2022년 제1차
고려대학교 의과대학
가정의학교실 연수강좌

의료의 중심, 주치의.
핵심진료능력의 강화.

고려대학교 의과대학 가정의학교실
Dept. of Family Medicine, Korea University College of Medicine

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KU MEDICINE KOREA UNIVERSITY MEDICINE

2022 연수강좌

개요

■ 일 시 : 2022년 4월 23일(토)
■ 평 점 : 대한의사협회 3점

프로그램

환영사	고려의대 가정의학과 과장 김양현
Session1. 만성질환 관리 기초 다지기	
심방세동의 치료: 항응고 치료, 심박수 조절, 동율동 전환	고려의대 순환기내과 김윤기
일차의료의를 위한 GLP-1 RA 총정리	고려의대 내분비내과 배재현
식이패턴에 따른 비만치료약물 선택	고려의대 가정의학과 한병덕
Session2. 특색있는 외래 만들기	
근골계통증의 약물치료, 기전과 적용	고려의대 재활의학과 강석
Post 코로나 우리가 알아야 할 예방접종	KMI한국의학연구소 신상엽
일차의료에서 흔히 사용하는 영양수액 총정리	고려의대 가정의학과 신고은

차례

고려대학교 의과대학 가정의학교실

2022 연수강좌

심방세동의 치료: 항응고 치료, 심박수 조절, 동율동 전환

김윤기
고려의대 순환기내과

Atrial Fibrillation

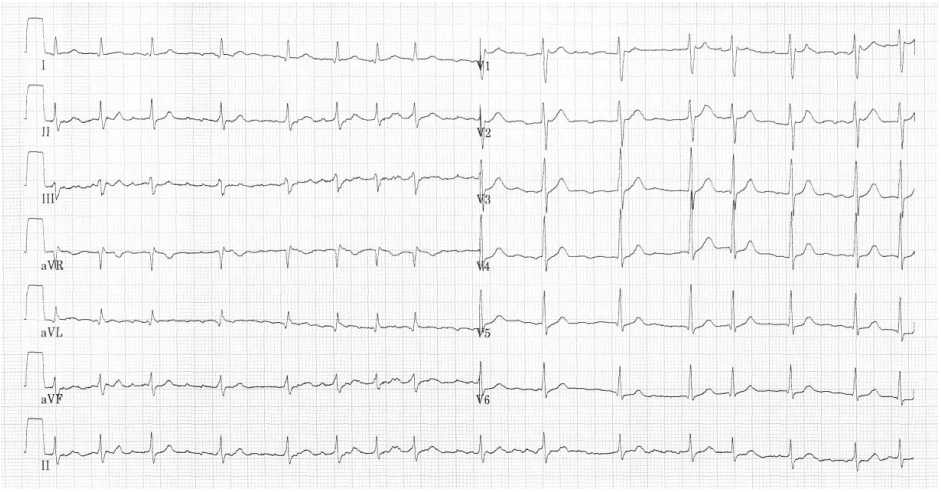
KU Medicine Anam Hospital
Arrhythmia Center

Yun Gi Kim

Objectives

- What is atrial fibrillation (AF)?
- What happens when you have AF?
- What should I do for AF?
- Why do I have to know about AF?

Atrial Fibrillation



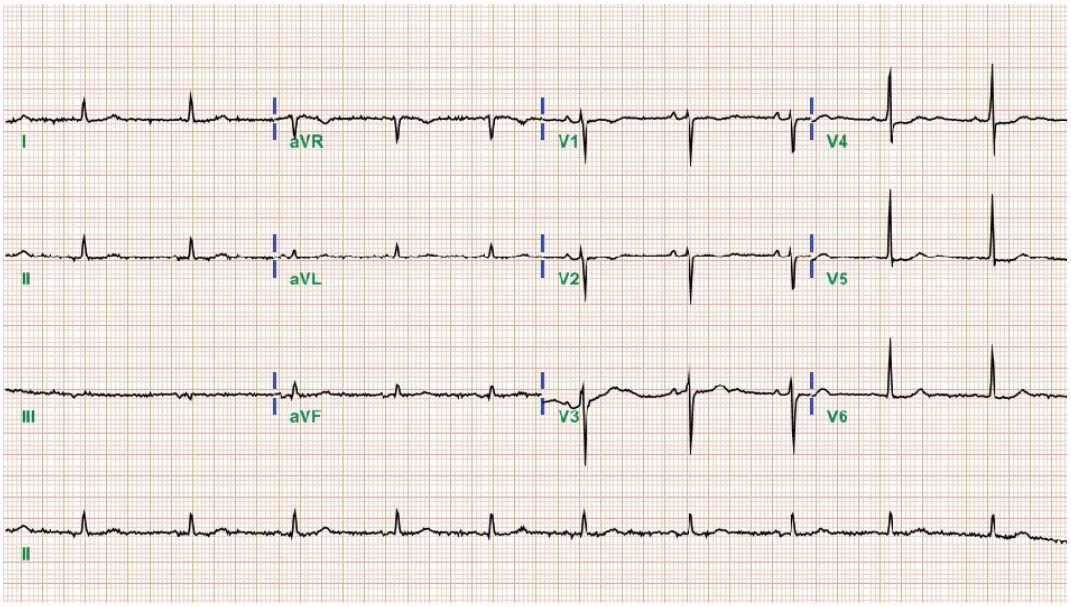
Chief Complaint

- 78 / Female
- Rt. hip pain
- She fell down 1 day ago (2016-07-05)
- Rt. inter-trochanteric fracture was diagnosed
- Cardiology consultation was done for Pre-Op risk evaluation

Past Medical History

- Underwent CAG in 2013 due to angina → no significant CAD
- Currently on HTN and DM medication
- Previous history of ischemic stroke on clopidogrel
- 150 cm, 45 kg
- Never smoker
- Non alcoholics
- No family history of cardiac disease

ECG



Progress

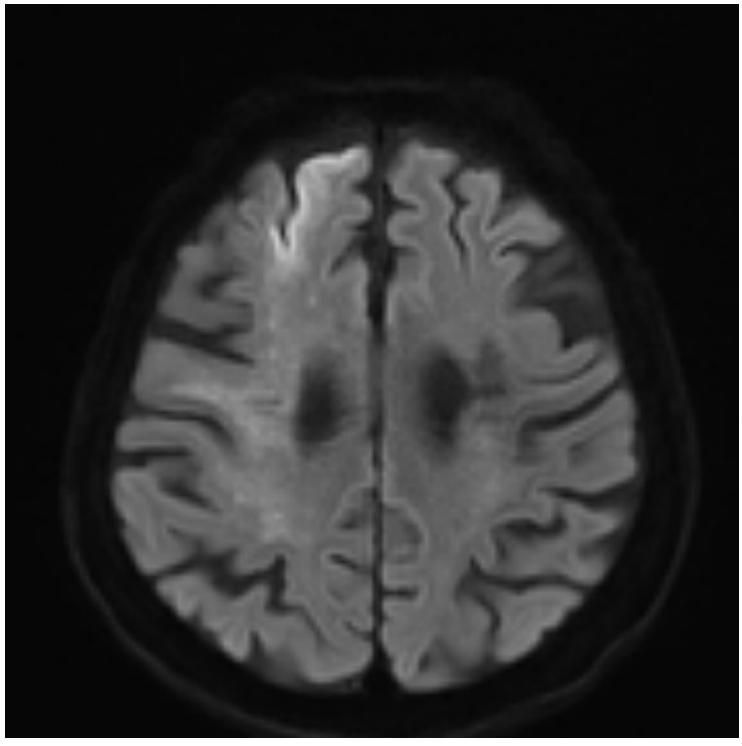
- She went to operating room but ECG showed AF with RVR (160)
  → CHA_2DS_2VASc 7 (age 2 + HTN 1 + DM 1 + CVA 2 + sex 1)
- Operation was delayed
- CA consultation for AF management was done
- Bridging anticoagulation was recommended

Progress

- She underwent 2 days of bridging enoxaparin and underwent operation in 2016-07-13 (8 days after fracture)
- The patient was stable in 2016-07-14
- Aspirin + Clopidogrel was given after operation
- However, sudden mental changed occurred in 2016-07-15

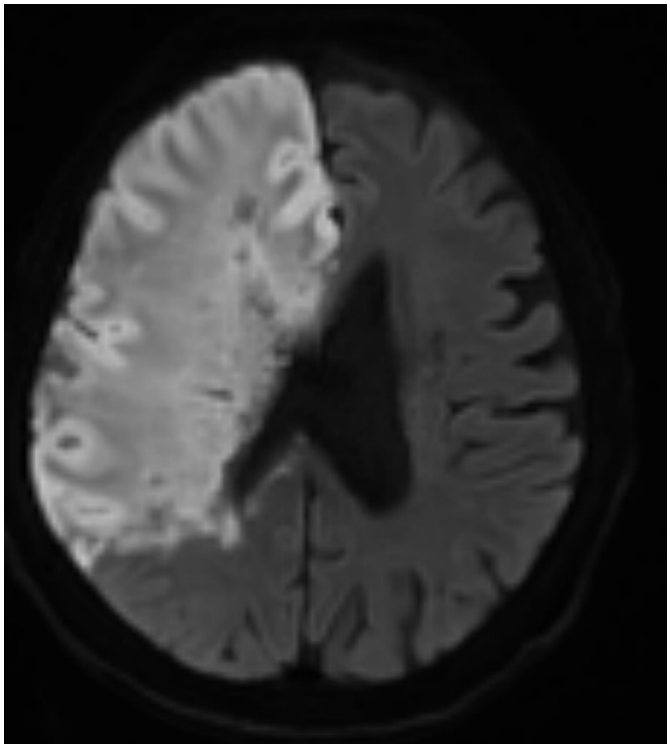
Progress

- MRI DWI 20 mins: no definite change
- **MRI DWI 5 hrs: Rt. ACA acute infarction**



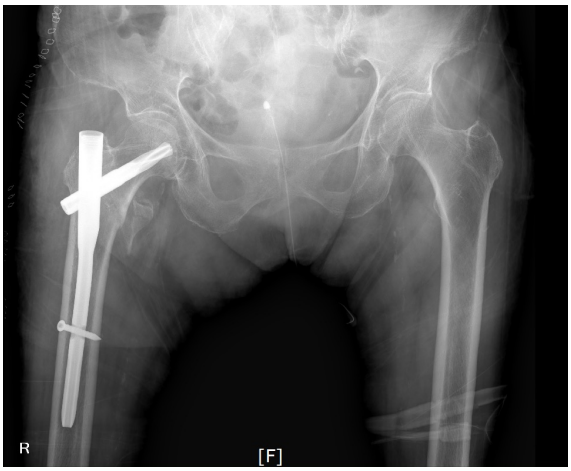
Progress

- MRI DWI 20 minutes: no definite change
- MRI DWI 5 hours: Rt. ACA acute infarction
- **MRI 5 days: Rt. MCA, ACA infarction**



Progress

- Discharged in 2016-08-26 with bed-ridden state
- Dabigatran + Aspirin



2020 ESC Guidelines

ESC European Society of Cardiology
European Heart Journal (2020) 00, 1–125
doi:10.1093/eurheartj/ehaa612
ESC GUIDELINES

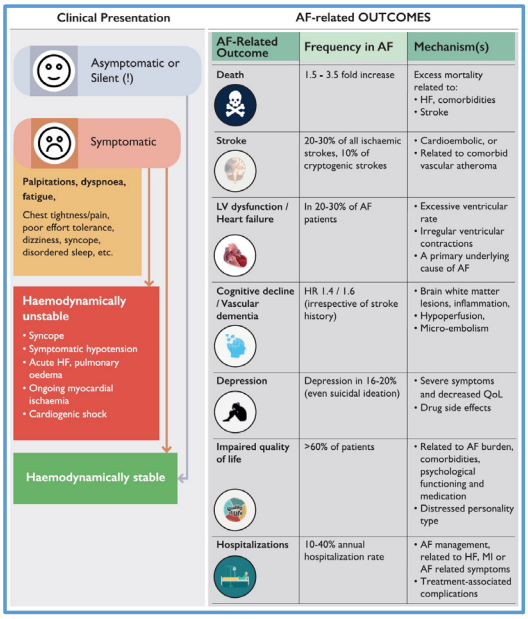
2020 ESC Guidelines for the diagnosis and management of atrial fibrillation developed in collaboration with the European Association of Cardio-Thoracic Surgery (EACTS)

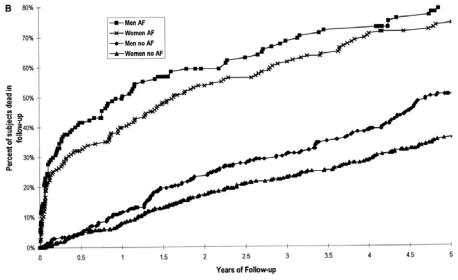
The Task Force for the diagnosis and management of atrial fibrillation of the European Society of Cardiology (ESC)

Developed with the special contribution of the European Heart Rhythm Association (EHRA) of the ESC

Hindricks G et al., Eur Heart J. 2020 Aug 29;00, 1-125.

What happens with AF?

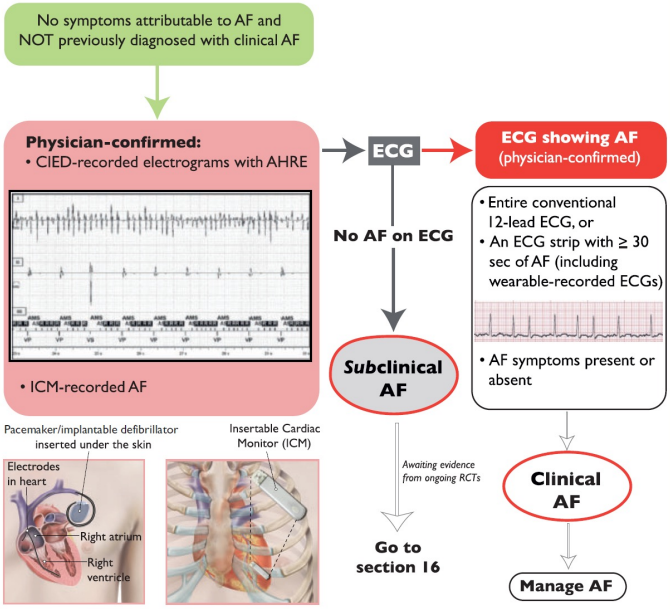




	Total				
	N	Death	P-Y	MR[a]	SMR (95% CI)
<20	215	9	1,321	6.8	21.93 (7.60–36.26)
20s	348	11	2,240	4.9	9.04 (3.70–14.39)
30s	669	36	4,018	9.0	10.26 (6.91–13.61)
40s	1,372	95	8,223	11.6	5.73 (4.58–6.88)
50s	2,515	333	13,438	24.8	5.89 (5.26–6.52)
60s	3,875	949	20,460	46.4	4.77 (4.47–5.08)
70s	4,118	1,618	15,624	103.6	3.78 (3.59–3.96)
≥80	2,299	1,428	5,468	261.1	2.77 (2.63–2.91)
Overall	15,411	4,479	70,791	63.3	3.67 (3.56–3.78)

Hindricks G et al., Eur Heart J. 2020 Aug 29;00, 1-125.
Circulation. 1998 Sep 8;98(10):946-52.
PLoS One. 2018 Dec 26;13(12):e0209687.

Diagnosis



Recommendations for diagnosis of AF

Recommendations	Class[a]	Level[b]
ECG documentation is required to establish the diagnosis of AF. • A standard 12-lead ECG recording or a single-lead ECG tracing of ≥30 s showing heart rhythm with no discernible repeating P waves and irregular RR intervals (when atrioventricular conduction is not impaired) is diagnostic of clinical AF.[6]	I	B

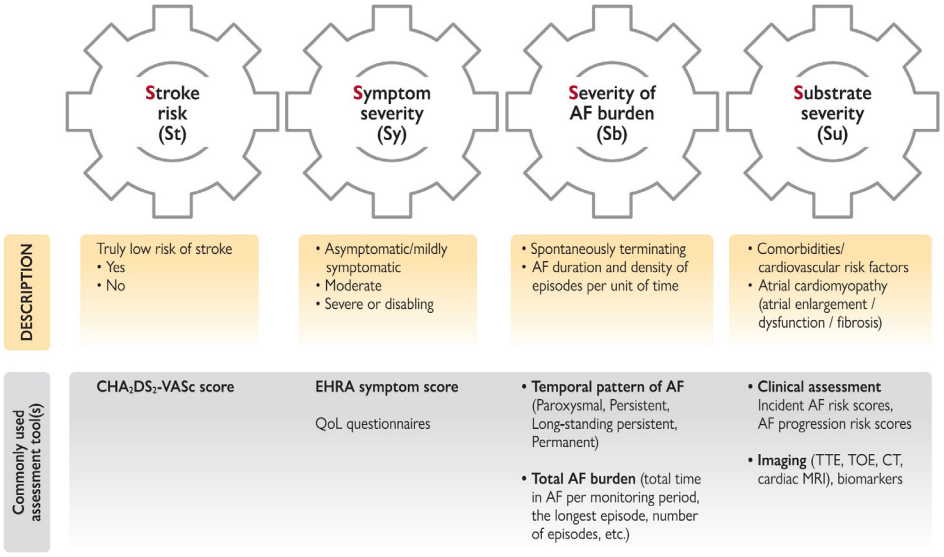
Hindricks G et al., Eur Heart J. 2020 Aug 29;00, 1-125.

Terminology

AF pattern	Definition
First diagnosed	AF not diagnosed before, irrespective of its duration or the presence/severity of AF-related symptoms.
Paroxysmal	AF that terminates spontaneously or with intervention within 7 days of onset.
Persistent	AF that is continuously sustained beyond 7 days, including episodes terminated by cardioversion (drugs or electrical cardioversion) after ≥7 days
Long-standing persistent	Continuous AF of >12 months' duration when decided to adopt a rhythm control strategy.
Permanent	AF that is accepted by the patient and physician, and no further attempts to restore/maintain sinus rhythm will be undertaken. Permanent AF represents a therapeutic attitude of the patient and physician rather than an inherent pathophysiological attribute of AF, and the term should not be used in the context of a rhythm control strategy with antiarrhythmic drug therapy or AF ablation. Should a rhythm control strategy be adopted, the arrhythmia would be re-classified as 'long-standing persistent AF'.

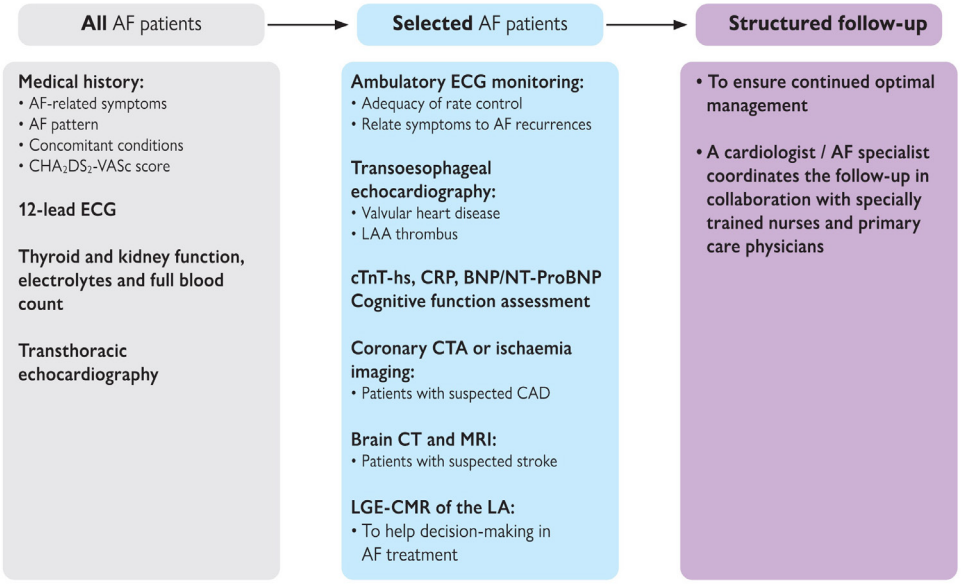
Hindricks G et al., Eur Heart J. 2020 Aug 29;00, 1-125.

Assessment of AF



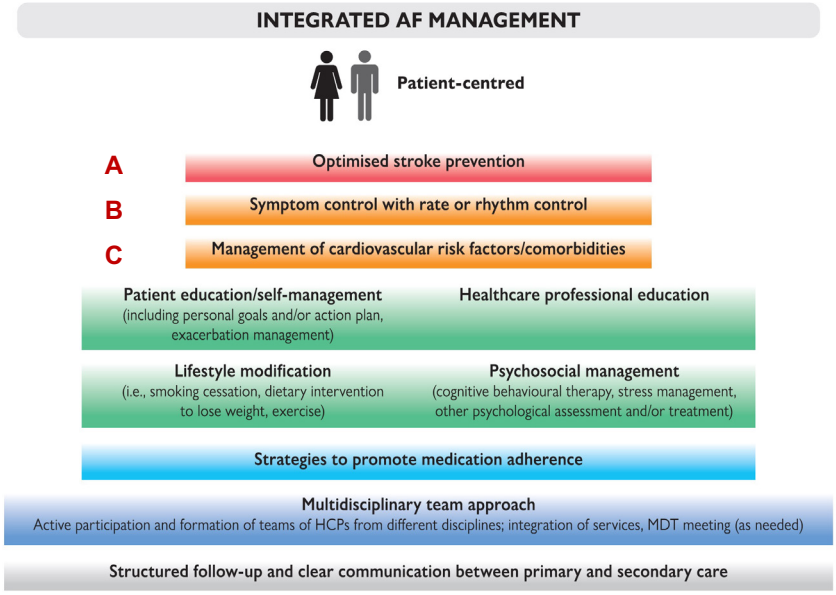
Hindricks G et al., Eur Heart J. 2020 Aug 29;00, 1-125.

Diagnostic Work-up



Hindricks G et al., Eur Heart J. 2020 Aug 29;00, 1-125.

Integrated Management



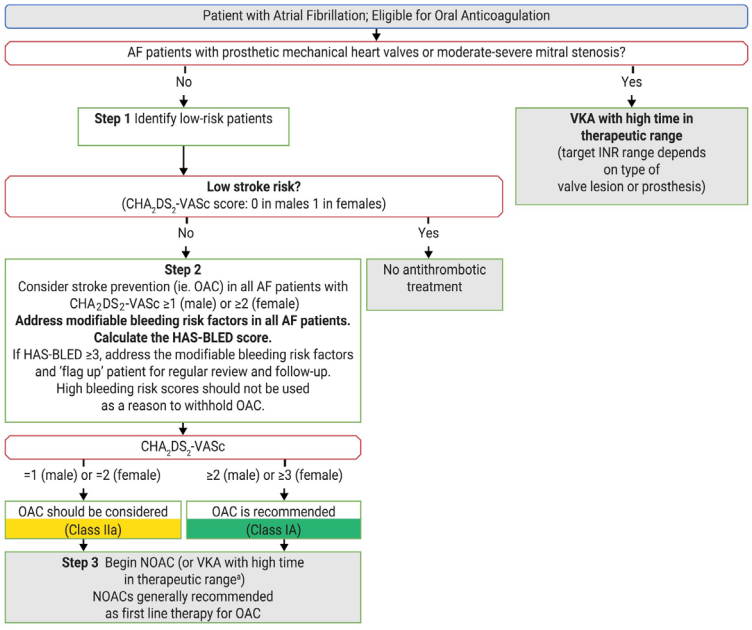
Hindricks G et al., Eur Heart J. 2020 Aug 29;00, 1-125.

Stroke Prevention: CHA_2DS_2-VASc

CHA_2DS_2-VASc score Risk factors and definitions		Points awarded	Comment
C	**Congestive heart failure** Clinical HF, or objective evidence of moderate to severe LV dysfunction, or HCM	1	Recent decompensated HF irrespective of LVEF (thus incorporating HFrEF or HFpEF), or the presence (even if asymptomatic) of moderate-severe LV systolic impairment on cardiac imaging[335]; HCM confers a high stroke risk[336] and OAC is beneficial for stroke reduction.[337]
H	**Hypertension** or on antihypertensive therapy	1	History of hypertension may result in vascular changes that predispose to stroke, and a well-controlled BP today may not be well-controlled over time.[324] Uncontrolled BP - the optimal BP target associated with the lowest risk of ischaemic stroke, death, and other cardiovascular outcomes is 120 - 129/<80 mmHg.[338]
A	**Age 75 years or older**	2	Age is a powerful driver of stroke risk, and most population cohorts show that the risk rises from age 65 years upwards.[339] Age-related risk is a continuum, but for reasons of simplicity and practicality, 1 point is given for age 65 - 74 years and 2 points for age ≥75 years.
D	**Diabetes mellitus** Treatment with oral hypoglycaemic drugs and/or insulin or fasting blood glucose >125 mg/dL (7 mmol/L)	1	Diabetes mellitus is a well-established risk factor for stroke, and more recently stroke risk has been related to duration of diabetes mellitus (the longer the duration of diabetes mellitus, the higher the risk of thromboembolism[340]) and presence of diabetic target organ damage, e.g. retinopathy.[341] Both type 1 and type 2 diabetes mellitus confer broadly similar thromboembolic risk in AF, although the risk may be slightly higher in patients aged <65 years with type 2 diabetes mellitus compared to patients with type 1 diabetes mellitus.[342]
S	**Stroke**Previous stroke, TIA, or thromboembolism	2	Previous stroke, systemic embolism, or TIA confers a particularly high risk of ischaemic stroke, hence weighted 2 points. Although excluded from RCTs, AF patients with ICH (including haemorrhagic stroke) are at very high risk of subsequent ischaemic stroke, and recent observational studies suggest that such patients would benefit from oral anticoagulation.[343–345]
V	**Vascular disease** Angiographically significant CAD, previous myocardial infarction, PAD, or aortic plaque	1	Vascular disease (PAD or myocardial infarction) confers a 17 - 22% excess risk, particularly in Asian patients.[346–348] Angiographically significant CAD is also an independent risk factor for ischaemic stroke among AF patients (adjusted incidence rate ratio 1.29, 95% CI 1.08 - 1.53).[349] Complex aortic plaque on the descending aorta, as an indicator of significant vascular disease, is also a strong predictor of ischaemic stroke.[350]
A	**Age 65 – 74 years**	1	See above. Recent data from Asia suggest that the risk of stroke may rise from age 50 - 55 years upwards and that a modified CHA_2DS_2-VASc score may be used in Asian patients.[351,352]
Sc	**Sex category (female)**	1	A stroke risk modifier rather than a risk factor.[353]
Maximum score		**9**	

Hindricks G et al., Eur Heart J. 2020 Aug 29;00, 1-125.

Stroke Prevention: Anticoagulation



Hindricks G et al., Eur Heart J. 2020 Aug 29;00, 1-125.

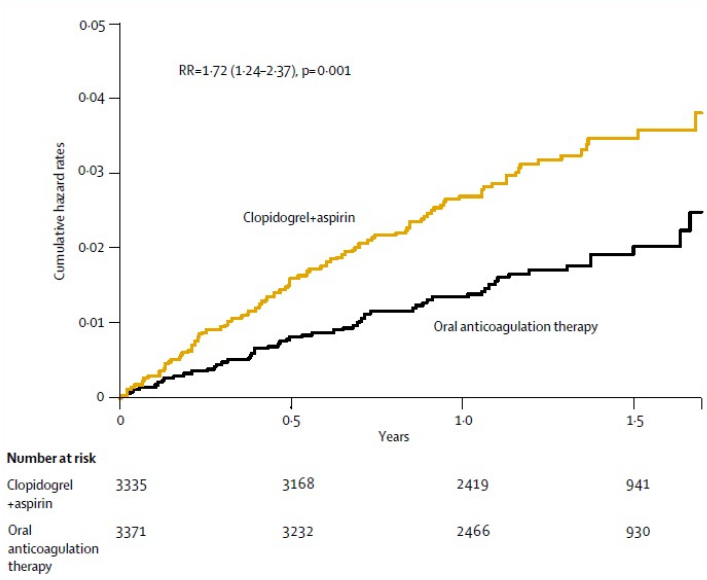
Warfarin vs. Aspirin

	Warfarin	Aspirin
Number of patients	488	485
Age (years)	81·5 (4·3)	81·5 (4·2)
Age group		
75–79	197 (40%)	200 (41%)
80–84	196 (40%)	190 (39%)
≥85	95 (19%)	95 (20%)
Male	267 (55%)	264 (54%)
Method of identification		
Practice register	342 (70%)	341 (70%)
Screening	146 (30%)	144 (30%)
CHADS2 score*		
1–2	349 (72%)	349 (72%)
3–6	139 (28%)	136 (28%)
On warfarin	194 (40%)	187 (39%)
On aspirin	203 (42%)	204 (42%)
History of stroke or TIA	64 (13%)	60 (12%)
History of hypertension	259 (53%)	269 (55%)
Systolic BP (mm Hg)	139·9 (19·2)	141·3 (19·9)
Diastolic BP (mm Hg)	78·1 (11·1)	78·9 (12·5)
Systolic BP (mm Hg)		
≤160	426 (87%)	408 (84%)
>160	62 (13%)	77 (16%)
Diabetes mellitus	68 (14%)	61 (13%)
Heart failure	96 (20%)	94 (19%)
Myocardial infarction	47 (10%)	56 (12%)
Angina	80 (16%)	75 (15%)

	Warfarin (n=488)		Aspirin (n=485)		Warfarin *vs* aspirin	
	n	Risk per year	n	Risk per year	RR (95% CI)	p
★ Stroke	21	1·6%	44	3·4%	0·46 (0·26–0·79)	0·003
By severity						
★ Fatal	13	1·0%	21	1·6%	0·59 (0·27–1·24)	0·14
★ Disabling non-fatal	8	0·6%	23	1·8%	0·33 (0·13–0·77)	0·005
Type of stroke*						
★ Ischaemic	10	0·8%	32	2·5%	0·30 (0·13–0·63)	0·0004
★ Haemorrhagic	6	0·5%	5	0·4%	1·15 (0·29–4·77)	0·83
Unknown	5	0·4%	7	0·5%	0·69 (0·17–2·51)	0·53
Other intracranial haemorrhage†	2	0·2%	1	0·1%	1·92 (0·10–113·3)	0·65
Systemic embolism‡	1	0·1%	3	0·2%	0·32 (0·01–3·99)	0·36
Total number of events	24	1·8%	48	3·8%	0·48 (0·28–0·80)	0·0027

Lancet 2007; 370: 493–503

Warfarin vs. Aspirin + Clopidogrel



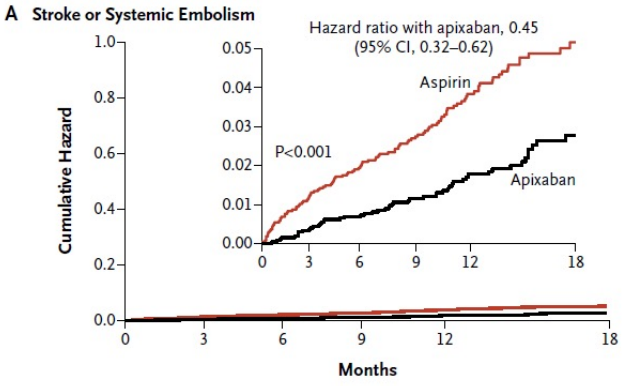
All stroke

Number at risk

Clopidogrel +aspirin	3335	3168	2419	941
Oral anticoagulation therapy	3371	3232	2466	930

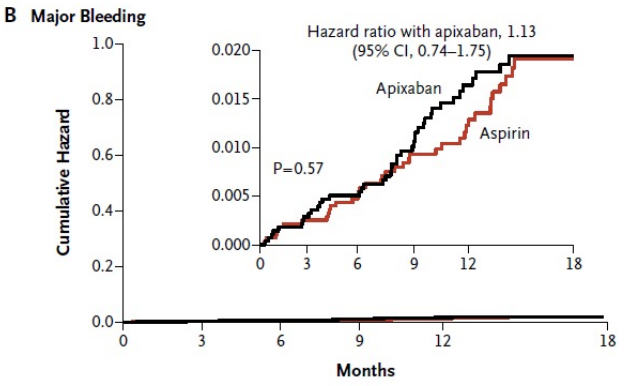
Lancet 2006; 367: 1903–12

Apixaban vs. Aspirin



No. at Risk

Aspirin	2791	2716	2530	2112	1543	628
Apixaban	2808	2758	2566	2125	1522	615

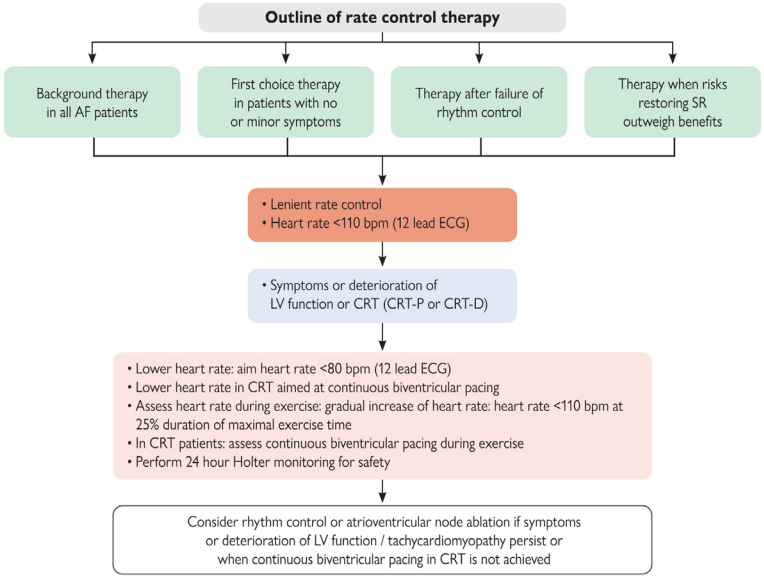


No. at Risk

Aspirin	2791	2738	2557	2140	1571	642
Apixaban	2808	2759	2566	2120	1521	622

N Engl J Med 2011;364:806-17.

Rate Control: Better Symptom Management



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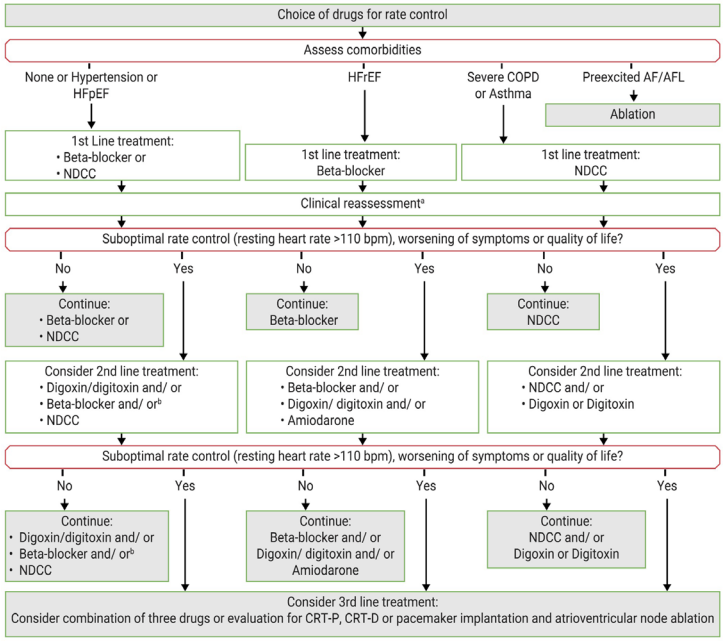
Rate Control: Better Symptom Management



Hindricks G et al., Eur Heart J. 2020 Aug 29;00, 1-125.

Rate Control: Better Symptom Management

	Intravenous administration	Usual oral maintenance dose	Contraindicated
Beta-blockers[b]			
Metoprolol tartrate	2.5 - 5 mg i.v. bolus; up to 4 doses	25 - 100 mg *b.i.d.*	In case of asthma use beta-1-blockers Contraindicated in acute HF and history of severe bronchospasm
Metoprolol XL (succinate)	N/A	50 - 400 mg *o.d.*	
Bisoprolol	N/A	1.25 - 20 mg *o.d.*	
Atenolol[c]	N/A	25 - 100 mg *o.d.*	
Esmolol	500 µg/kg i.v. bolus over 1 min; followed by 50 - 300 µg/kg/min	N/A	
Landiolol	100 µg/kg i.v. bolus over 1 min; followed by 10 - 40 µg/kg/min[505]	N/A	
Nebivolol	N/A	2.5 - 10 mg *o.d.*	
Carvedilol	N/A	3.125 - 50 mg *b.i.d.*	
Non-dihydropyridine calcium channel antagonists			
Verapamil	2.5 - 10 mg i.v. bolusover 5 min	40 mg b.i.d. to 480 mg (extended release) o.d.	Contraindicated in HFrEF Adapt doses in hepatic and renal impairment
Diltiazem	0.25 mg/kg i.v. bolus over 5 min, then 5 - 15 mg/h	60 mg t.i.d. to 360 mg (extended release) o.d.	
Digitalis glycosides			
Digoxin	0.5 mg i.v. bolus (0.75 - 1.5 mg over 24 hours in divided doses)	0.0625 - 0.25 mg o.d.	High plasma levels associated with increased mortality Check renal function before starting and adapt dose in CKD patients
Digitoxin	0.4 - 0.6 mg	0.05 - 0.1 mg o.d.	High plasma levels associated with increased mortality
Other			
Amiodarone	300 mg i.v. diluted in 250 mL 5% dextrose over 30 - 60 min (preferably via central venous cannula), followed by 900 - 1200 mg i.v. over 24 hours diluted in 500 - 1000 mL via a central venous cannula	200 mg o.d. after loading 3 × 200 mg daily over 4 weeks, then 200 mg daily[536] [d](reduce other rate controlling drugs according to heart rate)	In case of thyroid disease, only if no other options

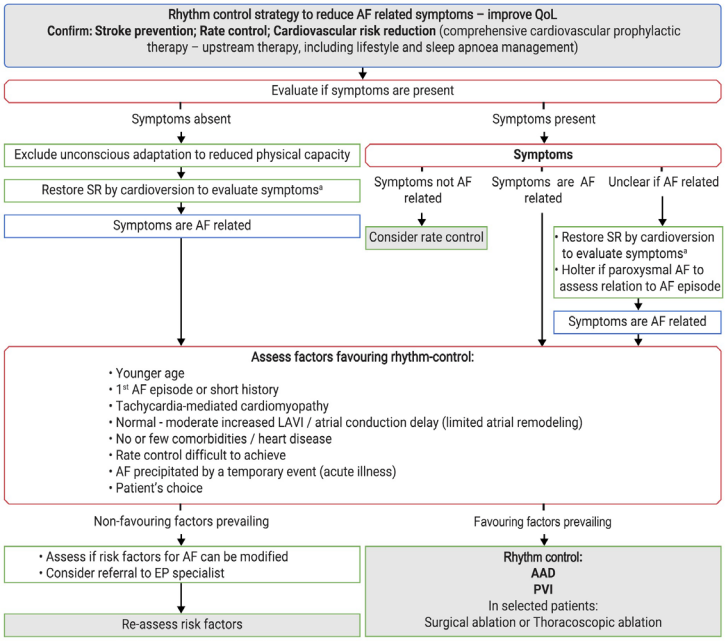
Hindricks G et al., Eur Heart J. 2020 Aug 29;00, 1-125.

