cyclical etidronatein the prevention of corticosteroid-induced bone loss. Ciblos Study Group. J Clin Endocrinol Metab 1998;83:1128–33 [63]	RCT	117 (59/58)
2	Adachi JD, Roux C, Pitt PI, et al. A pooled data analysis on the use of intermittentcyclical etidronate therapy for the prevention and treatment of corticosteroid-induced bone loss. J Rheumatol 2000;27:2424–31 [69]	meta-analysis	
3	S. Cohen, R.M. Levy, M. Keller, et al. Risedronate therapy prevents corticosteroid-induced bone loss: a twelve-month, multicenter, randomized, double-blind, placebo-controlled, parallel-group study Arthritis Rheum, 42 (1999), pp. 2309-2318 [44]	RCT	228 (151/ 77)
4	D.M. Reid, R.A. Hughes, R.F. Laan, et al. Efficacy and safety of daily risedronate in the treatment of corticosteroid-induced osteoporosis in men and women: a randomized trial. European Corticosteroid-Induced Osteoporosis Treatment Study. J Bone Miner Res, 15 (2000), pp. 1006-1013 [68]	RCT	290 (194 / 96)

5	S. Wallach, S. Cohen, D.M. Reid, et al. Effects of risedronate treatment on bone density and vertebral fracture in patients on corticosteroid therapy. Calcif Tissue Int, 67 (2000), pp. 277-285 [30]	RCT	509 (339/170)
6	D.M. Reid, J.P. Devogelaer, K. Saag, et al. Zoledronic acid and risedronate in the prevention and treatment on glucocorticoid induced osteoporosis (HORIZON): a multicentre, double-blind, double-dummy, randomised controlled trial. Lancet, 373 (2009), pp. 1253-1263 [54]	RCT	833 (416 / 417)
7	P.N. Sambrook, C. Roux, J.P. Devogelaer, et al. Bisphosphonates and glucocorticoid osteoporosis in men: results of a randomized controlled trial comparing zoledronic acid with risedronate. Bone, 50 (2012), pp. 289-295 [70]	RCT	265 (131/134)
8	J.A. Kanis, M. Stevenson, E.V. McCloskey, et al. Glucocorticoid-induced osteoporosis: a systematic review and cost-utility analysis. Health Technol Assess, 11 (2007), pp. iii-iv [71]	SR	

- 일차연구문헌 근거표

Author, Publication year	**Roux C, et al.**

	J Clin Endocrinol Metab. 1998 Apr;83(4):1128-33.
Title	Randomized trial of effect of cyclical etidronate in the prevention of corticosteroid-induced bone loss. Ciblos Study Group.
Methods	double-blind, randomized, multicenter, and parallel-group study
Participants	**N= 117 (중재군/비교군= 58 / 59)** **▸Inclusion criteria** - High-dose corticosteroids had to have been initiated within 90 days of study entry. - Low-dose prednisone in the year before the study was allowed, provided that the daily dose was less than 7.5 mg. - The treatment had to be expected to continue for at least 12 months, with the initial 90 days (of being in the study) at a mean daily dose of at least 7.5 mg of prednisone or its equivalent, with subsequent ongoing treatment at a mean cumulative dose of at least 2.5 mg/day **▸Exclusion criteria** - patients taking medications or presenting with diseases affecting bone or calcium metabolism were excluded. - particular, none had a history of treatment with any bisphosphonate, fluoride, estrogen, progestogen, or estrogen-like compounds within 1 yr, nor with calcitonin or supplemental vitamin D within the previous 6 months.

Interventions	▸(중재군) - oral etidronate 400 mg/day for 14 days, followed by 76 days of oral calcium carbonate (500 mg elemental calcium) cycled over 12 months ▸(비교군) - placebo for 14 days, followed by 76 days of oral calcium carbonate (500 mg elemental calcium) cycled over 12 months
Outcomes	▸**Primary outcome:** - the difference in percent change from baseline in bone mineral density of the lumbar spine between the groups at the end of year 1. ▸**Secondary outcomes:** - changes in femur bone density and in biochemical markers of bone remodeling. ▸**추적기간** - 1 year
Results	▸The mean (±sem) lumbar spine bone density changed 0.30 ± 0.61% and −2.79 ± 0.63% in the etidronate and placebo groups, respectively. The mean difference between groups after 1 yr was 3.0 ± 0.84% (P = 0.004). ▸The changes in the femoral neck and great trochanter were not different between the groups ▸There was a decrease in pyridinium crosslinks, significant from baseline at both 6 and 12 months, in the etidronate group. Osteocalcin increased in the placebo group, and difference between groups

	was− 25.07 ± 14.89% (P = 0.032) and −34.68 ± 19.77% (P = 0.051), at 6 and 12 months respectively ▸There was no significant difference between the groups in number of adverse experiences, including gastrointestinal disorders.

Author, Publication year	**S. Cohen. et al.** **Arthritis Rheum, 42 (1999), pp. 2309-2318**
Title	Risedronate therapy prevents corticosteroid-induced bone loss: a twelve-month, multicenter, randomized, double-blind, placebo-controlled, parallel-group study
Methods	multicenter, randomized, double-blind, placebo-controlled, parallel-group study
Participants	**N= 228 (중재군/비교군= 151 / 77)** ▸**Inclusion criteria** - Ambulatory patients, ages 18–85 years, with a variety of rheumatologic, pulmonary, and skin conditions, were eligible for the study if they had begun taking moderate to high doses of corticosteroids (≥7.5 mg/day mean daily dose of prednisone or prednisone equivalent) within the previous 3 months and were expected to continue treatment for another 12 months. ▸**Exclusion criteria**

	- Patients were excluded if they had a history of hyperparathyroidism, hyperthyroidism, or osteomalacia within 1 year prior to enrollment. - Patients were ineligible to participate if they had taken any drugs known to affect bone metabolism during the preceding year (e.g., bisphosphonates, estrogen or estrogenrelated drugs, or vitamin D at dosages .500 IU/day), including any treatment with corticosteroids prior to the current therapy. - Patients were excluded if they had any condition that would have interfered with the evaluation of lumbar spine bone mineral density (BMD), such as severe scoliosis, osteophytosis, or spinal fusion.
Interventions	▸(중재군) - risedronate 2.5mg/d + calcium 500mg/d (n=75) - risedronate 5mg/d + calcium 500mg/d (n=76) ▸(비교군) - risedronate 5mg/d + calcium 500mg/d (n=77)
Outcomes	▸**Primary outcome:** - the percentage of change in lumbar spine bone mineral density (BMD) ▸**Secondary outcomes:** - proximal femur BMD and incidence of vertebral fractures ▸**추적기간** - 1 year

Results	▸After 12 months, the lumbar spine BMD (mean +/- SEM) did not change significantly compared with baseline in the 5-mg (0.6 +/- 0.5%) or the 2.5-mg (-0.1 +/- 0.7%) risedronate groups, while it decreased in the placebo group (-2.8 +/- 0.5%; P < 0.05). ▸The mean differences in BMD between the 5-mg risedronate and the placebo groups were 3.8 +/- 0.8% at the lumbar spine (P < 0.001), 4.1 +/- 1.0% at the femoral neck (P < 0.001), and 4.6 +/- 0.8% at the femoral trochanter (P < 0.001). ▸A trend toward a decrease in the incidence of vertebral fracture was observed in the 5-mg risedronate group compared with the placebo group (5.7% versus 17.3%; P = 0.072). ▸Risedronate was well tolerated, and the incidence of upper gastrointestinal adverse events was comparable among the 3 groups.

Author, Publication year	**D.M. Reid et al.** **J Bone Miner Res, 15 (2000), pp. 1006-1013**
Title	Efficacy and safety of daily risedronate in the treatment of corticosteroid-induced osteoporosis in men and women: a randomized trial. European Corticosteroid-Induced Osteoporosis Treatment Study.
Methods	multicenter, double-blind study

Participants	**N= 290 (중재군/비교군= 194 / 96)** ▸**Inclusion criteria** - Ambulatory men and women aged 18–85 years were enrolled from 23 study centers in Europe. - All patients had been receiving oral corticosteroids (mean daily dose of prednisone≥ 7.5 mg, or equivalent) for at least 6 months. ▸**Exclusion criteria** - conditions that might interfere with the evaluation of spinal osteoporosis; history of hyperparathyroidism, hyperthyroidism, or osteomalacia within a year before the study; or history of sarcoidosis or cancer. - Patients were also excluded if they had taken (within 6–12 months, depending on the medication) or were still taking medication known to affect bone metabolism, including hormone replacement therapy.
Interventions	▸(중재군) - risedronate 2.5mg/d + calcium 1g/d + vit.D 400 IU/d (n=94) - risedronate 5mg/d + calcium 1g/d + vit.D 400 IU/d (n=100) ▸(비교군) - risedronate 5mg/d + calcium 1g/d + vit.D 400 IU/d (n=96)
Outcomes	▸**Primary outcome:**

	- lumbar spine bone mineral density (BMD) at month 12 ▸**Secondary outcomes:** - BMD at the femoral neck and trochanter and the incidence of vertebral fractures ▸**추적기간** - 1 year
Results	▸There were statistically significant treatment effects on BMD at 12 months at the lumbar spine ($p < 0.001$), femoral neck ($p = 0.004$), and trochanter ($p = 0.010$). ▸Risedronate 5 mg increased BMD at 12 months by a mean (SEM) of 2.9% (0.49%) at the lumbar spine, 1.8% (0.46%) at the femoral neck, and 2.4% (0.54%) at the trochanter, whereas BMD was maintained only in the control group. ▸Although not powered to show fracture efficacy, we observed a reduction in the incidence of vertebral fractures of 70% in the combined risedronate treatment groups, relative to placebo ($p = 0.042$). ▸Risedronate was well tolerated, had a good safety profile, and was not associated with gastrointestinal adverse events.

Author, Publication year	**Wallach S et al.**

	Calcif Tissue Int 67:277–285 (2002)
Title	Effects of risedronate treatment on bone density and vertebral fracture in patients on corticosteroid therapy
Methods	randomized, double-blind, placebo-controlled,
Participants	**N= 509(중재군/비교군= 339/170)** **▸Inclusion criteria** - ambulatory men and women, 18–85 years of age and receiving moderate-to-high doses of (equivalent to 7.5 mg prednisone daily or greater) oral corticosteroid therapy were enrolled in two parallel studies. - The patients were expected to continue on corticosteroid therapy for at least 12 months. - The diseases being treated included rheumatoid arthritis, polymyalgia rheumatica, temporal arteritis, chronic interstitial lung disease, chronic obstructive pulmonary disease, asthma, systemic lupus erythematosus, polymyositis, vasculitis, Behcet's disease, and a variety of skin diseases **▸Exclusion criteria** - evidence of metabolic bone disease other than CIO, recent use of HRT (within 1 year of enrollment) or other drugs known to affect bone metabolism, and any significant organic or psychiatric disease that could affect participation or interfere with the interpretation of the data.
Interventions	**▸(중재군)**

	- risedronate 2.5 mg/day + calcium 1 g/d + vitamin D 400 IU/d (n=165) - risedronate 5 mg/day + calcium 1 g/d + vitamin D 400 IU/d (n=174) **▸(비교군)** - placebo + calcium 1 g/d + vitamin D 400 IU/d
Outcomes	**▸Primary outcome:** - the difference between the placebo and active groups in lumbar spine bone mineral density (BMD) at 1 year **▸Secondary outcomes:** - changes in BMD at other sites, biochemical markers of bone turnover, and the incidence of vertebral fractures **▸추적기간** - 12 months
Results	▸the mean (SE) lumbar spine BMD increased 1.9 ± 0.38% from baseline in the risedronate 5 mg group ($P < 0.001$) and decreased 1.0 ± 0.4% in the placebo group ($P=0.005$). ▸BMD at the femoral neck, trochanter, and distal radius increased or was maintained with risedronate 5 mg treatment, but decreased in the placebo group. Midshaft radius BMD did not change significantly in either treatment group. The difference in BMD between the risedronate 5 mg and placebo groups was significant at all skeletal sites ($P <0.05$) except the midshaft radius at 1 year.

	▸The 2.5 mg dose also had a positive effect on BMD, although of a lesser magnitude than that seen with risedronate 5 mg. ▸A significant reduction of 70% in vertebral fracture risk was observed in the risedronate 5 mg group compared with the placebo group (P = 0.01).

Author, Publication year	**Reid DM, et al.** **Lancet 373:1253–1263 (2009)**
Title	Zoledronic acid and risedronate in the prevention and treatment of glucocorticoidinduced osteoporosis (HORIZON): a multicentre, double-blind, double-dummy, randomised controlled trial.
Methods	a multicentre, double-blind, double-dummy, randomised controlled trial.
Participants	**N= 833 (중재군/비교군= 416 / 417)** ▸**Inclusion criteria** - Men; pre-menopausal women; post-menopausal women NOS; - steroid>7.5mg/d; steroid duration<1mon; steroid duration 1-3mon; prevalent steroid use at least 3mon; - polymyalgia rheumatica; asthma or COPD; rheumatoid arthritis; SLE

	▸**Exclusion criteria** - age>85; pregnancy; carcinoma or suspected carcinoma; hyperparathyroidism; hypoparathyroidism; renal insufficiency; bisphosphonates; Medications that affect bone metabolism; serum 25-hydroxy-Vitamin D concentration <30 nmol/L
Interventions	▸(중재군) - zoledronic acid 5mg iv yearly + calcium 1g/d + Vit D 400 IU/d(treatment arm, n=272) - zoledronic acid 5mg iv yearly + calcium 1g/d + Vit D 400 IU/d (prevention arm, n=144) ▸(비교군) - Risedronate 5mg/d+ calcium 1g/d + Vit D 400 IU/d (treatment arm, n=273) - Risedronate 5mg/d + calcium 1g/d + Vit D 400 IU/d (prevention arm, n=144)
Outcomes	▸**Primary outcome:** - percentage change from baseline in lumbar spine bone mineral density ▸**Secondary outcomes:** - Changes in bone turnover biomarker concentrations ▸**추적기간** - 1 year
Results	▸Zoledronic acid was non-inferior and superior to risedronate for increase of lumbar spine bone mineral density in both the treatment (least-squares mean 4.06% [SE 0.28] vs 2.71% [SE 0.28], mean

	difference 1.36% [95% CI 0.67-2.05], p=0.0001) and prevention (2.60% [0.45] vs 0.64% [0.46], 1.96% [1.04-2.88], p<0.0001) subgroups at 12 months.