Rate Control: Better Symptom Management

Recommendations	Class[b]	Level[c]
Beta-blockers, diltiazem, or verapamil are recommended as first-choice drugs to control heart rate in AF patients with LVEF≥40%.[492,507,511,529]	I	B
Beta-blockers and/or digoxin are recommended to control heart rate in AF patients with LVEF<40%.[486,491,502,512,530–532]	I	B
Combination therapy comprising different rate controlling drugs[d] should be considered if a single drug does not achieve the target heart rate.[533,534]	IIa	B
A resting heart rate of <110 bpm (i.e. lenient rate control) should be considered as the initial heart rate target for rate control therapy.[488]	IIa	B
Atrioventricular node ablation should be considered to control heart rate in patients unresponsive or intolerant to intensive rate and rhythm control therapy, and not eligible for rhythm control by LA ablation, accepting that these patients will become pacemaker dependent.[516,523,535,536]	IIa	B
In patients with haemodynamic instability or severely depressed LVEF, intravenous amiodarone may be considered for acute control of heart rate.[504,514,515]	IIb	B

Hindricks G et al., Eur Heart J. 2020 Aug 29;00, 1-125.

Rhythm Control: Better Symptom Management



Recommendations	Class[a]	Level[b]
Rhythm control therapy is recommended for symptom and QoL improvement in symptomatic patients with AF.[551–553]	I	A

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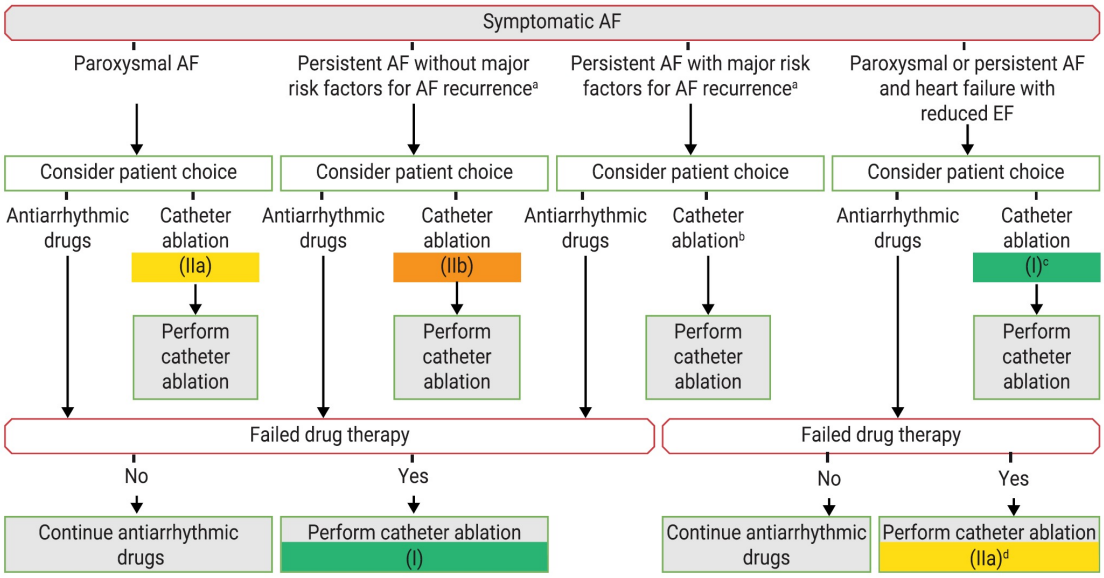
Rhythm Control: Better Symptom Management



Hindricks G et al., Eur Heart J. 2020 Aug 29;00, 1-125.

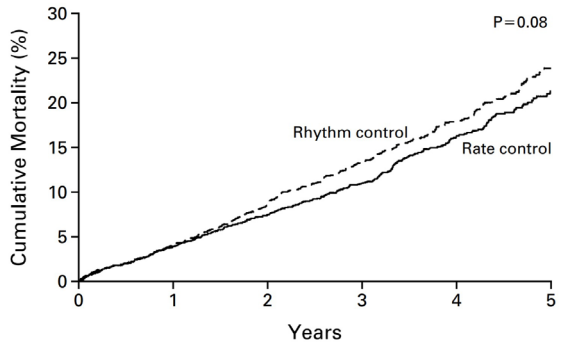
Rhythm Control with AADs

TABLE 2. DRUGS USED IN THE RATE-CONTROL GROUP AND THE RHYTHM-CONTROL GROUP.*

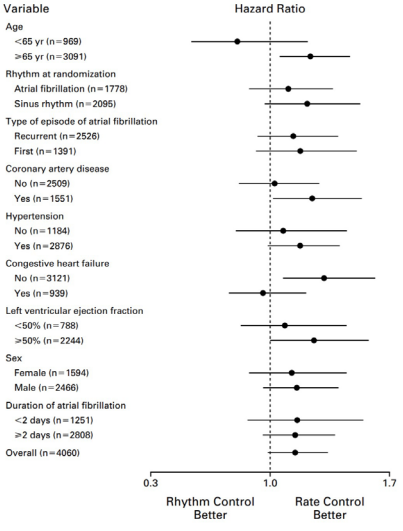
DRUG	RATE-CONTROL GROUP		RHYTHM-CONTROL GROUP	
	USED DRUG FOR INITIAL THERAPY	USED DRUG AT ANY TIME	USED DRUG FOR INITIAL THERAPY	USED DRUG AT ANY TIME
	no. of patients (%)			
Rate control				
Data available	1957	2027	1266	2033
Digoxin	949 (48.5)	1432 (70.6)	417 (32.9)	1106 (54.4)
Beta-blocker	915 (46.8)	1380 (68.1)	276 (21.8)	1008 (49.6)
Diltiazem	583 (29.8)	935 (46.1)	198 (15.6)	610 (30.0)
Verapamil	187 (9.6)	340 (16.8)	56 (4.4)	204 (10.0)
Rhythm control				
Data available	1265	2027	1960	2033
Amiodarone	2 (0.2)†	207 (10.2)	735 (37.5)	1277 (62.8)
Sotalol	1 (0.1)†	84 (4.1)	612 (31.2)	841 (41.4)
Propafenone	2 (0.2)†	45 (2.2)	183 (9.3)	294 (14.5)
Procainamide	0	30 (1.5)	103 (5.3)	173 (8.5)
Quinidine	2 (0.2)†	14 (0.7)	92 (4.7)	151 (7.4)
Flecainide	0	29 (1.4)	88 (4.5)	169 (8.3)
Disopyramide	0	7 (0.3)	42 (2.1)	87 (4.3)
Moricizine	0	2 (0.1)	14 (0.7)	35 (1.7)
Dofetilide	0	5 (0.2)	0	13 (0.6)

N Engl J Med. 2002 Dec 5;347(23):1825-33.

Rhythm Control with AADs

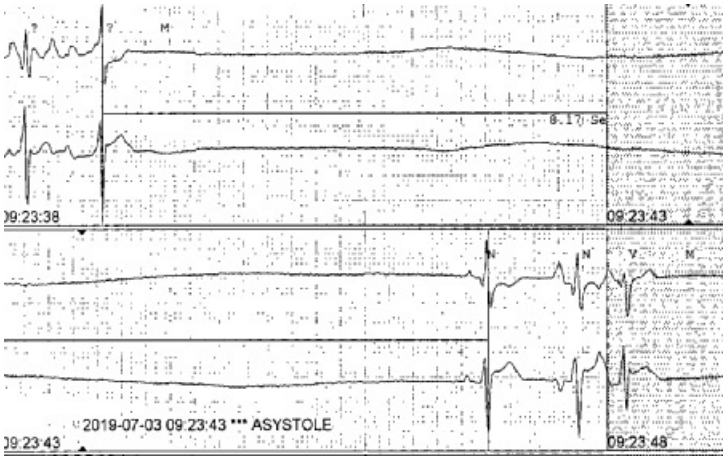


NO. OF DEATHS	number (percent)					
Rhythm control	0	80 (4)	175 (9)	257 (13)	314 (18)	352 (24)
Rate control	0	78 (4)	148 (7)	210 (11)	275 (16)	306 (21)

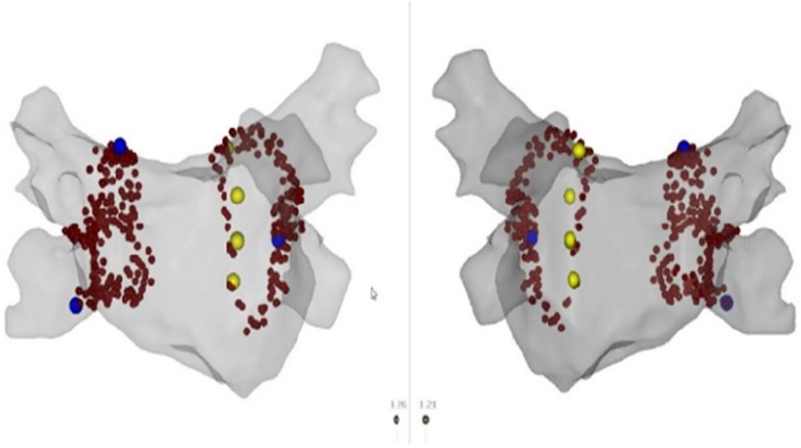


N Engl J Med. 2002 Dec 5;347(23):1825-33.

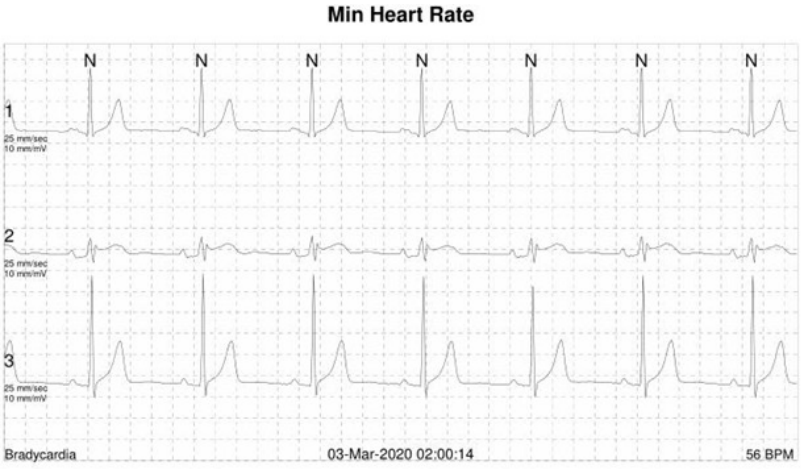
AF with TBS: AAD



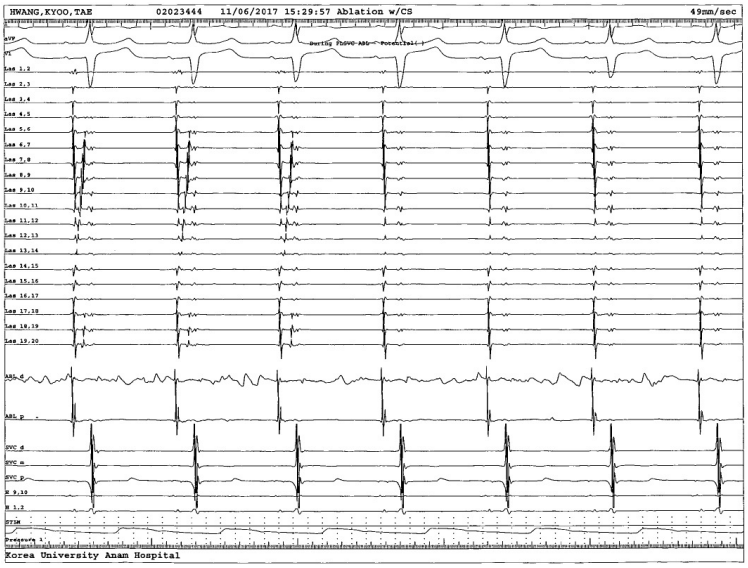
AF with TBS: RFCA

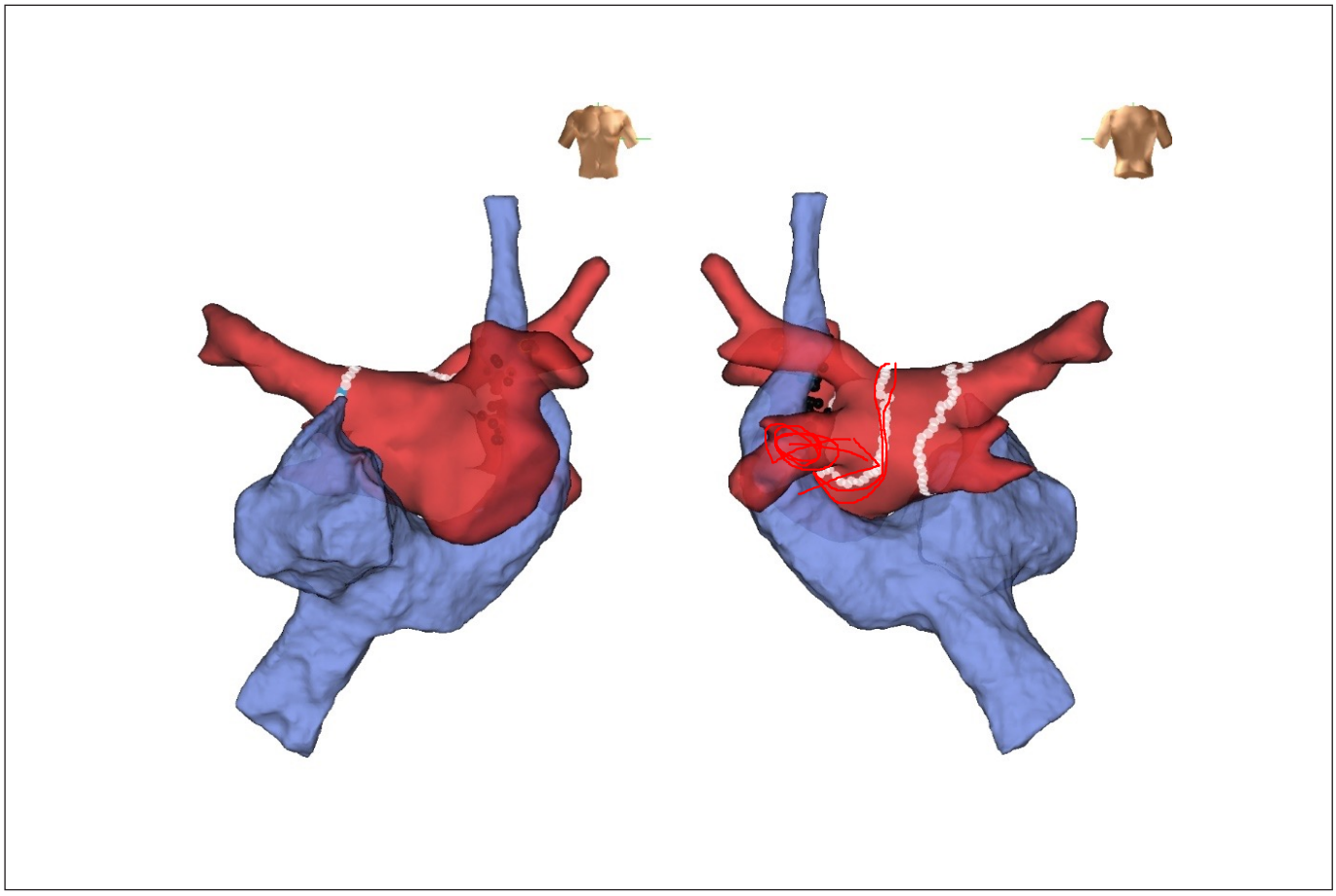


AF with TBS: post-RFCA



PLSVC Ablation



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전극도자절제술 5,000례
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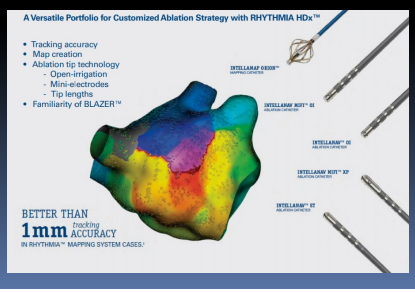
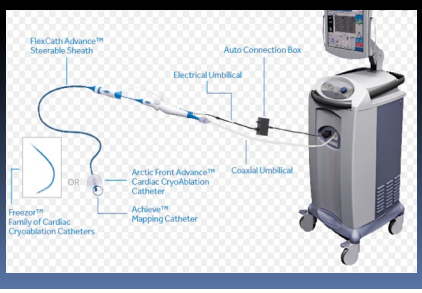




EAST-AFNET 4 Trial

The NEW ENGLAND JOURNAL of MEDICINE

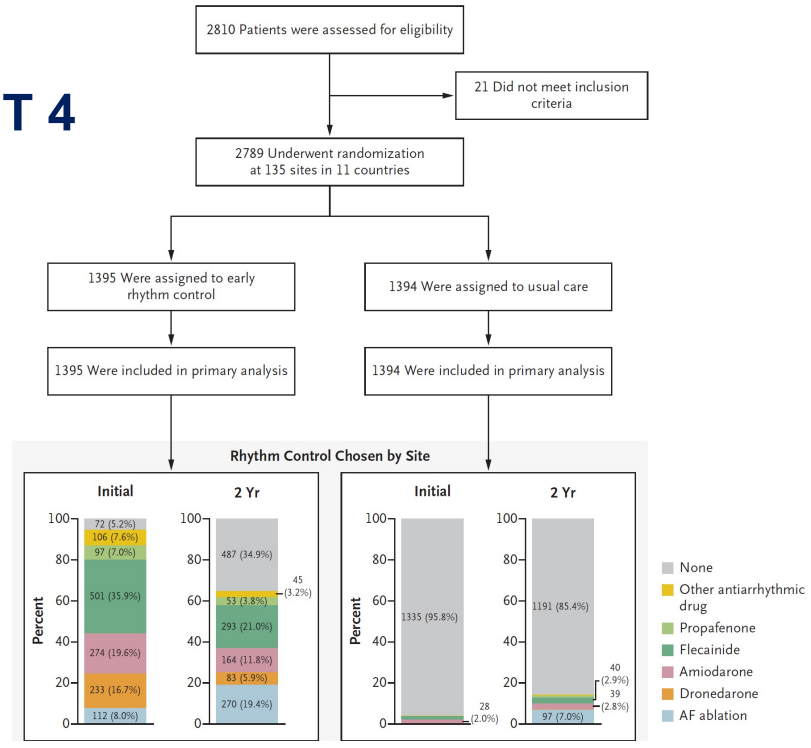
ESTABLISHED IN 1812 OCTOBER 1, 2020 VOL. 383 NO. 14

Early Rhythm-Control Therapy in Patients with Atrial Fibrillation

P. Kirchhof, A.J. Camm, A. Goette, A. Brandes, L. Eckardt, A. Elvan, T. Fetsch, I.C. van Gelder, D. Haase, L.M. Haegeli, F. Hamann, H. Heidbüchel, G. Hindricks, J. Kautzner, K.-H. Kuck, L. Mont, G.A. Ng, J. Rekosz, N. Schoen, U. Schotten, A. Suling, J. Taggeselle, S. Themistoclakis, E. Vettorazzi, P. Vardas, K. Wegscheider, S. Willems, H.J.G.M. Crijns, and G. Breithardt, for the EAST-AFNET 4 Trial Investigators*

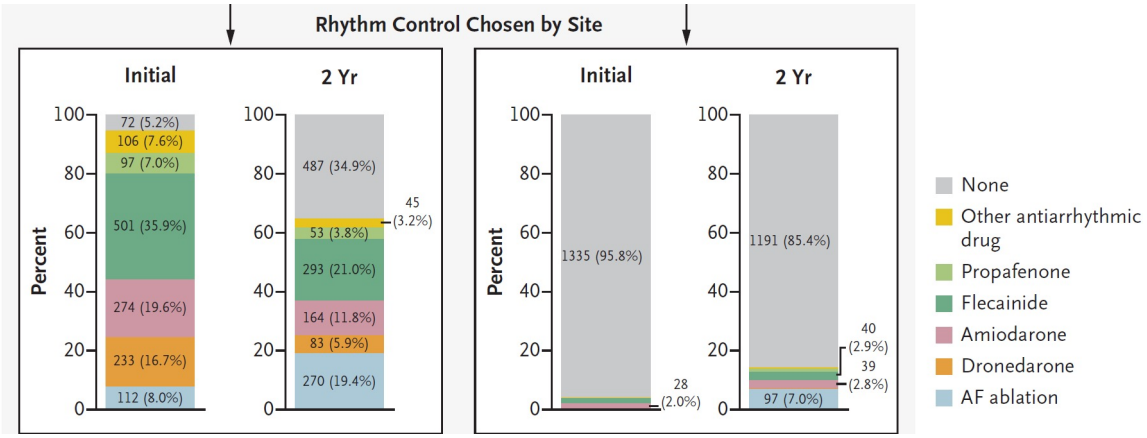
N Engl J Med 2020;383:1305-16.

EAST-AFNET 4 Trial



N Engl J Med 2020;383:1305-16.

EAST-AFNET 4 Trial



N Engl J Med 2020;383:1305-16.

EAST-AFNET 4 Trial

Table 1. Demographic and Clinical Characteristics of the Patients at Baseline.*

Characteristic	Early Rhythm Control (N=1395)	Usual Care (N=1394)
Age — yr	70.2±8.4	70.4±8.2
Female sex — no. (%)	645 (46.2)	648 (46.5)
Body-mass index†	29.2±5.4	29.3±5.4
Type of atrial fibrillation — no./total no. (%)		
First episode	528/1391 (38.0)	520/1394 (37.3)
Paroxysmal	501/1391 (36.0)	493/1394 (35.4)
Persistent	362/1391 (26.0)	381/1394 (27.3)
Sinus rhythm at baseline — no./total no. (%)	762/1389 (54.9)	743/1393 (53.3)
Median days since atrial fibrillation diagnosis (IQR)‡	36.0 (6.0–114.0)	36.0 (6.0–112.0)
Absence of atrial fibrillation symptoms — no./total no. (%)§	395/1305 (30.3)	406/1328 (30.6)
Previous cardioversion — no./total no. (%)	546/1364 (40.0)	543/1389 (39.1)
Concomitant cardiovascular conditions		
Previous stroke or transient ischemic attack — no. (%)	175 (12.5)	153 (11.0)
At least mild cognitive impairment — no./total no. (%)¶	582/1326 (43.9)	584/1341 (43.5)
Arterial hypertension — no. (%)	1230 (88.2)	1220 (87.5)
Blood pressure — mm Hg‖		
Systolic	136.5±19.4	137.5±19.3
Diastolic	80.9±12.1	81.3±12.0
Stable heart failure — no. (%)**	396 (28.4)	402 (28.8)
CHA_2DS_2-VASc score††	3.4±1.3	3.3±1.3
Valvular heart disease — no./total no. (%)	609/1389 (43.8)	642/1391 (46.2)
Chronic kidney disease of MDRD stage 3 or 4 — no. (%)‡‡	172 (12.3)	179 (12.8)
Medication at discharge — no./total no. (%)§§		
Oral anticoagulation with NOAC or VKA	1267/1389 (91.2)	1250/1393 (89.7)
Digoxin or digitoxin	46/1389 (3.3)	85/1393 (6.1)
Beta-blocker	1058/1389 (76.2)	1191/1393 (85.5)
ACE inhibitors or angiotensin II receptor blocker	953/1389 (68.6)	979/1393 (70.3)
Mineralocorticoid-receptor antagonist	90/1389 (6.5)	92/1393 (6.6)
Diuretic	559/1389 (40.2)	561/1393 (40.3)
Statin	628/1389 (45.2)	568/1393 (40.8)
Platelet inhibitor	229/1389 (16.5)	226/1393 (16.2)

N Engl J Med 2020;383:1305-16.

EAST-AFNET 4 Trial

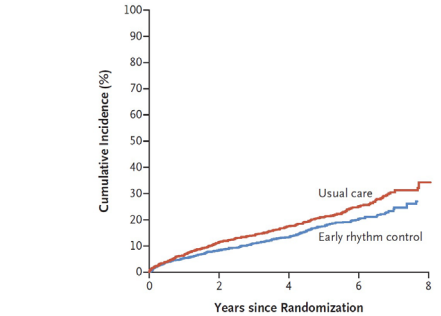


Table 2. Efficacy Outcomes.*

Outcome	Early Rhythm Control	Usual Care	Treatment Effect
First primary outcome — events/person-yr (incidence/100 person-yr)	249/6399 (3.9)	316/6332 (5.0)	0.79 (0.66 to 0.94)†
Components of first primary outcome — events/person-yr (incidence/100 person-yr)			
Death from cardiovascular causes	67/6915 (1.0)	94/6988 (1.3)	0.72 (0.52 to 0.98)‡
Stroke	40/6813 (0.6)	62/6856 (0.9)	0.65 (0.44 to 0.97)‡
Hospitalization with worsening of heart failure	139/6620 (2.1)	169/6558 (2.6)	0.81 (0.65 to 1.02)‡
Hospitalization with acute coronary syndrome	53/6762 (0.8)	65/6816 (1.0)	0.83 (0.58 to 1.19)‡
Second primary outcome — nights spent in hospital/yr	5.8±21.9	5.1±15.5	1.08 (0.92 to 1.28)§
Key secondary outcomes at 2 yr			
Change in left ventricular ejection fraction — %	1.5±9.8	0.8±9.8	0.23 (–0.46 to 0.91)¶
Change in EQ-5D score‖	–1.0±21.4	–2.7±22.3	1.07 (–0.68 to 2.82)¶
Change in SF-12 Mental Score**	0.7±10.6	1.6±10.1	–1.20 (–2.04 to –0.37)¶
Change in SF-12 Physical Score**	0.3±8.5	0.1±8.2	0.33 (–0.39 to 1.06)¶
Change in MoCA score	0.1±3.3	0.1±3.2	–0.14 (–0.39 to 0.12)¶
Sinus rhythm — no. of patients with feature/total no. (%)	921/1122 (82.1)	687/1135 (60.5)	3.13 (2.55 to 3.84)††
Asymptomatic — no. of patients with feature/total no. (%)‡‡	861/1159 (74.3)	850/1171 (72.6)	1.14 (0.93 to 1.40)††

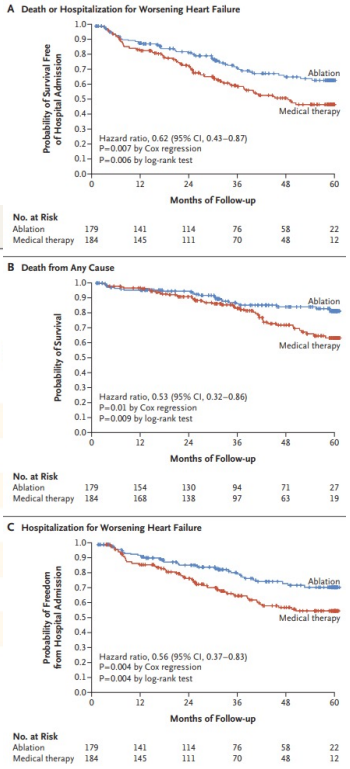
N Engl J Med 2020;383:1305-16.

RFCA vs. Medical
- CASTLE-AF

Table 2. Primary and Secondary Clinical End Points.*

End Point	Ablation (N=179)	Medical Therapy (N=184)	Hazard Ratio (95% CI)
	number (percent)		
Primary†	51 (28.5)	82 (44.6)	0.62 (0.43–0.87)
Secondary			
Death from any cause	24 (13.4)	46 (25.0)	0.53 (0.32–0.86)
Heart-failure hospitalization	37 (20.7)	66 (35.9)	0.56 (0.37–0.83)
Cardiovascular death	20 (11.2)	41 (22.3)	0.49 (0.29–0.84)
Cardiovascular hospitalization	64 (35.8)	89 (48.4)	0.72 (0.52–0.99)
Hospitalization for any cause	114 (63.7)	122 (66.3)	0.99 (0.77–1.28)
Cerebrovascular accident	5 (2.8)	11 (6.0)	0.46 (0.16–1.33)

NEJM. CASTLE-AF



RFCA vs. Medical
- CABANA RCT

Table 2. Primary and Secondary Outcomes by Intention-to-Treat Analysis

	Events, No. (%)		Kaplan-Meier 4-Year Event Rate, %				
	Catheter Ablation Group (n = 1108)	Drug Therapy Group (n = 1096)	Catheter Ablation Group (n = 1108)	Drug Therapy Group (n = 1096)	Absolute Reduction	Hazard Ratio (95% CI)[a]	*P* Value
Primary end point (death, disabling stroke, serious bleeding, or cardiac arrest)[b]	89 (8.0)	101 (9.2)	7.2	8.9	1.7	0.86 (0.65-1.15)[c]	.30
Components of primary end point							
Death	58 (5.2)	67 (6.1)	4.7	5.3	0.6	0.85 (0.60-1.21)	.38
Disabling stroke	3 (0.3)	7 (0.6)	0.1	0.7	0.6	0.42 (0.11-1.62)	.19
Serious bleeding	36 (3.2)	36 (3.3)	3.0	3.7	0.7	0.98 (0.62-1.56)	.93
Cardiac arrest	7 (0.6)	11 (1.0)	0.7	1.1	0.4	0.62 (0.24-1.61)	.33
Secondary end point							
Death or cardiovascular hospitalization	573 (51.7)	637 (58.1)	54.9	62.7	7.8	0.83 (0.74-0.93)	.001

JAMA . 2019 Apr 2;321(13):1261-1274.

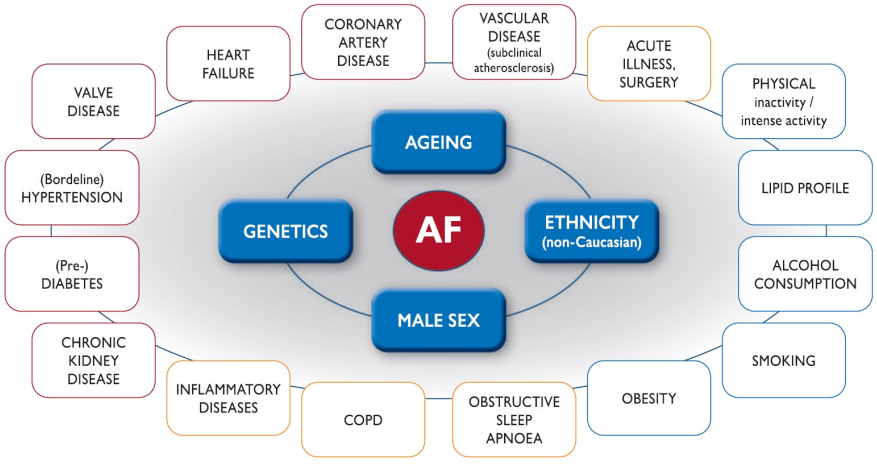
RFCA vs. Medical
- CABANA Real-World

Table 3 Outcomes in propensity score-weighted patients stratified by trial eligibility

	Number of events	Person years	Event rate	Number of events	Person years	Event rate	Absolute reduction in event rate (95% CI)	Hazard ratio (95% CI)	*P*-value
Trial eligible	Drug treated (*N* = 128 781)			Ablated (*N* = 6907)					
Composite	527	9454	5.57	388	10 105	3.84	1.73 (1.32–2.14)	0.70 (0.63–0.77)	<0.001
All-cause mortality	312	9811	3.18	200	10 499	1.90	1.27 (0.98–1.56)	0.60 (0.53–0.69)	<0.001
Ischaemic stroke	86	9698	0.88	50	10 436	0.48	0.40 (0.26–0.55)	0.56 (0.43–0.73)	<0.001
Major bleeding	185	9558	1.94	192	10 168	1.89	0.05 (-0.22 to 0.32)	1.00 (0.87–1.16)	0.99
Cardiac arrest	30	9809	0.31	13	10 497	0.12	0.19 (0.11–0.26)	0.41 (0.24–0.69)	0.001

Eur Heart J. 2019 Apr 21;40(16):1257-1264.

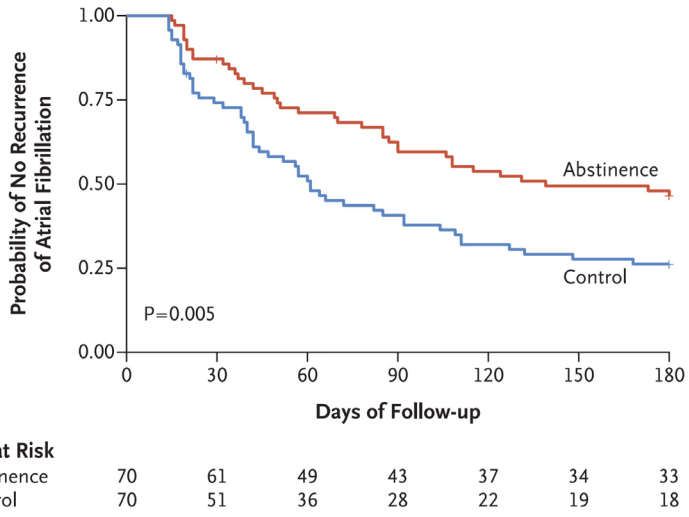
Risk Factors: Cardiovascular Risk Factors



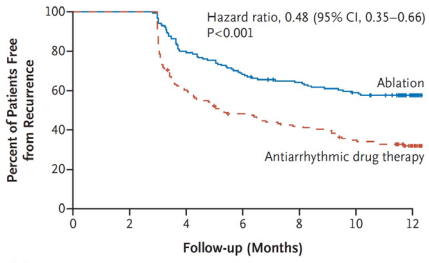
Recommendations	Class[a]	Level[b]
Identification and management of risk factors and concomitant diseases is recommended as an integral part of treatment in AF patients.[888]	I	B
Modification of unhealthy lifestyle and targeted therapy of intercurrent conditions is recommended to reduce AF burden and symptom severity.[245,636,887,889,1016,1052]	I	B
Opportunistic screening for AF is recommended in hypertensive patients.[26,172,222]	I	B
Attention to good BP control is recommended in AF patients with hypertension to reduce AF recurrences and risk of stroke and bleeding.[26,1035]	I	B
In obese patients with AF, weight loss together with management of other risk factors should be considered to reduce AF incidence, AF progression, AF recurrences, and symptoms.[898,899,1011]	IIa	B
Advice and management to avoid alcohol excess should be considered for AF prevention and in AF patients considered for OAC therapy.[324,1012,1014,1016]	IIa	B
Physical activity should be considered to help prevent AF incidence or recurrence, with the exception of excessive endurance exercise, which may promote AF.[1027–1033,1063]	IIa	C
Opportunistic screening for AF should be considered in patients with OSA.[172]	IIa	C
Optimal management of OSA may be considered, to reduce AF incidence, AF progression, AF recurrences, and symptoms.[650,651,1057–1061,1064,1065]	IIb	C

Hindricks G et al., Eur Heart J. 2020 Aug 29;00, 1-125.

Risk Factors: Cardiovascular Risk Factors



No. at Risk							
Abstinence	70	61	49	43	37	34	33
Control	70	51	36	28	22	19	18



No. at Risk							
Ablation	154	154	123	105	96	86	55
Antiarrhythmic drug therapy	149	149	89	69	60	49	27

N Engl J Med. 2020 Jan 2;382(1):20-28.
N Engl J Med 2021;384:305-15.

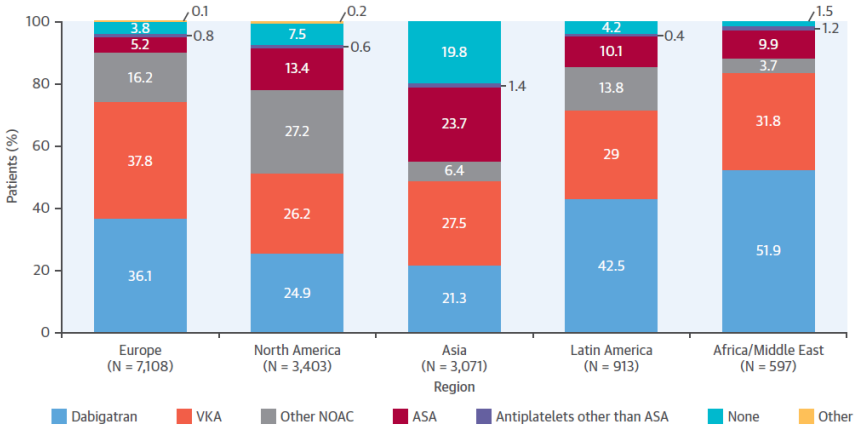
Conclusion

- **A:** Avoid stroke
- **B:** Better symptom control
- **C:** Cardiovascular risk factor management

Current Practice

CHA_2DS_2-VASc score categories*	
Low/moderate, score = 1†	2,093 (13.9)
High, score ≥2	12,999 (86.1)

CENTRAL ILLUSTRATION Stroke Prevention in AF: Antithrombotic Treatment per Region



Huisman, M.V. et al. J Am Coll Cardiol. 2017;69(7):777-85.

Patient distribution by antithrombotic therapy and region (N = 15,092). Other NOAC includes rivaroxaban, apixaban, and edoxaban. ASA = acetylsalicylic acid; NOAC = non-vitamin K antagonist oral anticoagulant(s); VKA = vitamin K antagonist(s).

J Am Coll Cardiol 2017;69:777–85

Thank you for listening!

고려대학교 의과대학 가정의학교실

2022 연수강좌

일차의료의를 위한 GLP-1 RA 총정리

배재현
고려의대 내분비내과

GLP-1 receptor agonists for the treatment of type 2 diabetes

Department of Internal Medicine, Korea University Anam Hospital
Jae Hyun Bae

Saturday, April 23, 2022

Classes and characteristics of antidiabetic medications

PROFILES OF ANTIHYPERGLYCEMIC MEDICATIONS

	MET	GLP1-RA	SGLT2i	DPP4i	AGi	TZD (moderate dose)	SU / GLN	COLSVL	BCR-QR	INSULIN	PRAML
HYPO	Neutral	Neutral	Neutral	Neutral	Neutral	Neutral	Moderate/ Severe / Mild	Neutral	Neutral	Moderate to Severe	Neutral
WEIGHT	Slight Loss	Loss	Loss	Neutral	Neutral	Gain	Gain	Neutral	Neutral	Gain	Loss
RENAL / GU	Contra-indicated if eGFR <30 mL/min/ 1.73 m²	Exenatide Not Indicated CrCl <30 Potential Benefit of LA GLP1-RA	Not Indicated for eGFR <45 mL/ min/1.73 m² See #1 Genital Mycotic Infections Potential CKD Benefit; See #1	Dose Adjustment Necessary (Except Linagliptin) Effective in Reducing Albuminuria	Neutral	Neutral	More Hypo Risk	Neutral	Neutral	More Hypo Risk	Neutral
GI Sx	Moderate	Moderate	Neutral	Neutral	Moderate	Neutral	Neutral	Mild	Moderate	Neutral	Moderate
CARDIAC: CHF	Neutral	Neutral	Prevent HF Hospitalization Manage HFrEF; See #2	See #4	Neutral	Moderate	Neutral	Neutral	Neutral	CHF Risk	Neutral
CARDIAC: ASCVD		Potential Benefit of LA GLP1-RA	See #3			May Reduce Stroke Risk	Possible ASCVD Risk	Lowers LDL-C	Safe	Neutral	
BONE	Neutral	Neutral	Neutral	Neutral	Neutral	Moderate Fracture Risk	Neutral	Neutral	Neutral	Neutral	Neutral
KETOACIDOSIS	Neutral	Neutral	DKA Can Occur in Various Stress Settings	Neutral	Neutral	Neutral	Neutral	Neutral	Neutral	Neutral	Neutral

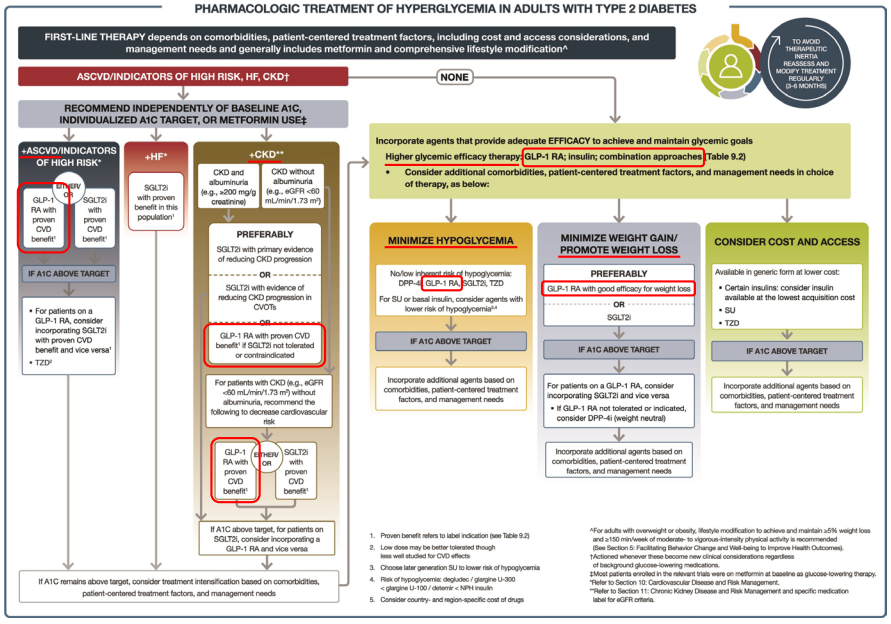
Few adverse events or possible benefits
Use with caution
Likelihood of adverse effects

1. Canagliflozin indicated for eGFR ≥30 mL/min/1.73 m² in patients with CKD 3 + albuminuria.
2. Dapagliflozin—potential primary prevention of HF hospitalization & demonstrated efficacy in HFrEF.
3. Empagliflozin—FDA approved to reduce CV mortality. Canagliflozin—FDA approved to reduce MACE events.
4. Possible increased hospitalizations for heart failure with alogliptin and saxagliptin.

DOI 10.4158/CS-2019-0472

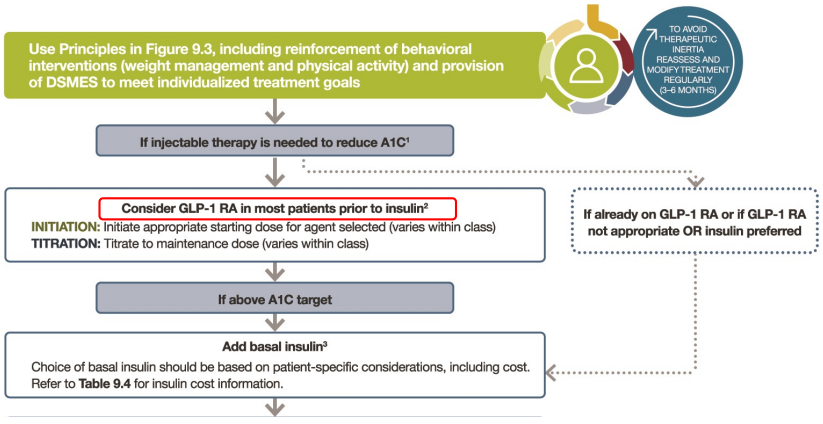
Garber AJ et al., Endocr Pract. 2020;26:107-39.

Pharmacologic treatment in people with type 2 diabetes



Draznin B et al., Diabetes Care. 2022;45(Suppl 1):S125-43.

Intensifying to injectable therapies in type 2 diabetes



1. Consider insulin as the first injectable if evidence of ongoing catabolism, symptoms of hyperglycemia are present, when A1C levels (>10% [86 mmol/mol]) or blood glucose levels (≥300 mg/dL [16.7 mmol/L]) are very high, or a diagnosis of type 1 diabetes is a possibility.
2. When selecting GLP-1 RA, consider: patient preference, A1C lowering, weight-lowering effect, or frequency of injection. If CVD, consider GLP-1 RA with proven CVD benefit. Oral or injectable GLP-1 RA are appropriate.
3. For patients on GLP-1 RA and basal insulin combination, consider use of a fixed-ratio combination product (IDegLira or iGlarLixi).

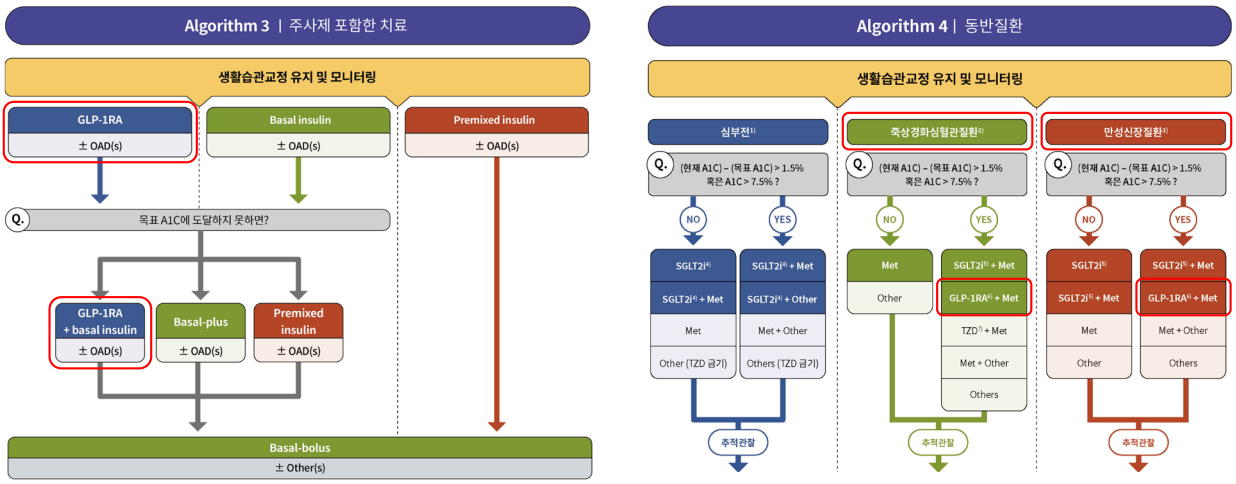
Draznin B et al., Diabetes Care. 2022;45(Suppl 1):S125-43.

대한당뇨병학회 진료지침: GLP-1수용체작용제 관련 내용

- 2형당뇨병의 약물치료
  - **강력한 혈당강하 효과**를 중점적으로 고려할 경우 **주사제를 포함한 치료**를 우선한다. **[무작위대조연구, 일반적권고]**
    - 혈당조절 강화를 위해 GLP-1수용체작용제와 기저인슐린을 병용할 수 있다. **[무작위대조연구, 제한적권고]**
  - **죽상경화심혈관질환을 동반**한 경우 병용요법 시 **심혈관이익**이 입증된 SGLT2억제제 혹은 GLP-1수용체작용제를 포함한 치료를 우선 고려한다. **[무작위대조연구, 제한적권고]**
  - 목표 당화혈색소에 도달하지 못한 경우 기존 약물의 증량 또는 다른 계열 약물과의 병용요법(2제 이상)을 조속히 시행한다. **(단, DPP-4억제제와 GLP-1수용체작용제는 병용하지 않는다.)** **[무작위대조연구, 일반적권고]**

대한당뇨병학회. 2021 당뇨병 진료지침 제7판.

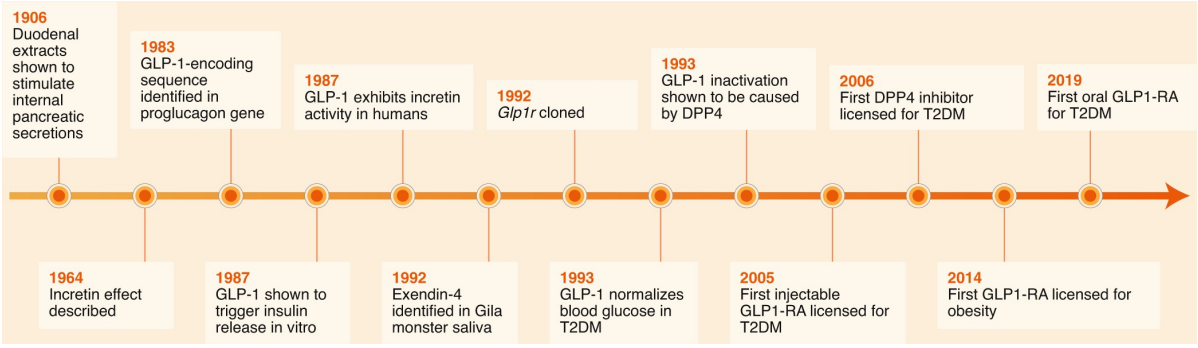
대한당뇨병학회 진료지침: GLP-1수용체작용제 관련 치료 알고리듬



GLP-1RA, glucagon-like peptide-1 receptor agonist; Met, metformin; OAD, oral antidiabetic drug; SGLT2i, sodium-glucose cotransporter 2 inhibitors; TZD, thiazolidinediones.

대한당뇨병학회. 2021 당뇨병 진료지침 제7판.

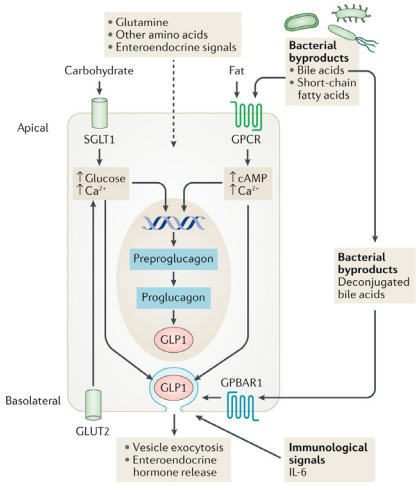
Timeline of GLP-1 discovery and clinical development



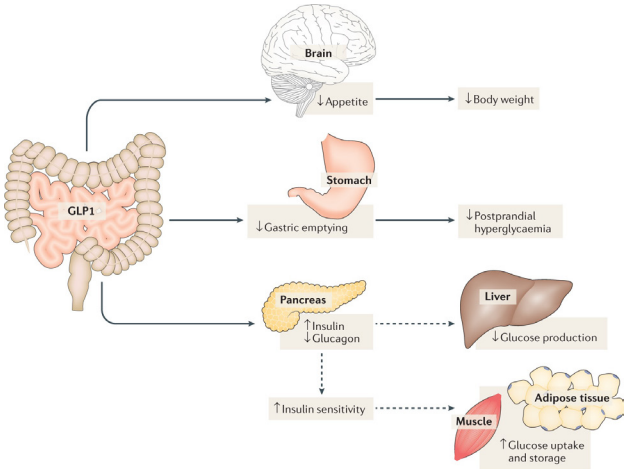
Gribble FM et al., Nat Metab. 2021;3:142-8.

GLP-1 secretion and antidiabetic effects of GLP-1

GLP-1 secretion from enteroendocrine L cells

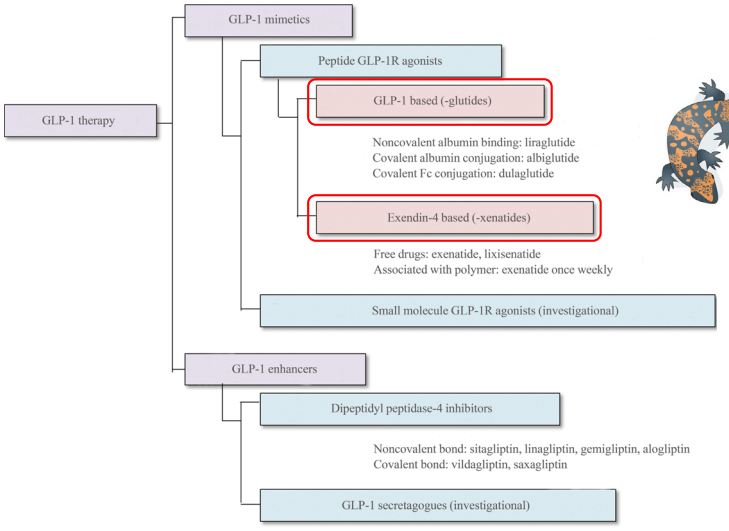


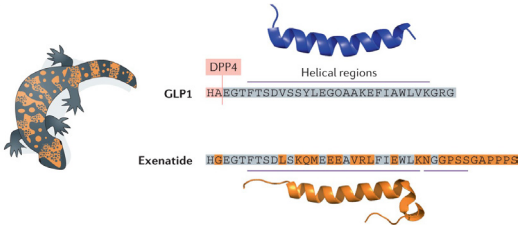
Effects of GLP-1 via GLP receptors on target tissues



Alicic RZ et al., Nat Rev Nephrol. 2021;17:227-44. Deacon CF, Nat Rev Endocrinol. 2020;16:642-53.

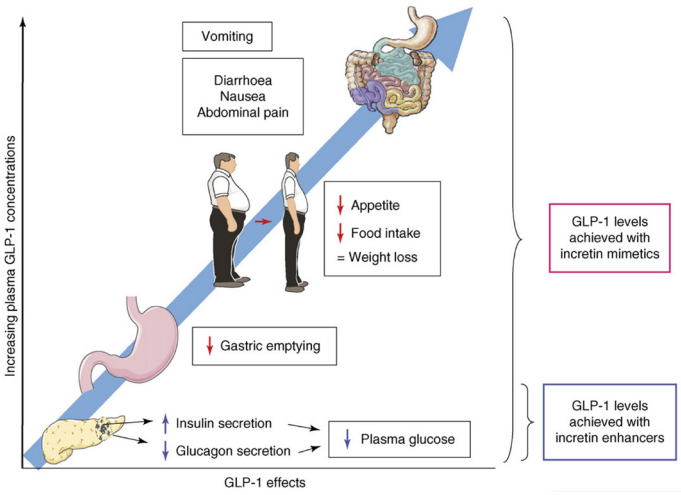
Classification of GLP-1-based therapies





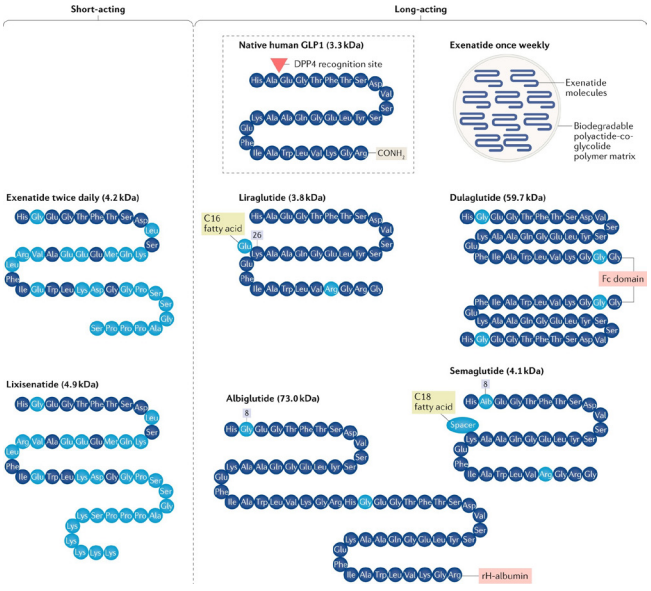
Cho YM et al., Endocrinol Metab. 2013;28:262-74. Muttenthaler M et al., Nat Rev Drug Discov. 2021;20:309-25.

Dose-response relationship for the effects of GLP-1



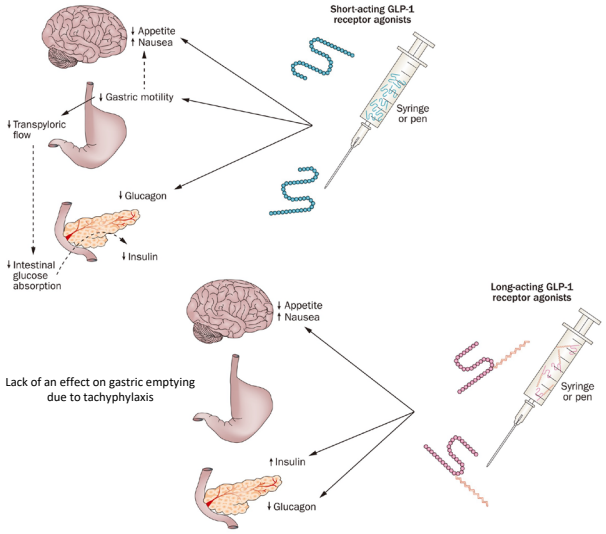
Holst JJ et al., Trends Mol Med. 2008;14:161-8.

Structure of native GLP-1 and GLP-1 receptor agonists



Andersen A et al., Nat Rev Endocrinol. 2018;14:390-403.

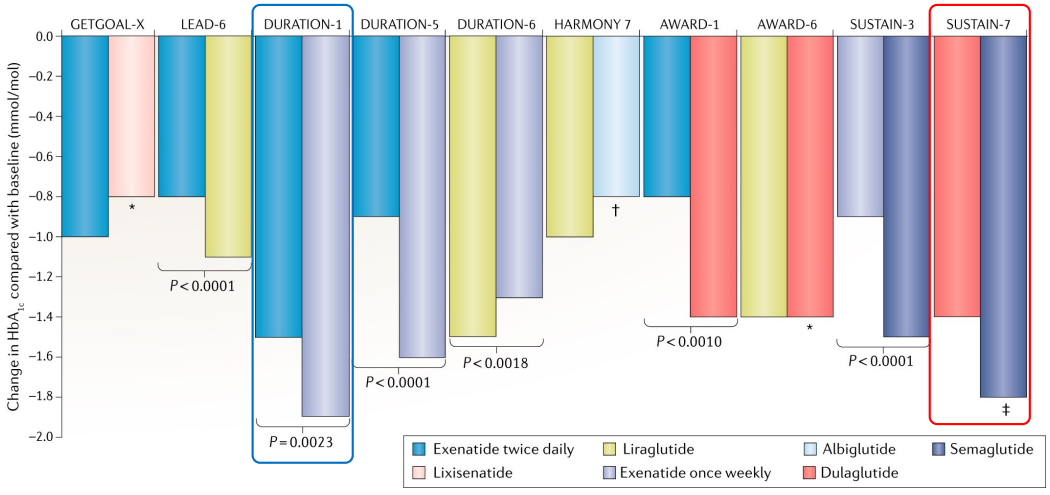
Comparison of short- vs. long-acting GLP-1 receptor agonists



Parameters	Short-acting GLP-1 receptor agonists	Long-acting GLP-1 receptor agonists
Compounds	Exenatide Lixisenatide	Albiglutide Dulaglutide Exenatide-LAR Liraglutide
Half-life	2–5 h	12 h–several days
Effects		
Fasting blood glucose levels	Modest reduction	Strong reduction
Postprandial hyperglycaemia	Strong reduction	Modest reduction
Fasting insulin secretion	Modest stimulation	Strong stimulation
Postprandial insulin secretion	Reduction	Modest stimulation
Glucagon secretion	Reduction	Reduction
Gastric emptying rate	Deceleration	No effect
Blood pressure	Reduction	Reduction
Heart rate	No effect or small increase (0–2 bpm)	Moderate increase (2–5 bpm)
Body weight reduction	1–5 kg	2–5 kg
Induction of nausea	20–50%, attenuates slowly (weeks to many months)	20–40%, attenuates quickly (~4–8 weeks)

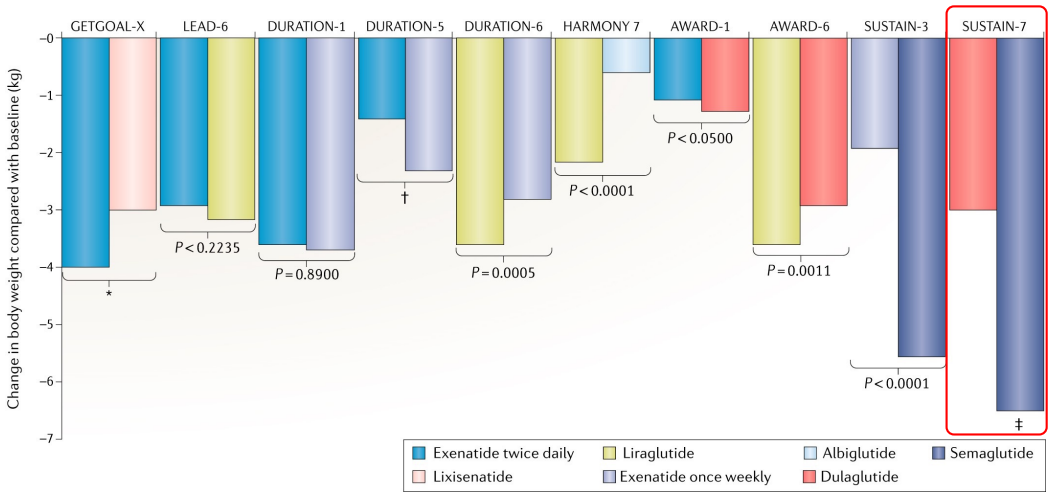
Meier JJ, Nat Rev Endocrinol. 2012;8:728-42.

HbA1c reductions in phase 3 head-to-head trials comparing GLP-1 receptor agonists in type 2 diabetes



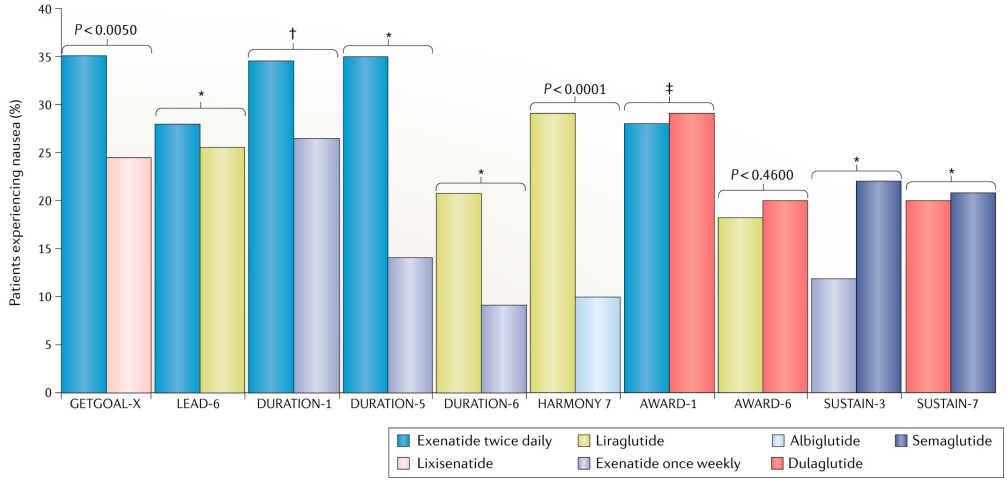
Andersen A et al., Nat Rev Endocrinol. 2018;14:390-403.

Body weight reductions in phase 3 head-to-head trials comparing GLP-1 receptor agonists in type 2 diabetes



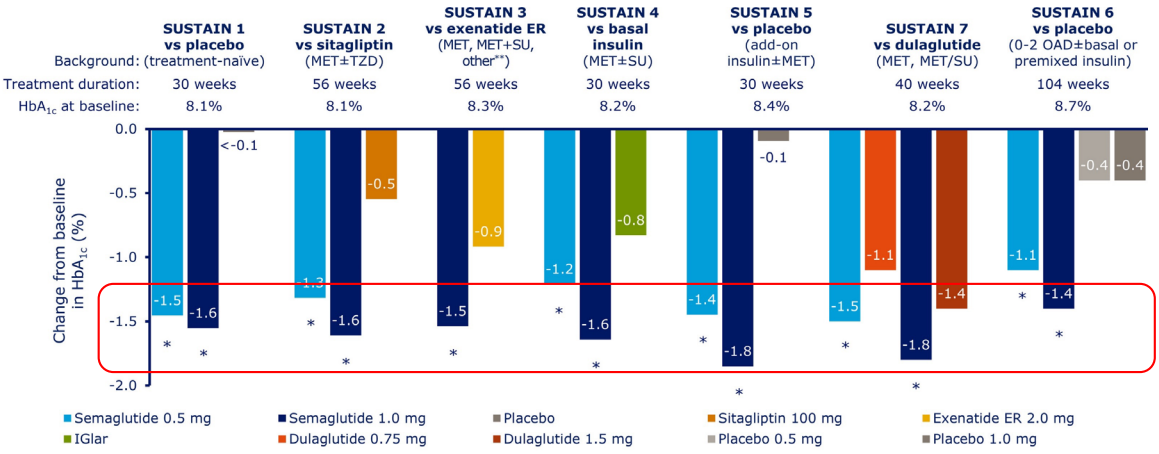
Andersen A et al., Nat Rev Endocrinol. 2018;14:390-403.

Percentage of patients with nausea in phase 3 head-to-head trials comparing GLP-1 receptor agonists in type 2 diabetes



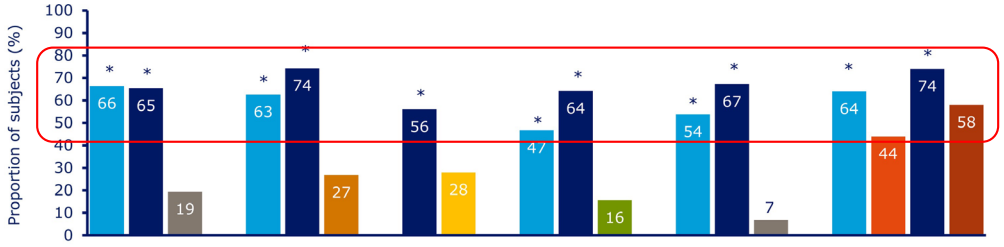
Andersen A et al., Nat Rev Endocrinol. 2018;14:390-403.

HbA1c reductions from baseline in SUSTAIN 1–7



Aroda VR et al., Diabetes Metab. 2019;45:409-18.

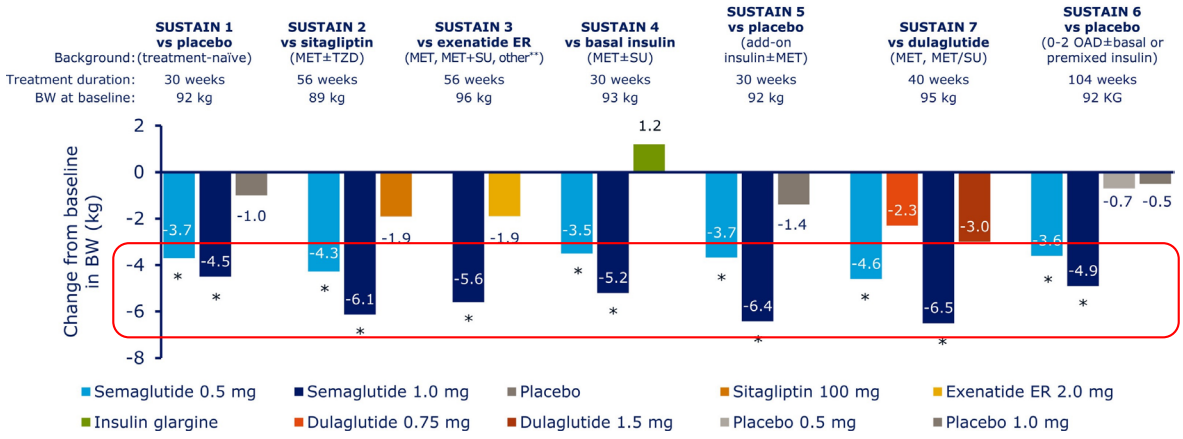
Proportions of people achieving HbA1c <7.0% in SUSTAIN 1–7



	SUSTAIN 1 vs placebo	SUSTAIN 2 vs sitagliptin	SUSTAIN 3 vs exenatide ER	SUSTAIN 4 vs Iglar	SUSTAIN 5 vs placebo	SUSTAIN 7 vs dulaglutide
Background:	(Monotherapy)	(MET, TZD, MET/TZD)	(1–2 OADs)	(MET, MET/SU)	(add-on insulin±MET)	(MET, MET/SU)
Treatment duration:	30 weeks	56 weeks	56 weeks	30 weeks	30 weeks	40 weeks
OR [95% CI] vs comparators:						
Semaglutide 0.5 mg	12.69 [6.57;24.52]	4.84 [3.51;6.68]		N/A	5.39 [3.72;7.81]	17.90 [8.26;38.78]
Semaglutide 1.0 mg	12.45 [6.46;23.99]	9.52 [6.75;13.43]		4.03 [2.90;5.59]	12.88 [8.73;19.02]	29.93 [13.65;65.61]

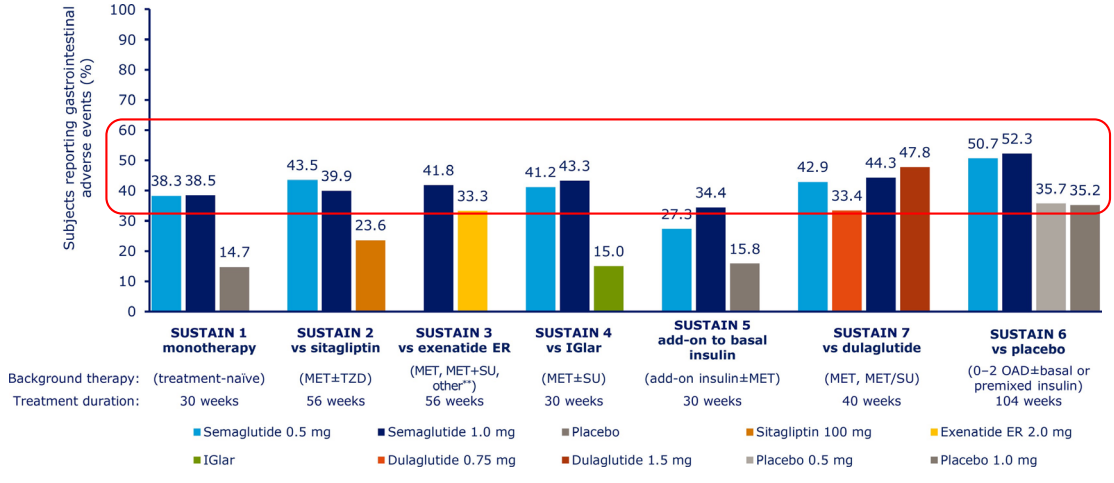
Aroda VR et al., Diabetes Metab. 2019;45:409-18.

Changes in body weight from baseline in SUSTAIN 1–7



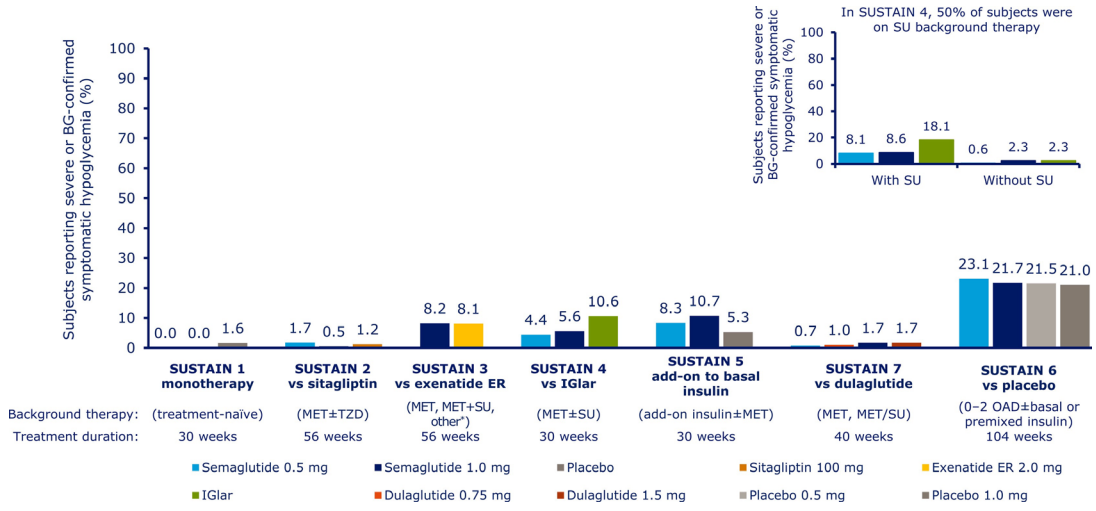
Aroda VR et al., Diabetes Metab. 2019;45:409-18.

Patient-reporting GI adverse events in SUSTAIN 1–7



Aroda VR et al., Diabetes Metab. 2019;45:409-18.

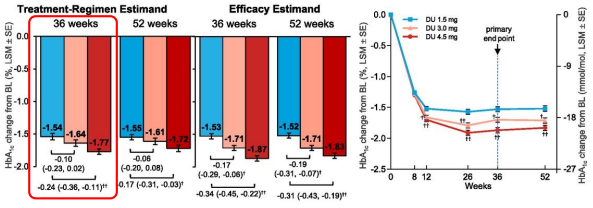
Severe or confirmed hypoglycemia in SUSTAIN 1–7



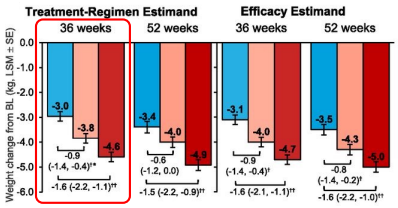
Aroda VR et al., Diabetes Metab. 2019;45:409-18.