Author, Publication year	**Sambrook PN, et al.** **LBone. 2012 Jan;50(1):289-95**
Title	Bisphosphonates and glucocorticoid osteoporosis in men: results of a randomized controlled trial comparing zoledronic acid with risedronate.
Methods	multinational, multicenter, randomized, double-blind, double-dummy, active-controlled, parallel-group study
Participants	**N= 265 (중재군/비교군= 131 / 134)** **▸Inclusion criteria** - Male patients aged 18–85 years, requiring high-doses of glucocorticoid therapy due to some underlying clinical conditions, and expected to continue the therapy for a minimum of 1 year were included in this sub-study report. **▸Exclusion criteria** - Major exclusion criteria were prior treatment with bisphosphonates or other drugs that may affect bone mineral metabolism (except in accordance with a predefined washout schedule), serum 25-hydroxyvitamin D

	concentration < 30 nmol/L, recent history of cancer or parathyroid disease, and renal impairment (creatinine clearance < 30 mL/min or proteinuria).
Interventions	▸(중재군) - zoledronic acid 5mg yearly +calcium 1g/d+ Vit D 400 IU/d ▸(비교군) - Risedronate 5mg daily + calcium 1g/d+ Vit D 400 IU/d
Outcomes	▸**Primary outcome:** - difference in percentage change from baseline in bone mineral density (BMD) at the lumbar spine (LS) at 12 months ▸**Secondary outcomes:** - percentage changes in BMD at total hip (TH) and femoral neck (FN), relative changes in bone turnover markers (β-CTx and P1NP), and overall safety. ▸**추적기간** - 1 year
Results	▸In the treatment subpopulation, ZOL increased LS BMD by 4.7% vs. 3.3% for RIS and at TH the percentage changes were 1.8% vs. 0.2%, respectively. ▸In the prevention subpopulation, bone loss was prevented by both treatments. At LS the percentage changes were 2.5% vs. -0.2% for ZOL vs. RIS and at TH the percentage changes were 1.1% vs.

-0.4%, respectively.

▸ZOL significantly increased lumbar spine BMD more than RIS at Month 12 in both the prevention population (p=0.0024) and the treatment subpopulation (p=0.0232) in men.

▸In the treatment subpopulation, ZOL demonstrated a significantly greater reduction in serum β-CTx and P1NP relative to RIS at all time-points. In the prevention subpopulation, ZOL significantly reduced β-CTx at all time-points, and P1NP at Month 3 (p=0.0297) only.

▸Both treatments were well tolerated in men, albeit with a higher incidence of influenza-like illness and pyrexia events post-infusion with ZOL.

지침4] 2010 CANADA

- **Reference**

	문헌정보	연구유형	연구대상자수 (치료군/비교군)
1	MacLean C, Newberry S, Maglione M, et al. Systematic review: comparative effectiveness of treatments to prevent fractures in men and women with low bone density or osteoporosis. Ann Intern Med	SR	

	2008;148:197-213 [72]		
2	Qaseem A, Snow V, Shekelle P, et al. Pharmacologic treatment of low bone density or osteoporosis to prevent fractures: a clinical practice guideline from the American College of Physicians. *Ann Intern Med* 2008;149:404-15 [73]	CPG	
3	Reid DM, Devogelaer JP, Saag K, et al. Zoledronic acid and risedronate in the prevention and treatment of glucocorticoid-induced osteoporosis (HORIZON): a multicentre, double-blind, double-dummy, randomised controlled trial. Lancet 2009;373:1253-63 [54]	RCT	833 (416/417)
4	Cranney A, Welch V, Adachi JD, et al. Calcitonin for the treatment and prevention of corticosteroid-induced osteoporosis. Cochrane Database *Syst Rev* 2000;(2): CD001983 [74]	SR	

- 일차연구문헌 근거표

Author, Publication year	**Reid DM, et al.**

	Lancet 373:1253–1263 (2009)
Title	Zoledronic acid and risedronate in the prevention and treatment of glucocorticoidinduced osteoporosis (HORIZON): a multicentre, double-blind, double-dummy, randomised controlled trial.
Methods	a multicentre, double-blind, double-dummy, randomised controlled trial.
Participants	**N= 833 (중재군/비교군= 416 / 417)** ▸**Inclusion criteria** - Men; pre-menopausal women; post-menopausal women NOS; - steroid>7.5mg/d; steroid duration<1mon; steroid duration 1-3mon; prevalent steroid use at least 3mon; - polymyalgia rheumatica; asthma or COPD; rheumatoid arthritis; SLE ▸**Exclusion criteria** - age>85; pregnancy; carcinoma or suspected carcinoma; hyperparathyroidism; hypoparathyroidism; renal insufficiency; bisphosphonates; Medications that affect bone metabolism; serum 25-hydroxy-Vitamin D concentration <30 nmol/L
Interventions	▸(중재군) - zoledronic acid 5mg iv yearly + calcium 1g/d + Vit D 400-1200IU/d (treatment arm, n=272) - zoledronic acid 5mg iv yearly + calcium 1g/d + Vit D 400-1200IU/d (prevention arm, n=144)

	▸(비교군) - Risedronate 5mg daily + + calcium 1g/d + Vit D 400-1200IU/d (treatment arm, n=273) - Risedronate 5mg daily + + calcium 1g/d + Vit D 400-1200IU/d (prevention arm, n=144)
Outcomes	▸**Primary outcome:** - percentage change from baseline in lumbar spine bone mineral density ▸**Secondary outcomes:** - Changes in bone turnover biomarker concentrations ▸**추적기간** - 1 year
Results	▸Zoledronic acid was non-inferior and superior to risedronate for increase of lumbar spine bone mineral density in both the treatment (least-squares mean 4.06% [SE 0.28] vs 2.71% [SE 0.28], mean difference 1.36% [95% CI 0.67-2.05], p=0.0001) and prevention (2.60% [0.45] vs 0.64% [0.46], 1.96% [1.04-2.88], p<0.0001) subgroups at 12 months.

- **Reference**

	문헌정보	연구유형	연구대상자수 (치료군/비교군)
1	Amiche MA, Albaum JM, Tadrous M et al. Efficacy of osteoporosis pharmacotherapies in preventing fracture among oral glucocorticoid users: a network meta-analysis. Osteoporos Int 2016;27:1989-98 [53]	SR	
2	Albaum JM, Youn S, Levesque LE, Gershon AS, Cadarette SM. Osteoporosis management among chronic glucocorticoid users: a systematic review. J Popul Ther Clin Pharmacol 2014;21:e486-504 [52]	SR	
3	Lekamwasam S, Adachi JD, Agnusdei D et al. A framework for the development of guidelines for the management of glucocorticoid induced osteoporosis. Osteoporos Int 2012a;23:2257-76 [48]	CPG	
4	Grossman JM, Gordon R, Ranganath VK et al. American College of Rheumatology 2010 recommendations for the prevention and treatment of glucocorticoid-induced osteoporosis. Arthritis Care Res (Hoboken) 2010;62:1515-26 [49]	CPG	

- 일차연구문헌 근거표 : 없음

▣ 핵심질문 3-3.

40세 이상 성인에서 테리파라티드는 글루코코르티코이드 유발 골다공증 예방과 치료에 효과적인가?

▣ PICO

Patients	Intervention	Comparators	Outcomes
40세 이상 성인	테리파라티드		글루코코르티코이드 유발 골다공증 예방과 치료 효과

▣ 권고비교표

	지침 1 (ACR)	지침2 (IOF-ECST)	지침3 (FRENCH)	지침4 (CANADA)	지침5 (NOGG)
출판년도	2017	2012	2014	2010	2017

AGREE 평가점수	89	67	56	44	67
권고문	Adults age≥40 years at moderate and high risk of fracture, If bisphosphonate treatment is not appropriate, teriparatide should be used rather than the patient receiving no additional treatment beyond calcium and vitaminD.	1 Bone-protective treatment should be started at the onset of glucocorticoid therapy in patients at increased risk of fracture. 2. Alendronate, etidronate, risedronate, zoledronic acid and teriparatide are the front-line therapeutic options for the majority of patients.	Teriparatide can be prescribed as the first-line drug in patients at high fracture risk and is reimbursed by the French statutory healthcare system in patients with at least two prevalent vertebral fractures at diagnosis	Teriparatide should be considered for those at high risk for fracture who are taking glucocorticoids (≥ three months cumulative therapy during the preceding year at a prednisone equivalent dose ≥ 7.5 mg daily)	1. Women and men age ≥70 years with a previous fragility fracture, or taking high doses of glucocorticoids (≥7.5 mg/day prednisolone), should be considered for bone protective therapy. 2.Bone-protective treatment should be started at the onset of glucocorticoid therapy in individuals at high risk of fracture. 3. Alendronate and risedronate are first line treatment options.

					Where these are contraindicated or not tolerated, zoledronic acid or teriparatide are alternative options
근거수준,권고등급	I / A	I / A	I / A	I / A	I / A

▣ 근거 내용 정리

[지침1] ACR 2017

-reference

	문헌정보	연구유형	연구대상자수 (치료군/비교군)
1	Lane NE, Sanchez S, Modin GW, Genant HK, Pierini E, Arnaud CD. Parathyroid hormone treatment can reverse corticosteroid-induced	RCT	51 (28/23)

	osteoporosis. Results of a randomized controlled clinical trial. J Clin Invest 1998; 102(8):1627-33 [76]		
2	Hopkins RB, Goeree R, Pullenayegum E, Adachi JD, Papaioannou A, Xie F, et al. The relative efficacy of nine osteoporosis medications for reducing the rate of fractures in post-menopausal women. BMC Musculoskelet Disord. 2011;12:209 [41]	SR	
3	Neer RM, Arnaud CD, Zanchetta JR, Prince R, Gaich GA, Reginster JY, et al. Effect of parathyroid hormone (1-34) on fractures and bone mineral density in postmenopausal women with osteoporosis. N Engl J Med. 2001;344(19):1434-1441 [77]	RCT	1,627 (544/1,083)
4	Stevenson M, Jones ML, De Nigris E, Brewer N, Davis S, Oakley J. A systematic review and economic evaluation of alendronate, etidronate, risedronate, raloxifene and teriparatide for the prevention and treatment of postmenopausal osteoporosis. Health Technol Assess. 2005;9(22):1-160 [78]	SR	
5	Vestergaard P, Jorgensen NR, Mosekilde L, Schwarz P. Effects of parathyroid hormone alone or in combination with antiresorptive therapy on bone mineral density and fracture risk—a meta-analysis. Osteoporos Int. 2007;18(1):45-57 [79]	a meta-analysis	

- **일차연구문헌 근거표**

Author, Publication year	**N. E. Lane, et al.** **J Clin Invest 1998; 102(8):1627-33.**
Title	Parathyroid hormone treatment can reverse corticosteroid-induced osteoporosis. Results of a randomized controlled clinical trial.
Methods	a randomized controlled clinical trial.
Participants	**N= 51 (중재군/비교군= 28/23)** **▸Inclusion criteria:** - Postmenopausal women, 50–82 yr of age, with a variety of chronic noninfectious inflammatory diseases, were eligible for the study if they had osteoporosis defined by low bone mass (>2.5 SD below mean young normal values at the lumbar spine or femoral neck), had been menopausal for ≥ 3 yr, had been taking hormone replacement therapy (Premarin 0.6 25 mg a day or an equivalent dose of another estrogen) for ≥1 yr, had been treated with prednisone or its equivalent for the previous 12 mo at a mean daily dose of 5.0–20 mg, and were expected to continue corticosteroid treatment for at least 1 yr

	▸**Exclusion criteria:** - Patients were excluded from the study if they had secondary osteoporosis other than from rheumatic diseases and corticosteroids, renal or hepatic dysfunction, or abnormalities on spinal radiographs that precluded accurate measurements of the lumbar spine by quantitative computed tomography (QCT) or dual-energy x-ray absorptiometry (DXA).
Interventions	▸(중재군) - hPTH (1-34) 25 mcg daily + Premarin 0.6 25 mg a day or an equivalent dose of another estrogen + 1500mg/d + VIt.D 800 IU/d ▸(비교군) - Premarin 0.6 25 mg a day or an equivalent dose of another estrogen + 1500mg/d + VIt.D 800 IU/d
Outcomes	▸**Primary outcome:** **-** bone mineral density (BMD) measurements of the lumbar spine by quantitative computed tomography (QCT) ▸**Secondary outcomes:** - BMD measurements of the lumbar spine, hip, and forearm by dual-energy x-ray absorptiometry (DXA); and biochemical markers of bone turnover. ▸ 추적기간

	- 12 months
Results	▸The mean(±SE) changes in BMD of the lumbar spine by QCT and DXA in the PTH group were 35±5.5% and 11±1.4%, respectively, compared with a relatively small change of 1.7±1.8% and 0±0.9% in the estrogen-only group. ▸The differences in mean percentage between the groups at 1 yr were 33.5% for the lumbar spine by QCT (*P*<0.001) and 9.8% for the lumbar spine by DXA (*P*<0.001). ▸The changes in the hip and forearm were not significantly different between or within the groups. During the first 3 mo of PTH treatment, markers of bone formation increased to nearly 150%, whereas markers of bone resorption increased only 100%, suggesting an early uncoupling of bone turnover in favor of formation.
Author, Publication year	**Neer RM et al.** **N Engl J Med. 2001;344(19):1434-1441**