Efficacy and safety of dulaglutide 3.0 mg and 4.5 mg vs. 1.5 mg in metformin treated type 2 diabetes (AWARD-11)

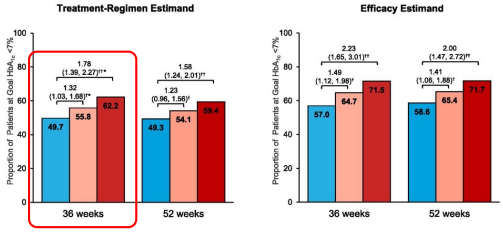
Change in HbA1c from baseline to week 36 (primary efficacy measure)

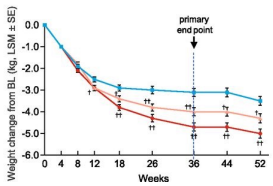


Change in body weight from baseline



Proportion of patients achieving HbA1c <7.0%

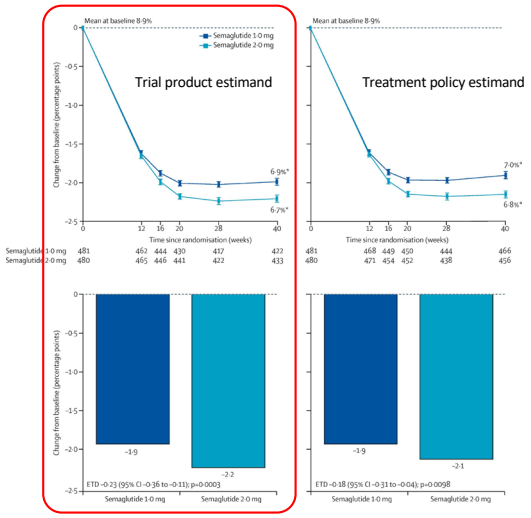




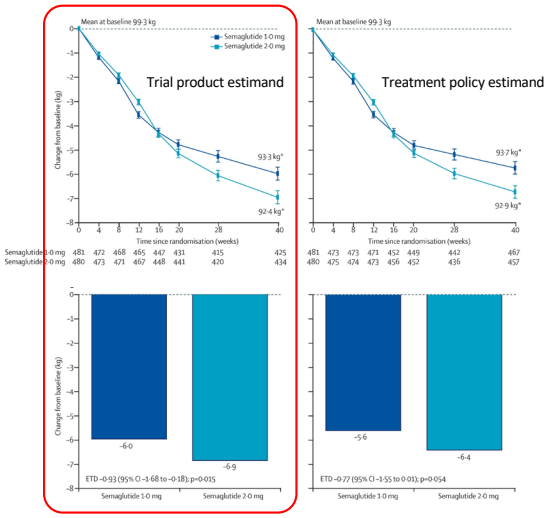
Frías JP et al., Diabetes Care. 2021;44:765-73.

Efficacy and safety of once-weekly semaglutide 2.0 mg vs. 1.0 mg in type 2 diabetes (SUSTAIN FORTE)

Change in HbA1c from baseline at week 40



Change in body weight from baseline at week 40



Frias JP et al., Lancet Diabetes Endocrinol. 2021;9:563-74.

Effects of weekly semaglutide 2.4 mg for obesity

	STEP 1 (Wilding et al, 2021)[2]	STEP 2 (Davies et al, 2021)[3]	STEP 3 (Wadden et al, 2021)[4]	STEP 4 (Rubino et al, 2021)[5]
Population	1961 adults with BMI ≥30 kg/m² or ≥27 kg/m² with ≥1 weight-related comorbidity	1595 adults with BMI ≥27 kg/m² with type 2 diabetes	611 adults with BMI ≥30 kg/m² or ≥27 kg/m² with ≥1 weight-related comorbidity	902 adults with BMI >30 kg/m² or >27 kg/m² with >1 weight-related comorbidity entered 20-week run-in; 806 who reached 2·4 mg dose semaglutide entered randomisation
Randomisation scheme	Randomised 2:1 to semaglutide 2·4 mg *vs* placebo	Randomised 1:1:1 to semaglutide 2·4 mg *vs* semaglutide 1·0 mg *vs* placebo	Randomised 2:1 to semaglutide 2·4 mg *vs* placebo	Randomised 2:1 to continued semaglutide 2·4 mg *vs* placebo
Background treatment	Both groups received lifestyle intervention	All groups received lifestyle intervention	Both groups received low-calorie diet for 8 weeks and intensive behavioural therapy (ie, 30 counselling visits)	Both groups received lifestyle intervention
Mean change in bodyweight at week 68				
Semaglutide 2·4 mg	−14·9%	−9·6%*	−16·0%	−7·9% from week 20; −17·4% from baseline
Placebo	−2·4%	−3·4%	−5·7%	+6·9% from week 20; −5·9% from baseline
Proportion of participants with >5% weight loss at week 68				
Semaglutide 2·4 mg	86·4%	68·8%	86·6%	88·7%
Placebo	31·5%	28·5%	47·6%	47·6%

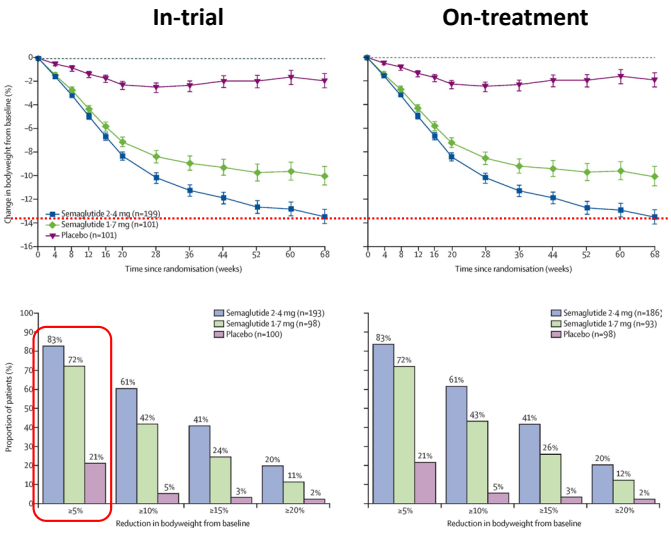
*Mean change in bodyweight at week 68 was −6·99% for semaglutide 1·0 mg weekly.

For weight management | **For weight management in T2D** | **For maximizing weight loss** | **For maintaining weight loss**

Ryan DH, Lancet Diabetes Endocrinol. 2021;9:252-4.

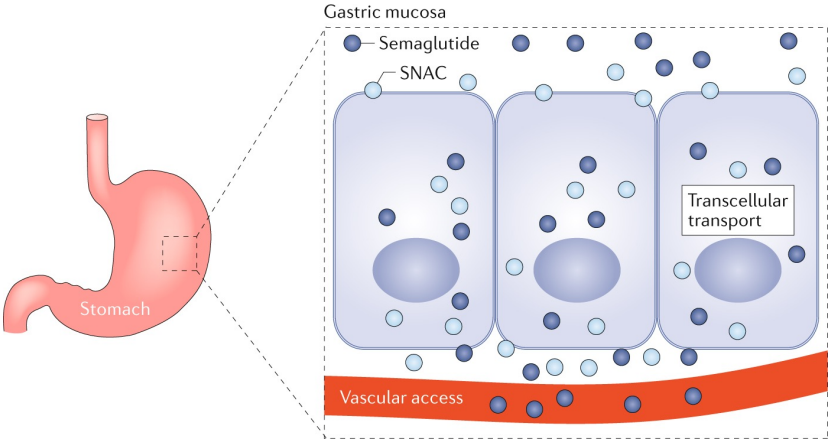
Semaglutide 2.4 mg once weekly in adults with overweight or obesity in an east Asian population (STEP 6)

	Total (n=401)
Full analysis set	
Age, years	51 (11)
Sex	
Female	148 (37%)
Male	253 (63%)
Country	
Japan	360 (90%)
South Korea	41 (10%)
Ethnicity	
Asian	401 (100%)
Bodyweight, kg	87·5 (15·2)
BMI, kg/m²	
Mean	31·9 (4·3)
<30	170 (42%)
30–<35	155 (39%)
35–<40	50 (12%)
≥40	26 (6%)
Comorbidities at screening†	
Dyslipidaemia	346 (86%)
Hypertension	299 (75%)
Non-alcoholic fatty liver disease	179 (45%)
Elevated HbA_{1c}	158 (39%)
Type 2 diabetes	99 (25%)
Kidney disease	56 (14%)
Obstructive sleep apnoea	40 (10%)



Kadowaki T et al., Lancet Diabetes Endocrinol. 2022;10:193-206.

Absorption of oral semaglutide in the stomach

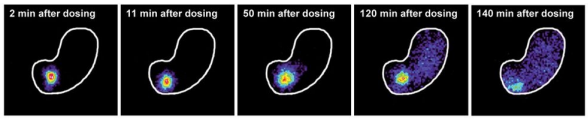


SNAC, sodium N-[8-(2-hydroxybenzoyl)amino] caprylate.

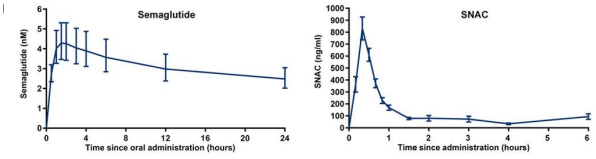
Drucker DJ, Nat Rev Drug Discov. 2020;19:277-89.

Anatomical site of absorption of oral semaglutide in health individuals

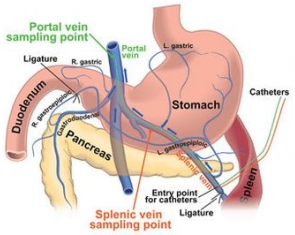
Gamma scintigraphic imaging of tablet erosion

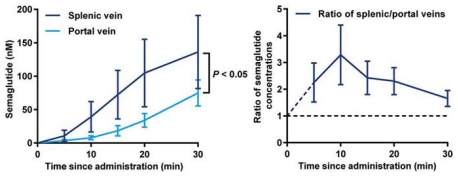


Plasma concentrations of semaglutide and SNAC after a single dose of semaglutide



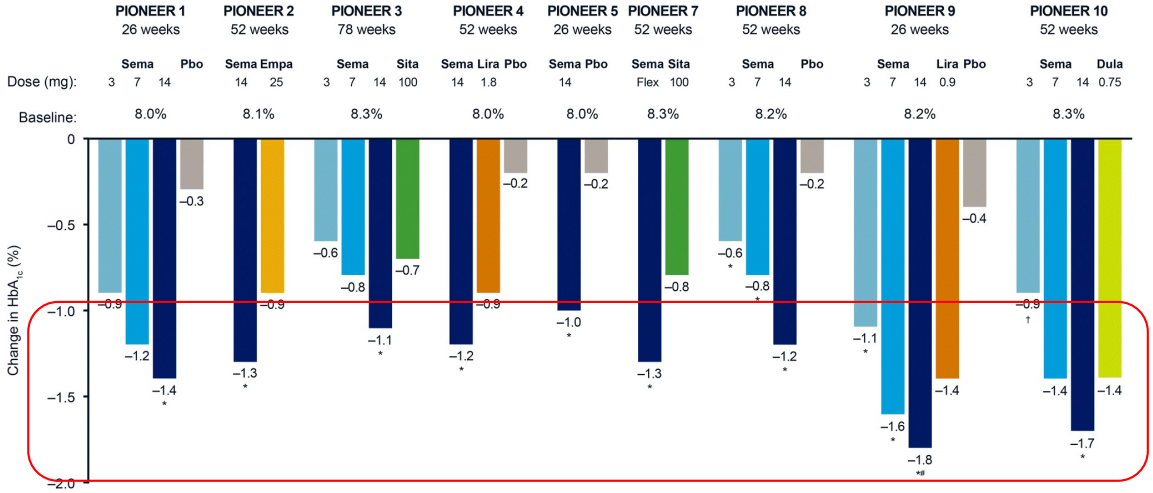
Plasma semaglutide concentrations in the splenic and portal veins





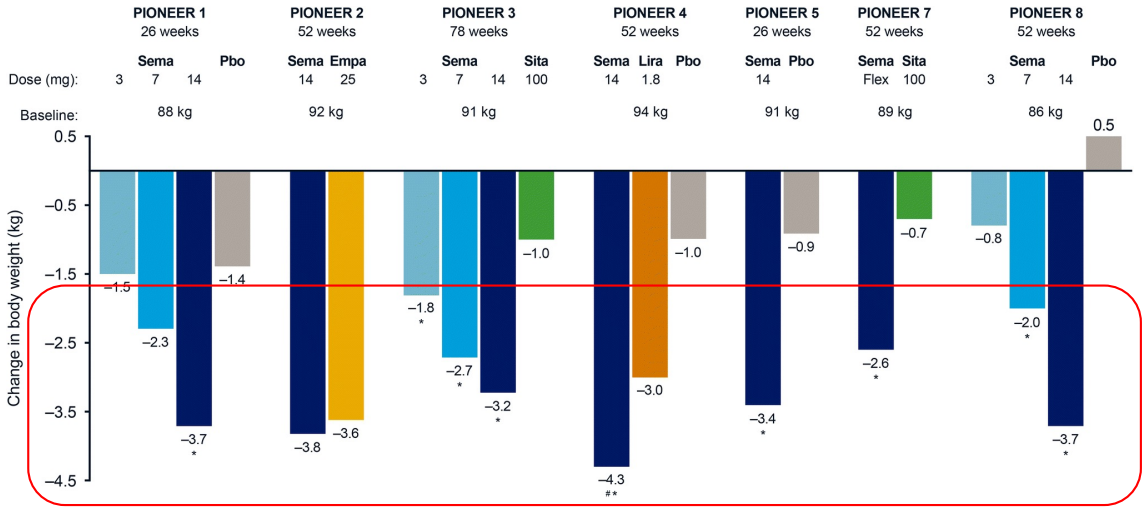
Buckley ST et al., Sci Transl Med. 2018;10:eaar7047.

Changes in HbA1c from baseline in the PIONEER program



Rasmussen MF, Diabetol Int. 2020;11:76-86.

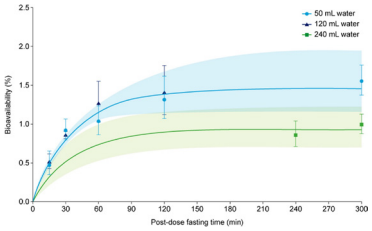
Changes in body weight from baseline in the PIONEER program

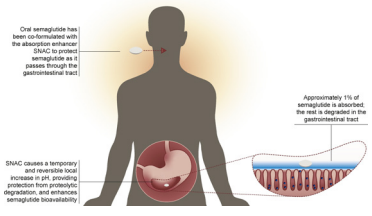


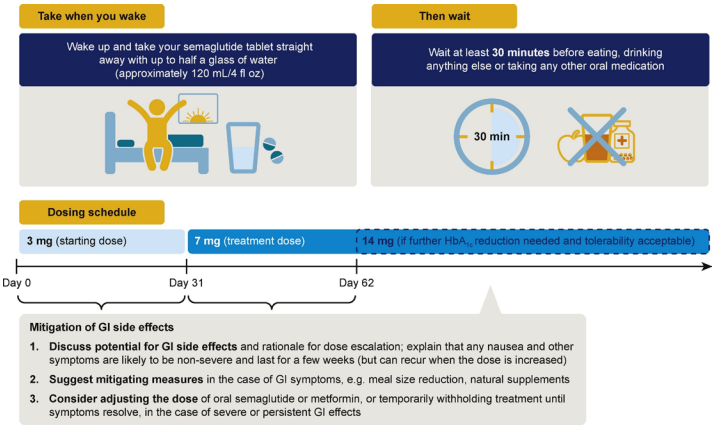
Rasmussen MF, Diabetol Int. 2020;11:76-86.

Oral semaglutide dosing instructions

Oral semaglutide bioavailability vs. post-dosing fasting time by water volume

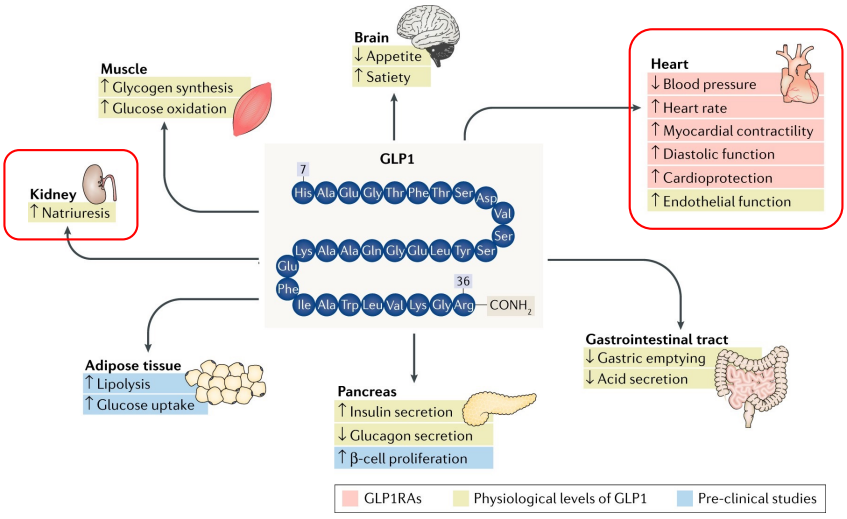






Seidu S et al., Prim Care Diabetes.2021;15:59-68. Overgaard RV et al., Clin Pharmacokinet. 2021;60:1335-48.

Pleiotropic effects of GLP-1 and GLP-1 receptor agonists



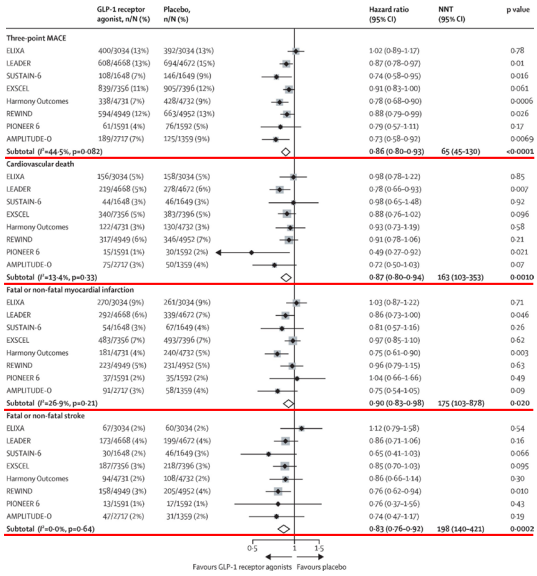
Andersen A et al., Nat Rev Endocrinol. 2018;14:390-403.

Summary of CV outcome trials with GLP-1 receptor agonists in patients with type 2 diabetes

	ELIXA	LEADER	SUSTAIN-6	EXSCEL	REWIND	PIONEER-6
Enrolled patient, *n*	6,068	9,340	3,297	14,752	9,901	3,183
Drug	Lixisenatide	Liraglutide	Semaglutide	Exenatide ER	Dulaglutide	Oral semaglutide
Median duration of follow-up, yrs	2.1	3.8	2.1	3.2	5.4	1.3
Mean baseline HbA1c, %	7.7	8.7	8.7	8.0	7.2	8.2
Mean duration of diabetes, yrs	9.3	12.8	13.9	12	9.5	14.9
Baseline prevalence of CVD/HF, %	100	81	72	73	31	85
Baseline prevalence of HF, %	22	18	24	16	9	NR
MACE, HR (95% CI)	1.02 (0.89–1.17)	**0.87 (0.78–0.97)**	**0.74 (0.58–0.95)**	0.91 (0.83–1.00)	**0.88 (0.79–0.99)**	0.79 (0.57–1.11)
Fatal or nonfatal MI, HR (95% CI)	1.03 (0.87–1.22)	0.86 (0.73–1.00)	0.74 (0.51–1.08)	0.97 (0.85–1.10)	0.96 (0.79–1.15)	1.18 (0.73–1.90)
Fatal or nonfatal stroke, HR (95% CI)	1.12 (0.79–1.58)	0.86 (0.71–1.06)	**0.61 (0.38–0.99)**	0.85 (0.70–1.03)	**0.76 (0.62–0.94)**	0.74 (0.35–1.57)
CV death, HR (95% CI)	0.98 (0.78–1.22)	**0.78 (0.66–0.93)**	0.98 (0.65–1.48)	0.88 (0.76–1.02)	0.91 (0.78–1.06)	**0.49 (0.27–0.92)**
Hospitalization for HF, HR (95% CI)	0.96 (0.75–1.23)	0.87 (0.73–1.05)	0.86 (0.48–1.55)	0.94 (0.78–1.13)	0.93 (0.77–1.12)	1.11 (0.77–1.61)
Renal composite outcome, HR (95% CI)	0.84 (0.68–1.02)	**0.78 (0.67–0.92)**	**0.64 (0.46–0.88)**	0.88 (0.76–1.01)	**0.85 (0.77–0.93)**	**0.64 (0.46–0.88)**
All-cause mortality, HR (95% CI)	0.94 (0.78–1.13)	**0.85 (0.74–0.97)**	1.05 (0.74–1.50)	**0.86 (0.77–0.97)**	0.90 (0.80–1.01)	**0.51 (0.31–0.84)**

Pfeffer MA, et al. N Engl J Med. 2015;373:2247-57. Marso SP, et al. N Engl J Med. 2016;375:311-22. Marso SP, et al. N Engl J Med. 2016;375:1834-44.
Holman RR, et al. N Engl J Med. 2017;377:1228-39. Gerstein HC, et al. Lancet. 2019;394:121-30. Husain M, et al. N Engl J Med. 2019;381:841-51.

Risk of MACE and each components from RCTs of GLP-1 receptor agonists in type 2 diabetes



	GLP-1 receptor agonist, n/N (%)	Placebo, n/N (%)	Hazard ratio (95% CI)	NNT (95% CI)	p value
Three-point MACE					
ELIXA	400/3034 (13%)	392/3034 (13%)	1·02 (0·89–1·17)		0·78
LEADER	608/4668 (13%)	694/4672 (15%)	0·87 (0·78–0·97)		0·01
SUSTAIN-6	108/1648 (7%)	146/1649 (9%)	0·74 (0·58–0·95)		0·016
EXSCEL	839/7356 (11%)	905/7396 (12%)	0·91 (0·83–1·00)		0·061
Harmony Outcomes	338/4731 (7%)	428/4732 (9%)	0·78 (0·68–0·90)		0·0006
REWIND	594/4949 (12%)	663/4952 (13%)	0·88 (0·79–0·99)		0·026
PIONEER 6	61/1591 (4%)	76/1592 (5%)	0·79 (0·57–1·11)		0·17
AMPLITUDE-O	189/2717 (7%)	125/1359 (9%)	0·73 (0·58–0·92)		0·0069
Subtotal (I^2=44·5%, p=0·082)			**0·86 (0·80–0·93)**	**65 (45–130)**	**<0·0001**
Cardiovascular death					
ELIXA	156/3034 (5%)	158/3034 (5%)	0·98 (0·78–1·22)		0·85
LEADER	219/4668 (5%)	278/4672 (6%)	0·78 (0·66–0·93)		0·007
SUSTAIN-6	44/1648 (3%)	46/1649 (3%)	0·98 (0·65–1·48)		0·92
EXSCEL	340/7356 (5%)	383/7396 (5%)	0·88 (0·76–1·02)		0·096
Harmony Outcomes	122/4731 (3%)	130/4732 (3%)	0·93 (0·73–1·19)		0·58
REWIND	317/4949 (6%)	346/4952 (7%)	0·91 (0·78–1·06)		0·21
PIONEER 6	15/1591 (1%)	30/1592 (2%)	0·49 (0·27–0·92)		0·021
AMPLITUDE-O	75/2717 (3%)	50/1359 (4%)	0·72 (0·50–1·03)		0·07
Subtotal (I^2=13·4%, p=0·33)			**0·87 (0·80–0·94)**	**163 (103–353)**	**0·0010**
Fatal or non-fatal myocardial infarction					
ELIXA	270/3034 (9%)	261/3034 (9%)	1·03 (0·87–1·22)		0·71
LEADER	292/4668 (6%)	339/4672 (7%)	0·86 (0·73–1·00)		0·046
SUSTAIN-6	54/1648 (3%)	67/1649 (4%)	0·81 (0·57–1·16)		0·26
EXSCEL	483/7356 (7%)	493/7396 (7%)	0·97 (0·85–1·10)		0·62
Harmony Outcomes	181/4731 (4%)	240/4732 (5%)	0·75 (0·61–0·90)		0·003
REWIND	223/4949 (5%)	231/4952 (5%)	0·96 (0·79–1·15)		0·63
PIONEER 6	37/1591 (2%)	35/1592 (2%)	1·04 (0·66–1·66)		0·49
AMPLITUDE-O	91/2717 (3%)	58/1359 (4%)	0·75 (0·54–1·05)		0·09
Subtotal (I^2=26·9%, p=0·21)			**0·90 (0·83–0·98)**	**175 (103–878)**	**0·020**
Fatal or non-fatal stroke					
ELIXA	67/3034 (2%)	60/3034 (2%)	1·12 (0·79–1·58)		0·54
LEADER	173/4668 (4%)	199/4672 (4%)	0·86 (0·71–1·06)		0·16
SUSTAIN-6	30/1648 (2%)	46/1649 (3%)	0·65 (0·41–1·03)		0·066
EXSCEL	187/7356 (3%)	218/7396 (3%)	0·85 (0·70–1·03)		0·095
Harmony Outcomes	94/4731 (2%)	108/4732 (2%)	0·86 (0·66–1·14)		0·30
REWIND	158/4949 (3%)	205/4952 (4%)	0·76 (0·62–0·94)		0·010
PIONEER 6	13/1591 (1%)	17/1592 (1%)	0·76 (0·37–1·56)		0·43
AMPLITUDE-O	47/2717 (2%)	31/1359 (2%)	0·74 (0·47–1·17)		0·19
Subtotal (I^2=0·0%, p=0·64)			**0·83 (0·76–0·92)**	**198 (140–421)**	**0·0002**

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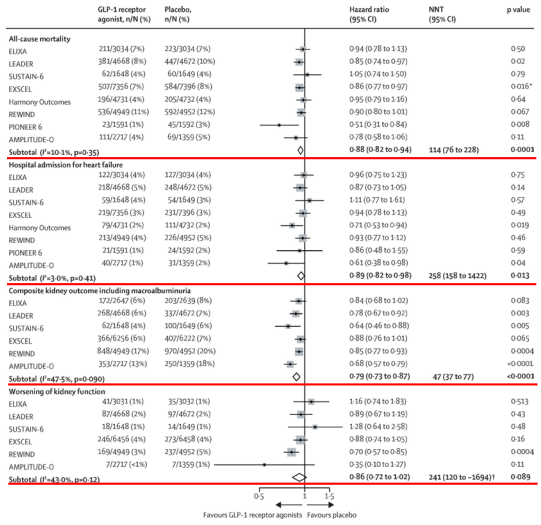
Favours GLP-1 receptor agonists Favours placebo

Sattar N et al., Lancet Diabetes Endocrinol. 2021;9:653-62.

Risk of all-cause mortality, hospitalization for heart failure, and kidney outcomes from RCTs of GLP-1 receptor agonists in type 2 diabetes



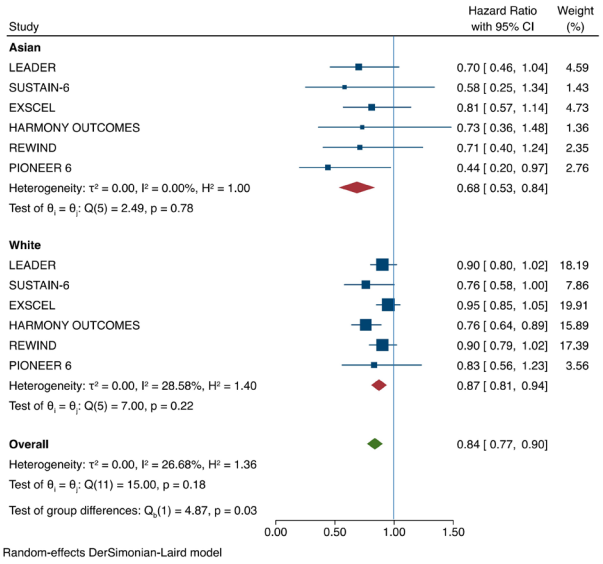
	GLP-1 receptor agonist, n/N (%)	Placebo, n/N (%)	Hazard ratio (95% CI)	NNT (95% CI)	p value
All-cause mortality					
ELIXA	211/3034 (7%)	223/3034 (7%)	0·94 (0·78 to 1·13)		0·50
LEADER	381/4668 (8%)	447/4672 (10%)	0·85 (0·74 to 0·97)		0·02
SUSTAIN-6	62/1648 (4%)	60/1649 (4%)	1·05 (0·74 to 1·50)		0·79
EXSCEL	507/7356 (7%)	584/7396 (8%)	0·86 (0·77 to 0·97)		0·016*
Harmony Outcomes	196/4731 (4%)	205/4732 (4%)	0·95 (0·79 to 1·16)		0·64
REWIND	536/4949 (11%)	597/4952 (12%)	0·90 (0·80 to 1·01)		0·067
PIONEER 6	23/1591 (1%)	45/1592 (3%)	0·51 (0·31 to 0·84)		0·008
AMPLITUDE-O	111/2717 (4%)	69/1359 (5%)	0·78 (0·58 to 1·06)		0·11
Subtotal (I^2=10·1%, p=0·35)			**0·88 (0·82 to 0·94)**	**114 (76 to 228)**	**0·0001**
Hospital admission for heart failure					
ELIXA	122/3034 (4%)	127/3034 (4%)	0·96 (0·75 to 1·23)		0·75
LEADER	218/4668 (5%)	248/4672 (5%)	0·87 (0·73 to 1·05)		0·14
SUSTAIN-6	59/1648 (4%)	54/1649 (3%)	1·11 (0·77 to 1·61)		0·57
EXSCEL	219/7356 (3%)	231/7396 (3%)	0·94 (0·78 to 1·13)		0·49
Harmony Outcomes	79/4731 (2%)	111/4732 (2%)	0·71 (0·53 to 0·94)		0·019
REWIND	213/4949 (4%)	226/4952 (5%)	0·93 (0·77 to 1·12)		0·46
PIONEER 6	21/1591 (1%)	24/1592 (2%)	0·86 (0·48 to 1·55)		0·59
AMPLITUDE-O	40/2717 (1%)	31/1359 (2%)	0·61 (0·38 to 0·98)		0·04
Subtotal (I^2=3·0%, p=0·41)			**0·89 (0·82 to 0·98)**	**258 (158 to 1422)**	**0·013**
Composite kidney outcome including macroalbuminuria					
ELIXA	172/2647 (6%)	203/2639 (8%)	0·84 (0·68 to 1·02)		0·083
LEADER	268/4668 (6%)	337/4672 (7%)	0·78 (0·67 to 0·92)		0·003
SUSTAIN-6	62/1648 (4%)	100/1649 (6%)	0·64 (0·46 to 0·88)		0·005
EXSCEL	366/6256 (6%)	407/6222 (7%)	0·88 (0·76 to 1·01)		0·065
REWIND	848/4949 (17%)	970/4952 (20%)	0·85 (0·77 to 0·93)		0·0004
AMPLITUDE-O	353/2717 (13%)	250/1359 (18%)	0·68 (0·57 to 0·79)		<0·0001
Subtotal (I^2=47·5%, p=0·090)			**0·79 (0·73 to 0·87)**	**47 (37 to 77)**	**<0·0001**
Worsening of kidney function					
ELIXA	41/3031 (1%)	35/3032 (1%)	1·16 (0·74 to 1·83)		0·513
LEADER	87/4668 (2%)	97/4672 (2%)	0·89 (0·67 to 1·19)		0·43
SUSTAIN-6	18/1648 (1%)	14/1649 (1%)	1·28 (0·64 to 2·58)		0·48
EXSCEL	246/6456 (4%)	273/6458 (4%)	0·88 (0·74 to 1·05)		0·16
REWIND	169/4949 (3%)	237/4952 (5%)	0·70 (0·57 to 0·85)		0·0004
AMPLITUDE-O	7/2717 (<1%)	7/1359 (1%)	0·35 (0·10 to 1·27)		0·11
Subtotal (I^2=43·0%, p=0·12)			**0·86 (0·72 to 1·02)**	**241 (120 to −1694)†**	**0·089**

0·5 1 1·5

Favours GLP-1 receptor agonists Favours placebo

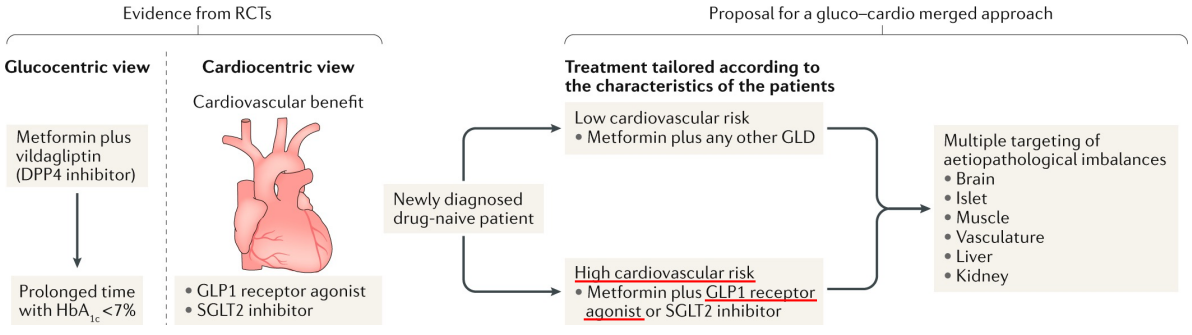
Sattar N et al., Lancet Diabetes Endocrinol. 2021;9:653-62.

Risk of MACE in GLP-1 RA CVOTs according to ethnicity



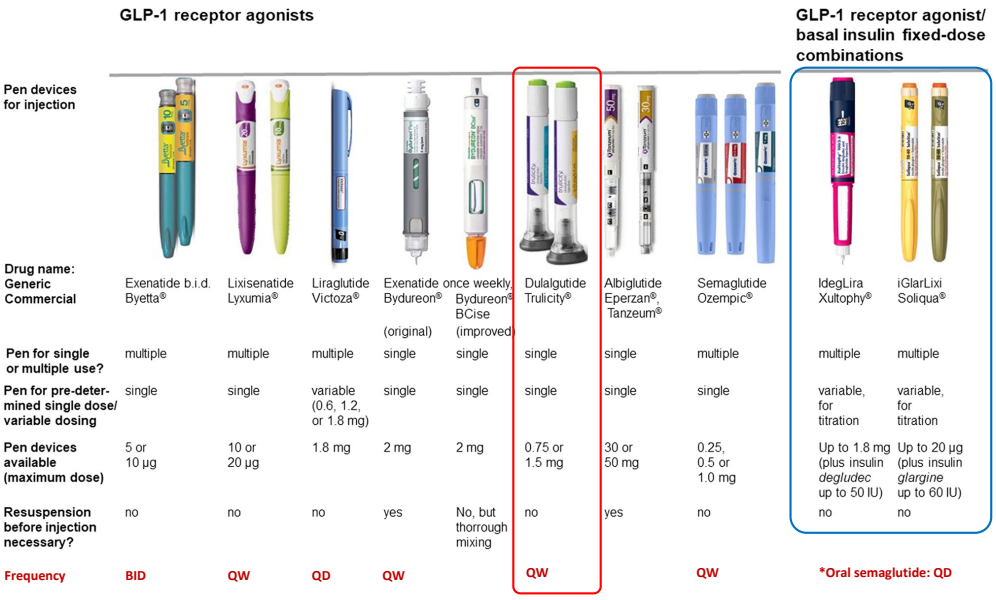
Lee MMY et al., Diabetes Care. 2021;44:1236-41.

Proposal for merging the glucocentric and the cardiocentric view of type 2 diabetes treatment



Prattichizzo F et al., Nat Rev Endocrinol. 2020;16:15-16.

Injection devices for GLP-1 receptor agonists



	GLP-1 receptor agonists								GLP-1 receptor agonist/ basal insulin fixed-dose combinations	
Drug name: Generic Commercial	Exenatide b.i.d. Byetta®	Lixisenatide Lyxumia®	Liraglutide Victoza®	Exenatide once weekly Bydureon® (original)	Bydureon® BCise (improved)	Dulalgutide Trulicity®	Albiglutide Eperzan® Tanzeum®	Semaglutide Ozempic®	IdegLira Xultophy®	iGlarLixi Soliqua®
Pen for single or multiple use?	multiple	multiple	multiple	single	single	single	single	multiple	multiple	multiple
Pen for pre-determined single dose/ variable dosing	single	single	variable (0.6, 1.2, or 1.8 mg)	single	single	single	single	single	variable, for titration	variable, for titration
Pen devices available (maximum dose)	5 or 10 µg	10 or 20 µg	1.8 mg	2 mg	2 mg	0.75 or 1.5 mg	30 or 50 mg	0.25, 0.5 or 1.0 mg	Up to 1.8 mg (plus insulin *degludec* up to 50 IU)	Up to 20 µg (plus insulin *glargine* up to 60 IU)
Resuspension before injection necessary?	no	no	no	yes	No, but thorrough mixing	no	yes	no	no	no
Frequency	BID	QW	QD	QW		QW		QW	*Oral semaglutide: QD	

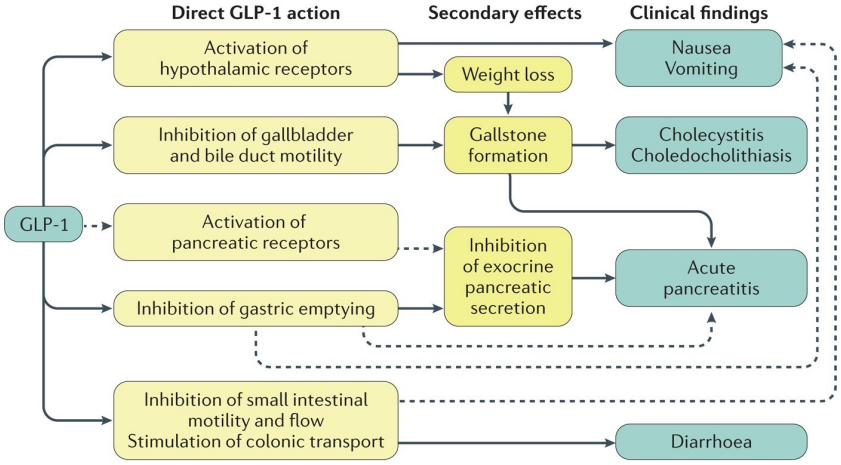
Nauck MA et al., Eur J Endocrinol. 2019;181:R211-34.

Dosing and kidney dose adjustment of GLP-1 receptor agonists

Agent	Route and frequency of administration	Half-life	General recommended dosing for glycaemic control	Recommended kidney dose adjustment
GLP1R agonists				
Exenatide[a]	Subcutaneous injection; twice daily	~2.4 hours	Initially, 5 µg twice daily within the 60-minute period before the morning and evening meals; can increase to 10 µg twice daily after 1 month of therapy based on clinical response	Not recommended for patients with CrCl <30 ml/min; caution recommended when initiating or escalating the dose in patients with CrCl 30–50 ml/min
Lixisenatide[a]	Subcutaneous injection; once daily	~3 hours	Initially, 10 µg once daily within the 60-minute period before the first meal of the day; on day 15, increase to 20 µg once daily	Not recommended for patients with CrCl <15 ml/min
Liraglutide[b]	Subcutaneous injection; once daily	~13 hours	Initially, 0.6 mg once daily at any time of day; after 1 week of the 0.6 mg dose, increase to 1.2 mg once daily; if additional glycaemic control is required, can increase to 1.8 mg once daily after ≥1 week of treatment with the 1.2 mg dose	No dosage adjustments required
Exenatide XR[b]	Subcutaneous injection; once weekly	~1 week	2 mg once weekly at any time of day	Not recommended for patients with an eGFR <45 ml/min/1.73 m^2 or with kidney failure
Dulaglutide[b]	Subcutaneous injection; once weekly	~5 days	Initially, 0.75 mg once weekly at any time of day; if additional glycaemic control is required, can increase to 1.5 mg once weekly	No dosage adjustments required
Semaglutide[b]	Subcutaneous injection; once weekly	~1 week	Initially, 0.25 mg once weekly at any time of day; after 4 weeks on the 0.25 mg dose, increase to 0.5 mg once weekly; if additional glycaemic control is required, can increase to 1 mg once weekly after ≥4 weeks of treatment with the 0.5 mg dose	No dosage adjustments required
	Oral; once daily	~1 week	Initially, 3 mg once daily at least 30 minutes before intake of the first food, fluid or other oral medications of the day; to be taken with no more than 120 ml of plain water only; after 30 days on the 3 mg dose, increase to 7 mg once daily; if additional glycaemic control is required, can increase to 14 mg once daily after ≥30 days of treatment with the 7 mg dose	No dosage adjustments required

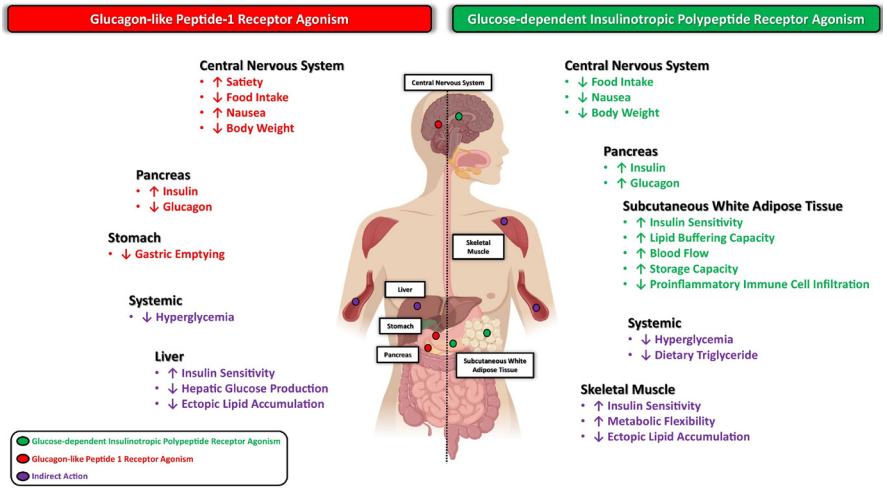
Alicic RZ et al., Nat Rev Nephrol. 2021;17:227-44.c

Potential mechanisms underlying GI adverse events of GLP-1 receptor agonists



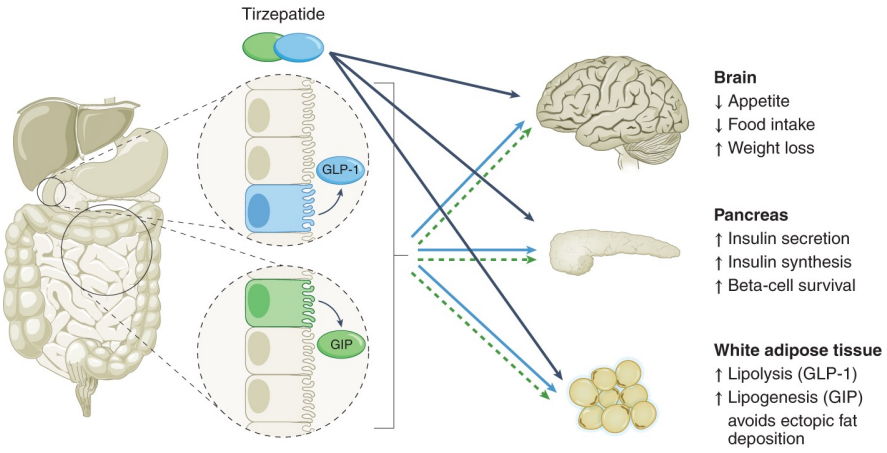
Meier JJ et al., Nat Rev Gastroenterol Hepatol. 2016;13:630-2.

Pleiotropic benefits of dual GIP/GLP-1 receptor agonist therapy in type 2 diabetes



Meier JJ et al., Nat Rev Gastroenterol Hepatol. 2016;13:630-2.

Key metabolic actions of a dual GLP-1 and GIP agonist



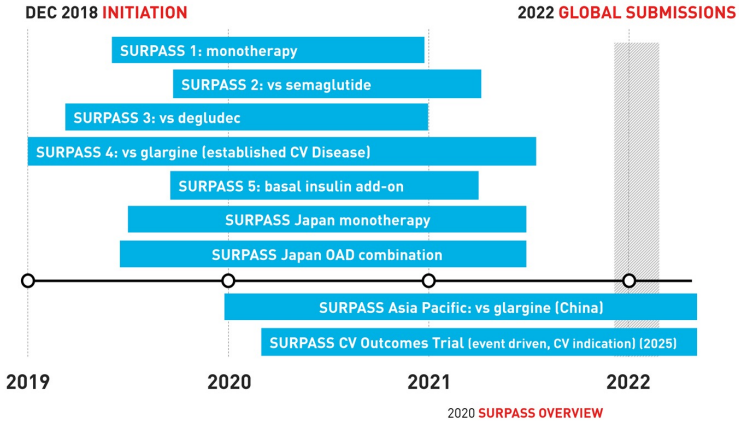
Moura FA et al., Nat Med. 2022;28:450-1.

SURPASS CLINICAL PROGRAM

DESIGNED TO DELIVER ROBUST DATASET WITH MULTIPLE HEAD-TO-HEAD TRIALS

Lilly

SURPASS TYPE 2 DIABETES PROGRAM



2020 SURPASS OVERVIEW

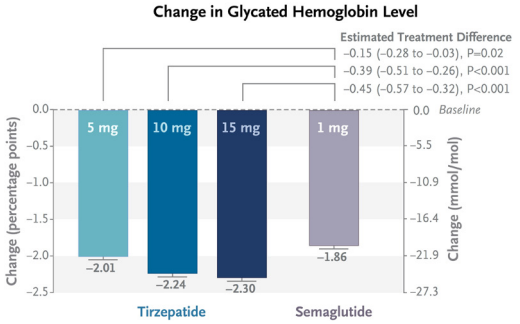
OTHER INDICATIONS

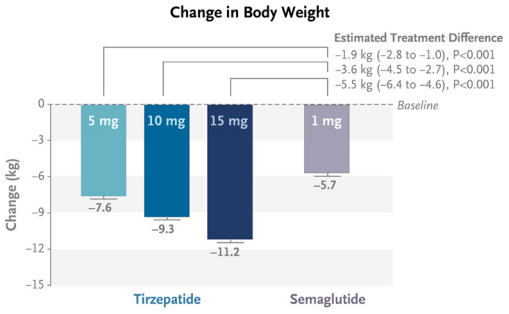
2022

Obesity **Phase 3** – initial SURMOUNT readout

NASH **Phase 2** – SYNERGY-NASH readout

Tirzepatide vs. semaglutide once weekly in type 2 diabetes (SURPASS-2)



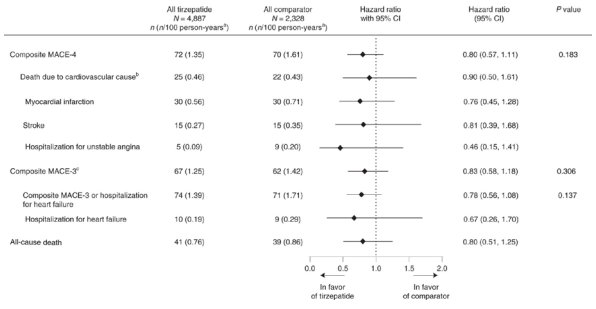


- **Primary efficacy outcome: change in HbA1c level from baseline at week 40**
- **Adverse events**
  - Similar across the groups (most comment: GI events)
  - Serious adverse events: 5.3% to 7.0% in the tirzepatide group vs. 28% in the semaglutide group

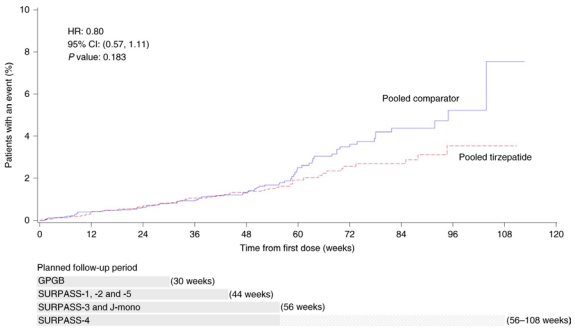
Frías JP et al., N Engl J Med. 2021;385:503-15.c

Tirzepatide and the risk of cardiovascular events in type 2 diabetes : meta-analysis of phase 2 and phase 3 trials

CV outcomes of pooled tirzepatide vs. comparators



Adjusted Kaplan-Meier plot of time to first occurrence of MACE-4



Phase 2 trial: 18F-MC-GPGB; Global phase 3 trials: SURPASS 1-1 to SURPASS 5; Regional (Japan) phase 3 trial: SURPASS J-mono.

Sattar N et al., Nat Med. 2022;28:591-8.

Summary

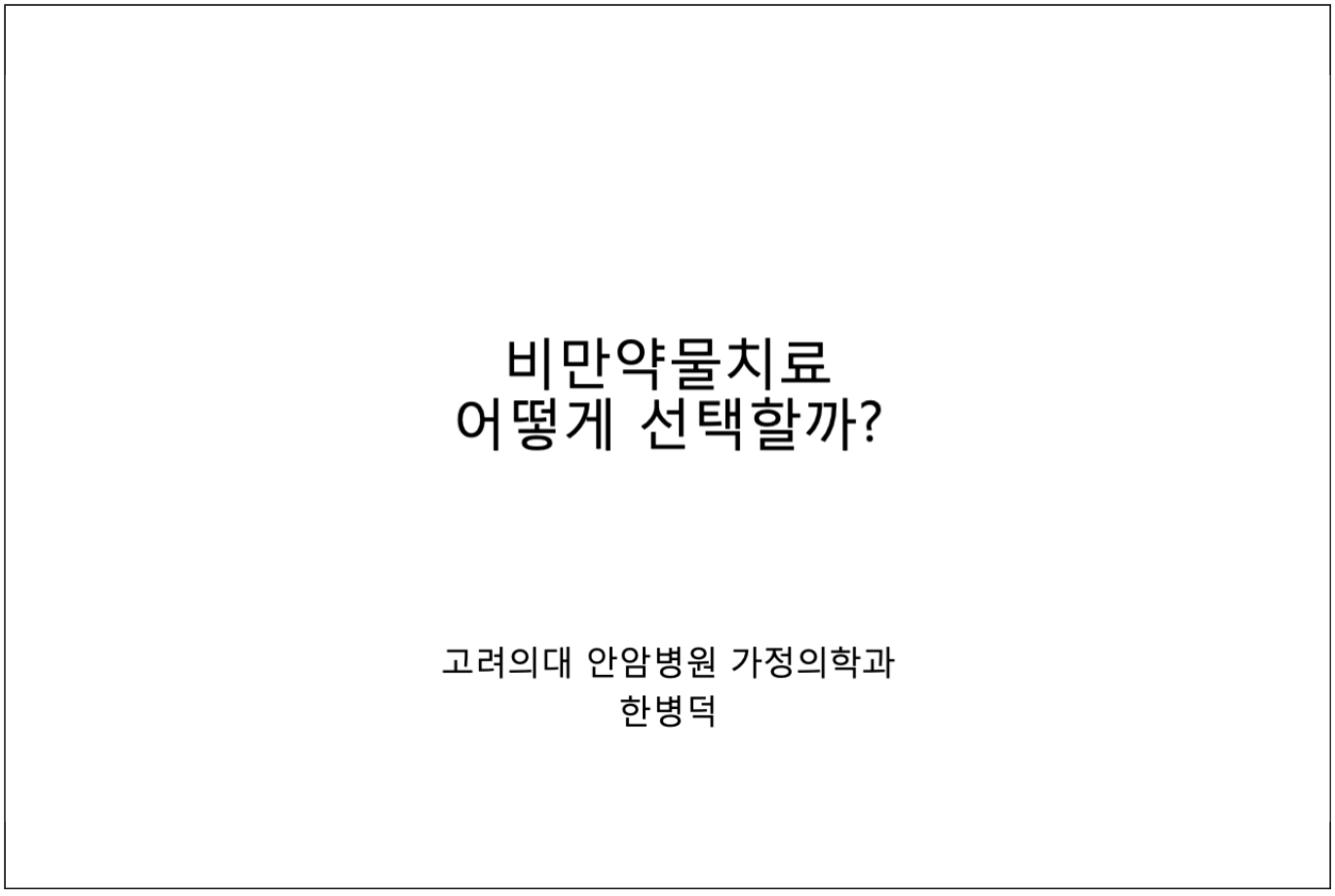
- GLP-1 stimulates insulin secretion from pancreatic β-cells and suppresses the release of glucagon from α-cells, and promotes satiety in response to the ingestion of nutrients.
- GLP-1 receptor agonists were developed with different chemical structures and pharmacokinetic profiles for the treatment of type 2 diabetes owing to the short half-life of GLP-1.
- GLP-1 receptor agonists lower fasting and postprandial plasma concentrations of glucose and reduce body weight, with minimal risk of hypoglycemia.
- Some GLP-1 receptor agonists have positive effects on cardiovascular and kidney outcomes in patients with type 2 diabetes.
- Oral semaglutide and a dual GIP and GLP-1 agonist (tirzepatide) will extend our armamentarium of medications for treating patients with type 2 diabetes and obesity.

고려대학교 의과대학 가정의학교실

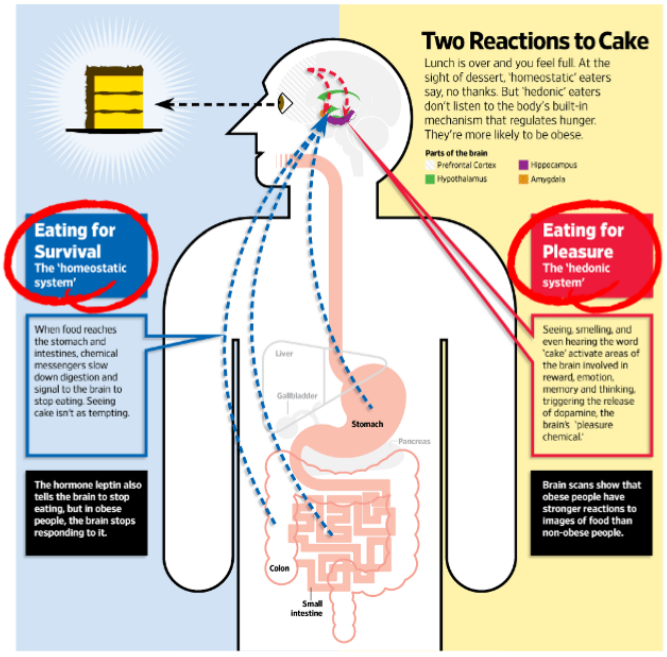
2022 연수강좌

식이패턴에 따른 비만치료약물 선택

한병덕
고려의대 가정의학과



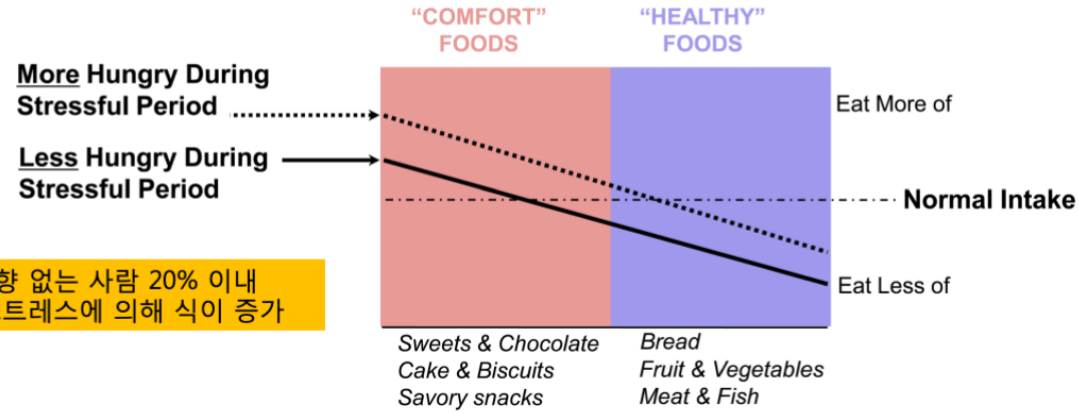
Two Reaction to Cake



Emotional hunger vs Physical hunger

Emotional hunger	Physical hunger
Emotional hunger comes on suddenly	Physical hunger comes on gradually
Emotional hunger feels like it needs to be satisfied instantly	Physical hunger can wait
Emotional hunger craves specific comfort foods	Physical hunger is open to options—lots of things sound good
Emotional hunger isn't satisfied with a full stomach.	Physical hunger stops when you're full
Emotional eating triggers feelings of guilt, powerlessness, and shame	Eating to satisfy physical hunger doesn't make you feel bad about yourself

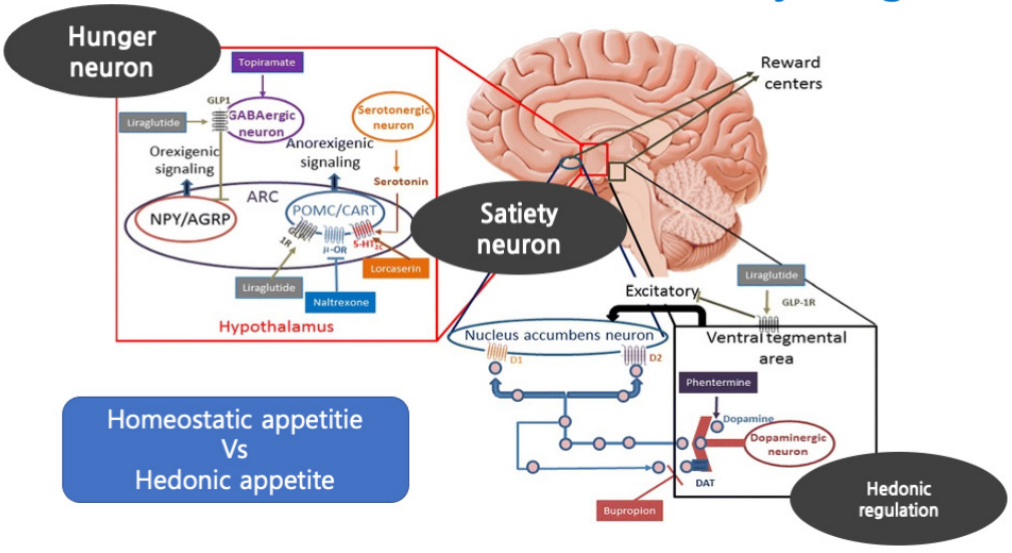
Stress and Food intake



- Stress 와 식이 영향 없는 사람 20% 이내
- 40 % 이상에서 스트레스에 의해 식이 증가

2009 Trends in Endocrinology and Metabolism- Stress-induced obesity and the emotional nervous system

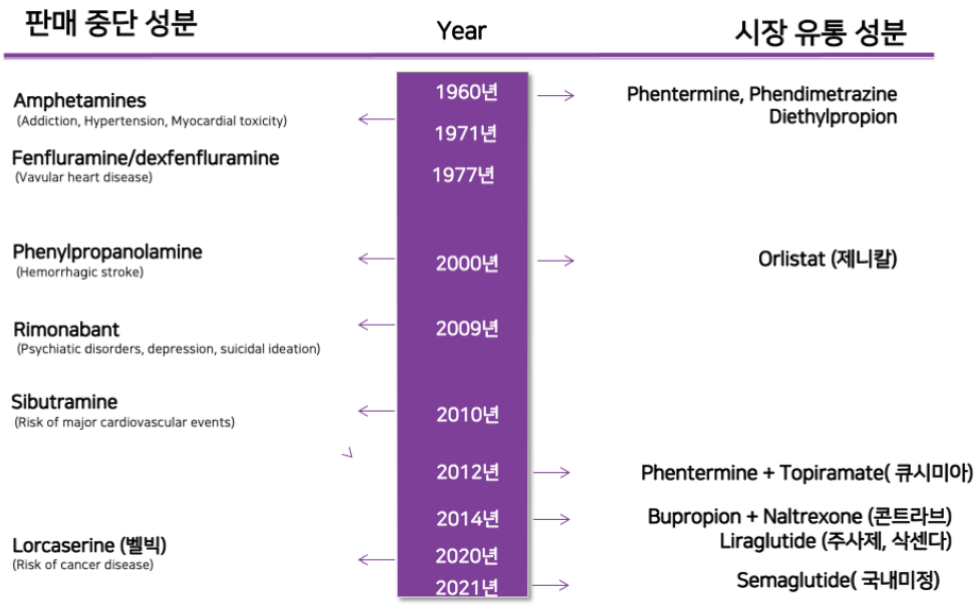
Mechanism of action of antiobesity drugs



Homeostatic appetitie
Vs
Hedonic appetite

Mancini and de Melo Diabetol Metab Syndr (2017) 9:44

비만 치료의 약물 종류



Obesity drug and Psychotropic effects

Drug	Approved for obesity	Favourable psychotropic effects	Unfavourable psychotropic effects	Euphoria addiction
Olistat	Yes	No	No	
Liraglutide	Yes	No	No	
Phentermine Dexaphetamine	Yes(3month) No	Improvements in executive functioning, mood elevation, increased vigor/activity	Anger/hostility, depression, paranoia, hyperlocomotion, psychosis	Yes
Bupropion	Yes(combination)	Improvements in executive functioning	Hyperlocomotion psychosis	Yes
Naltrexone	Yes(combination)	Reduces craving		
Topiramate	Yes(combination)	Mood improvement		
Locarserin	No	Reduces impulsive behavior	Fatigue, depression, cognitive impairment	
Rimonabant Taranabant	No No	Increased vigor/activity	Anger/hostility, anxiety, depression, suicide risk	

비만 치료약물 가이드

Phentermine

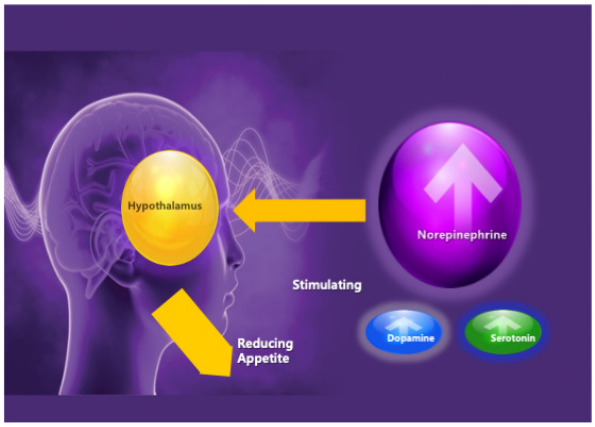
- CNS자극
- Diethypropion, Phendimetrazine, Mazindol
- 12주 단기 요법 권고
- 구갈, 수면장애, 빈맥, 심계항진, 혈압 상승, 두통
- 의존, 중독?
- 저비용-고효율, 고효율-고위험??

Orlistat(Xenical®, Orliet®)

- 리파제 억제제 - 지방흡수차단(30%)
- 장기처방
- 당뇨병 발생 감소
- 지방 변, 변실금, 복통, 간 손상

Phentermine Mechanism

- NE 분비 촉진하여 식욕을 억제
- 약간 Dopamine 분비도 증가 시킨다.
- 한가지 약물로는 식욕 억제 효과 강력한 편 (Net weight loss 7.4kg)
- Heart rate 증가, BP증가, 불면증, 떨림



Phentermine Clinical Trial

Effects on Weight Reduction and Safety of Short-Term Phentermine Administration in Korean Obese People

Kyoung Kon Kim,[1] Hi-Jung Cho,[2] Hee-Cheol Kang,[2] Bang-Bu Youn,[2] and Kyu-Rae Lee[1]

Departments of Family Medicine, [1]Gachon University Gil Medical Center, Incheon; [2]Yonsei University College of Medicine, Seoul, Korea.

		Phentermine (n = 24)	Placebo (n = 12)	*p* value
Weight (kg)	Baseline	78.0 ± 11.5	77.4 ± 9.4	
	14th week	70.5 ± 11.8	74.3 ± 10.5	
	Change	-7.5 ± 2.7	-3.1 ± 3.2	< 0.001†
Waist (cm)	Baseline	93.1 ± 6.8	91.1 ± 8.0	
	14th week	85.8 ± 8.1	87.8 ± 7.3	
	Change	-7.3 ± 3.3	-3.3 ± 4.7	< 0.001†

	Phentermine (n = 29)*	Placebo (n = 24)	*p* value
Any adverse event	28 (96.6)	18 (75.0)	0.021†
Dry mouth	16 (55.2)	4 (16.7)	0.004†
Insomnia	10 (34.5)	0 (0.0)	0.001†

- 단기간 체중 감량효과는 좋으나 부작용 발현이 높음 -> Any adverse event 96.6%

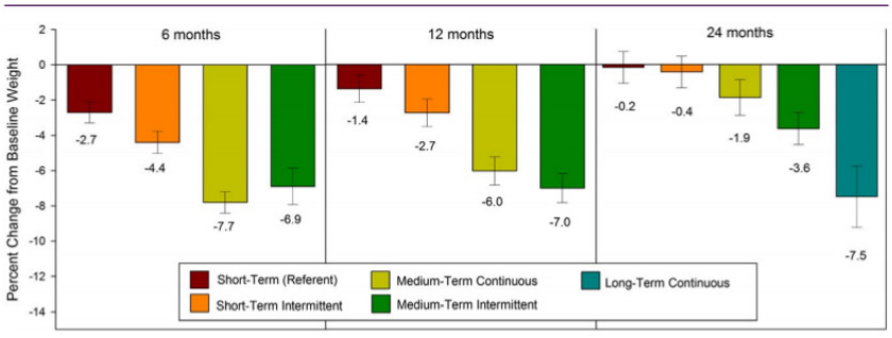
Ref. Yonsei Med J Vol. 47, No.5 , 2006

Phentermine, 길게 쓰면 안되요?

Safety and Effectiveness of Longer-Term Phentermine Use: Clinical Outcomes from an Electronic Health Record Cohort

Kristina H. Lewis [1,2], Heidi Fischer[3], Jamy Ard [1], Lee Barton[3], Daniel H. Bessesen[4], Matthew F. Daley[5], Jay Desai[6], Stephanie L. Fitzpatrick[7], Michael Horberg[8], Corinna Koebnick[3], Caryn Oshiro[9], Ayae Yamamoto[3], Deborah R. Young[3], and David E. Arterburn[10]

	On-label users		Off-label users			
	Short-term referent (*n* = 6,764)	Short-term intermittent (*n* = 2,938)	Medium-term continuous (*n* = 1,703)	Medium-term intermittent (*n* = 2,423)	Long-term continuous (*n* = 144)	Total (*N* = 13,972)
Sex[b]						
Female	5,611 (83.1%)	2,523 (85.8%)	1,402 (82.3%)	2,047 (84.3%)	116 (80.6%)	11,699 (83.7%)
Race/ethnicity[c]						
Non-Hispanic white	3,007 (44.5%)	1,093 (37.2%)	894 (52.5%)	1,181 (48.6%)	80 (55.6%)	6,255 (44.8%)
Non-Hispanic black	1,370 (20.3%)	786 (26.7%)	253 (14.9%)	446 (18.4%)	19 (13.2%)	2,874 (20.6%)
Hispanic	1,749 (25.9%)	764 (26.0%)	367 (21.6%)	564 (23.2%)	27 (18.8%)	3,471 (24.8%)
Asian	305 (4.5%)	137 (4.7%)	101 (5.9%)	107 (4.4%)	12 (8.3%)	662 (4.7%)
Other	324 (4.8%)	162 (5.5%)	88 (5.2%)	130 (5.4%)	6 (4.2%)	710 (5.1%)
Age (y)[c]	43.7 (10.9)	42.3 (10.6)	44.3 (10.4)	43.7 (10.5)	46.5 (10.0)	43.5 (10.7)
BMI (kg/m^2)[c]						
Mean (SD)	38.0 (7.5)	37.0 (6.9)	38.4 (7.0)	37.6 (6.8)	37.5 (7.1)	37.8 (7.2)
27-29.9	687 (10.2%)	381 (13%)	118 (6.9%)	234 (9.6%)	14 (9.7%)	1,434 (10.3%)
30-34.9	1,977 (29.3%)	979 (33.3%)	477 (28%)	738 (30.4%)	45 (31.3%)	4,216 (30.2%)
35-39.9	1,890 (28.0%)	773 (26.3%)	519 (30.5%)	735 (30.3%)	46 (31.9%)	3,963 (28.4%)
40-49.9	1,733 (25.7%)	673 (22.9%)	472 (27.7%)	593 (24.4%)	30 (20.8%)	3,501 (25.1%)
≥50.0	468 (6.9%)	136 (4.6%)	117 (6.9%)	128 (5.3%)	9 (6.3%)	858 (6.1%)
Hypertension diagnosis[d]	1,443 (21.4%)	578 (19.6%)	357 (21%)	476 (19.6%)	35 (24.3%)	2,889 (20.7%)
Diabetes diagnosis[c,d]	824 (12.2%)	299 (10.2%)	224 (13.2%)	253 (10.4%)	24 (16.7%)	1,624 (11.6%)
Smoking status[c,e]						
Never users	4,211 (62.3%)	1,870 (63.6%)	1,035 (60.8%)	1,469 (60.5%)	69 (47.9%)	8,654 (61.9%)
Ever users	2,298 (34%)	944 (32.1%)	612 (35.9%)	849 (35%)	65 (45.1%)	4,768 (34.1%)
Missing/unknown	246 (3.6%)	128 (4.4%)	56 (3.3%)	110 (4.5%)	10 (6.9%)	550 (3.9%)
Area families below poverty level[f]						
Missing[e,g]	234 (3.5%)	146 (5%)	56 (3.3%)	93 (3.8%)	9 (6.3%)	538 (3.9%)
<5%	1,568 (23.2%)	686 (23.3%)	445 (26%)	612 (25.2%)	38 (26.4%)	3,349 (24%)
5-<10%	1,779 (26.3%)	769 (26.1%)	448 (26.2%)	656 (27%)	37 (25.7%)	3,682 (26.4%)
10-<20%	1,812 (26.8%)	798 (27.1%)	443 (25.9%)	629 (25.9%)	35 (24.3%)	3,717 (26.6%)
≥20%	1,362 (20.2%)	543 (18.5%)	318 (18.6%)	438 (18%)	25 (17.4%)	2,686 (19.2%)
Follow-up duration (y)[c]	1.6 (1.1)	2.2 (0.9)	1.6 (1.0)	2.4 (0.8)	2.3 (0.8)	1.9 (1.0)
Median percent of follow-up on phentermine	9%	16%	33%	42%	75%	19%
Daily phentermine dose[c]						
<37.5 mg	3,688 (54.6%)	1,528 (51.9%)	1,120 (65.8%)	1,526 (62.9%)	89 (61.8%)	7,951 (56.9%)
37.5 mg	3,053 (45.2%)	1,404 (47.7%)	580 (34.1%)	892 (36.7%)	53 (36.8%)	5,982 (42.8%)
Missing[g]	14 (0.2%)	10 (0.3%)	3 (0.2%)	10 (0.4%)	2 (1.4%)	39 (0.3%)



Early responder

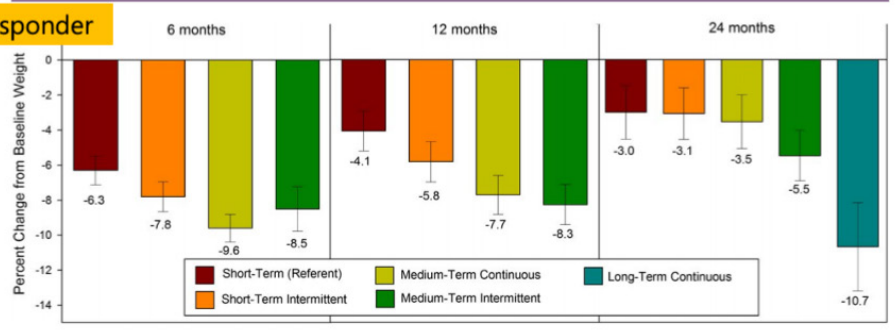


TABLE 4 Change in heart rate (HR) and blood pressure (BP) over follow-up: results from multivariable linear models using time-varying exposure[a]

		Heart rate results					
		6 months		12 months		24 months	
		Parameter estimate	*n* (%) enrolled	Parameter estimate	*n* (%) enrolled	Parameter estimate (95% CI)	*n* (%) enrolled with VS data[b]
Intercept[c]						to 1.86)	n/a
Short-term[c]							2,534 (91%)
Short-term intermittent[c]						to 0.91)	1,533 (93%)
Medium-term continuous[c]						to 0.90)	610 (90%)
Medium-term intermittent[c]						to 1.49)	1,360 (95%)
Long-term continuous[c]						5.14)	96 (90%)
Intercept[c]	ΔSBP (m					3.19)[e]	n/a
	ΔDBP (m					to 0.98)	
Short-term[c]	ΔSBP (m						2,592 (92%)
	ΔDBP (m						
Short-term intermittent[c]	ΔSBP (m					to 1.00)[i]	1,560 (94%)
	ΔDBP (mmHg)	0.08 (−0.46 to 0.61)[d]		0.21 (−0.31 to 0.73)		0.4 (−0.18 to 0.98)	
Medium-term continuous[c]	ΔSBP (mmHg)	−0.5 (−1.12 to 0.12)[d]	2,402 (76%)	−1.11 (−1.88 to −0.33)[h]	1,395 (80%)	−0.94 (−2.05 to 0.17)[i]	622 (90%)
	ΔDBP (mmHg)	0.36 (−0.11 to 0.82)[d]		−0.39 (−0.95 to 0.18)		−0.12 (−0.93 to 0.69)	
Medium-term intermittent[c]	ΔSBP (mmHg)	−1.18 (−2.98 to 0.61)[d]	183 (80%)	−0.92 (−1.74 to −0.09)[h]	1,200 (88%)	−0.41 (−1.25 to 0.43)[i]	1,383 (95%)
	ΔDBP (mmHg)	−0.81 (−2.16 to 0.53)[d]		−0.19 (−0.79 to 0.41)		0.12 (−0.49 to 0.73)	
Long-term continuous[c]	ΔSBP (mmHg)	n/a		n/a		−3.31 (−5.85 to −0.76)[i]	99 (91%)
	ΔDBP (mmHg)					−0.69 (−2.54 to 1.16)	

	Hazard ratio	CI[b]
Short-term (referent)	Reference	
Short-term intermittent	0.74	0.29-1.91
Medium-term intermittent	0.50	0.14-1.74
Medium & long-term continuous combined[c]	1.58	0.69-3.63

Liraglutied

GLP-1 이란?

- Incretin family
- 장의 L-cell에서 주로 분비
- 인슐린 분비 유도
- 글루카곤 분비 억제

- 식욕 감소
- 혈당 강하
- 체중감소
- 염증지표 감소

- 반감기 : 2분

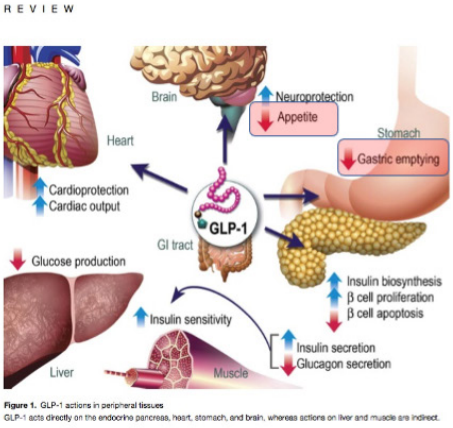
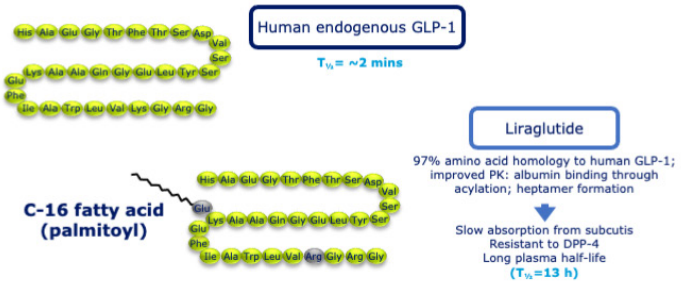


Figure 1. GLP-1 actions in peripheral tissues
GLP-1 acts directly on the endocrine pancreas, heart, stomach, and brain, whereas actions on liver and muscle are indirect.