Title	Effect of parathyroid hormone (1-34) on fractures and bone mineral density in postmenopausal women with osteoporosis..
Methods	a randomized controlled clinical trial.
Participants	**N= 51 (중재군/비교군= 28/23)** ▸**Inclusion criteria:** - Women were eligible for enrollment if they were ambulatory, if a period of at least five years had elapsed since menopause, and if they had at least one moderate or two mild atraumatic vertebral fractures on radiographs of the thoracic and lumbar spine, and an ambulatory status.6 For women with fewer than two moderate fractures, an additional criterion for enrollment was a value for bone mineral density of the hip or lumbar spine that was at least 1 SD below the mean value in normal premenopausal white women (age range, 20 to 35 years). ▸**Exclusion criteria:** - We excluded women with illnesses that affect bone or calcium metabolism, urolithiasis within the preceding 5 years, impaired hepatic function, a serum creatinine concentration exceeding 2 mg per deciliter (177 μmol per liter), or alcohol or drug abuse, as well as women who had taken drugs that alter bone metabolism within the previous 2 to 24 months (depending on the drug)
Interventions	▸(중재군) - parathyroid hormone (1-34) 20μg + 1000 mg calcium + 400 to 1200 IU of vitamin D

	- parathyroid hormone (1-34) 40μg + 1000 mg calcium + 400 to 1200 IU of vitamin D ▸(비교군) - placebo + 1000 mg of calcium and 400 to 1200 IU of vitamin D
Outcomes	▸**Primary outcome:** **-** new vertebral faractures ▸**Secondary outcomes:** - new nonvertebral fragility fractures - bone mineral density in lumbar spine and femoral neck - total-body bone mineral - side effects ▸ 추적기간 - median duration 21 months
Results	▸New vertebral fractures occurred in 14 percent of the women in the placebo group and in 5 percent and 4 percent, respectively, of the women in the 20-μg and 40-μg parathyroid hormone groups; the respective relative risks of fracture in the 20-μg and 40-μg groups, as compared with the placebo group, were 0.35 and 0.31 (95 percent confidence intervals, 0.22 to 0.55 and 0.19 to 0.50). ▸New nonvertebral fragility fractures occurred in 6 percent of the women in the placebo group and in 3 percent of those in each parathyroid hormone group (relative risk, 0.47 and 0.46, respectively [95 percent confidence intervals, 0.25 to 0.88 and 0.25 to 0.86]). ▸As

compared with placebo, the 20-μg and 40-μg doses of parathyroid hormone increased bone mineral density by 9 and 13 more percentage points in the lumbar spine and by 3 and 6 more percentage points in the femoral neck; the 40-μg dose decreased bone mineral density at the shaft of the radius by 2 more percentage points.

▸Both doses increased total-body bone mineral by 2 to 4 more percentage points than did placebo.

▸Parathyroid hormone had only minor side effects (occasional nausea and headache).

[지침2] 2010 IOF-ECTS

- **reference**

	문헌정보	연구유형	연구대상자수 (치료군/비교군)
1	Burshell AL, Moricke R, Correa-Rotter R, Chen P, Warner MR, Dalsky GP, Taylor KA, Krege JH (2010) Correlations between	a randomized, double-blind, double-	157 (80/77)

	biochemical markers of bone turnover and bone density responses in patients with glucocorticoid-induced osteoporosis treated with teriparatide or alendronate. Bone 46:935–939 [80]	dummy, active-comparator controlled trial	
2	Devogelaer JP, Adler RA, Recknor C, See K,Warner MR,Wong M, Krohn K (2010) Baseline glucocorticoid dose and bone mineral density response with teriparatide or alendronate therapy in patients with glucocorticoid-induced osteoporosis. J Rheumatol 37:141–148 [81]	a randomized, double-blind, double-dummy clinical trial	387 (195/192)
3	Langdahl BL, Marin F, Shane E, Dobnig H, Zanchetta JR, Maricic M, Krohn K, See K, Warner MR (2009) Teriparatide versus alendronate for treating glucocorticoid-induced osteoporosis: an analysis by gender and menopausal status. Osteoporos Int 20:2095–2104 [51]	a randomized, double-blind study	277 (134/143)
4	Saag KG, Zanchetta JR, Devogelaer JP, Adler RA, Eastell R, See K, Krege JH, Krohn K, Warner MR (2009) Effects of teriparatide versus alendronate for treating glucocorticoid-induced osteoporosis: 36-month results of a randomized, double-blind, controlled trial. Arthritis Rheum 60:3346–3355 [50]	RCT	428 (214/214)

- **일차연구문헌 근거표**

Author, Publication year	**Burshell AL et al.** **Bone 46:935–939**
Title	Correlations between biochemical markers of bone turnover and bone density responses in patients with glucocorticoid-induced osteoporosis treated with teriparatide or alendronate.
Methods	a randomized, double-blind, double-dummy, active-comparator controlled trial
Participants	**N= 157 (중재군/비교군= 80/77)** **▸Inclusion criteria:** - patients on ≥5 mg/day of prednisolone or equivalent for ≥3 months, either T score ≤−2.0 (LS or TH) or T score of ≤1.0 plus at least one VF **▸Exclusion criteria:** - N/R

Interventions	▸(중재군) - teriparatide 20 μg/day ▸(비교군) - aldendronate 10 mg/day
Outcomes	▸**Primary outcome:** **-** changes in serum bone turnover markers ▸**Secondary outcomes:** - changes in lumbar spine (LS) and femoral neck (FN) BMD ▸ 추적기간 - 18 months
Results	▸In the teriparatide group, increases in LS and FN BMD at 18 months were not significantly correlated with baseline marker concentrations (P>0.05) but were correlated with the increases in PINP at 1 and 6 months (P<0.05). ▸In the alendronate group, the increase in FN BMD at 18 months was positively correlated with baseline marker concentrations (P<0.05) and negatively correlated with change in PINP and Sβ-CTX at 1 and 6 months. ▸In addition, in the alendronate group, the increase in LS BMD was negatively correlated with change in Sβ-CTX at 1 month (P<0.05). ▸Increases in BMD at the spine and hip were independent of baseline bone turnover in

	the teriparatide group, while increases in hip BMD were dependent on baseline bone turnover in the alendronate group

Author, Publication year	**Devogelaer et al.** **J Rheumatol 37:141–148**
Title	Baseline glucocorticoid dose and bone mineral density response with teriparatide or alendronate therapy in patients with glucocorticoid-induced osteoporosis.
Methods	a randomized, double-blind, double-dummy clinical trial
Participants	**N= 387 (중재군/비교군= 195/192)** **▸Inclusion criteria:** - patients on ≥5 mg/day of prednisolone or equivalent for ≥3 months, either T score ≤−2.0 (LS or TH) or T score of ≤1.0 plus at least one fragility fracture **▸Exclusion criteria:** - N/R

Interventions	▸(중재군) - teriparatide 20 μg/day ▸(비교군) - aldendronate 10 mg/day
Outcomes	▸**Primary outcome:** **-** LS BMD at 18 months. ▸**Secondary outcomes:** - FN, and TH BMD at 18 months ▸ 추적기간 - 18 months
Results	▸Baseline LS, FN, and TH BMD were similar between groups, and between glucocorticoid dose categories within each group. LS BMD increases at the low, medium, and high glucocorticoid doses were 8.1%, 6.6%, and 4.6%, respectively, with teriparatide, and 3.6%, 2.8%, and 2.3% with alendronate. ▸Analyzed as a continuous variable, higher glucocorticoid doses had a negative, but nonsignificant, effect on the percentage increase in LS BMD in both groups. ▸Glucocorticoid dose did not significantly affect FN or TH BMD increases in either group. Across the 3 glucocorticoid dose categories, the overall LS BMD increases were different for both treatments combined (p = 0.033), but the relative differences

	between the treatment groups were not different (interaction, p = 0.52).

Author, Publication year	**Langdahl et al.** **Osteoporos Int 20:2095–2104**
Title	Teriparatide versus alendronate for treating glucocorticoid-induced osteoporosis: an analysis by gender and menopausal status.
Methods	a multicenter, randomized, double-blind study
Participants	**N= 277 (중재군/비교군= 134/143)** ▸**Inclusion criteria:** - patients on ≥5 mg/day of prednisolone or equivalent for ≥3 months, either T score ≤−2.0 (LS or TH) or T score of ≤1.0 plus at least one fragility fracture ▸**Exclusion criteria:** - skeletal diseases other than GIO, malignancies, Paget's disease, impaired renal functions, untreated thyroid diseases, heparin therapy, excess alcohol

Interventions	▸(중재군) - teriparatide 20 μg/day ▸(비교군) - alendronate 10 mg/day
Outcomes	▸**Primary outcome:** **-** change in lumbar spine BMD ▸**Secondary outcomes:** - change in hip BMD, change in bone biomarkers, fracture incidence, and safety. ▸ 추적기간 - 18 months
Results	▸At 18 months, mean percent increases from baseline in lumbar spine BMD were significantly greater in the teriparatide versus alendronate group in postmenopausal women (7.8% versus 3.7%, p<0.001), premenopausal women (7.0% versus 0.7%, p<0.001), and men (7.3% versus 3.7%, p=0.03). ▸Radiographic vertebral fractures occurred in one teriparatide (one postmenopausal) and ten alendronate patients (six postmenopausal, four men), and nonvertebral fractures occurred in 12 teriparatide (nine postmenopausal, two premenopausal, one man) and eight alendronate patients (six postmenopausal, two men). The proportion of patients reporting adverse events in teriparatide versus alendronate groups was consistent

	across subgroups.

Author, Publication year	**Saag KG et al.** **Arthritis Rheum. 2009 Nov;60(11):3346-55**
Title	Effects of Teriparatide Versus Alendronate for Treating Glucocorticoid-Induced Osteoporosis Thirty-Six–Month Results of a Randomized, Double-Blind, Controlled Trial Arthritis Rheum.
Methods	a Randomized, Double-Blind, Controlled Tria
Participants	**N= 428 (중재군/비교군= 214/214)** **▸Inclusion criteria** - Ambulatory patients were eligible for enrollment - if they met the following criteria: - an age of 21 years or more, - a history of sustained glucocorticoid therapy, - and a T score (the number of standard deviations above or below the mean value in normal adults) for bone mineral density at the lumbar spine or total hip of either −2.0 or less or −1.0 or less in addition to at least one fragility fracture during treatment with glucocorticoids. - Sustained glucocorticoid therapy was defined as a mean daily dose of 5 mg or more of prednisone or its equivalent for 3 or more consecutive months immediately preceding the

	screening visit. ▸**Exclusion criteria** - Patients were excluded if they had fewer than three lumbar vertebrae that could be evaluated on dual energy x-ray absorptiometry, abnormal laboratory values, unresolved skeletal diseases other than glucocorticoid-induced osteoporosis, - a history of cancer within 5 years before screening (with the exception of superficial basal-cell or squamous-cell carcinomas of the skin that had been definitively treated), - an increased risk of osteosarcoma - gastrointestinal disorders that would be likely to reduce tolerance of oral alendronate, or substantial renal impairment (on the basis of the Cockcroft–Gault formula). - Patients were excluded if they had received a bisphosphonate for more than 2 weeks within 6 months before enrollment or for more than 2 years within the previous 3 years and for nontrivial exposure to other osteoporosis therapies.
Interventions	▸(중재군) - teriparatide 20 μg/day ▸(비교군) - alendronate 10 mg/day
Outcomes	▸**Primary outcome:** - BMD change at 18months

	▸**Secondary outcomes:** - Fracture ▸**추적기간** - 36 months
Results	▸Increases in BMD from baseline were significantly greater in the teriparatide group than in the alendronate group, and at 36 months were 11.0% versus 5.3% for lumbar spine, 5.2% versus 2.7% for total hip, and 6.3% versus 3.4% for femoral neck (*P* < 0.001 for all). ▸Fewer subjects had vertebral fractures in the teriparatide group than in the alendronate group (3 [1.7%] of 173 versus 13 [7.7%] of 169; *P* 0.007), with most occurring during the first 18 months. There was no significant difference between groups in the incidence of nonvertebral fractures (16 [7.5%] of 214 subjects taking teriparatide versus 15 [7.0%] of 214 subjects taking alendronate; *P* 0.843).

[지침3] 2014 FRENCH

- **reference**

	문헌정보	연구유형	연구대상자수

			(치료군/비교군)
1	Saag KG, Shane E, Boonen S, et al. Teriparatide or alendronate in glucocorticoid-induced osteoporosis. N Engl J Med 2007;357:2028–39 [45]	RCT	428 (214/214)
2	Saag KG, Zanchetta JR, Devogelaer JP, Adler RA, Eastell R, See K, Krege JH, Krohn K, Warner MR (2009) Effects of teriparatide versus alendronate for treating glucocorticoid-induced osteoporosis: 36-month results of a randomized, double-blind, controlled trial. Arthritis Rheum 60:3346–3355 [50]	RCT	428 (214/214)

- **일차연구문헌 근거표**

Author, Publication year	**Saag KG et al.** **N Engl J Med 2007;357:2028–39.**
Title	Teriparatide or alendronate in glucocorticoid-induced osteoporosis.
Methods	randomized, double-blind, controlled trial,

Participants	**N= 428 (중재군/비교군= 214/214)** ▸**Inclusion criteria** - women and men with osteoporosis (ages, 22 to 89 years) who had received glucocorticoids for at least 3 months (prednisone equivalent, 5 mg daily or more). ▸**Exclusion criteria** - NR
Interventions	▸(중재군) - teriparatide 20 μg/day ▸(비교군) - alendronate 10 mg/day
Outcomes	▸**Primary outcome:** - the change in bone mineral density at the lumbar spine. ▸**Secondary outcomes:** - changes in bone mineral density at the total hip and in markers of bone turnover, the time to changes in bone mineral density, the incidence of fractures, and safety. ▸**추적기간** - 36 months

Results	▸At the last measurement, the mean (±SE) bone mineral density at the lumbar spine had increased more in the teriparatide group than in the alendronate group (7.2±0.7% vs. 3.4±0.7%, P<0.001). ▸A significant difference between the groups was reached by 6 months (P<0.001). At 12 months, bone mineral density at the total hip had increased more in the teriparatide group. ▸Fewer new vertebral fractures occurred in the teriparatide group than in the alendronate group (0.6% vs. 6.1%, P¼0.004); the incidence of nonvertebral fractures was similar in the two groups (5.6% vs. 3.7%, P¼0.36). Significantly more patients in the teriparatide group had at least one elevated measure of serum calcium.

Author, Publication year	**Saag KG et al.** **Arthritis Rheum. 2009 Nov;60(11):3346-55**
Title	Effects of Teriparatide Versus Alendronate for Treating Glucocorticoid-Induced Osteoporosis Thirty-Six–Month Results of a Randomized, Double-Blind, Controlled Trial Arthritis Rheum.
Methods	a Randomized, Double-Blind, Controlled Trial
Participants	**N= 428 (중재군/비교군= 214/214)**

‣**Inclusion criteria**

- Ambulatory patients were eligible for enrollment
- if they met the following criteria:
- an age of 21 years or more,
- a history of sustained glucocorticoid therapy,
- and a T score (the number of standard deviations above or below the mean value in normal adults) for bone mineral density at the lumbar spine or total hip of either −2.0 or less or −1.0 or less in addition to at least one fragility fracture during treatment with glucocorticoids.
- Sustained glucocorticoid therapy was defined as a mean daily dose of 5 mg or more of prednisone or its equivalent for 3 or more consecutive months immediately preceding the screening visit.

‣**Exclusion criteria**

- Patients were excluded if they had fewer than three lumbar vertebrae that could be evaluated on dual energy x-ray absorptiometry, abnormal laboratory values, unresolved skeletal diseases other than glucocorticoid-induced osteoporosis,
- a history of cancer within 5 years before screening (with the exception of superficial basal-cell or squamous-cell carcinomas of the skin that had been definitively treated),
- an increased risk of osteosarcoma
- gastrointestinal disorders that would be likely to reduce tolerance of oral alendronate, or substantial renal impairment (on the basis of the Cockcroft–Gault formula).
- Patients were excluded if they had received a bisphosphonate for more than 2 weeks

	within 6 months before enrollment or for more than 2 years within the previous 3 years and for nontrivial exposure to other osteoporosis therapies.
Interventions	▸(중재군) - teriparatide 20 μg/day ▸(비교군) - alendronate 10 mg/day
Outcomes	▸**Primary outcome:** - BMD change at 18months ▸**Secondary outcomes:** - Fracture ▸**추적기간** - 36 months
Results	▸Increases in BMD from baseline were significantly greater in the teriparatide group than in the alendronate group, and at 36 months were 11.0% versus 5.3% for lumbar spine, 5.2% versus 2.7% for total hip, and 6.3% versus 3.4% for femoral neck (*P* < 0.001 for all). ▸Fewer subjects had vertebral fractures in the teriparatide group than in the alendronate group (3 [1.7%] of 173 versus 13 [7.7%] of 169; *P* 0.007), with most occurring during the first 18 months. There was no significant difference between groups in the

	incidence of nonvertebral fractures (16 [7.5%] of 214 subjects taking teriparatide versus 15 [7.0%] of 214 subjects taking alendronate; *P* 0.843).

[지침4] 2010 CANADA

- **reference**

	문헌정보	연구유형	연구대상자수 (치료군/비교군)
1	MacLean C, Newberry S, Maglione M, et al. Systematic review: comparative effectiveness of treatments to prevent fractures in men and women with low bone density or osteoporosis. *Ann Intern Med* 2008;148:197-213 [72]	SR	
2	Qaseem A, Snow V, Shekelle P, et al. Pharmacologic treatment of low bone density or osteoporosis to prevent fractures: a clinical practice guideline from the American College of Physicians. *Ann Intern Med* 2008;149:404-15 [73]	clinical practice guideline	

- **일차연구문헌 근거표 : 없음.**

[지침5] 2017 NOGG

- **reference**

	문헌정보	연구유형	연구대상자수 (치료군/비교군)
1	Albaum JM, Youn S, Levesque LE, Gershon AS, Cadarette SM. Osteoporosis management among chronic glucocorticoid users: a systematic review. J Popul Ther Clin Pharmacol. 2014;21(3):e486-504 [52]	SR	
2	Amiche MA, Albaum JM, Tadrous M et al. Efficacy of osteoporosis pharmacotherapies in preventing fracture among oral glucocorticoid users: a network meta-analysis. Osteoporos Int 2016;27:1989-98 [53]	meta-analysis	

3	Lekamwasam S, Adachi JD, Agnusdei D et al. A framework for the development of guidelines for the management of glucocorticoid-induced osteoporosis. Osteoporos Int 2012a;23:2257-76 [48]	clinical practice guideline	
4	Grossman JM, Gordon R, Ranganath VK et al. American College of Rheumatology 2010 recommendations for the prevention and treatment of glucocorticoid-induced osteoporosis. Arthritis Care Res (Hoboken) 2010;62:1515-26 [49]	clinical practice guideline	

- **일차연구문헌 근거표 : 없음.**

▣ 핵심질문 3-4.

40세 이상 성인에서 데노수맙 사용은 글루코코르티코이드 유발 골다공증 예방과 치료에 효과적인가?

▣ PICO

Patients	Intervention	Comparators	Outcomes
40세 이상 성인	데노수맙		글루코코르티코이드 유발 골다공증 예방과 치료 효과

▣ 권고비교표

	지침1 (ACR)	지침2 (IOF-ECTS)	지침3 (FRENCH)	지침4 (CANADA)	지침5 (NOGG)
출판년도	2017	2012	2014	2010	2017
AGREE 평가점수	89	67	56	44	67
권고문	If neither oral nor IV bisphosphonates nor	NA	NA	NA	NA

	teriparatide treatment is appropriate, denosumab should be used rather than the patient receiving no additional treatment beyond calcium and vitamin D.				
근거수준,권고등급	II / B	NA	NA	NA	NA

▣ 근거 내용 정리

[지침1] 2017 ACR

- **Reference**

	문헌정보	연구유형	연구대상자수

			(치료군/비교군)
1	Effects of denosumab on bone mineral density and bone turnover in patients with rheumatoid arthritis receiving concurrent glucocorticoids or bisphosphonates. Ann Rheum Dis. 2010 May;69(5):872-5 [82]	RCT	90 (61/29)
2	Effect of denosumab on Japanese patients with rheumatoid arthritis: a dose–response study of AMG 162 (Denosumab) in patients with RheumatoId arthritis on methotrexate to Validate inhibitory effect on bone Erosion (DRIVE)—a 12-month, multicentre, randomised, double-blind, placebo-controlled, phase II clinical trial. Ann Rheum Dis. 2016 Jun;75(6):983-90 [83]	RCT	340 (88 / 252)

- **일차연구문헌 근거표**

Author, Publication year	**Dore RK et al.** **Ann Rheum Dis. 2010 May;69(5):872-5**
Title	Effects of denosumab on bone mineral density and bone turnover in patients with rheumatoid arthritis receiving concurrent glucocorticoids or bisphosphonates
Methods	a randomised, double-blind, placebo-controlled study

Participants	**N=90 (중재군/비교군= 61/29)** ▸**Inclusion criteria** - activeRA for ≥24 weeks and were receiving methotrexate - patients using ≥2.5 mg/day of prednisone (or equivalent) for ≥90 days during the study. ▸**Exclusion criteria** - NR
Interventions	▸(중재군) - denosumab 60 mg (n=28) - denosumab 180 mg (n=33) ▸(비교군) - placebo
Outcomes	▸**Primary outcome:** - comparisons of changes in BMD and bone turnover markers from baseline through 12 months ▸**Secondary outcomes:** - the correlation between BMD changes and baseline values of bone turnover markers. ▸추적기간 - 12 month

Results	▸Denosumab treatment increased mean lumbar spine and hip BMD and reduced sCTx-I and P1NP compared with placebo through 12 months, regardless of baseline BMD or marker levels or concomitant bisphosphonate or glucocorticoid use.

Author, Publication year	**Takeuchi et al.** **Ann Rheum Dis. 2016 Jun;75(6):983-90**
Title	Effect of denosumab on Japanese patients with rheumatoid arthritis: a dose–response study of AMG 162 (Denosumab) in patients with RheumatoId arthritis on methotrexate to Validate inhibitory effect on bone Erosion (DRIVE)—a 12-month, multicentre, randomised, double-blind, placebo-controlled, phase II clinical trial.
Methods	multicentre, randomised, placebo-controlled phase III study
Participants	**N= 340 (중재군/비교군= 252/88)** **▸Inclusion criteria** - disease duration of RA between 6 month and <5 years, - 20–74 years old, - use of methotrexate for at least 8 weeks prior to first investigational product (IP) administration - confirmed at least 6 swollen joints among 58 joints at thescreening by investigator assessment.

	- presence of bone erosion as assessed by the investigator on radiographs or meeting the following criteria at a screening: C-reactive protein (CRP) ≥1.0 mg/dL or erythrocyte sedimentation rate ≥28 mm/h and positive for anticyclic citrullinated peptide antibodies or RF>20 IU/mL. ▸**Exclusion criteria** **-** classified RA functional status as class IV10 and previous or current treatment with any biologics for RA treatment. - Bisphosphonate use and the use of oral glucocorticoid >10 mg/day (prednisolone equivalent) were prohibited throughout the study
Interventions	▸(중재군) - denosumab 60 mg every 6 months, or every 3 months, or every 2 months ▸(비교군) - placebo
Outcomes	▸**Primary outcome:** - change from the baseline in the modified Sharp erosion score at 12 months. ▸**Secondary outcomes:** **-** change from the baseline in the modified Sharp erosion score at 6 months, - change from the baseline in themodified Sharp joint space narrowing (JSN) score and the modified total Sharp score (TSS) at 6 and 12 months - percent change from the baseline in BMD at the LS and TH at 6 and 12 months

	▸추적기간 - 12 month
Results	▸Denosumab significantly inhibited the progression of bone erosion at 12 months compared with the placebo, and the mean changes of the modified Sharp erosion score at 12 months ▸denosumab increased bone mineral density. No apparent difference was observed in the safety profiles of denosumab and placebo.

[지침2] 2012 IOF-ECTS

- **Reference** – 없음

- **일차연구문헌 근거표** – 없음

[지침3] 2014 FRENCH

- **Reference** – 없음

- **일차연구문헌 근거표** – 없음

[지침4] 2010 CANADA

- **Reference** – 없음

- **일차연구문헌 근거표** – 없음

[지침5] 2017 NOGG

- **Reference** – 없음

- **일차연구문헌 근거표** – 없음

▣ 핵심질문 3-5.

폐경 후 여성에서 선택적 에스트로겐 수용체 조절제 사용은 글루코코르티코이드 유발 골다공증 예방과 치료에 효과적인가?

▣ PICO

Patients	Intervention	Comparators	Outcomes
폐경 후 여성	선택적 에스트로겐 수용체 조절제		글루코코르티코이드 유발 골다공증 예방과 치료

▣ 권고비교표

	지침1 (ACR)	지침2 (IOF-ECTS)	지침3 (FRENCH)	지침4 (CANADA)	지침5 (NOGG)
출판년도	2017	2012	2014	2010	2017
AGREE 평가점수	89	67	56	44	67
권고문	Adults age≥40 years at moderate and high	NA	NA	NA	NA

	risk of fracture, For postmenopausal women in whom none of these medications is appropriate, raloxifene should be used rather than the patient receiving no additional treatment beyond calcium and vitamin D				
근거수준, 권고등급	I/B	NA	NA	NA	NA

▣ 근거 내용 정리

[지침1] 2017 ACR

- **Reference**

	문헌정보	연구유형	연구대상자수 (치료군/비교군)
1	Mok, C. C., Ying, K. Y., To, C. H., Ho, L. Y., Yu, K. L., Lee, H. K. Ma, K. M. Raloxifene for prevention of glucocorticoid-induced bone loss: a 12-month randomised double-blinded placebo-controlled trial. Ann Rheum Dis. 2011 May;70(5):778-84 [75]	RCT	90 (61/29)

- **일차연구문헌 근거표**

Author, Publication year	Mok CC et al. Ann Rheum Dis. 2011 May;70(5):778-84.
Title	Raloxifene for prevention of glucocorticoid-induced bone loss: a 12-month randomised double-blinded placebo-controlled trial.
Methods	randomised double-blinded placebo-controlled trial.
Participants	**N= 90 (중재군/비교군= 28 (60mg), 33(180mg)/ 29): subgroup analysis** **▸Inclusion criteria**

	- postmenopausal for ≥12 months, - having been receiving a stable dose of corticosteroids (prednisone≤10 mg/day or equivalent) for ≥6 months prior to entry, - patients expected to be on corticosteroid treatment throughout the study period, - written consent could be obtained. ▸**Exclusion criteria** - patients with hypercoagulability risk factors (eg, positive anti-phospholipid antibodies) or a history of thromboembolism) - history of allergic reactions or intolerance to raloxifene or other SERMs; - patients receiving bisphosphonates, parathyroid hormone, SERMs, anticonvulsants or anticytokine therapies within 6 months prior to entry; - patients with known bone disorders such as osteomalacia, renal osteodystrophy and hyperparathyroidism; - patients with undiagnosed uterine bleeding; - patients with serum creatinine level of≥200 μmol/litre.
Interventions	▸(중재군) - raloxifene (60mg/day) + calcium 1000mg/day + calcitriol (0.25μg/day) ▸(비교군) - placebo + calcium 1000mg/day + calcitriol (0.25μg/day)
Outcomes	▸**Primary outcome**

	- BMD of the hip and spine ▸**Secondary outcomes** - bone turnover markers and new vertebral fractures ▸추적기간 - 12 month
Results	▸At month 12, a significant gain in the lumbar spine (+1.3±0.4%; p=0.004) and total hip BMD (+1.0±0.4%; p=0.01) was observed in patients treated with raloxifene but a significant decrease in BMD of the lumbar spine (-0.9±0.4%; p=0.045) and hip (-0.8±0.3%; p=0.01) occurred in the placebo group. ▸The femoral neck BMD did not change significantly in favour of raloxifene. Three new fractures developed exclusively in the patients treated with placebo. ▸Bone formation (serum osteocalcin and procollagen type I N-terminal) and resorption (urine deoxypyridinoline and type I collagen) markers decreased significantly in the raloxifene group but not in patients treated with placebo. ▸Leg cramps were numerically more frequent in the raloxifene group (7% vs 0%) but thromboembolism was not reported in any patients.