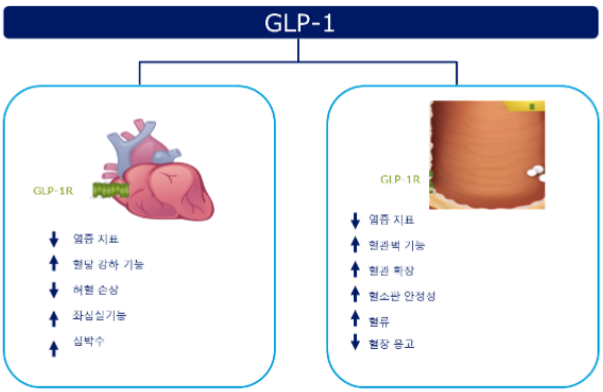
Liraglutide, human GLP-1 analogue[1-2]



DPP-4, dipeptidyl peptidase-4; GLP-1, glucagon-like peptide-1; PK, pharmacokinetics; $T_{½}$, plasma half-life

1. Knudsen *et al. J Med Chem* 2000;43:1664–9; 2. Degn *et al. Diabetes* 2004;53:1187–94

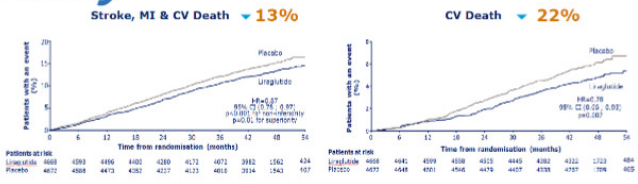
Cardiovascular Effect



GLP-1, glucagon-like peptide-1; GLP-1R, glucagon-like peptide-1 receptor
1. Adapted from: Drucker DJ. *Cell Metab* 2016;24:15-30

Liraglutide 연구결과

LEADER – Liraglutide CV safety



in more than 9,000 patients for period upto 4.5 years
in T2D patients with liraglutide at dose upto 1.8 mg

The primary composite outcome in the time-to-event analysis was the first occurrence of death from cardiovascular causes, non-fatal myocardial infarction, or non-fatal stroke. The cumulative incidences were estimated with the use of the Kaplan–Meier method, and the hazard ratios with the use of the Cox proportional-hazard regression model. The data analyses are truncated at 54 months, because less than 10% of the patients had an observation time beyond 54 months.
CI: confidence interval; CV: cardiovascular; HR: hazard ratio.
Marso SP et al. *N Engl J Med* 2016. DOI: 10.1056/NEJMoa1603827.

임상 요약[1-5]

Key efficacy outcomes with liraglutide 3.0 mg

SCALE Obesity and Prediabetes[1,2]	SCALE Diabetes[3]	SCALE Maintenance[4]	SCALE Sleep Apnoea[5]
-9.2% change in body weight after 1 year	**-6.0%** change in body weight after 56 weeks	**81%** maintained ≥5% weight loss after 1 year	**-12.2** events p/h vs. 6.1 with placebo
80% reduction in the risk of T2D over 3 years	**-1.3%** change in HbA_{1c} from baseline	**6.2%** additional weight loss with liraglutide 3.0 mg*	**-5.7%** change in body weight after 32 weeks

*Following lifestyle intervention induced weight loss of ≥5% over a 12 week run in period

1. Pi-Sunyer *et al. N Engl J Med* 2015;373:11–22; 2. le Roux *et al. Lancet* 2017;389:1399–409; 3. Davies *et al. JAMA* 2015;314:687–99;
4. Wadden *et al. Int J Obes (Lond)* 2013;37:1443–51; 5. Blackman *et al. Int J Obes (Lond)* 2016;40:1310–19

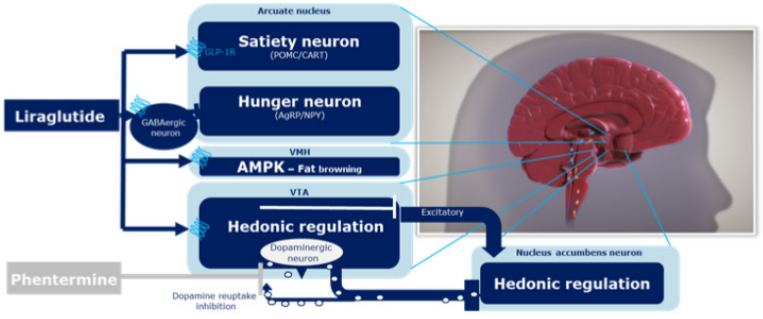
METABOLIC EFFECTS OF GLP-1

Appetite[1]

- ↑ Satiety
- ↑ Fullness
- ↓ Hunger
- ↓ Prospective food consumption
- ↓ Energy intake

GLP-1 effect on	Effect of GLP-1	Subjects/patients/system (experimental conditions) [Reference(s)]
Insulin secretion	Glucose-dependent stimulation	Isolated islets [163] Perfused pancreas [164] Healthy subjects [26, 64] Type 2 diabetic patients [34, 141]
Glucagon secretion	Glucose-dependent (?) suppression	Perfused pancreas [67, 83] Healthy subjects [64, 71] Type 2 diabetic patients [34, 79]
Islet insulin content	Stimulation of (pro)insulin biosynthesis	Insulinoma cells in culture [69]
Food intake	Reduction	Mice (after i.c.v. administration) [38, 118, 119] Humans (intravenous infusion of GLP-1) [39]
Gastric emptying	Deceleration	Healthy subjects [87, 90, 130] Type 2 diabetic patients [89]
Gastric acid secretion	Reduction	Healthy subjects [91, 92]
Insulin sensitivity	Equivocal	Healthy subjects [108] Type 1 diabetic patients [107] Type 2 diabetic patients [109]

식욕억제 기전



1. Mancini and de Melo Diabetol Metab Syndr (2017) 9:44, 2. Jacobson et al., Br J Clin Pharmacol / 68:6 / 898–905, 2009; 3. Beirsa et al., Diabetes 2014 Oct; 63(10): 3346-3358. VMH: Ventromedial nucleus of the hypothalamus AMPK: AMP activated kinase, VTA, Ventral tegmental area

정신신경학적 증상 – 위약군과 차이 없음

	Liraglutide 3.0 mg (n=3384)	Placebo (n=1941)
Number of subjects, n (%)	366 (10.8)	197 (10.1)
Number of events	459	245
Event rate per 100 PYE	15.4	15.3

✓ 불안증 및 우울증 발생은 위약군과 차이가 없었습니다.

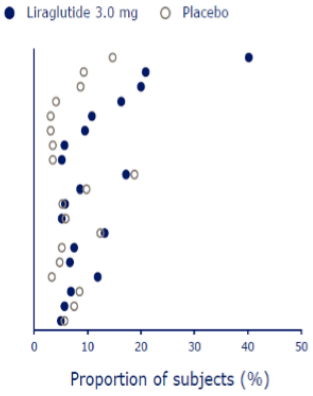
✓ 가장 흔하게 보고된 증상은 불면증 입니다.

✓ 삭센다®는 정신질환 관련 금기사항은 없습니다.

1. 삭센다® 제품설명서. 2. Saxenda® [summary of product characteristics]. Bagsværd, Denmark: Novo Nordisk A/S; June-2017 3. Larsen et al., JAMA Psychiatry.4. Novo Nordisk Briefing Document: Liraglutide 3.0 mg for weight management NDA 206-321. 5. FDA Endocrinologic and Metabolic Drugs Advisory Committee Meeting. September 11, 2014. doi:10.1001/jamapsychiatry.2017.1220. Data are based on NN8022-1839, -1923, -3970, -1922 and -1807 trials. Events were identified by a MedDRA search for SOC psychiatric disorders (including all primary and secondary preferred terms within the SOC) MedDRA, Medical Dictionary for Regulatory Activities; PYE; patient years of exposure; SOC, system organ class

Liraglutide 의 흔한 Adverse events

	Liraglutide 3.0 mg %	Placebo %
Nausea	40.2	14.7
Diarrhoea	20.9	9.3
Constipation	20.0	8.7
Vomiting	16.3	4.1
Decreased appetite	10.8	3.1
Dyspepsia	9.5	3.1
Abdominal pain upper	5.7	3.5
Abdominal pain	5.2	3.5
Nasopharyngitis	17.2	18.8
Upper respiratory tract infection	8.6	9.8
Influenza	5.8	5.3
Sinusitis	5.2	5.9
Headache	13.2	12.4
Fatigue	7.5	5.2
Dizziness	6.7	4.8
Hypoglycaemia	11.9	3.3
Back pain	6.9	8.5
Injection site haematoma	5.7	7.5
Arthralgia	5.0	5.7



삭센다 부작용실태조사
고려대 구로병원 외

- 연구대상 : 1249명(종합병원1073, 개인의원 176)
- 부작용 경험 : 206명(종합병원 117, 개인의원 89
- 중대한 이상반응보고는 없었음

순위	전체(N=291)		리라글루티드 사용 용량(mg)					
	부작용	N	0.6	1.2	1.8	2.4	3	미상
1	오심	106	11	26	42	10	14	3
2	소화불량	53	1	8	31	7	4	2
3	발진, 피부장애	24	1	7	7	4	1	4
4	설사	23	2	9	8	1	3	0
5	변비	17	1	2	4	3	6	1
6	어지러움	15	1	4	5	1	1	4
7	역류성소화장애	11	1	3	4	0	1	2
8	구토	10	4	3	1	0	2	0
9	피로, 쇠약	9	3	3	3	0	0	0
10	두통	4	1	1	1	1	0	0
11	저혈당	4	1	0	2	0	0	0
12	불면	3	1	0	1	1	0	0
13	우울	2	0	1	0	0	1	0
14	심계항진	2	0	0	0	1	1	0
15	주사부위 멍	2	0	1	0	0	0	1
16	호흡곤란	2	0	2	0	0	0	0
17	생리불순	1	0	1	0	0	0	0
18	근육통	1	0	0	1	0	0	0
19	혈압상승	1	1	0	0	0	0	0
20	기침	1	0	1	0	0	0	0

투약방법

- 식사와 관계없이 1일 1회 피하주사
- 매일 같은 시간에 투여
- 복부, 대퇴부, 상완부에 주사 가능
- 시작용량 1일 1회 0.6 mg → 1주일 후 1.2 mg → 1주일 후 1.8 mg → 1주일 후 2.4 mg → 1주일 후 3.0 mg로 증량
- 약물 투여를 빠뜨린 경우

① 평소 투여 시간에서 12시간 미만: 가능한 빨리 빠뜨린 용량을 투여할 것

② 다음 투여까지 남은 시간이 12시간 미만: 다음 번 예정된 투여량으로 1일 1회 투여를 재개

③ 3일 이상 투여하지 않은 경우: 초기용량부터 다시 증량하며 재개

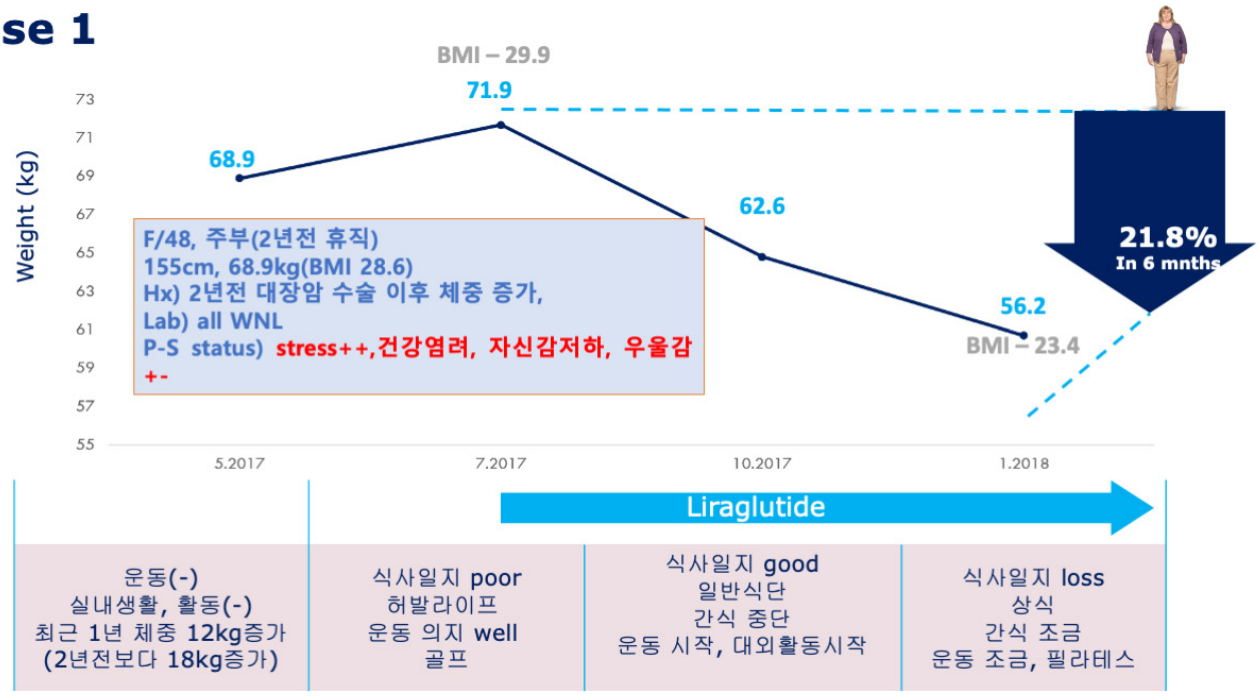
비만 치료약물 가이드

Liraglutide(Saxenda)

- 다양한 기전의 식욕억제 작용
- 심혈관계 안전성 및 유효성
- 정신의학적 안전성
- 장기간 처방에 유리

- Injection
- 고비용
- 위장장애가 흔하다

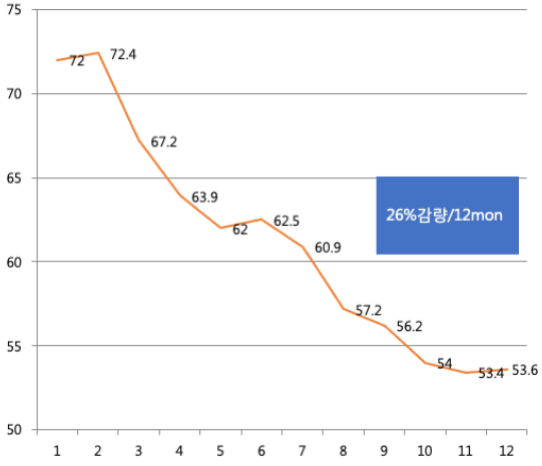
Case 1



This model image is only patient examples, not real patients.

Case 2.

피리부는 선생님



- 병원 직원
- 160cm 72.4 kg -> 53.6kg
- Locaserine(10kg) -> liraglutide (9kg) (3.0)
- 식사일지
- 우울감 -> 자신감
- 날씬한척
- 연애준비

- 이후 삭센다 유지 요법 : 1.2유지

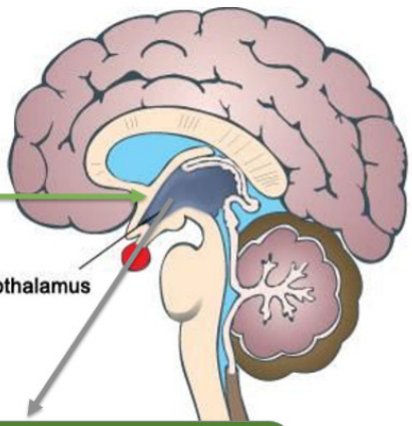
Phentermine/Topiramate

Topiramate Mechanism

1979년 경구용혈당강하제로 최초 개발
1999년 항경련치료 중 체중감소 효과 발견

토피라메이트

GABA 수용체를 증강

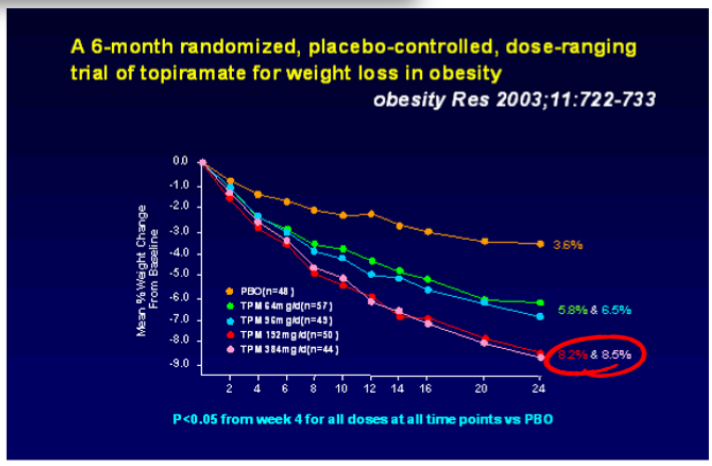


- 열생산 촉진, 발열작용
- 당, 지질대사 를 좋게 함 → 지방의 침착을 방해
- 폭식빈도의 감소, 식욕 및 체중의 감소
- 비향정(내성 없음), 1년 이상 지속되는 꾸준한 효과
- 부작용: 저림현상, 쳐짐, 집중력 저하

Topiramate Clinical Trial

A 6-Month Randomized, Placebo-Controlled, Dose-Ranging Trial of Topiramate for Weight Loss in Obesity

George A. Bray, Priscilla Hollander,† Samuel Klein,‡ Robert Kushner,§ Brian Levy,¶ Martin Fitchet,¶ and Barbara H. Perry,¶ for the U.S. Topiramate Research Group*



Ref. Bray et al 2003-Obesity_Research

Known Side-Effects Associated with Phentermine and Topiramate

- Phentermine[1]
  - Dry mouth
  - Insomnia
  - Headache
  - Dizziness
  - Fatigue
  - Palpitation
- Topiramate[2]
  - Paresthesia
  - Fatigue
  - Nausea / Diarrhea
  - Dizziness
  - Dysgeusia
  - Somnolence
  - Attention / language / memory
  - Depression / anxiety / mood

❖Known Teratogenicity

AEs with Phen/Top ER as expected and consistent with individual drugs

[1]Kim KK, et al. *Yonsei Med J* 2006;47:614-25
[2]TOPAMAX® Package Insert 2011

사용상 주의사항

- **임신 가능성 여부**
  - 토피라메이트 성분 때문에 임신 중에 복용 시 구순구개파열 의 위험을 높힐 수 있습니다.
  - 복용 중 임신을 계획하신다면, 복용 중단 한달 이후 계획하시기 바랍니다.

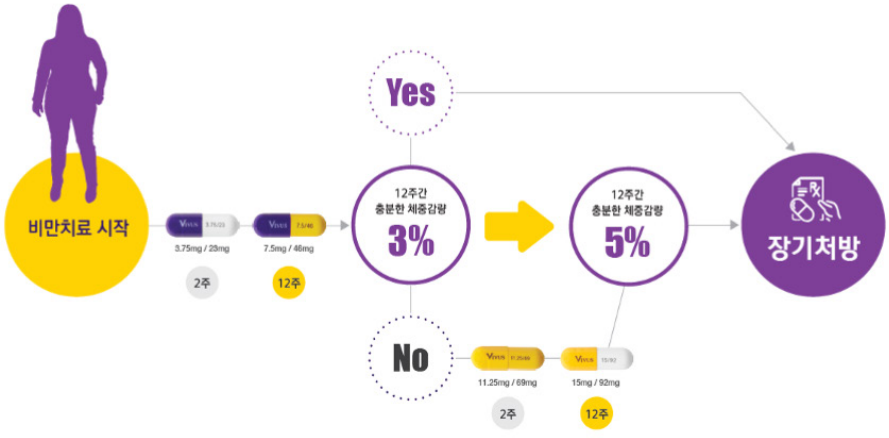
- **조절되지 않는 고혈압 환자 및 폐동맥 고혈압 환자** 는 금기 입니다.

- **갑상선 기능 항진증 환자** 는 금기 입니다.

- **녹내장 기왕력 환자**
  - 토피라메이트 성분으로 안압 상승의 우려가 있습니다.
  - 복용 중 갑자기 시력이 저하되거나 안압 상승이 발생하면 복용을 중단하고 안과 진료를 받으시길 바랍니다.

- 간기능 (Child-pugh score 7-9) , 신기능 (30 이하) 저하 환자
  - 중증도 간기능, 신기능 저하 환자에서는 **7.5/46mg 까지만 사용이 가능합니다.**

투약방법



투약방법

- 식사와 관계없이 1일 1회 복약
- 매일 같은 시간에 복약
- 3.75/23mg 2주 → 7.5/46mg 12주

  효과 有 ➔ 유지

  효과 無 ➔11.25/69mg 2주 → 15/92mg 유지
- 녹내장, 폐동맥 폐쇄성질환, 임신가능성 확인 요함

비만 치료약물 가이드

Phentermine/Topiramate

- **펜터민 - CNS에서 NE 증가시켜 식욕을 억제**
- **토피라메이트 - gaba활성화, 글루타메이트 수용체 차단**
- **약용량 반응관계**
- **혈압, 혈당, 지질수치 향상**
- **부작용 - 구갈, 이상감각, 수면장애, 어지럼증**
- **주의 - 녹내장, 심혈관질환 과거력**
- **금기 - 임신**
- **장기간 처방 가능**
- **강력한 체중감량 효과**

CASE 2
내가 .. 내가 당뇨라니

2020.09.

CASE 2. 어둡고 조용한 30세 연구원

- 2021. 07.30 (초진일)
- M / 30
- 173cm / 121kg(BMI 40.5) / BP 170/97
- Lab

  HbA1c 8.7

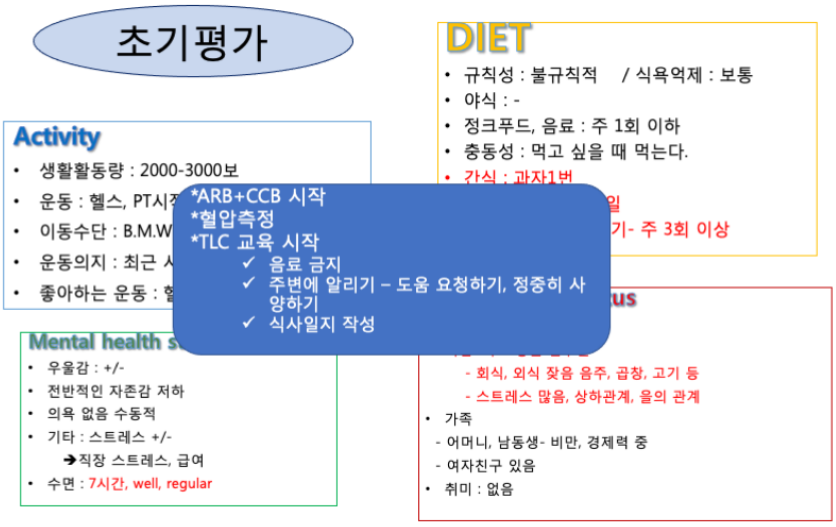
  LDL 106 / TG 76 /HDL 51

  AST 46 / ALT 80
- A/S (+/+) 1병 1회, 1갑
- 성인 최저 체중 : 90kg / 성인 최고 체중 : 123kg
- 이전 비만클리닉 경험 : none
- 운동 : 헬스장 (1달째)
- 동거인 : 어머니(비만), 아버지(마른편), 동생(비만)

- 식사 3끼 규칙적(저녁을 많이 먹는다) 야식은 잘 안먹는다
- 탄수화물 : 좋아하는 밀가루, 피자,
- 음료 : 탄산좋아한다. 차마시려고 노력중
- 정크푸드 : 2-3/wk

- 다이어트 실패이유- 맛있는게 많았다.
- 스트레스 : +- 스트레스 받으면 먹는게 조금 영향
- 우울감 : 급여때문,,
- 역류증상

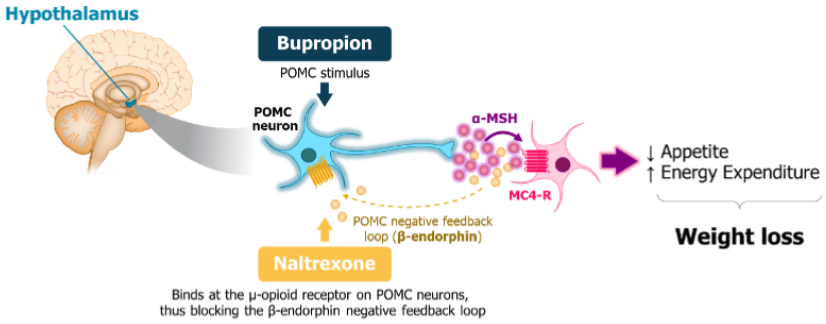
- 목표 몸무게 75kg /1년



Naltrexone/Bupropion

Mechanism of Naltrexone/Bupropion SR

식욕중추



- Bupropion : NE, 도파민의 재흡수 억제 → 도파민에 의한 POMC 활성 자극 → **식욕억제**
- Naltrexone : β-endorphin의 POMC 자가저해 억제 → POMC 활성 지속 → **식욕억제**

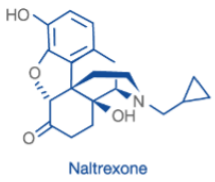
보상중추

*** 도파민– 음식 섭취 행동 유발에 관여, 오피오이드 – 음식 섭취 후 즐거운 감정에 관여**

Bupropion과 Naltrexone은 각각 뇌의 보상중추에 작용하여 식품에 의한 중독증상을 억제
→ **식탐(Craving)억제**

Pharmacological Research 2014:1–11.

Naltrexone



Naltrexone

분류	전문/392[해독제]
작용기전	**Opioid receptor antagonist** : 아편상 활성은 갖지 않으면서, 수용체와 결합하여 아편상의 작용을 저해
효능효과	알코올 의존성 치료 및 아편류의 효과 차단
FDA 승인	1984년: 아편중독 치료제로 승인
용법용량	Daily dose: 50 mg/d
부작용	위장관계 (구역, 구토, 복통 등)
Weight loss 관련 ?	날트렉손 장기간 사용 시 5% 미만의 체중감소 관찰. → β-endorphin의 μ-opioid receptor 결합 억제. 즉, POMC의 자가저해 억제 !

Naltrexone – Opioid와 상호작용 가능

- Opioid 제제를 장기 복용하다가 중단한 환자에게 contrave를 투여할 경우, 충분한 휴약 기간(1주일 이상) 이후에 투여한다

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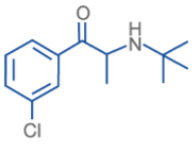
Bupropion



Bupropion

분류	전문/117[정신신경용제]
작용기전	Norepinephrine-dopamine reuptake inhibitor
효능효과	우울증 금연 시 니코틴 의존을 치료하기 위한 단기간의 보조요법
FDA 승인	1985년: 항우울제로 승인
용법용량	Daily dose: 300 mg/d, 최대 400~450 mg/d
부작용	불면증, 두통, 간질성 발작 등
Weight loss 관련?	부프로피온 300-400 mg/d 장기간 사용 시 5% 미만의 체중감소 관찰. → Dopamine이 POMC 자극

Bupropion

- Seizure risk를 상승 가능성
- Psychotics, antidepressants, theophylline, systemic corticosteroids 와 병용시 주의
- -도파민 제제 (levodopa, amantadine) 와 병용할 경우 부작용 발생 증가

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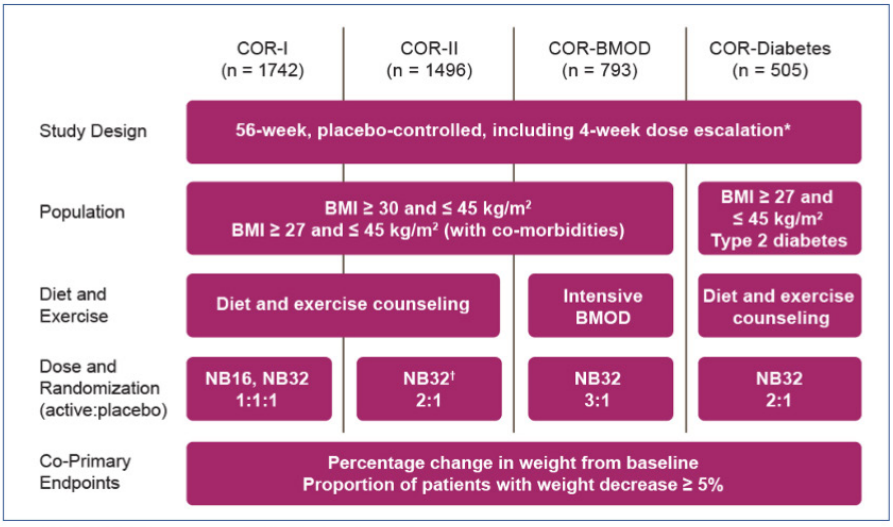
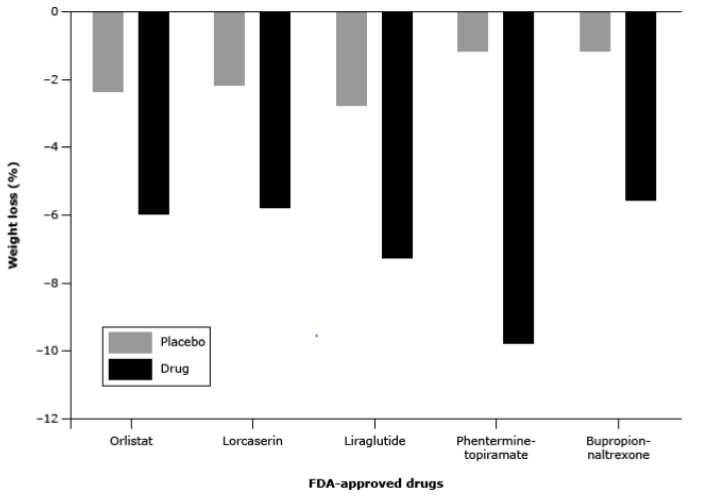
Contrave Obesity Research (COR) design



* For COR-II, full dose was reached by the start of week 5
† With exploration of NB48 in NB32 non-responders

	COR-I		COR-II		COR-BMOD		COR-Diabetes	
	NB 32/360	Placebo	NB 32/360	Placebo	NB 32/360	Placebo	NB 32/360	Placebo
Intent-to-Treat	n=538	n=536	n=820	n=474	n=565	n=196	n=321	n=166
%change in BW	–5.4%	–1.3%	–5.6%	–1.2%	–8.1%	–4.9%	–3.7%	–1.7%
≥ 5% weight loss	42%	17%	47.9%	16.9%	57%	43%	36%	18%
≥ 10% weight loss	21%	7%	28.1%	6.1%	35%	21%	15%	5%
Completers	n=296	n=290	n=434	n=267	n=301	n=106	n=175	n=100
%change in BW	–8.1%	–1.8%	–8.2%	–1.4%	–11.5%	–7.3%	–5.9%	–2.2%
≥ 5% weight loss	62%	23%	64.9%	21.7%	80.4%	60.4%	53.1%	24%
≥ 10% weight loss	34%	11%	39.4%	7.9%	55.2%	30.2%	26.3%	8.0%

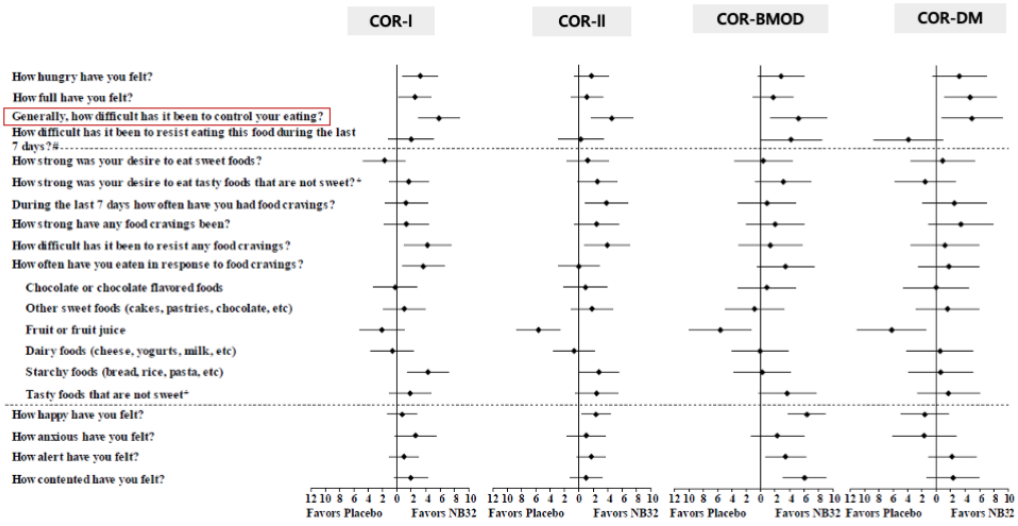
Weight loss at 12 months for FDA-approved drugs



Courtesy of George A Bray, MD.
Data from: Khera R, Murad MH, Chandar AK, et al. Association of pharmacological treatments for obesity with weight loss and adverse events: A systematic review and meta-analysis. JAMA 2016; 315:2424. doi: 10.1001/jama.2016.7602

Graphic 115096 Version 1.0

Control of Eating Questionnaire



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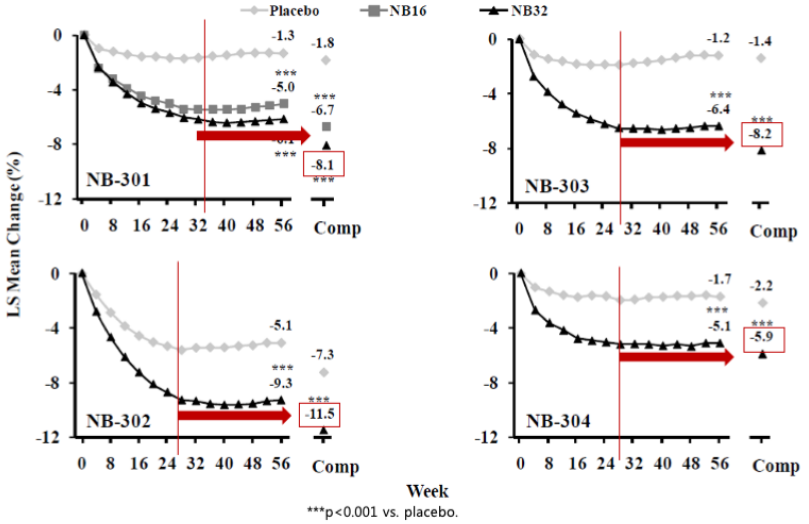
Food and Drug Administration. CONTRAVE®

Body Weight, Percent Change from Baseline to Each Visit by Phase 3 Study (mITT-LOCF)



1. 4주차부터 유의적인 체중감량이 관찰.
2. 최대 체중감량은 28~40주에 관찰
3. 장기간 체중감량이 유지되는 일관된 경향을 관찰.

Food and Drug Administration. CONTRAVE®

우울증 / 불안 / 초조

- Lorc
  - D
  - S
- Phe
  - D
  - In
  - A

Table 3. Adverse Reactions Reported by Obese or Overweight Patients With an Incidence (%) of at Least 2% Among Patients Treated with CONTRAVE and More Common than with Placebo

Adverse Reaction	CONTRAVE 32 mg/360 mg N=2545 %	Placebo N=1515 %
Nausea	32.5	6.7
Constipation	19.2	7.2
Headache	17.6	10.4
Vomiting	10.7	2.9
Dizziness	9.9	3.4
Insomnia	9.2	5.9
Dry mouth	8.1	2.3
Diarrhea	7.1	5.2
Anxiety	4.2	2.8
Hot flush	4.2	1.2
Fatigue	4.0	3.4
Tremor	4.0	0.7

.3%

비만 치료약물 가이드

Naltrexone/Bupropion(Contrave®)

- 날트렉손 - Opioid receptor antagonist
- 부프로피온 - POMC에 작용
- 시상하부, 중뇌변연계 작용-식욕억제, 식탐억제
- 장기간 처방가능
- 부작용 - 구역, 변비, 수면장애, 두통, 어지럼증
- 금기 - uncontrolled HTN, Seizure, pregnancy, breastfeeding, chronic opioid use, Eating disorder
- CVD safety concern
- DEA Schedule drug으로 분류되지 않음(항정X)
- Major depressive disorder, seasonal affective disorder, attention-deficit disorder, 금연 고려 시 고려 가능

Case 3. 처음 비만 치료를 시작하는 대사증후군 여성환자

- F / 54
- 155cm / 71kg(BMI 29.5) / WC 91cm / BP120/80
- Lab)FBS 120+- / Hba1c 6.2
  TG 180~255 /HDL 40~45
  LDL 130~155
- A/S(+/-) 3회 1.5병
- 운동 : (-) / 직업 : 사무직
- 일상활동 : 자가운전, 사무직, 활동없는 편, 좌식생활
- 식사습관 : 규칙적(+ 3끼), 충동성(-), 습관성(-), 간식(+-), 야식(+)
- 우울감(+-) : 긍정적 태도 보이나 외모 및 건강에 대한 자신감 저하, 계속된 생활습관 교정 실패에 대한 스트레스
- 수면 well
- 가족관계 : 지지적 안정적

Case1. 처음 비만 치료를 시작하는 대사증후군 여성환자

- 탄수화물 : 빵, 분식
- 고지방식품 : 술안주, 치킨
- 외식빈도 : 매일 1-2끼
- 음료 : 커피 (믹스커피1잔, 아메리카노 1잔), 생과일 주스 1잔
- 좋아하는 음식 : 안주류, 디저트류

- 출산전 몸무게 : 50kg
- 10년간 최저 몸무게 : 60??kg
- 이전 다이어트 시도 : 운동 , 다이어트 선식, 홈쇼핑
- 목표 : 55kg(16kg 감량)/6month

고려대학교 의과대학 가정의학교실

KU MEDICINE KOREA UNIVERSITY MEDICINE

2022 연수강좌

근골계통증의 약물치료, 기전과 적용

강석
고려의대 재활의학과

Management of musculoskeletal pain

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2022.04.23.

Contents

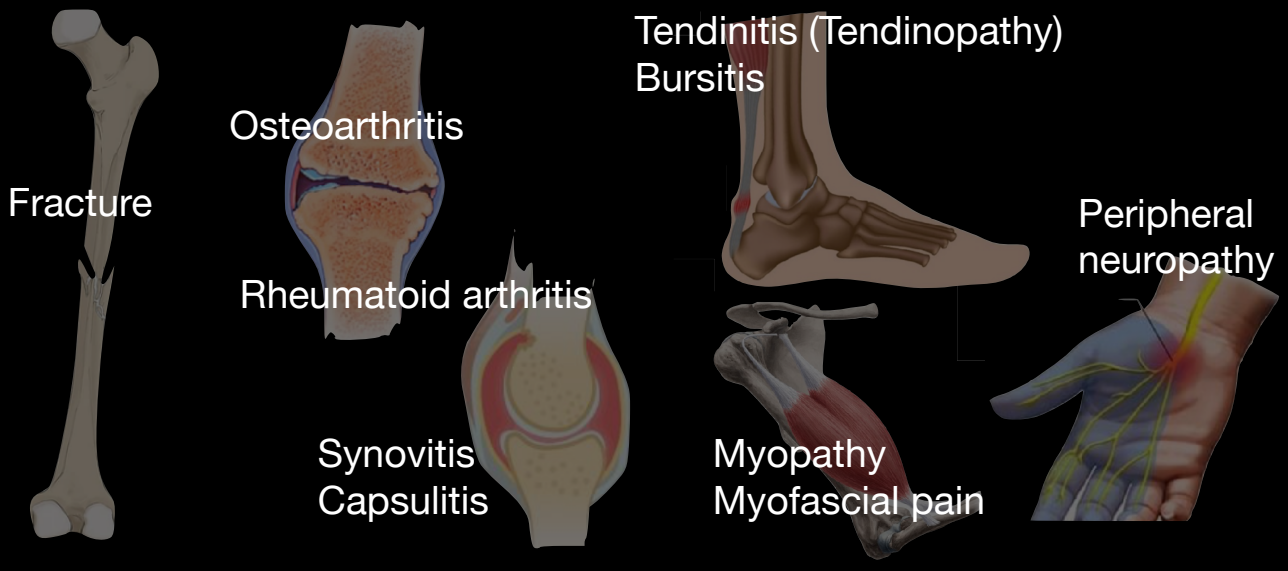
- Musculoskeletal system and disorders
- Causes of musculoskeletal pain
- General principle of the musculoskeletal pain management
- Common musculoskeletal pain disorders
- Chronic pain management

Musculoskeletal system and disorders

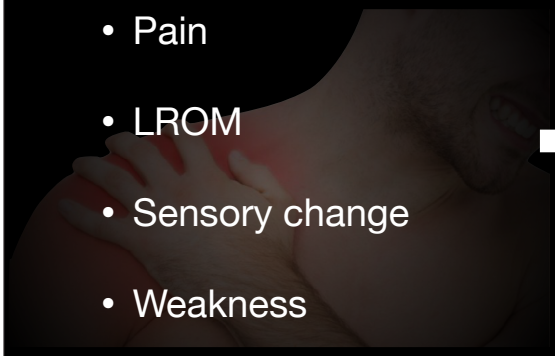
Musculoskeletal system

- Bone, cartilage
- Joint capsule, synovium, bursa
- Muscle, ligament, tendon
- Peripheral nerve

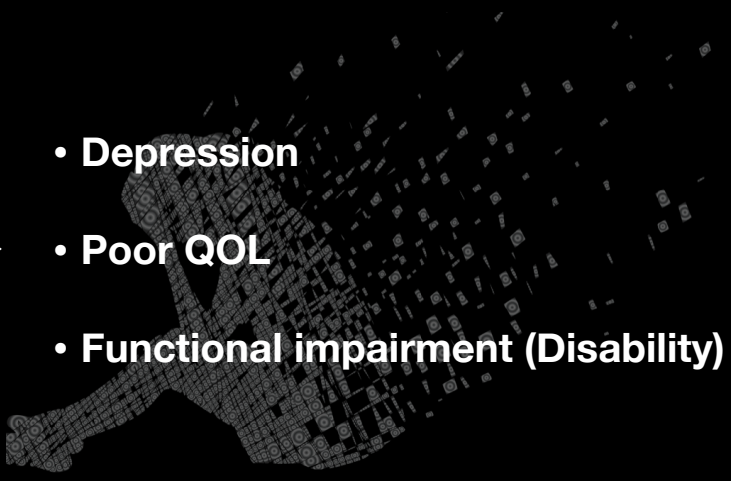
Common disorders in MSK system



Symptoms of MSK disorders



- Pain
- LROM
- Sensory change
- Weakness



- **Depression**
- **Poor QOL**
- **Functional impairment (Disability)**

Causes of MSK pain

Trauma

Overloading

Overuse

Degenerative changes

Infection, hereditary, systemic disorder

Tissue damage

↓

Inflammatory response

↓

Activation of nociceptors

↓

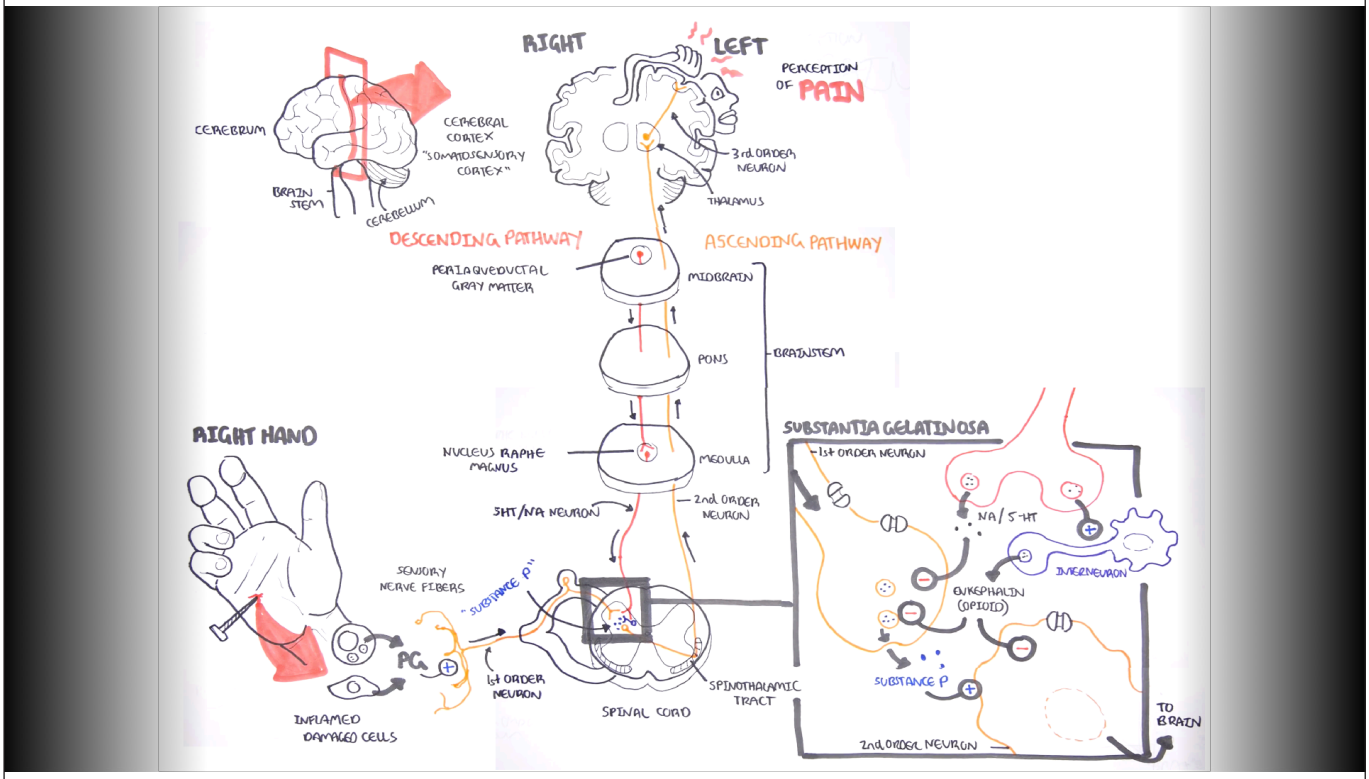
Dorsal root ganglion

↓

Spinothalamic tract

↓

Cerebral cortex



Types of pain and causes

	NOCICEPTIVE/SOMATIC PAIN	VISCERAL PAIN	NEUROPATHIC/CENTRAL PAIN
Description	• Deep somatic pain: dull/aching • Superficial somatic pain: sharp, pricking • Burning, localized, reproducible	• Crampy and dull • Vague in location	• Burning, tingling, shooting, stabbing, electric-like • May be associated with numbness, tingling
Causes	• Noxious perception from tissue damage can originate from the skin, muscle, bone, or fascia • Mediated by somatic nervous system	• Internal structures of solid or hollow organs/autonomic nervous system. Gastrointestinal • Mediated by ANS	• Primary lesion or dysfunction of the pain-sensing nervous system (CNS or PNS)

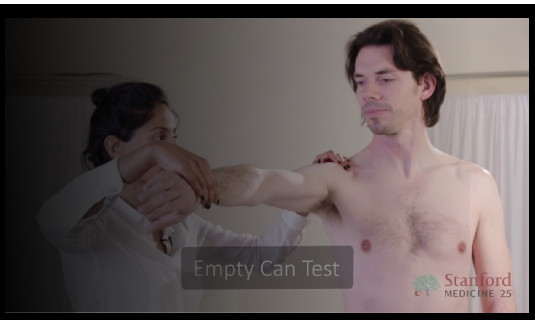
Note: ANS = autonomic nervous system; CNS = central nervous system; PNS = peripheral nervous system.

General principle of the MSK pain management

Approach to MSK disorders

- **Involved structures**
- **Systemic or localized**
- **Clinical course**
  - progressive
  - stationary
  - wax and wane
  - restorative

Diagnosis and Assessment



Physical examinations
- Functional assessment
- Neurologic examination

Radiologic examinations
- X-ray, CT - bone and joint
- MRI, Ultrasound - Soft tissue

Laboratory examinations
- Inflammatory marker
- Enzymes
- Antibodies

Principle for conservative management of MSK disorder

Alleviate pain

– Medications, physical modalities, injections

Functional recovery

– Stretching, strengthening and stabilizing exercises

Prevent additional injury

– Avoid trauma or overuse

Acute MSK injury

Protect

Rest

Ice

Compress

Elevate

Conservative treatment for the MSK pain

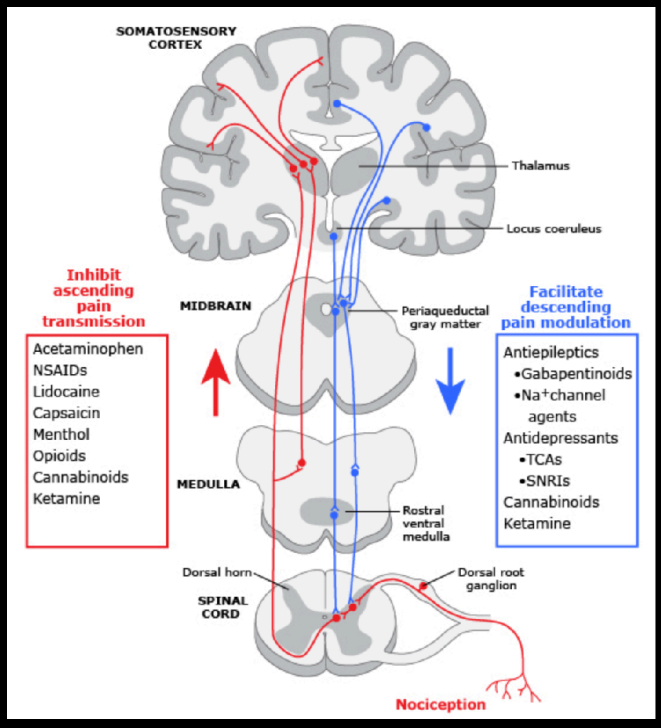
Medications

Injections

Physical therapy

Exercise

Braces

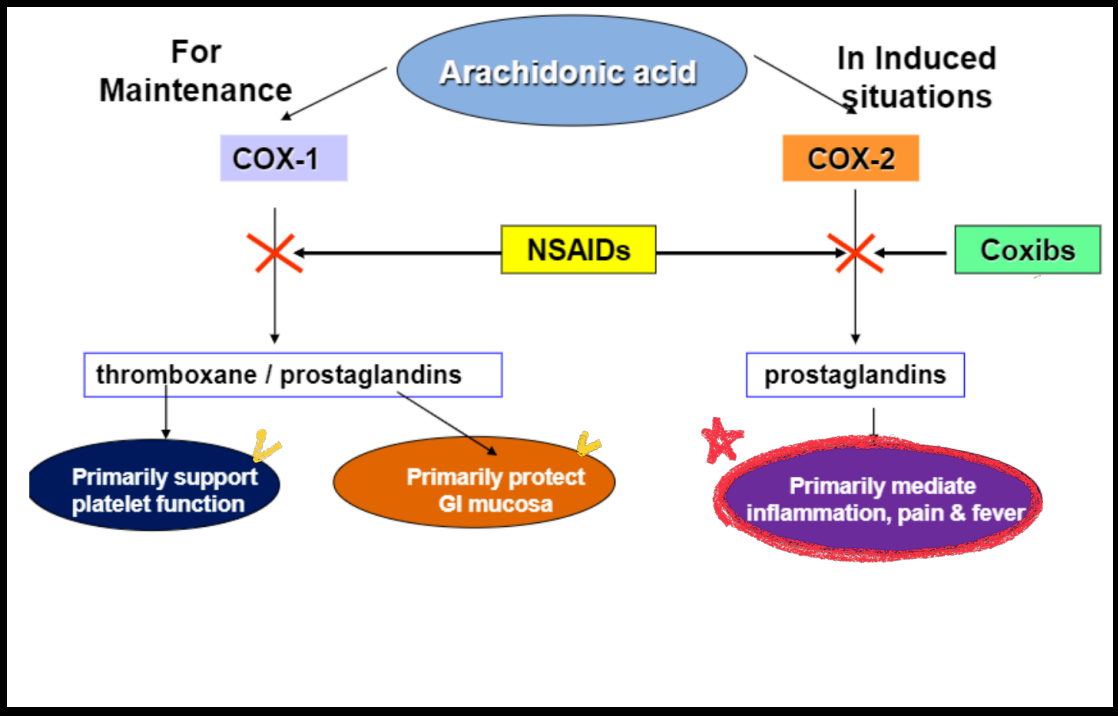


nociceptive pain

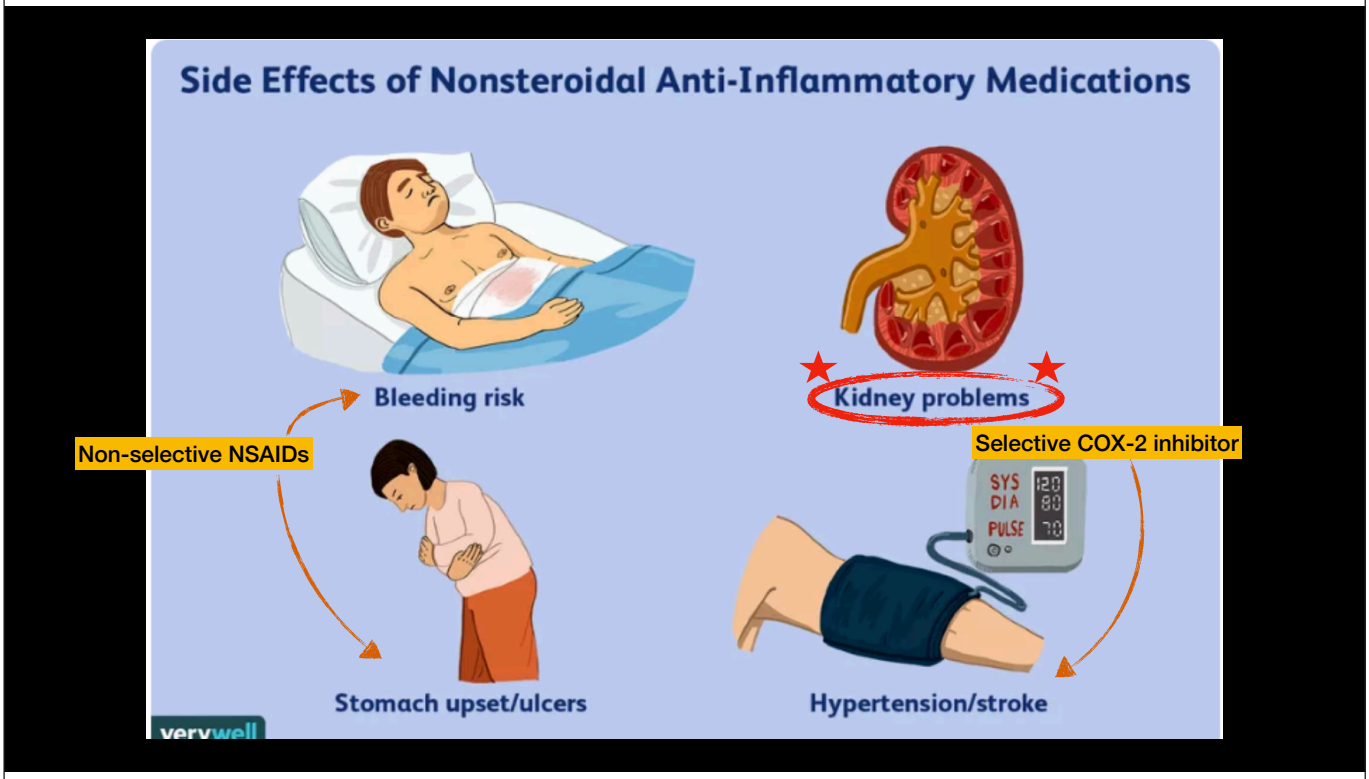
- NSAIDs
- Acetaminophen
- Tramadol
- Opioid

neuropathic pain

- Gabapentin
- Pregabalin
- Anticonvulsant
- Antidepressant

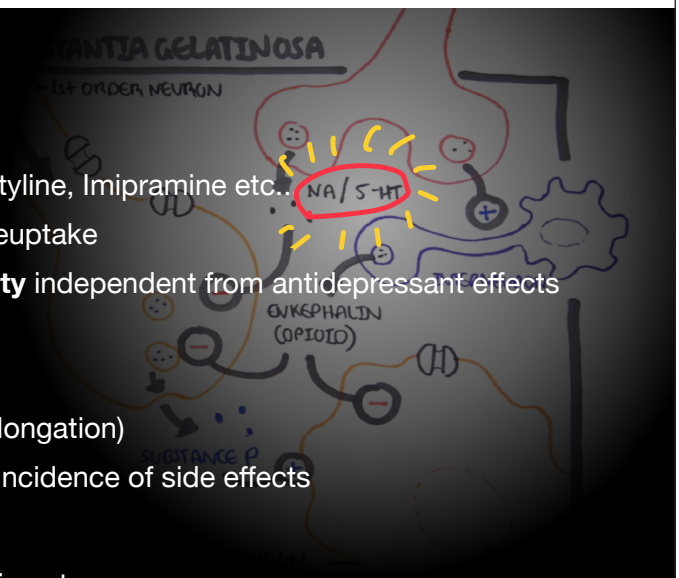


MEDICATION	LESS COX-2 SELECTIVITY	MORE COX-2 SELECTIVITY
Meloxicam		XXX
Celecoxib		XXX
Diclofenac		X
Sulindac (Most common to cause liver failure)		X
Ibuprofen	X	
Naproxen	X	
Salicylate	X	
Indomethacin	XX	
Ketorolac	XXX	


Side Effects of Nonsteroidal Anti-Inflammatory Medications
Bleeding risk
Kidney problems
Non-selective NSAIDs
Selective COX-2 inhibitor
SYS 120
DIA 80
PULSE 70
Stomach upset/ulcers
Hypertension/stroke
verywell


Acetaminophen
• Inhibit PG synthesis within the CNS
• Analgesic and antipyretic effect
• No anti-inflammatory effect
• Hepatotoxicity
타이레놀
10정

Antidepressant



TCA

- Amitriptyline, Nortriptyline, Imipramine etc...
- Inhibit 5HT and NE reuptake
  → **analgesic property** independent from antidepressant effects
- Side effects
  - Somnolence
  - Arrhythmia (QT prolongation)
- Nortriptyline - lower incidence of side effects

SNRI

- Venlafaxine, Duloxetine etc...
- Inhibit 5HT and NE reuptake
- Effective for neuropathic pain, fibromyalgia

Anticonvulsant - membrane stabilizing agent

Gabapentin (Neurontin)
Pregabalin (Lyrica)

- Voltage-gated calcium channels at the alpha 2-delta subunit in the central nervous system
- Pregabalin may provide analgesia more quickly than gabapentin
- Diabetic neuropathy, Post-herpetic neuralgia, Radicular pain, Spinal cord injury, Central pain
- Side effect - dizziness and sedation

Valproic acid (Depakote)
Lamotrigine
Carabamazepine

Injections

- Decrease acute inflammatory response
- Alleviate pain and improve functions
- Stimulate tissue healing process and regeneration

• Corticosteroid injections: intraarticular, epitendinous, perineurial

• Viscosupplement IA injection: degenerative arthritis

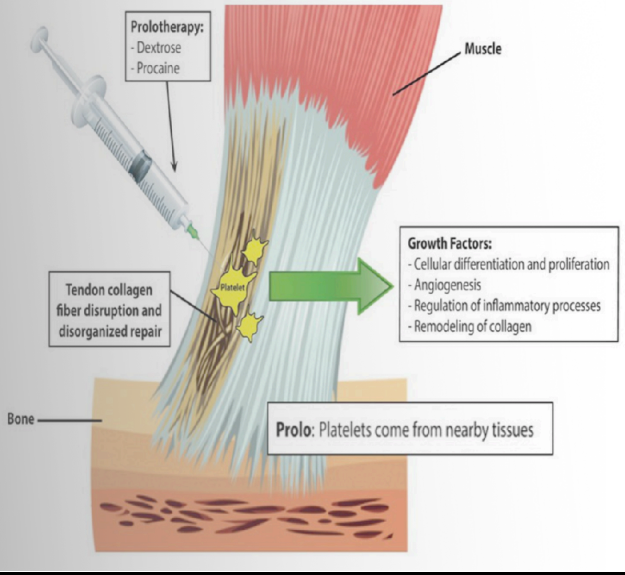
• Prolotherapy: tendinopathy, enthesopathy

Prolotherapy

15% dextrose & lidocaine solution

Frequency: q 3-6 weeks

a promising option for the treatment of painful musculoskeletal conditions, particularly when other standard treatments have proved ineffective.



Therapeutic Exercises

- Stabilization exercise - core exercise, scapular stabilization exercise
- Muscle pain - Stretching exercise
- Arthritis - Isometric strengthening exercise
- Tendinopathy - Eccentric contraction exercise

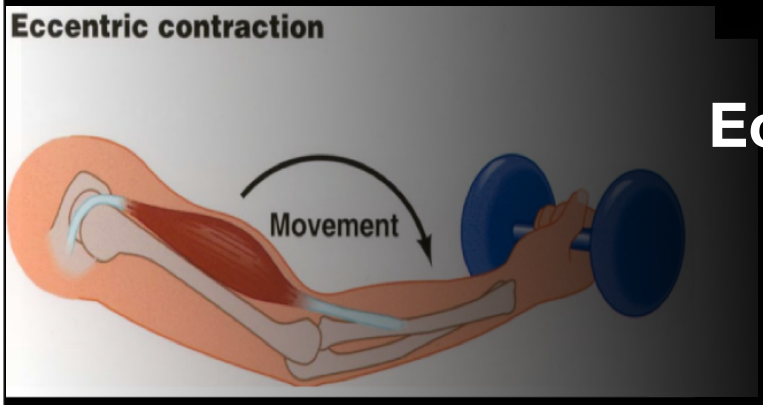
Physical modality

- Cold therapy: Ice pack, Vapocoolant (cold spray) etc…
- Superficial heat: Hot pack, Infrared, Paraffin bath etc…
- Deep heat: Ultrasound, Microwave…
- Electrotherapy: TNES, Interferential current therapy…

Isometric exercise

Isotonic exercise

Isokinetic exercise



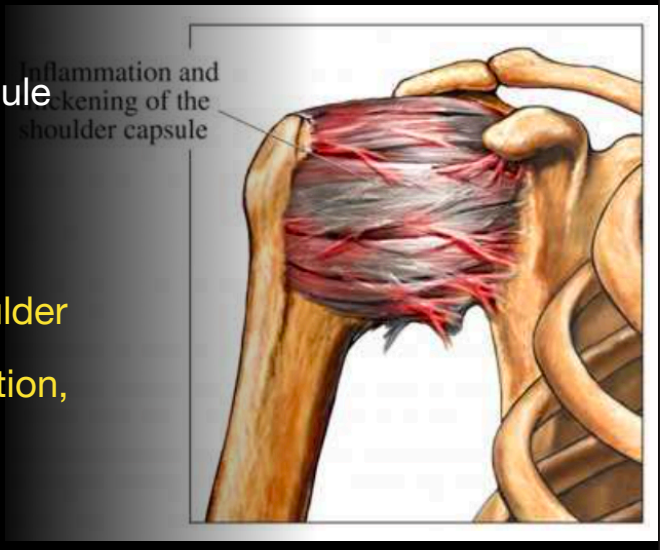
Eccentric contraction

Concentric contraction

Common MSK pain disorders

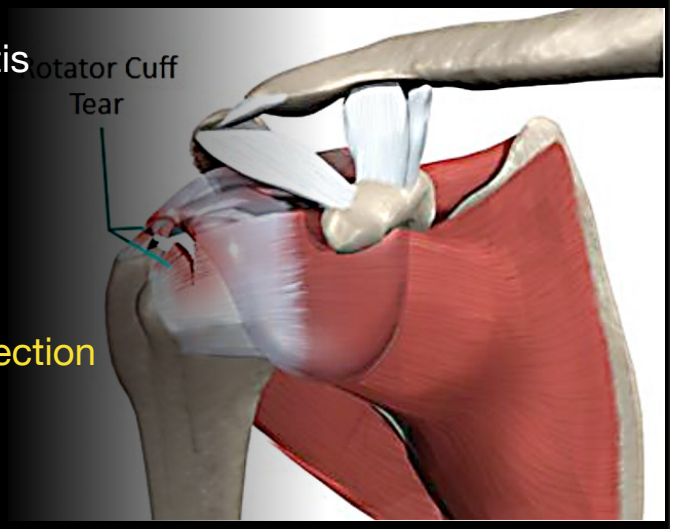
Adhesive capsulitis (Frozen shoulder)

- Inflammation of shoulder joint capsule
- Adhesion of synovial membrane
- Decrease of joint volume
- Painful LROM and stiffness of shoulder
- Treatment - NSAID, IA steroid injection, PROM exercise



Rotator cuff tendinopathy

- Combined with subacromial bursitis
- Result of impingement syndrome
- Treatment
  - NSAID, Acetaminophen
  - bursa or epitendinous steroid injection
  - scapular stabilization exercise
  - eccentric contraction exercise



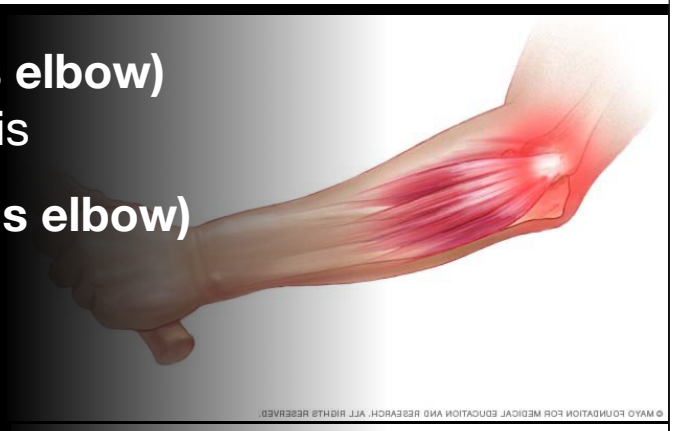
Lateral epicondylitis (Tennis elbow)

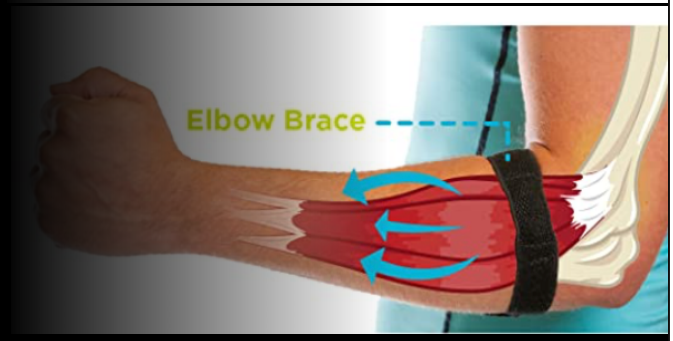
- Common extensor tendinitis

Medial epicondylitis (Golfer's elbow)

- Common flexor tendinitis

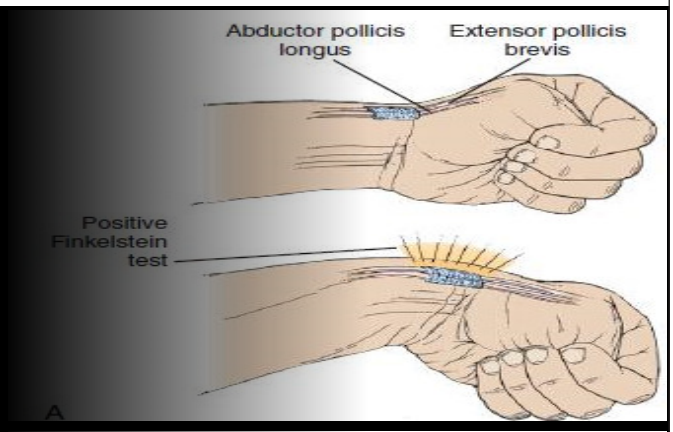
- Treatment
  - NSAID, Acetaminophen
  - steroid injection
  - prolotherapy
  - ESWT
  - eccentric contraction exercise
  - brace





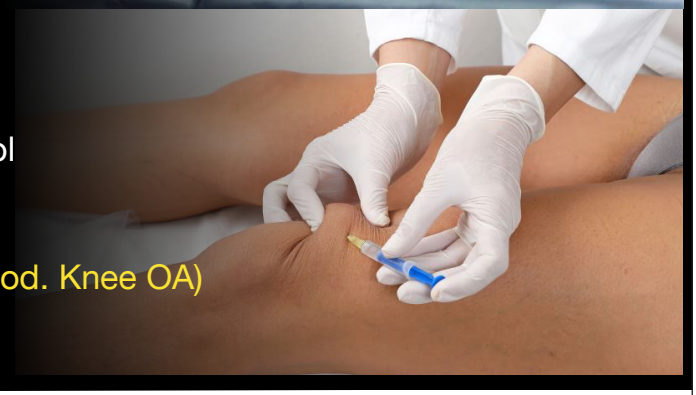
DeQuervain's disease

- APL, EPB tendinitis
- Treatment
  - NSAID, steroid injection
  - eccentric contraction exercise
  - thumb spica splint



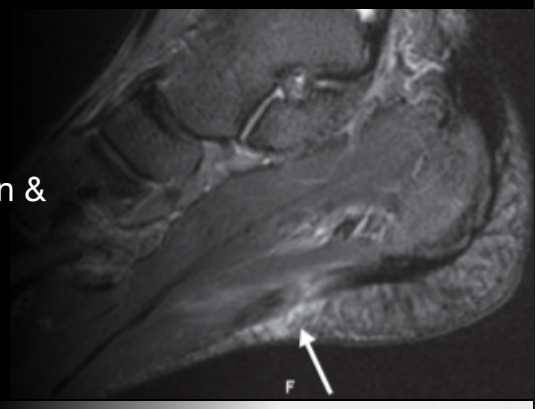
Knee Osteoarthritis

- Regular exercise
  - isometric strengthening
  - aerobic exercise
- Activity modification
- Brace
- Acetaminophen, NSAIDs, Tramadol
- IA steroid injection
- IA Hyaluronate injection (mild to mod. Knee OA)



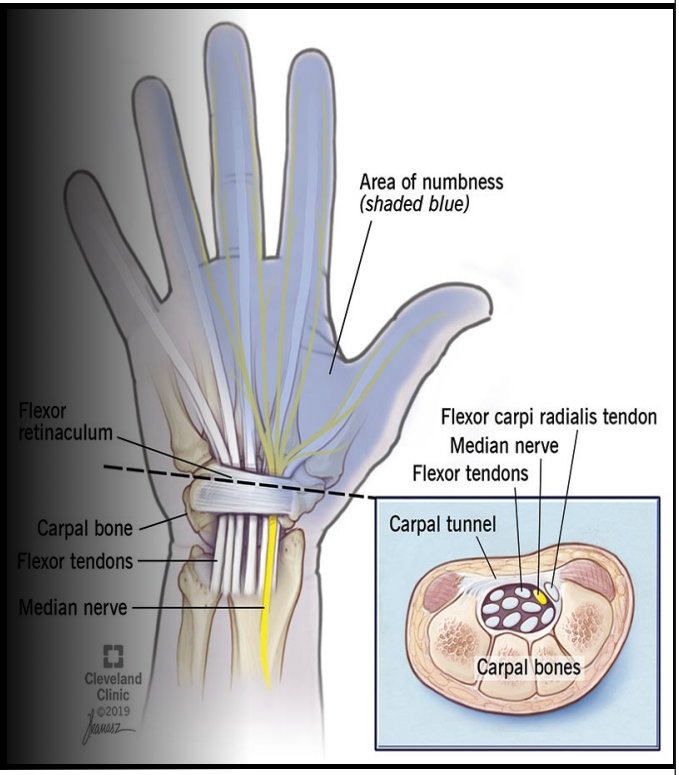
Plantar fasciitis

- Enthesopathy at the calcaneus / Inflammation & pain in the plantar fascia
- Treatment
  - NSAID, Acetaminophen
  - Stretching, eccentric contraction exercise
  - Resting night splint
  - Local steroid injection
  - Prolotherapy
  - ESWT

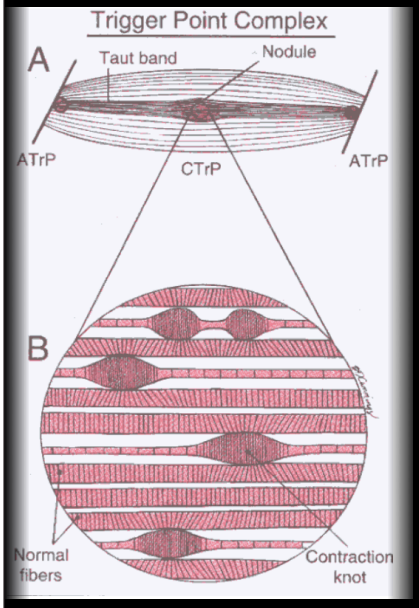


Carpal tunnel syndrome

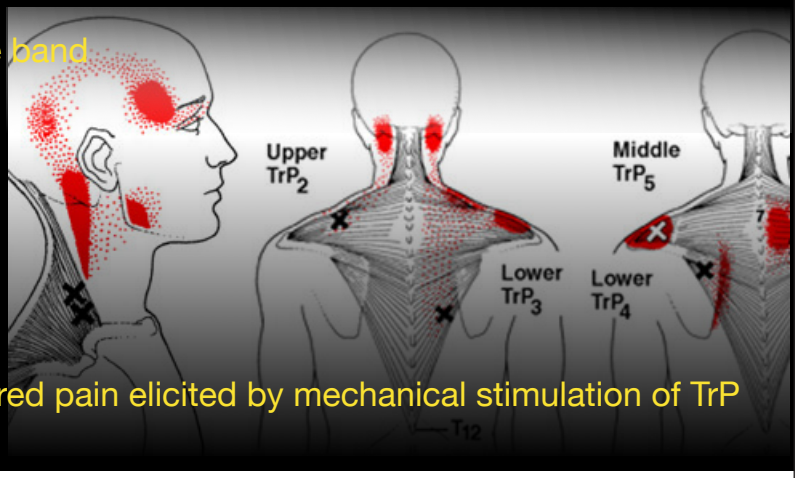
- Median nerve entrapment at the wrist
- Treatment
  - NSAID
  - Gabapentin or pregabalin
  - Stretching exercise
  - Resting night splint
  - Local steroid injection



Myofascial pain syndrome



- Most common MSK pain
- Myofascial trigger point - Exquisite tenderness in a taut muscle band

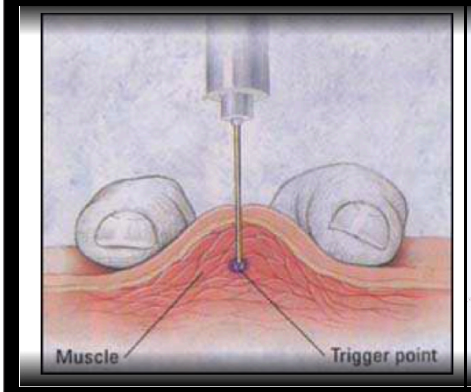


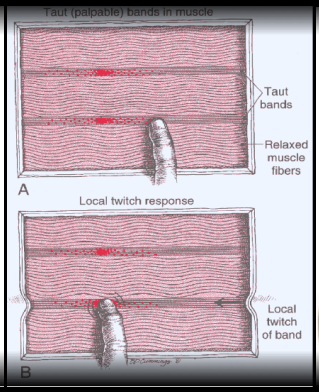
- Referred pain elicited by mechanical stimulation of TrP

Myofascial pain syndrome

- Treatment

- Trigger point injection





- Stretching exercise

Chronic pain management

Revised definition of pain

Pain
An unpleasant sensory and emotional experience associated with, or resembling that associated with, actual or potential tissue damage.
Notes
▪ Pain is always a personal experience that is influenced to varying degrees by biological, psychological, and social factors.
▪ Pain and nociception are different phenomena. Pain cannot be inferred solely from activity in sensory neurons.
▪ Through their life experiences, individuals learn the concept of pain.
▪ A person's report of an experience as pain should be respected.[1]
▪ Although pain usually serves an adaptive role, it may have adverse effects on function and social and psychological well-being.
▪ Verbal description is only one of several behaviors to express pain; inability to communicate does not negate the possibility that a human or a nonhuman animal experiences pain.