[지침2] 2012 IOF-ECTS

- **Reference** – 없음

- **일차연구문헌 근거표** – 없음

[지침3] 2014 FRENCH

- **Reference** – 없음

- **일차연구문헌 근거표** – 없음

[지침4] 2010 CANADA

- **Reference** – 없음

- **일차연구문헌 근거표** – 없음

[지침5] 2017 NOGG

- **Reference** – 없음

- **일차연구문헌 근거표** – 없음

▣ 핵심질문 4.

임신을 계획하고 있는 여성에서 치료 약제 사용은 안전한가?

▣ PICO

Patients	Intervention	Comparators	Outcomes
글루코코르티코이드 유발 골다공증 환자 중 임신가능성 있는 여성	골다공증 치료 약제		임신 중 약제 안전성

▣ 권고비교표

	지침 1 (ACR)	지침 2 (IOF-ECTS)	지침 3 (FRENCH)	지침 4 (Canada)	지침5(NOGG)
출판년도	2017	2012	2014	2010	2017
AGREE 평가점수	89	67	56	44	67

권고문	1. Because of the lack of safety data and the potential fetal harm associated with denosumab and high-dose IV bisphosphonates should be used only in women who are at high risk of fracture in whom treatment with an oral bisphosphonate and teriparatide is not appropriate. 2. There is a lack of data on the safety of currently available OP treatments during pregnancy. Therefore, these guidelines do not include	Caution is advised in the use of bisphosphonates in women of childbearing age.	Women should be advised against starting a pregnancy during the treatment and within 6 months after its discontinuation.	N/A	Caution is advised in the use of bisphosphonates in women of childbearing age.

	recommendations about OP prevention or treatment, other than calcium and vitamin D intake and lifestyle modification, in women who are pregnant.				
근거수준, 권고등급	IV /I	IV/I	IV/I	N/A	IV/I

▣ 근거 내용 정리

[지침1] 2017 ACR

- **Reference** : 없음

- **일차연구문헌 근거표** : 없음

[지침 2] 2012　IOF-ECTS

- **reference**

	문헌정보	연구유형	연구대상자수 (치료군/비교군)
1	Patlas N, Golomb G, Yaffe P, Pinto T, Breuer E, Ornoy A (1999) Transplacental effects of bisphosphonates on fetal skeletal ossification and mineralization in rats. Teratology 60:68–73 [84]	animal study	
2	Losada I, Sartori L, Di Gianantonio E, Zen M, Clementi M, Doria A (2010) Bisphosphonates in patients with autoimmune rheumatic diseases: can they be used in women of childbearing age? Autoimmun Rev 9:547–552 [85]	SR	
3	Levy S, Fayez I, Taguchi N, Han JY, Aiello J, Matsui D, Moretti M, Koren G, Ito S (2009) Pregnancy outcome following in utero exposure to bisphosphonates. Bone 44:428–430 [86]	prospective cohort study	42 (21/21)
4	Ornoy A, Wajnberg R, Diav-Citrin O (2006) The outcome of pregnancy following pre-pregnancy or early pregnancy alendronate treatment. Reprod Toxicol 22:578–579 [87]	prospective observational study	case 24/ control 790

[지침3] 2014 FRENCH

- **Reference** : 없음

- **일차연구문헌 근거표** : 없음

[지침4] 2010 CANADA

- **Reference** : 없음

- **일차연구문헌 근거표** : 없음

[지침5] 2017 NOGG

- **Reference** : 없음

- **일차연구문헌 근거표** : 없음

▣ 핵심질문 5.

글루코코르티코이드 유발 골다공증환자에서 신체계측/영상학적/생화학적 방법을 이용하여 얼마간의 간격으로 모니터링 할 것인가?

▣ PICO

Patients	Intervention	Comparators	Outcomes
글루코코르티코이드 유발 골다공증 환자에서	신체계측/영상학적/생화학적 방법을 이용하여 얼마간의 간격으로 추적관찰을 하는 것이	그 외의 간격(다른 간격)으로 추적 관찰을 하거나 추적 관찰을 하지 않는 것에 비하여	환자의 골밀도 및 생화학적 변화를 가장 효율적으로 확인할 수 있는가?

▣ 권고비교표

	지침 1 (ACR, 2017)	지침 2 (IOF)	지침 3 (French)	지침 4 (CANADA)	지침 5 (NOGG)
출판년도	2017	2012	2014	2010	2017
AGREE 평가점수	89	67	56	44	67

권고문	1) In all adults and children who continue GC treatment, a clinical fracture risk reassessment should be performed every 12 months. 2) For adults ≥ 40 years of age who continue GC treatment and are not treated with an OP medication beyond calcium and vitamin D, reassessment with FRAX, with BMD testing if available, should be completed every 1–3years. 3) For adults ≥ 40 years old who received an OP	1) Measurement of BMD at appropriate intervals 2) Annual height measurement 3) Vertebral fracture assessment by X-ray or DXA if fracture is suspected 4) Assessment of adherence to therapy, including calcium and vitamin D, at each visit 5) Measurement of serum PINP after 3 months of teriparatide therapy	1) Given the rapid onset of bone loss, annual BMD measurement is recommended during the first 2 years of glucocorticoid therapy in the absence of osteoporosis drug therapy or at the end of an osteoporosis drug sequence. Subsequently, the frequency of BMD measurement should be determined based on the BMD values, glucocorticoid dose, and level of control of the underlying disease 2) Clinical follow-up may be sufficient to	NA	NA

	treatment in the past but are no longer being treated with an OP medication other than calcium and vitamin D, BMD testing should be done every 2–3 years. 4) For all adults <40 years of age who continue GC treatment and are at moderate-to-high fracture risk (history of previous fracture, BMD Z score<-3, received very high-dose prednisone ≥30 mg/day and cumulative dose >5 gm] in the previous year, risks for poor		assess adherence 3) Given the rapid onset of bone loss, annual BMD measurement is recommended during the first 2 years of GC therapy in the absence of osteoporosis drug therapy or at the end of an osteoporosis drug sequence. Subsequently, the frequency of BMD measurement should be determined based on the BMD values, glucocorticoid dose, and level of control of the underlying disease 4) Vertebral height measurement once a		

	medication adherence or absorption, or multiple OP risk factors), BMD testing should be done every 2–3 years. 5) For adults ≥ 40 years old who continue GC treatment and are currently treated with an OP medication in addition to calcium and vitamin D, BMD testing should be completed every 2–3 years during treatment in high-risk patients such as those receiving very high-dose GCs (initial prednisone dose ≥30 mg/day, cumulative		year: vertebral fractures result in height loss, which is a nonspecific sign of vertebral disease 5) A morphological assessment of the spine is indicated in patients with back pain or height loss ≥ 2 cm during follow-up		

	dose >5 gm in the previous year), a history of OP fracture occurring after ≥18 months of treatment with antifracture medication (other than calcium and vitamin D), risks for poor medication adherence or absorption, or other significant OP risk factors. 6) For all adults <40 years of age who continue GC treatment and are at moderate-to-high fracture risk (history of previous fracture, BMD Z score<-3, received very high-dose				

	prednisone ≥30 mg/day and cumulative dose >5 gm] in the previous year, risks for poor medication adherence or absorption, or multiple OP risk factors), BMD testing should be done every 2–3years.				
근거수준, 권고등급	전문가 합의, B	전문가 합의, B	전문가 합의, B	NA	NA

▣ 근거 내용 정리

[지침1] 2017 ACR

- **reference** : 없음

- **일차연구문헌 근거표** : 없음

[지침2] 2010 IOF-ECTS

- **reference** :

	문헌정보	연구유형	연구대상자수 (치료군/비교군)
1	Timing of repeat BMD measurements: Development of an absolute risk-based prognostic model – J Bone Miner Res 2009 [88]	Retrospective cohort study(Level III)	Nonosteoporotic Women: 1008, men: 750
2	What is the role of serial bone mineral density measurements in patient management? - 2002 Journal of clinical densitometry [89]	Panel discussion	
3	Clinical value of monitoring BMD in patients treated with bisphosphonates for osteoporosis – 2009 Jounral of bone and mineral research [90]	Expert opinion	
4	Markers of bone turnover for the prediction of fracture risk and monitoring of osteoporosis treatment: a need for international reference standards – 2011 Osteoporosis international [91]	Expert opinion	
5	Development of an algorithm for using PINP to monitor treatment of patients with teriparatide* - 2006 Current medial research and opinion[92]	Expert opinion	

-일차연구문헌 근거표

Author, **Publication year**	**Steven et al.** **J Bone Miner Res 2009**
Title	Timing of repeat BMD measurements: Development of an absolute risk-based prognostic model
Methods	Retrospective cohort study(Level III)
Participants	**N = 1758 (Women: 1008, Men: 750)** ▸Inclusion criteria - Femoral neck BMD score greater than –2.5(nonosteoporosis) ▸Exclusion criteria - Femoral neck BMD score less than –2.5(osteoporosis)
Interventions	No intervention
Outcomes	▸**Primary outcome** - 346 women (34%), 160 men (21%) developed osteoporosis or sustained low-trauma fracture ▸**Secondary outcome** - The risk of osteoporosis or fracture increased with advancing age and lower BMD levels. - Using predicted risk of 10% as a cut-off level for repeating BMD measurement, the estimated time to

	reach the cut-off level varied from 1.5 to 10.6 years. ▸추적기간 - median 7.1 years
Results	▸Based on an individual's current age and BMD T-score, it is possible to estimate the optimal time to repeat BMD testing for the individual. ▸The prognostic model and approach presented in this study may help improve the individualization and management of osteoporosis.

Author, Publication year	**Leon et al., 2002** **2002 Journal of clinical densitometry**
Title	What is the role of serial bone mineral density measurements in patient management?
Methods	Panel discussion
Results	▸Except for patients with expected rapid bone loss, there is rarely an indication for repeating bone mass measurement in less than 1yr. ▸Because it is difficult to predict the rate of loss in an individual patient, a more practical approach is to repeat PA spine measurement in 1 to 2 years in treated patients.

	▸Because the Level of least significant change(LSC) and the expected change in BMD with therapy are often similar in magnitude, there is little value in monitoring patients on antiresorptive treatment at an interval more frequent than 1 year.

Author, Publication year	**Nelson et al., 2009** **2009 Jounral of bone and mineral research**
Title	Clinical value of monitoring BMD in patients treated with bisphosphonates for osteoporosis
Methods	Expert opinion(Level V)
Conclusions	▸The authors suggest that until there is good evidence to do otherwise, clinicians should consider a follow-up BMD test 1yr after starting pharmacologic therapy for osteoporosis and thereafter at intervals determinded by individual patient circumstances. ▸The true purpose of monitoring BMD in patients treated for osteoporosis is to identify the small but substantial number of patients who experience a significant decrease in BMD. These patients should be considered for further evaluation to search for the cause or causes of their decline BMD, which may include poor compliance with the treatment program, deficient calcium/vitamin D intake, malabsorption, confounding disease/disorders/medications with adverse skeletal effects, or true nonresponse to drug.

Author, Publication year	**S. Vasikaran et al., 2011** **2011 Osteoporosis international**
Title	Markers of bone turnover for the prediction of fracture risk and monitoring of osteoporosis treatment: a need for international reference standards
Methods	Expert opinion(Level V)
Conclusions	Identification of secondary osteoporosis ▸The clinical approach to the patient at risk of fractures should always include a consideration of secondary osteoporosis. The level of BMD has proven less useful in selecting individuals for further workup for secondary osteoporosis. It is possible that bone turnover markers could be used for this purpose. ▸Low bone turnover markers may be found in glucocorticoid-induced osteoporosis.

Author, Publication year	**Richard Eastell et al., 2006** **2006 Current medial research and opinion**
Title	Development of an algorithm for using PINP to monitor treatment of patients with teriparatide
Methods	Expert opinion(Level V)

Conclusions	Algorithm for monitoring PINP ▸PINP is measured prior to the initiation of teriparatide, and again after 1-3months of teriparatide therapy. Because alendronate-pretreated patients switched to teriparatide showed PINP response rate of 79% at 1month and 97% at 3months, a 3-month PINP follow-up assessment may be more helpful than earlier assessment in this group of patients.

[지침3] 2014 FRENCH

- **reference** : 없음

- **일차연구문헌 근거표 : 없음.**

[지침4] 2010 CANADA

- **reference** : 없음

- **일차연구문헌 근거표 : 없음.**

[지침5] 2017 NOGG

- **reference** : 없음

- **일차연구문헌 근거표 : 없음.**

▣ 핵심질문 6

글루코코르티코이드 유발 골다공증 치료 중 골절 위험도를 재평가하여 낮은 골절위험도로 확인되었을 경우 치료 중단을 고려할 수 있는가?

▣ PICO

Patients	Intervention	Comparators	Outcomes
글루코코르티코이드 유발 골다공증 진단 후 이에 대한 치료 중인 환자에서	여러 형태로 골절의 위험도를 재평가 했을 때, 낮은 골절위험도로 확인되었을 경우	골다공증 치료를 지속하는 것에 비하여	골다공증 치료를 중단하는 것의 이득/손실이 어떻게 되는가?

▣ 권고비교표

	지침 1 (ACR, 2017)	지침 2 (IOF)	지침 3 (french)	지침 4 (canada)	지침 5 (NOGG)
출판년도	2017	2012	2014	2010	2017
AGREE 평가점수	89	67	56	44	67

권고문	For adults ≥40 years of age who are treated with OP medication in addition to calcium and vitamin D and are discontinuing GC treatment, discontinuation of the OP medication is recommended if fracture risk at the time of GC discontinuation is assessed to be low. Otherwise, the OP treatment course should be completed or continued until the fracture risk is assessed to be low	If glucocorticoid therapy is stopped, withdrawal of bone-protective therapy may be considered, but if glucocorticoids are continued long term, bone protection should be maintained	Osteoporosis drug discontinuation can be considered in patients who meet all the following criteria: no fracture during treatment AND prednisone-equivalent dose≤ 7.5 mg/d AND no new risk factors AND optimal control of under-lying disease activity AND no change in BMD values (with change defined as a decrease ≥ 0.03 g/cm^2 at one or both sites). In every case, the decision to stop osteoporosis drug therapy should rest on a case-by-case	For patients undergoing long-term glucocorticoid therapy, the appropriate duration of osteoporosis treatment is unknown.	If glucocorticoid therapy is stopped, withdrawal of bone-protective therapy may be considered, but if glucocorticoids are continued long term, bone protection should be maintained in the majority of cases

			evaluation of the risk/benefit ratio.		
근거수준, 권고등급	전문가합의, B	전문가합의, B	전문가합의, B	전문가합의, B	전문가합의, B

▣ 근거 내용 정리

[지침1] 2017 ACR

- **reference** : 없음

- **일차연구문헌 근거표** : 없음

[지침2] 2010 IOF-ECTS

- **reference** : 없음

- **일차연구문헌 근거표** : 없음

[지침3] 2014 FRENCH

- **reference** : 없음

- **일차연구문헌 근거표** : 없음

[지침4] 2010 CANADA

- **reference** : 없음

- **일차연구문헌 근거표 : 없음.**

[지침5] 2017 NOGG

- **reference** : 없음

- **일차연구문헌 근거표 : 없음.**

▣ 핵심질문 7

글루코코르티코이드 유발 골다공증 치료 실패를 어떻게 정의할 것인가?

▣ PICO

Patients	Intervention	Comparators	Outcomes
글루코코르티코이드 유발 골다공증 진단 후 이에 대한 치료 중인 환자에서	어떠한 임상 양상 및 영상의학적/생화학적 계측치를 보일 경우		치료의 실패로 정의할 수 있는가?

▣ 권고비교표

	지침 1 (ACR, 2017)	지침 2 (French)	지침 3 (FRENCH)	지침 4 (CANADA)	지침 5 (NOGG)
출판년도	2017	2014	2014	2010	2017
AGREE 평가점수	89	56	56	44	67

권고문	Follow up treatment recommendation Initial treatment failure: For adults ≥40 years of age who are continuing GC treatment who have had a fracture that occurred ≥18 months after beginning treatment with an oral bisphosphonate or had a significant decline in BMD (≥10%/year) after 1 year of treatment, Treat with another class of OP medication or an IV bisphosphonate is recommended rather than the patient	No data are available on switching or combining osteoporosis drugs in patients with significant bone loss (BMD decrease≥ 0.03 g/cm^2) or bone frailty fractures during combined long-termglucocorticoid therapy and osteoporosis drug therapy. Advice from a bone disease specialist should ideally be obtained	NA	NA	NA

	receiving no additional treatment beyong calcium and vitamin D alone or continuing oral bisphosphonate treatment. Treatment if moderate-to-high fracture risk persists after BP therapy: For adults ≥40 years of age who have completed 5 years of bisphosphonate treatement who are continuing GC treatment and are assessed to be at moderate to high risk of fracture, continuation of active OP treatment is				

	recommended rather than the patient receiving no additional treatment beyond calcium and vitamin D.				
근거수준, 권고등급	전문가합의, B	전문가합의, B	NA	NA	NA

▣ 근거 내용 정리

[지침1] 2017 ACR

- **reference** : 없음

- **일차연구문헌 근거표** : 없음

[지침2] 2010 IOF-ECTS

- **reference** : 없음

- **일차연구문헌 근거표** : 없음

[지침3] 2014 FRENCH

- **reference** : 없음

- **일차연구문헌 근거표** : 없음

[지침4] 2010 CANADA

- **reference** : 없음

- **일차연구문헌 근거표 : 없음.**

[지침5] 2017 NOGG

- **reference** : 없음

- **일차연구문헌 근거표 : 없음.**

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부록 8: 수용성, 적용성 평가

▣ 권고의 수용성, 적용성 평가

▣ 핵심질문 (KQ1) : 글루코코르티코이드를 사용하는 환자에서 비약물적 치료가 GIOP 예방과 치료에 효과적인가?

구분	지침 1 (ACR)	지침 2 (IOF-ESTS)	지침 3 (FRENCH)	지침 4 (CANADA)	지침 5 (NOGG)
권고	All adults taking prednisone at a dose of ≥2.5 mg/day for ≥3 months Optimize calcium intake (800–1,000 mg/day) and vitamin D intake (600–800 IU/day) and lifestyle modifications (balanced diet,	Tobacco use and alcohol abuse should be avoided, and appropriate levels of physical exercise should be encouraged.	Encourage smoking cessation and a decrease of excessive alcohol use to a reasonable level	1. Exercises involving resistance training appropriate for the individual's age and functional capacity and/or weightbearing aerobic exercises are recommended for those with osteoporosis or at risk for osteoporosis	Regular weight-bearing exercise should be advised, tailored according to the needs and abilities of the individual patient.

구분	지침 1 (ACR)	지침 2 (IOF-ESTS)	지침 3 (FRENCH)	지침 4 (CANADA)	지침 5 (NOGG)
	maintaining weight in the recommended range, smoking cessation, regular weight-bearing or resistance training exercise, limiting alcohol intake to 1–2 alcoholic beverages/day) over no treatment or over any of these treatments alone.			[grade B]. 2. Exercises to enhance core stability and thus to compensate for weakness or postural abnormalities are recommended for individuals who have had vertebral fractures [grade B]. 3. Exercises that focus on balance, such as tai chi, or on balance and gait training should be considered for those at risk of	

구분		지침 1 (ACR)	지침 2 (IOF-ESTS)	지침 3 (FRENCH)	지침 4 (CANADA)	지침 5 (NOGG)
					falls [grade A].	
수용성	인구 집단(유병률, 발생률 등)이 유사하다	예	예	예	예	예
	가치와 선호도가 유사하다	예	예	예	예	예
	권고로 인한 이득은 유사하다	예	예	예	예	예
	해당 권고는 수용할만하다.	예	예	예	예	예
적용성	해당 중재/장비는 이용 가능하다.	예	예	예	예	예
	필수적인 전문기술이 이용 가능하다	예	예	예	예	예
	법률적/제도적 장벽이 없다.	예	예	예	예	예
	해당 권고는 적용할만하다.	예	예	예	예	예

▣ 핵심질문 (KQ2) : 40세 미만에서 어떤 약물 치료가 GIOP 예방과 치료에 효과적인가?

▣ 핵심질문 (KQ2-1) : 40세 미만에서 칼슘과 비타민 D 보충은 GIOP 예방과 치료에 효과적인가?

구분	지침 1 (ACR)	지침 2 (IOF-ESTS)	지침 3 (FRENCH)	지침 4 (CANADA)	지침 5 (NOGG)
권고	All adults taking prednisone at a dose of ≥2.5 mg/day for ≥3 months Optimize calcium intake (800–1,000 mg/day) and vitamin D intake (600–800 IU/day) and lifestyle modifications (balanced diet, maintaining weight in the recommended range, smoking	1. Advise good nutrition especially with calcium and vitamin D 2. Adequate calcium intake should be achieved through dietary intake if possible, with the use of supplements if necessary. 3. An adequate vitamin D status should be maintained,	1. Ensure adequate intakes of calcium (preferably via a balanced diet) and vitamin D 2. Routine prescription of calcium supplements is not recommended 3. The serum levelof 25-OH vitamin D should be maintained at the optimal value,which has been set at 30	1. For healthy adults at low risk of vitamin D deficiency, routine supplementation with 400–1000 IU (10–25 μg) vitamin D 3 daily is recommended [grade D]. 2. For individuals receiving pharmacologic therapy for osteo-porosis, measurement of serum 25-	General recommendation (GIOP를 포함한) - A daily calcium intake of between 700 and 1200mg should be advised, if possible achieved through dietary intake, with use of supplements if necessary. It is recommended that in postmenopausal

구분	지침 1 (ACR)	지침 2 (IOF-ESTS)	지침 3 (FRENCH)	지침 4 (CANADA)	지침 5 (NOGG)
	cessation, regular weight-bearing or resistance training exercise, limiting alcohol intake to 1–2 alcoholic beverages/day) over no treatment or over any of these treatments alone.	using supplements if required	ng/mL (75 nmoL/L) [52] based on findingsfrom biological and clinical studies that did not focus specificallyon glucocorticoid-induced osteoporosis 4. In patients with vitamin D insufficiency or deficiency, a loading dose of vitamin D should be given to elevate the serum 25-OH vita-min D level above the target of 30 ng/mL	hydroxyvitamin D should follow three to four months of adequate supplementation and should not be repeated if an optimal level (≥ 75 nmol/L) is achieved [grade D].	women and men ≥50 years who are at increased risk of fracture, a daily dose of 800 IU of cholecalciferol should be advised(Grade A recommendation). Intermittent administration of large doses of vitamin D e.g. ≥100,000 IU is not advised, based on recent reports of an associated increased risk of fracture and falls

구분		지침 1 (ACR)	지침 2 (IOF-ESTS)	지침 3 (FRENCH)	지침 4 (CANADA)	지침 5 (NOGG)
				5. The maintenance dose is 800 to 1200 IU/day (or the equivalent of 100,000 IU every 2–3 months). The currently available data do not support the use of high-dose vitamin D supplementation (500,000 or 600,000 IU once or twice every year)		
수용성	인구 집단(유병률, 발생률 등)이 유사하다	예	예	예	예	예
	가치와 선호도가 유사하다	예	예	예	예	예
	권고로 인한 이득은 유사하다	예	예	예	예	예

구분		지침 1 (ACR)	지침 2 (IOF-ESTS)	지침 3 (FRENCH)	지침 4 (CANADA)	지침 5 (NOGG)
	해당 권고는 수용할만하다.	예	예	예	예	예
적용성	해당 중재/장비는 이용 가능하다.	예	예	예	예	예
	필수적인 전문기술이 이용 가능하다	예	예	예	예	예
	법률적/제도적 장벽이 없다.	예	예	예	예	예
	해당 권고는 적용할만하다.	예	예	예	예	예

▣ **핵심질문 (KQ2-2) : 40세 미만에서 비스포스포네이트 사용은 GIOP 예방과 치료에 효과적인가?**

구분	지침 1 (ACR)	지침 2 (IOF-ESTS)	지침 3 (FRENCH)	지침 4 (CANADA)	지침 5 (NOGG)
권고	1. For adults <40 years of age (women not of childbearing potential and men) with a history of OP fracture, or those continuing GC treatment (≥6 months at a dose of ≥7.5 mg/day) who have either a hip or spine BMD Z score <-3 or bone loss of ≥10%/year at the hip or spine as assessed by dual x-ray	1. Data on the effects of pharmacological interventions in this population are sparse, particularly with regard to fracture risk. 2.Bone-protective therapy may be appropriate in some premenopausal women and younger men, particularly in individuals with a previous history of fracture or receiving high doses of	1. osteoporosis drug therapy should be given to patients with established bone frailty documented by a history of low-energy fracture 2. Osteoporosis drug therapy should not be given routinely to patients without a history of low-energy fracture. Instead, the treatment decision should rely on an evaluation of these	N/A	Bone protective therapy may be appropriate in some premenopausal women and younger men, particularly in individuals with a previous history of fracture or receiving high doses of glucocorticoids

구분	지침 1 (ACR)	지침 2 (IOF-ESTS)	지침 3 (FRENCH)	지침 4 (CANADA)	지침 5 (NOGG)
	absorptiometry (DXA), an oral bisphosphonate should be used rather than the patient receiving no additional treatment beyond calcium and vitamin D. 2. For adults 30 years of age who are receiving very high dose GC treatment (initial prednisone dose of ≥30 mg/day [or equivalent GC exposure] and a cumulative annual	glucocorticoids. 3. Caution is advised in the use of bisphosphonates in women of childbearing age.	verity of the underlying disease, glucocorticoid dose, expected treatment duration, and BMD values 3. When bisphosphonates are used off-label, preference should be given to a bisphosphonate with a limited carry-over effect (risedronate)		

구분		지침 1 (ACR)	지침 2 (IOF-ESTS)	지침 3 (FRENCH)	지침 4 (CANADA)	지침 5 (NOGG)
		dose of >5 gm) (Table 3), oral bisphosphonate treatment should be initiated.				
수용성	인구 집단(유병률, 발생률 등)이 유사하다	예	예	예	N/A	예
	가치와 선호도가 유사하다	예	예	예	N/A	예
	권고로 인한 이득은 유사하다	예	예	예	N/A	예
	해당 권고는 수용할만하다.	예	예	예	N/A	예
적용성	해당 중재/장비는 이용 가능하다.	예	예	예	N/A	예
	필수적인 전문기술이 이용 가능하다	예	예	예	N/A	예
	법률적/제도적 장벽이 없다.	예	예	예	N/A	예
	해당 권고는 적용할만하다.	예	예	예	N/A	예

▣ 핵심질문 (KQ2-3) : 40세 미만에서 부갑상선호르몬 사용은 GIOP 예방과 치료에 효과적인가?

구분	지침 1 (ACR)	지침 2 (IOF-ESTS)	지침 3 (FRENCH)	지침 4 (CANADA)	지침 5 (NOGG)
권고	1. For adults <40 years of age (women not of childbearing potential and men) with a history of OP fracture, or those continuing GC treatment (≥6 months at a dose of ≥7.5 mg/day) who have either a hip or spine BMD Z score <-3 or bone loss of ≥10%/year at the hip or spine as assessed by dual x-ray	1. Data on the effects of pharmacological interventions in this population are sparse, particularly with regard to fracture risk. 2.Bone-protective therapy may be appropriate in some premenopausal women and younger men, particularly in individuals with a previous history of fracture or receiving high doses	NA	NA	Bone protective therapy may be appropriate in some premenopausal women and younger men, particularly in individuals with a previous history of fracture or receiving high doses of glucocorticoids

구분	지침 1 (ACR)	지침 2 (IOF-ESTS)	지침 3 (FRENCH)	지침 4 (CANADA)	지침 5 (NOGG)
	absorptiometry (DXA), If treatment with an oral bisphosphonate is not appropriate, the same alternative medications listed for adults <40 years of age are recommended with the exception of raloxifene, which is not used in men and premenopausal women 2. For adults 30 years of age who are receiving very	of glucocorticoids. 3. Caution is advised in the use of bisphosphonates in women of childbearing age.			

구분	지침 1 (ACR)	지침 2 (IOF-ESTS)	지침 3 (FRENCH)	지침 4 (CANADA)	지침 5 (NOGG)
	highdose GC treatment (initial prednisone dose of ≥30 mg/day [or equivalent GC exposure] and a cumulative annual dose of >5 gm) (Table 3), oral bisphosphonate treatment should be initiated. If treatment with an oral bisphosphonate is not appropriate, the age-related recommendations for				

구분		지침 1 (ACR)	지침 2 (IOF-ESTS)	지침 3 (FRENCH)	지침 4 (CANADA)	지침 5 (NOGG)
		secondline therapy (Table 2) should be followed (with adjustments for women of childbearing potential as outlined in these guidelines).				
수용성	인구 집단(유병률, 발생률 등)이 유사하다	예	예	N/A	N/A	예
	가치와 선호도가 유사하다	예	예	N/A	N/A	예
	권고로 인한 이득은 유사하다	예	예	N/A	N/A	예
	해당 권고는 수용할만하다.	예	예	N/A	N/A	예
적용성	해당 중재/장비는 이용 가능하다.	예	예	N/A	N/A	예
	필수적인 전문기술이 이용 가능하다	예	예	N/A	N/A	예
	법률적/제도적 장벽이 없다.	예	예	N/A	N/A	예
	해당 권고는 적용할만하다.	예	예	N/A	N/A	예

▣ 핵심질문 (KQ2-4) : 40세 미만에서 데노수맙 사용은 GIOP 예방과 치료에 효과적인가?

구분		지침 1 (ACR)	지침 2 (IOF-ESTS)	지침 3 (FRENCH)	지침 4 (CANADA)	지침 5 (NOGG)
권고		If treatment with an oral bisphosphonate is not appropriate, the same alternative medications listed for adults≥40 years of age are recommended with the exception of raloxifene, which is not used in men and premenopausal women.	N/A	N/A	N/A	N/A
수용성	인구 집단(유병률, 발생률 등)이 유사하다	예	N/A	N/A	N/A	N/A
	가치와 선호도가 유사하다	예	N/A	N/A	N/A	N/A

구분		지침 1 (ACR)	지침 2 (IOF-ESTS)	지침 3 (FRENCH)	지침 4 (CANADA)	지침 5 (NOGG)
	권고로 인한 이득은 유사하다	예	N/A	N/A	N/A	N/A
	해당 권고는 수용할만하다.	예	N/A	N/A	N/A	N/A
적용성	해당 중재/장비는 이용 가능하다.	예	N/A	N/A	N/A	N/A
	필수적인 전문기술이 이용 가능하다	예	N/A	N/A	N/A	N/A
	법률적/제도적 장벽이 없다.	예	N/A	N/A	N/A	N/A
	해당 권고는 적용할만하다.	예	N/A	N/A	N/A	N/A

▣ 핵심질문 (KQ3) : 40세 이상에서 어떤 약물 치료가 GIOP 예방과 치료에 효과적인가?

▣ 핵심질문 (KQ3-1) : 40세 이상에서 칼슘과 비타민 D 보충은 GIOP 예방과 치료에 효과적인가?

구분	지침 1 (ACR)	지침 2 (IOF-ESTS)	지침 3 (FRENCH)	지침 4 (CANADA)	지침 5 (NOGG)
권고	All adults taking prednisone at a dose of ≥2.5 mg/day for ≥3 months Optimize calcium intake (800–1,000 mg/day) and vitamin D intake (600–800 IU/day) and lifestyle modifications (balanced diet, maintaining weight in the recommended range, smoking	1. Advise good nutrition especially with calcium and vitamin D 2. Adequate calcium intake should be achieved through dietary intake if possible, with the use of supplements if necessary. 3. An adequate vitamin D status should be maintained,	1. Ensure adequate intakes of calcium (preferably via a balanced diet) and vitamin D 2. Routine prescription of calcium supplements is not recommended 3. The serum levelof 25-OH vitamin D should be maintained at the optimal value,which has been set at 30	NOT GIOP 1. The total daily intake of elemental calcium (through diet and supplements) for individuals over age 50 should be 1200 mg [grade B]. 2. For healthy adults at low risk of vitamin D deficiency, routine supplementation with 400–1000 IU (10–25 μg) vitamin D 3 daily	NOT GIOP, General 1. A daily calcium intake of between 700 and 1200mg should be advised, if possible achieved through dietary intake, with use of supplements if necessary. 2. In postmenopausal women and older men (≥50 ears) at increased risk of

구분	지침 1 (ACR)	지침 2 (IOF-ESTS)	지침 3 (FRENCH)	지침 4 (CANADA)	지침 5 (NOGG)
	cessation, regular weight-bearing or resistance training exercise, limiting alcohol intake to 1–2 alcoholic beverages/day) over no treatment or over any of these treatments alone.	using supplements if required	ng/mL (75 nmoL/L) [52] based on findingsfrom biological and clinical studies that did not focus specificallyon glucocorticoid-induced osteoporosis 4. In patients with vitamin D insufficiency or deficiency, a loading dose of vitamin D should be given to elevate the serum 25-OH vita-min D level above the target of 30 ng/mL	is recommended [grade D]. 3. For adults over age 50 at moderate risk of vitamin D defi-ciency, supplementation with 800–1000 IU (20–25 µg) vitamin D 3 daily is recommended. To achieve optimal vitamin D status, daily supplementation with more than 1000 IU (25 µg) may be required. Daily doses up to 2000 IU (50 µg) are safe and do not	fracture a daily dose of 800IU cholecalciferol should be advised. 3. In postmenopausal women and older men receiving bone protective therapy for osteoporosis, calcium supplementation should be given if the dietary intake is below 700 mg/day, and vitamin D supplementation considered in those at risk of, or with

구분	지침 1 (ACR)	지침 2 (IOF-ESTS)	지침 3 (FRENCH)	지침 4 (CANADA)	지침 5 (NOGG)
			5. The maintenance dose is 800 to 1200 IU/day (or the equivalent of 100,000 IU every 2–3 months). The currently available data do not support the use of high-dose vitamin D supplementation (500,000 or 600,000 IU once or twice every year)	necessitate monitoring [grade C]. 4. For individuals receiving pharmacologic therapy for osteo-porosis, measurement of serum 25-hydroxyvitamin D should follow three to four months of adequate supplementation and should not be repeated if an optimal level (≥ 75 nmol/L) is achieved [grade D].	evidence of, vitamin D insufficiency.

구분		지침 1 (ACR)	지침 2 (IOF-ESTS)	지침 3 (FRENCH)	지침 4 (CANADA)	지침 5 (NOGG)
수용성	인구 집단(유병률, 발생률 등)이 유사하다	예	예	예	예	예
	가치와 선호도가 유사하다	예	예	예	예	예
	권고로 인한 이득은 유사하다	예	예	예	예	예
	해당 권고는 수용할만하다.	예	예	예	예	예
적용성	해당 중재/장비는 이용 가능하다.	예	예	예	예	예
	필수적인 전문기술이 이용 가능하다	예	예	예	예	예
	법률적/제도적 장벽이 없다.	예	예	예	예	예
	해당 권고는 적용할만하다.	예	예	예	예	예

▣ **핵심질문 (KQ3-2) : 40세 이상에서 비스포스포네이트 사용은 GIOP 예방과 치료에 효과적인가?**

구분	지침 1 (ACR)	지침 2 (IOF-ESTS)	지침 3 (FRENCH)	지침 4 (CANADA)	지침 5 (NOGG)
권고	1) Women ≥40 years of age and not of childbearing potential and men ≥40 years of age (Figure 3) who are at moderate to high risk of fracture should be treated with an oral bisphosphonate. 2) For patients in whom oral bisphosphonates are not appropriate (for example, due to comorbidities, patient preference, or	1) Bone-protective treatment should be started at the onset of glucocorticoid therapy in patients at increased risk of fracture. 2) Alendronate, etidronate, risedronate, zoledronic acid and teriparatide are the front-line therapeutic options for the majority of patients.	1) Postmenopausal women and men older than 50 years of ages hould be considered at high risk for fractures and therefore eligiblefor osteoporosis drug therapy if they meet the following criteria - history of bone frailty fracture after 50 years of age - T-score ≤ − 2.5 at the lumbar spine and/or femur	1) For individuals over age 50 who are on long-term glucocorticoid therapy (≥ three months cumulative therapy during the preceding year at a prednisone equivalent dose ≥ 7.5 mg daily), a bisphosphonate (alendronate,risedronate, zoledronic acid) should be initiated at the outset and should be continued for at	1) Women and men age ≥70 years with a previous fragility fracture, or taking high doses of glucocorticoids (≥7.5 mg/day prednisolone), should be considered for bone protective therapy. 2) Bone-protective treatment should be started at the onset of glucocorticoid therapy in individuals at high

구분	지침 1 (ACR)	지침 2 (IOF-ESTS)	지침 3 (FRENCH)	지침 4 (CANADA)	지침 5 (NOGG)
	concerns about adherence with an oral medication regimen), IV bisphosphonates should be used rather than the patient receiving no additional treatment beyond calcium and vitamin D.		- age ≥ 70 years, since in this age group FRAX® scores evaluating the fracture risk are similar in women starting glucocorticoid therapy and in women with a history of fracture - long-term high dose glucocorticoid therapy (≥7.5mg/d prednisone equivalent for longer than 3	least the duration of the glucocorticoid therapy 2) For long-term glucocorticoid users who are intolerant of first line therapies, calcitonin or etidronate may be considered for preventing loss of bone mineral density	risk of racture. 3) Alendronate and risedronate are first line treatment options. Where these are contraindicated or not tolerated, zoledronic acid or teriparatide are alternative options

구분	지침 1 (ACR)	지침 2 (IOF-ESTS)	지침 3 (FRENCH)	지침 4 (CANADA)	지침 5 (NOGG)
			months); selection of this dose cutoff is based on its use in most clinical trials as aninclusion criterion and on epidemiological data showing that the relative risk of vertebral fracture increases from 2.6 with dosesof 2.5 to 7.5 mg/d to 5.2 with doses > 7.5 mg/d 2) Among bisphosphonates,		

구분		지침 1 (ACR)	지침 2 (IOF-ESTS)	지침 3 (FRENCH)	지침 4 (CANADA)	지침 5 (NOGG)
				zoledronic acid or risedronate is always an appropriate choice		
수용성	인구 집단(유병률, 발생률 등)이 유사하다	예	예	예	예	예
	가치와 선호도가 유사하다	예	예	예	예	예
	권고로 인한 이득은 유사하다	예	예	예	예	예
	해당 권고는 수용할만하다.	예	예	예	예	예
적용성	해당 중재/장비는 이용 가능하다.	예	예	예	예	예
	필수적인 전문기술이 이용 가능하다	예	예	예	예	예
	법률적/제도적 장벽이 없다.	예	예	예	예	예
	해당 권고는 적용할만하다.	예	예	예	예	예

▣ **핵심질문 (KQ3-3) : 폐경 후 여성에서 선택적 에스트로겐 수용체 조절제 사용은 GIOP 예방과 치료에 효과적인가?**

구분		지침 1 (ACR)	지침 2 (IOF-ESTS)	지침 3 (FRENCH)	지침 4 (CANADA)	지침 5 (NOGG)
권고		Adults age≥40 years at moderate and high risk of fracture, For postmenopausal women in whom none of these medications is appropriate, raloxifene should be used rather than the patient receiving no additional treatment beyond calcium and vitamin D	NA	NA	NA	NA
수용성	인구 집단(유병률, 발생률 등)이 유사하다	예	NA	NA	NA	NA
	가치와 선호도가 유사하다	예	NA	NA	NA	NA

구분		지침 1 (ACR)	지침 2 (IOF-ESTS)	지침 3 (FRENCH)	지침 4 (CANADA)	지침 5 (NOGG)
	권고로 인한 이득은 유사하다	예	NA	NA	NA	NA
	해당 권고는 수용할만하다.	예	NA	NA	NA	NA
적용성	해당 중재/장비는 이용 가능하다.	예	NA	NA	NA	NA
	필수적인 전문기술이 이용 가능하다	예	NA	NA	NA	NA
	법률적/제도적 장벽이 없다.	예	NA	NA	NA	NA
	해당 권고는 적용할만하다.	예	NA	NA	NA	NA

▣ **핵심질문 (KQ3-4) : 40세 이상에서 부갑상선호르몬은 GIOP 예방과 치료에 효과적인가?**

구분	지침 1 (ACR)	지침 2 (IOF-ESTS)	지침 3 (FRENCH)	지침 4 (CANADA)	지침 5 (NOGG)
권고	Adults age≥40 years at moderate and high risk of fracture, If bisphosphonate treatment is not appropriate, teriparatide should be used rather than the patient receiving no additional treatment beyond calcium and vitaminD.	1 Bone-protective treatment should be started at the onset of glucocorticoid therapy in patients at increased risk of fracture. 2. Alendronate, etidronate, risedronate, zoledronic acid and teriparatide are the front-line therapeutic options for the majority of patients.	Teriparatide can be prescribed as the first-line drug in patients at high fracture risk and is reimbursed by the French statutory healthcare system in patients with at least two prevalent vertebral fractures at diagnosis	Teriparatide should be considered for those at high risk for fracture who are taking glucocorticoids (≥ three months cumulative therapy during the preceding year at a prednisone equivalent dose ≥ 7.5 mg daily)	1. Women and men age ≥70 years with a previous fragility fracture, or taking high doses of glucocorticoids (≥7.5 mg/day prednisolone), should be considered for bone protective therapy. 2.Bone-protective treatment should be started at the onset of glucocorticoid therapy in individuals at high

구분		지침 1 (ACR)	지침 2 (IOF-ESTS)	지침 3 (FRENCH)	지침 4 (CANADA)	지침 5 (NOGG)
						risk of fracture. 3. Alendronate and risedronate are first line treatment options. Where these are contraindicated or not tolerated, zoledronic acid or teriparatide are alternative options
수용성	인구 집단(유병률, 발생률 등)이 유사하다	예	예	예	예	예
	가치와 선호도가 유사하다	예	예	예	예	예
	권고로 인한 이득은 유사하다	예	예	예	예	예
	해당 권고는 수용할만하다.	예	예	예	예	예
적용성	해당 중재/장비는 이용 가능하다.	예	예	예	예	예

구분		지침 1 (ACR)	지침 2 (IOF-ESTS)	지침 3 (FRENCH)	지침 4 (CANADA)	지침 5 (NOGG)
	필수적인 전문기술이 이용 가능하다	예	예	예	예	예
	법률적/제도적 장벽이 없다.	예	예	예	예	예
	해당 권고는 적용할만하다.	예	예	예	예	예

▣ **핵심질문 (KQ3-5) : 40세 이상에서 데노수맙 사용은 GIOP 예방과 치료에 효과적인가?**

구분		지침 1 (ACR)	지침 2 (IOF-ESTS)	지침 3 (FRENCH)	지침 4 (CANADA)	지침 5 (NOGG)
권고		If neither oral nor IV bisphosphonates nor teriparatide treatment is appropriate, denosumab should be used rather than the patient receiving no additional treatment beyond calcium and vitamin D.	NA	NA	NA	NA
수용성	인구 집단(유병률, 발생률 등)이 유사하다	예	NA	NA	NA	NA
	가치와 선호도가 유사하다	예	NA	NA	NA	NA
	권고로 인한 이득은 유사하다	예	NA	NA	NA	NA
	해당 권고는 수용할만하다.	예	NA	NA	NA	NA

구분		지침 1 (ACR)	지침 2 (IOF-ESTS)	지침 3 (FRENCH)	지침 4 (CANADA)	지침 5 (NOGG)
적용성	해당 중재/장비는 이용 가능하다.	예	NA	NA	NA	NA
	필수적인 전문기술이 이용 가능하다	예	NA	NA	NA	NA
	법률적/제도적 장벽이 없다.	예	NA	NA	NA	NA
	해당 권고는 적용할만하다.	예	NA	NA	NA	NA

▣ 핵심질문 (KQ4) : 임신을 계획하고 있는 여성에서 치료 약제 사용은 안전한가?

구분	지침 1 (ACR)	지침 2 (IOF-ESTS)	지침 3 (FRENCH)	지침 4 (CANADA)	지침 5 (NOGG)
권고	1. Because of the lack of safety data and the potential fetal harm associated with denosumab and high-dose IV bisphosphonates should be used only in women who are at high risk of fracture in whom treatment with an oral bisphosphonate and teriparatide is not appropriate. 2. There is a lack of data	Caution is advised in the use of bisphosphonates in women of childbearing age.	Women should be advised against starting a pregnancy during the treatment and within 6 months after its discontinuation.	N/A	Caution is advised in the use of bisphosphonates in women of childbearing age.

구분		지침 1 (ACR)	지침 2 (IOF-ESTS)	지침 3 (FRENCH)	지침 4 (CANADA)	지침 5 (NOGG)
		on the safety of currently available OP treatments during pregnancy. Therefore, these guidelines do not include recommendations about OP prevention				
수용성	인구 집단(유병률, 발생률 등)이 유사하다	예	예	예	NA	예
	가치와 선호도가 유사하다	예	예	예	NA	예
	권고로 인한 이득은 유사하다	예	예	예	NA	예
	해당 권고는 수용할만하다.	예	예	예	NA	예
적용성	해당 중재/장비는 이용 가능하다.	예	예	예	NA	예
	필수적인 전문기술이 이용 가능하다	예	예	예	NA	예

구분		지침 1 (ACR)	지침 2 (IOF-ESTS)	지침 3 (FRENCH)	지침 4 (CANADA)	지침 5 (NOGG)
	법률적/제도적 장벽이 없다.	예	예	예	NA	예
	해당 권고는 적용할만하다.	예	예	예	NA	예

▣ 핵심질문 (KQ5) : GIOP환자에서 신체계측/영상학적/생화학적 방법을 이용하여 얼마간의 간격으로 모니터링 할 것인가?

(GIOP 환자의 치료 반응을 어떻게 모니터링 할 것 인가?)

구분	지침 1 (ACR)	지침 2 (IOF-ESTS)	지침 3 (FRENCH)	지침 4 (CANADA)	지침 5 (NOGG)
권고	1) In all adults and children who continue GC treatment, a clinical fracture risk reassessment should be performed every 12 months. 2) For adults ≥ 40 years of age who continue GC treatment and are not treated with an OP medication beyond calcium and vitamin D, reassessment with	1) Measurement of BMD at appropriate intervals 2) Annual height measurement 3) Vertebral fracture assessment by X-ray or DXA if fracture is suspected 4) Assessment of adherence to therapy, including calcium and vitamin D, at each visit 5) Measurement of BMD at appropriate	1) Given the rapid onset of bone loss, annual BMD measurement is recommended during the first 2 years of glucocorticoid therapy in the absence of osteoporosis drug therapy or at the end of an osteoporosis drug sequence. Subsequently, the frequency of BMD measurement should	NA	NA

구분	지침 1 (ACR)	지침 2 (IOF-ESTS)	지침 3 (FRENCH)	지침 4 (CANADA)	지침 5 (NOGG)
	FRAX, with BMD testing if available, should be completed every 1–3years. 3) For adults ≥ 40 years old who received an OP treatment in the past but are no longer being treated with an OP medication other than calcium and vitamin D, BMD testing should be done every 2–3 years. 4) For all adults <40 years of age who	intervals 6) Annual height measurement 7) Vertebral fracture assessment by X-ray or DXA if fracture is suspected 8) Measurement of serum PINP after 3 months of teriparatide therapy	be determined based on the BMD values, glucocorticoid dose, and level of control of the underlying disease 2) Clinical follow-up may be sufficient to assess adherence 3) Given the rapid onset of bone loss, annual BMD measurement is recommended during the first 2 years of GC therapy in the absence of osteoporosis drug therapy or at the end		

구분	지침 1 (ACR)	지침 2 (IOF-ESTS)	지침 3 (FRENCH)	지침 4 (CANADA)	지침 5 (NOGG)
	continue GC treatment and are at moderate-to-high fracture risk (history of previous fracture, BMD Z score<-3, received very high-dose prednisone ≥30 mg/day and cumulative dose >5 gm] in the previous year, risks for poor medication adherence or absorption, or multiple OP risk factors), BMD testing should be done every		of an osteoporosis drug sequence. Subsequently, the frequency of BMD measurement should be determined based on the BMD values, glucocorticoid dose, and level of control of the underlying disease 4) Vertebral height measurement once a year: vertebral fractures result in height loss, which is a nonspecific sign of vertebral disease		

구분	지침 1 (ACR)	지침 2 (IOF-ESTS)	지침 3 (FRENCH)	지침 4 (CANADA)	지침 5 (NOGG)
	2–3 years. 5) For adults ≥ 40 years old who continue GC treatment and are currently treated with an OP medication in addition to calcium and vitamin D, BMD testing should be completed every 2–3 years during treatment in high-risk patients such as those receiving very high-dose GCs (initial prednisone dose ≥30 mg/day, cumulative		5) A morphological assessment of the spine is indicated in patients with back pain or height loss ≥ 2 cm during follow-up		

구분	지침 1 (ACR)	지침 2 (IOF-ESTS)	지침 3 (FRENCH)	지침 4 (CANADA)	지침 5 (NOGG)
	dose >5 gm in the previous year), a history of OP fracture occurring after ≥18 months of treatment with antifracture medication (other than calcium and vitamin D), risks for poor medication adherence or absorption, or other significant OP risk factors. 6) For all adults <40 years of age who continue GC treatment				

구분	지침 1 (ACR)	지침 2 (IOF-ESTS)	지침 3 (FRENCH)	지침 4 (CANADA)	지침 5 (NOGG)
	and are at moderate-to-high fracture risk (history of previous fracture, BMD Z score<-3, received very high-dose prednisone ≥30 mg/day and cumulative dose >5 gm] in the previous year, risks for poor medication adherence or absorption, or multiple OP risk factors), BMD testing should be done every 2–3years.				

구분		지침 1 (ACR)	지침 2 (IOF-ESTS)	지침 3 (FRENCH)	지침 4 (CANADA)	지침 5 (NOGG)
수용성	인구 집단(유병률, 발생률 등)이 유사하다	예	예	예	NA	NA
	가치와 선호도가 유사하다	예	예	예	NA	NA
	권고로 인한 이득은 유사하다	예	예	예	NA	NA
	해당 권고는 수용할만하다.	예	예	예	NA	NA
적용성	해당 중재/장비는 이용 가능하다.	예	예	예	NA	NA
	필수적인 전문기술이 이용 가능하다	예	예	예	NA	NA
	법률적/제도적 장벽이 없다.	예	예	예	NA	NA
	해당 권고는 적용할만하다.	예	예	예	NA	NA

▣ 핵심질문 (KQ6) : GIOP 치료 중 골절 위험도를 재평가하여 낮은 골절위험도로 확인되었을 경우 치료 중단을 고려할 수 있는가?

(GIOP 치료 중 어떤 경우에 치료 중단을 고려할 수 있는가?)

구분	지침 1 (ACR)	지침 2 (IOF-ESTS)	지침 3 (FRENCH)	지침 4 (CANADA)	지침 5 (NOGG)
권고	For adults ≥40 years of age who are treated with OP medication in addition to calcium and vitamin D and are discontinuing GC treatment, discontinuation of the OP medication is recommended if fracture risk at the time of GC discontinuation is assessed to be low.	If glucocorticoid therapy is stopped, withdrawal of bone-protective therapy may be considered, but if glucocorticoids are continued long term, bone protection should be maintained	Osteoporosis drug discontinuation can be considered in patients who meet all the following criteria: no fracture during treatment AND prednisone-equivalent dose≤ 7.5 mg/d AND no new risk factors AND optimal control of under-lying disease activity AND no change in BMD values (with change defined	For patients undergoing long-term glucocorticoid therapy, the appropriate duration of osteoporosis treatment is unknown.	If glucocorticoid therapy is stopped, withdrawal of bone-protective therapy may be considered, but if glucocorticoids are continued long term, bone protection should be maintained in the majority of cases

구분		지침 1 (ACR)	지침 2 (IOF-ESTS)	지침 3 (FRENCH)	지침 4 (CANADA)	지침 5 (NOGG)
		Otherwise, the OP treatment course should be completed or continued until the fracture risk is assessed to be low		as a decrease ≥ 0.03 g/cm^2 at one or both sites). In every case, the decision to stop osteoporosis drug therapy should rest on a case-by-case evaluation of the risk/benefit ratio.		
수용성	인구 집단(유병률, 발생률 등)이 유사하다	예	예	예	예	예
	가치와 선호도가 유사하다	예	예	예	예	예
	권고로 인한 이득은 유사하다	예	예	예	예	예
	해당 권고는 수용할만하다.	예	예	예	예	예
적용성	해당 중재/장비는 이용 가능하다.	예	예	예	예	예
	필수적인 전문기술이 이용 가능하다	예	예	예	예	예
	법률적/제도적 장벽이 없다.	예	예	예	예	예

구분		지침 1 (ACR)	지침 2 (IOF-ESTS)	지침 3 (FRENCH)	지침 4 (CANADA)	지침 5 (NOGG)
	해당 권고는 적용할만하다.	예	예	예	예	예

▣ 핵심질문 (KQ7) : GIOP치료 실패를 어떻게 정의할 것인가?

구분	지침 1 (ACR)	지침 2 (IOF-ESTS)	지침 3 (FRENCH)	지침 4 (CANADA)	지침 5 (NOGG)
권고	Follow up treatment recommendation Initial treatment failure: For adults ≥40 years of age who are continuing GC treatment who have had a fracture that occurred ≥18 months after beginning treatment with an oral bisphosphonate or had a significant decline in BMD (≥10%/year) after 1 year of treatment,	No data are available on switching or combining osteoporosis drugs in patients with significant bone loss (BMD decrease≥ 0.03 g/cm^2) or bone frailty fractures during combined long-termglucocorticoid therapy and osteoporosis drug therapy. Advice from a bone disease specialist should ideally be	NA	NA	NA

구분	지침 1 (ACR)	지침 2 (IOF-ESTS)	지침 3 (FRENCH)	지침 4 (CANADA)	지침 5 (NOGG)
	Treat with another class of OP medication or an IV bisphosphonate is recommended rather than the patient receiving no additional treatment beyong calcium and vitamin D alone or continuing oral bisphosphonate treatment. Treatment if moderate-to-high fracture risk persists after BP therapy: For adults ≥40 years of	obtained			

구분		지침 1 (ACR)	지침 2 (IOF-ESTS)	지침 3 (FRENCH)	지침 4 (CANADA)	지침 5 (NOGG)
		age who have completed 5 years of bisphosphonate treatement who are continuing GC treatment and are assessed to be at moderate to high risk of fracture, continuation of active OP treatment is recommended rather than the patient receiving no additional treatment beyond calcium and vitamin D.				
수용성	인구 집단(유병률, 발생률 등)이 유사하다	예	예	NA	NA	NA

구분		지침 1 (ACR)	지침 2 (IOF-ESTS)	지침 3 (FRENCH)	지침 4 (CANADA)	지침 5 (NOGG)
	가치와 선호도가 유사하다	예	예	NA	NA	NA
	권고로 인한 이득은 유사하다	예	예	NA	NA	NA
	해당 권고는 수용할만하다.	예	예	NA	NA	NA
적용성	해당 중재/장비는 이용 가능하다.	예	예	NA	NA	NA
	필수적인 전문기술이 이용 가능하다	예	예	NA	NA	NA
	법률적/제도적 장벽이 없다.	예	예	NA	NA	NA
	해당 권고는 적용할만하다.	예	예	NA	NA	NA