Chronic pain syndromes

Chronic MPS

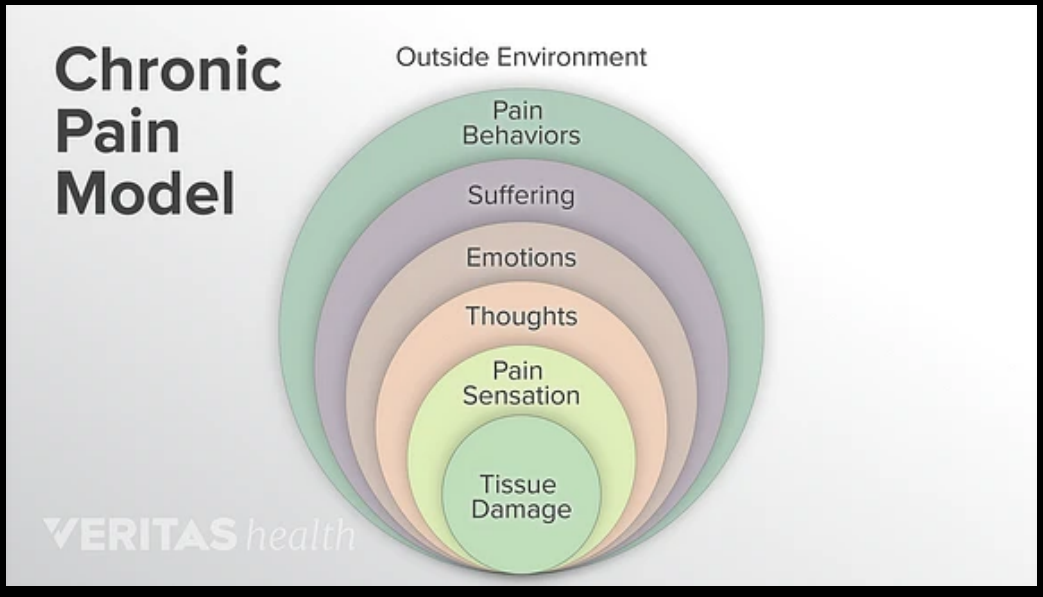
Fibromyalgia

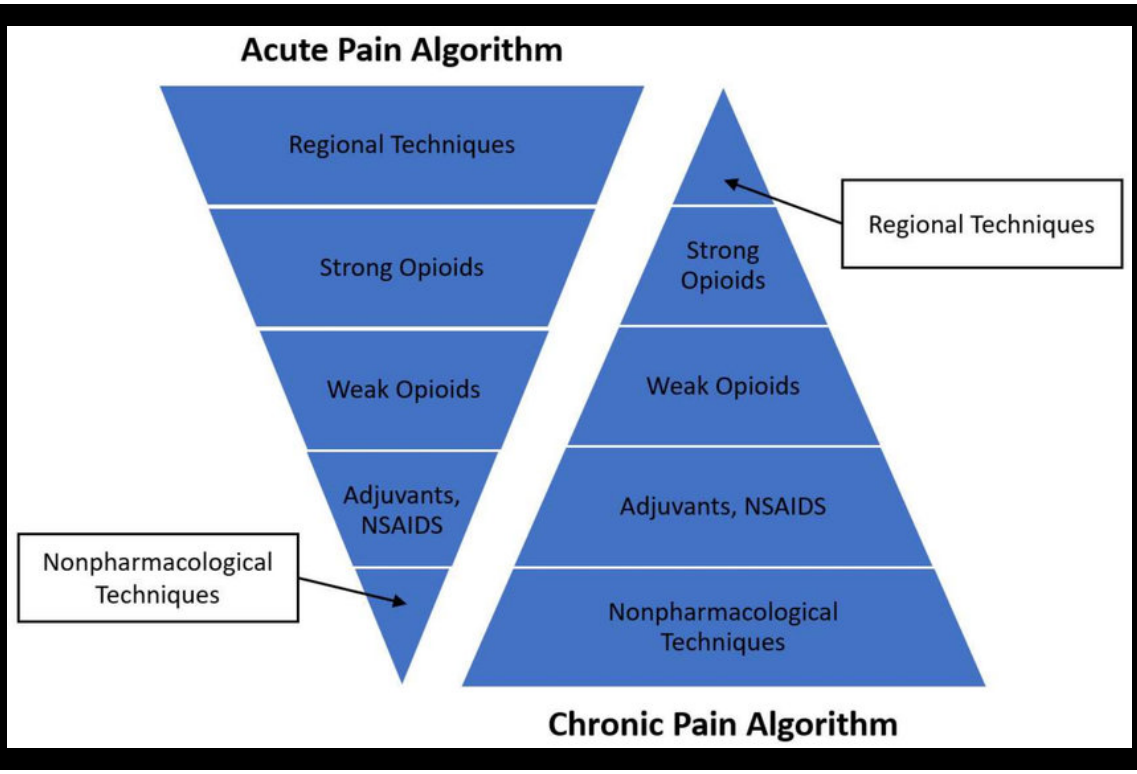
Chronic LBP

Chronic fatigue syndrome

Complex Regional Pain Syndrome (CRPS)

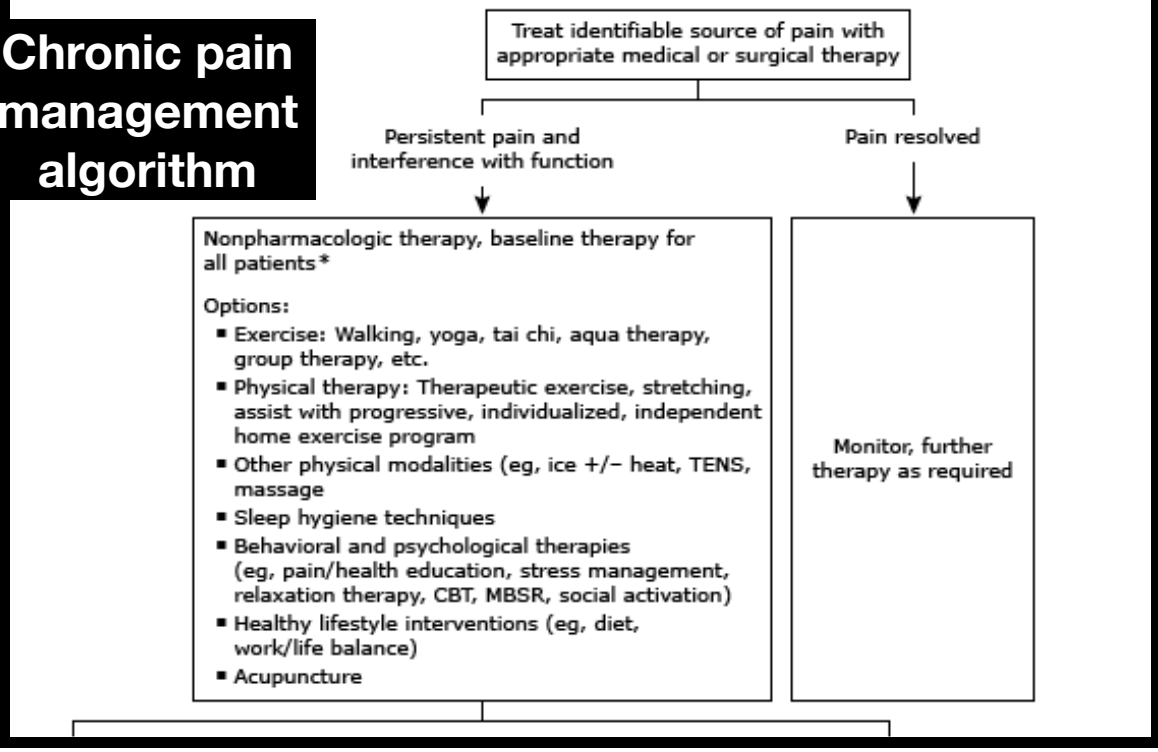
Somatization or conversion disorders

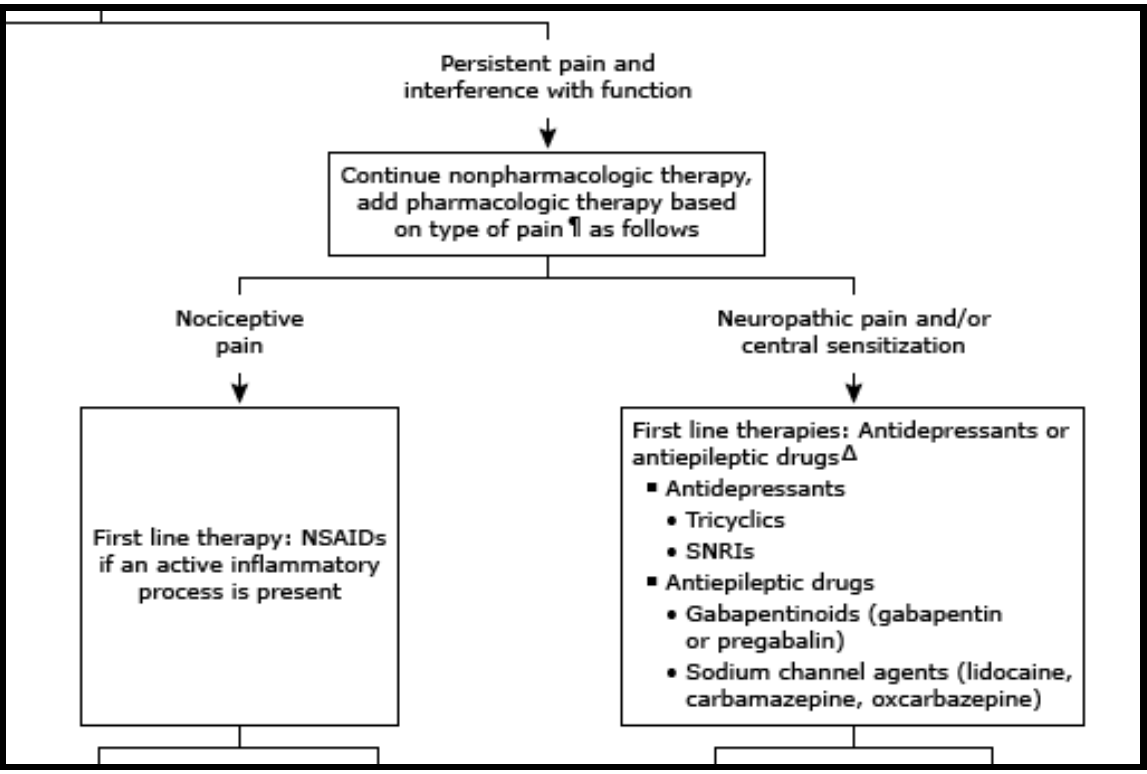


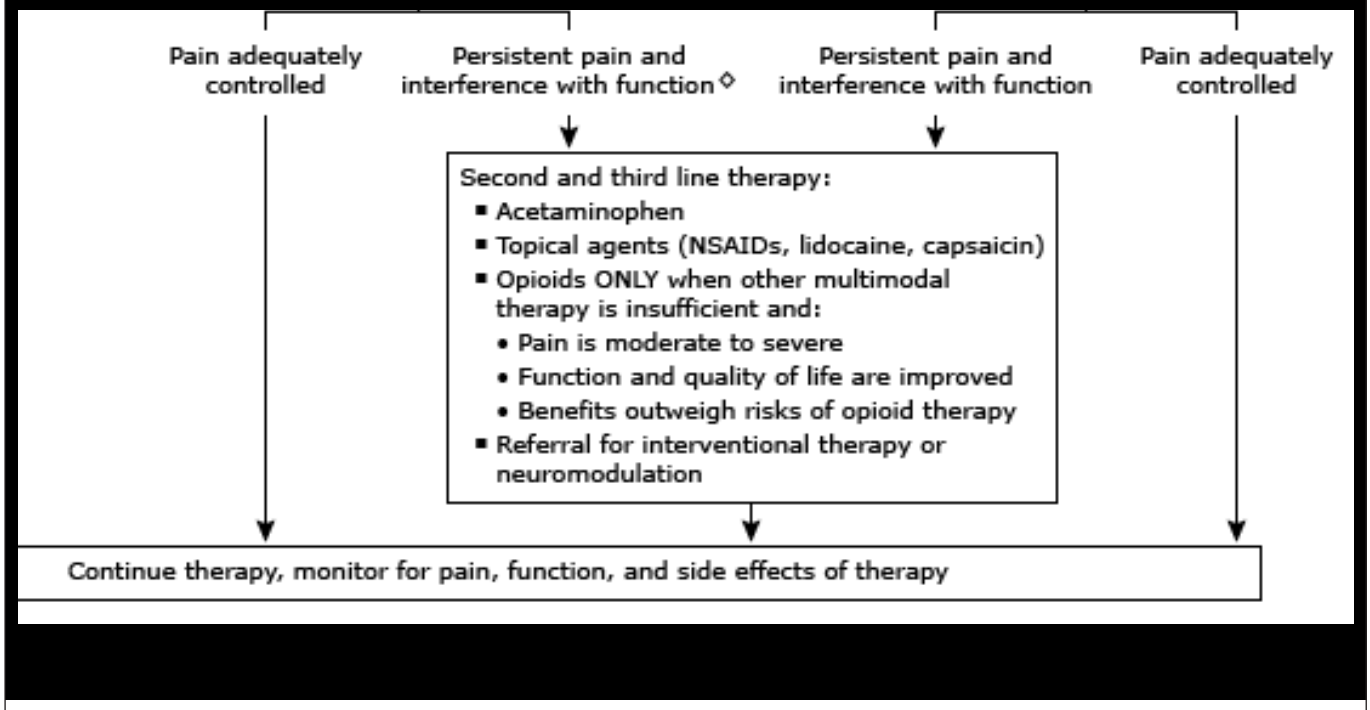

Acute Pain Algorithm
Regional Techniques
Strong Opioids
Weak Opioids
Adjuvants, NSAIDS
Nonpharmacological Techniques
Regional Techniques
Strong Opioids
Weak Opioids
Adjuvants, NSAIDS
Nonpharmacological Techniques
Chronic Pain Algorithm

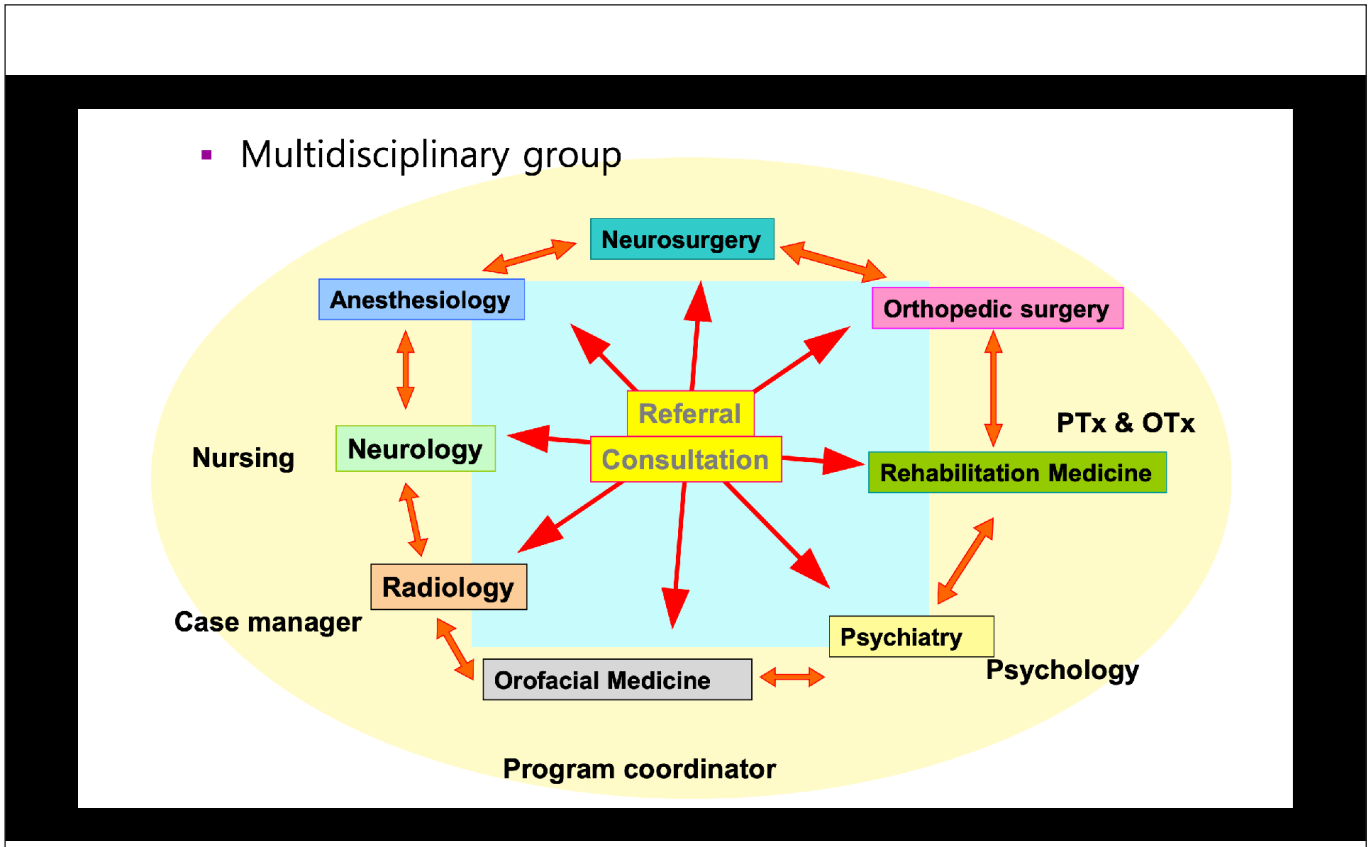

Non pharmacologic management of chronic pain
Physical therapy
Therapeutic exercise
Stretching
Psychological therapy
Cognitive-behavioral therapy
Mind-body therapy
Complementray and integrative health therapies
Spinal manipulation
Acupuncture
Physical modality

Chronic pain management algorithm






Pain adequately controlled
Persistent pain and interference with function◇
Persistent pain and interference with function
Pain adequately controlled
Second and third line therapy:
Acetaminophen
Topical agents (NSAIDs, lidocaine, capsaicin)
Opioids ONLY when other multimodal therapy is insufficient and:
Pain is moderate to severe
Function and quality of life are improved
Benefits outweigh risks of opioid therapy
Referral for interventional therapy or neuromodulation
Continue therapy, monitor for pain, function, and side effects of therapy


Multidisciplinary group
Neurosurgery
Anesthesiology
Orthopedic surgery
Referral
Consultation
Nursing
Neurology
PTx & OTx
Rehabilitation Medicine
Radiology
Case manager
Psychiatry
Psychology
Orofacial Medicine
Program coordinator

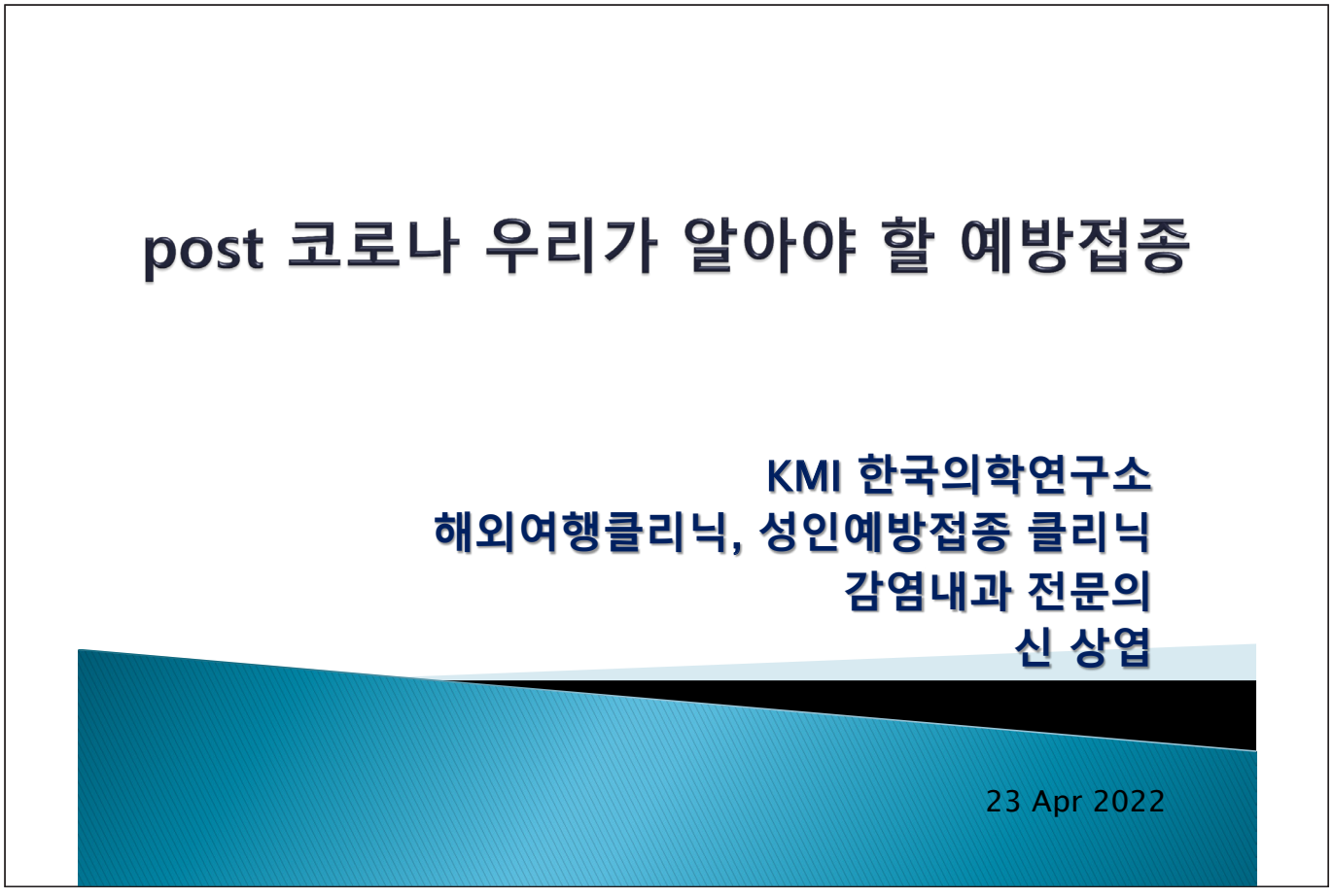

Thank you!

고려대학교 의과대학 가정의학교실

2022 연수강좌

Post 코로나 우리가 알아야 할 예방접종

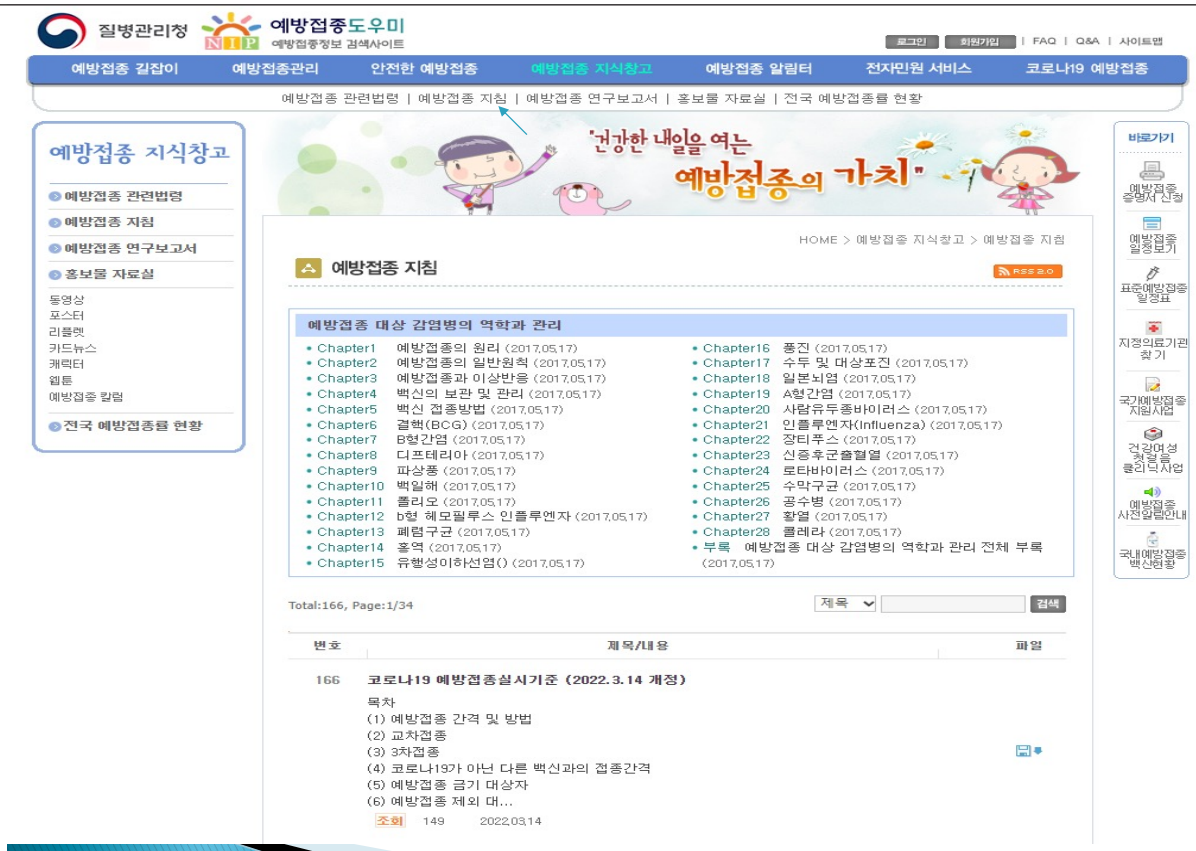
신상엽
KMI한국의학연구소



post 코로나 우리가 알아야 할 예방접종

I. 성인예방접종 개요 (Know where)

II. 최근 업데이트 된 백신과 특징 (Know how)



https://nip.kdca.go.kr/irgd/index.html

발 간 등 록 번 호
11-1352159-000081-14

Guidelines

2018

성인 예방접종 안내서
제2판

Guidelines for Adult Immunization

for Adult

Immunization

질병관리본부

ISBN 978-89-6838-593-3 (PDF)

질병관리본부

2 성인 예방접종 일정

표 1-1 성인 예방접종 일정표는 각 연령대에 따라 권장되는 예방접종을 한 눈에 볼 수 있도록 정리하여 보건의료인과 일반인이 쉽게 활용하도록 한 표이다. 면역의 증거가 없는 해당 연령의 건강한 성인에게 일반적으로 권장되는 예방접종도 있지만(연령 권장), 개인이 가지고 있는 질환, 직업 및 상황에 따른 위험군에게 권장되는 예방접종도 있다(위험군 권장). 또한 성인대상 예방접종 중 그 중요성이 특히 강조되어 국가예방접종으로 무료접종이 지원되는 대상과 백신은 따로 표시하였다. 표 1-2는 일반적으로 건강한 성인에게 권장되는 예방접종을 열거하였다.

표 1-1. 성인 예방접종 일정표

대상감염병	백신종류	만 19~29세	만 30~39세	만 40~49세	만 50~59세	만 60~64세	만 65세 이상
인플루엔자[1]	Flu	위험군에 대해 매년 1회			매년 1회		
파상풍/디프테리아/백일해	Tdap/Td	Tdap으로 1회 접종, 이후 매 10년 마다 Td 1회					
폐렴구균[2]	PPSV23	위험군에 대해 1회 또는 2회					1회
	PCV13	위험군 중 면역저하자, 무비증, 뇌척수액누출, 인공와우 이식 환자에 대해 1회					
A형간염[3]	HepA	2회		항체검사 후 2회	위험군에 대해 항체검사 후 2회 접종		
B형간염[4]	HepB	위험군 또는 3회 접종/감염력이 없을 경우 항체 검사 후 3회 접종					
수두[5]	Var	위험군 또는 접종력/감염력이 없을 경우 항체검사 후 2회 접종					
홍역/유행성이하선염/풍진[6]	MMR	위험군 또는 접종력/감염력이 없을 경우 1회 또는 2회 접종 ; 가임 여성은 풍진 항체 검사 후 접종					
사람유두종바이러스 감염증	HPV	만 25-26세 이하 여성 총 3회					
대상포진	HZV					1회	
수막구균[7]	MCV4	위험군에 대해 1회 또는 2회					
B형 헤모필루스 인플루엔자[8]	Hib	위험군에 대해 1회 또는 3회					

연령 권장 : 면역의 증거가 없는(과거 감염력이 없고 예방접종력이 없거나 불확실) 대상 연령의 성인에게 권장됨
※ 연령권장의 경우에도 해당 질병의 위험군(각주 참고)에게는 접종을 더욱 권장함
위험군 권장 : 특정 기저질환, 상황 등에 따라 해당 질병의 위험군에게 권장
국가예방접종사업으로 무료접종

[감염병별 위험군]

1) 인플루엔자 위험군: 만성질환자, 면역저하자, 임신부, 의료기관 종사자, 집단시설 거주자, 위험군을 돌보거나 함께 거주하는 자 등

2) 폐렴구균 위험군
- i) 면역 기능이 저하된 환자: HIV 감염증, 만성 신부전과 신증후군, 면역억제제나 방사선 치료를 요하는 질환(악성 종양, 백혈병, 림프종, 호지킨병) 혹은 고형 장기 이식, 선천성 면역결핍질환 등
- ii) 기능적 또는 해부학적 무비증 또는 비장 기능 장애 환자, 겸상구 빈혈 혹은 헤모글로빈증
- iii) 면역 기능은 정상이며, 뇌척수액 누출, 인공와우 이식 상태
- iv) 면역 기능은 정상이나 다음과 같은 질환을 가진 환자: 만성 심장 질환, 만성 폐 질환, 만성 간 질환, 당뇨병 등

3) A형간염 위험군: 만성간질환자, 혈액제제를 자주 투여 받는 혈우병 환자, 보육시설 종사자, A형간염 바이러스에 노출될 위험이 있는 의료인 및 실험실 종사자, A형간염 유행지역 여행자 또는 근무 예정자, 음식물을 다루는 요식업체 종사자, 남성 동성애자, 약물중독자, 최근 2주 이내에 A형간염 환자와의 접촉자

4) B형간염 위험군: 만성 간질환 환자, 혈액투석환자, HIV 감염인, 혈액제제를 자주 투여받는 환자, B형간염 바이러스에 노출될 위험이 높은 환경에 있는 사람

5) 수두 위험군: 수두 유행 가능성이 있는 환경에 있는 사람(의료인, 학교 혹은 유치원 교사, 학생, 영유아와 함께 거주하는 사람, 수두 유행지역 여행자), 면역저하 환자의 보호자, 가임기 여성 중 수두에 면역이 없는 사람

6) 홍역/유행성이하선염/풍진 위험군 : 의료인, 홍역/유행성이하선염/풍진 유행국가 해외여행자, 가임기 여성 중 면역이 없는 사람 등

7) 수막구균 위험군: 해부학적 또는 기능적 무비증, 보체결핍 환자, 군인(특히 신병), 직업적으로 수막구균에 노출되는 실험실 근무자, 수막구균 감염병이 유행하는 지역에서 현지인과 밀접하게 접촉이 예상되는 여행자 또는 체류자

8) b형 헤모필루스 인플루엔자 위험군: 침습성 Hib 감염 고위험군인 기능적·해부학적 무비증, 보체결핍, 겸상적혈구빈혈증, 조혈모세포 이식 환자

[백신별 접종 기준] ※ 상세내용은 2장 '감염병별 예방접종' 참조

- **인플루엔자 백신:** '(고시) 예방접종의 실시기준 및 방법'에 따라 만 50세 이상 성인 및 연령에 상관없이 위험군에 대해 매년 1회 접종 ※ 만 65세 이상 성인은 국가예방접종사업 대상으로 무료접종 가능
- **파상풍/디프테리아/백일해 백신:** 모든 연령 성인에 대해 Tdap으로 1회 접종, 이 후 매 10년마다 Td 1회 접종
- **폐렴구균 23가 다당 백신(PPSV23):** 만 65세 이상 성인 및 폐렴구균 감염 위험군에 대해 1회 접종
  ※ 만 65세 이상 성인은 국가예방접종 대상으로 보건소(보건지소)에서 무료접종 가능
- **폐렴구균 단백결합 백신(PCV13):** 폐렴구균 감염 위험군 중 면역저하자, 기능적·해부학적 무비증, 뇌척수액누출, 인공와우이식 환자에 대해 접종
- **A형간염 백신:** 면역의 증거가 없는 만 20~39세 성인 또는 위험군에 대해 2회 접종
- **B형간염 백신:** 면역의 증거가 없는 성인 또는 위험군에 대해 항체 검사 후 3회 접종
- **수두 백신:** 면역의 증거가 없는 1970년 이후 출생자 또는 위험군에 대해 항체검사 후 2회 접종
- **홍역/유행성이하선염/풍진 백신:** 면역의 증거가 없는 1968.1.1일 이후 출생자(홍역) 및 위험군에 대해 항체검사 확인 후 접종하거나 비용을 고려하여 검사 없이 접종할 수도 있음
  ※ 의료인은 진료 중 노출 위험과 감염 시 의료기관 내 환자에게 전파할 위험이 높아 2회 접종을 권고
- **사람유두종바이러스 감염증 백신:** 이전에 예방접종을 완료하지 못한 만 25~26세 이하 여성에 대해 3회 접종
- **대상포진 백신:** 만 60세 이상 성인을 대상으로 접종. 과거 대상포진을 앓은 경우 자연면역을 얻는 효과가 있으나 예방접종을 원하는 경우 접종 가능(최소 6~12 개월 경과 후 접종 권장)
- **수막구균 백신:** 위험군에 대해 1회(정상면역이나 노출위험 있는 경우) 또는 2회(해부학적 또는 기능적 무비증, 보체결핍, HIV 감염인) 접종
- **b형 헤모필루스 인플루엔자 백신:** 위험군에 대해 1회 또는 3회(조혈모세포이식환자) 접종

대상감염병	백신종류	만 19~29세	만 30~39세	만 40~49세	만 50~59세	만 60~64세	만 65세 이상
인플루엔자[1]	Flu	위험군에 대해 매년 1회			매년 1회		
파상풍/디프테리아/백일해	Tdap/Td	Tdap으로 1회 접종, 이후 매 10년 마다 Td 1회					
폐렴구균[2]	PPSV23	위험군에 대해 1회 또는 2회					1회
	PCV13	위험군 중 면역저하자, 무비증, 뇌척수액누출, 인공와우 이식 환자에 대해 1회					
A형간염[3]	HepA	2회		항체검사 후 2회	위험군에 대해 항체검사 후 2회 접종		
B형간염[4]	HepB	위험군 또는 3회 접종/감염력이 없을 경우 항체 검사 후 3회 접종					
수두[5]	Var	위험군 또는 접종력/감염력이 없을 경우 항체검사 후 2회 접종					
홍역/유행성 이하선염/풍진[6]	MMR	위험군 또는 접종력/감염력이 없을 경우 1회 또는 2회 접종 ; 가임 여성은 풍진 항체 검사 후 접종					
사람유두종 바이러스 감염증	HPV	만 25~26세 이하 여성 총 3회					
대상포진	HZV					1회	
수막구균[7]	MCV4	위험군에 대해 1회 또는 2회					
B형 헤모필루스 인플루엔자[8]	Hib	위험군에 대해 1회 또는 3회					

연령 권장 : 면역의 증거가 없는(과거 감염력이 없고 예방접종력이 없거나 불확실) 대상 연령의 성인에게 권장됨
※ 연령권장의 경우에도 해당 질병의 위험군(각주 참고)에게는 접종을 더욱 권장함
위험군 권장 : 특정 기저질환, 상황 등에 따라 해당 질병의 위험군에게 권장
국가예방접종사업으로 무료접종

표 1-2. 건강한 성인에게 일반적으로 권장되는 예방접종

예방접종 종류	접 종 대 상
인플루엔자	만 50세 이상 성인 (매년 1회 접종)
폐렴구균[1]	만 65세 이상 성인
파상풍 · 디프테리아 · 백일해 (Tdap 또는 Td)[2]	모든 성인 (매 10년마다 접종)
대상포진[3]	만 60세 이상 성인
A형간염[4]	만 20~39세 성인

1) 폐렴구균 23가 다당 백신으로 1회 접종
2) 이전에 Tdap 접종력이 없는 경우 처음 1회는 Tdap으로 접종 이후 Td 접종
3) 대상포진을 앓은 경우 자연면역을 얻는 효과가 있으나 예방접종을 원하는 경우 접종 가능하며, 최소 6~12 개월이 경과한 후 접종하는 것을 권장
4) 6개월 이상 간격으로 2회 접종

3 질환(상황)에 따른 성인 예방접종 권장표

질환(상황)에 따라 접종 필요성이 강조
다른 권고기준(연령, 위험인자 등)에 해당할 경우 접종
금기
고려할 필요 없음

구분	당뇨병	만성 심혈관 질환	만성 폐질환	만성 신질환	만성 간질환	항암 치료 중인 고형암	이식 이외 면역 억제제 사용	장기 이식	조혈 모세포 이식	무비증	HIV 감염 CD4 <200/㎕	HIV 감염 CD4 ≥200/㎕	임신부
인플루엔자 (Flu)													
폐렴구균 (PPSV)													가)
폐렴구균 (PCV)													
파상풍/디프테리아 (백일해) (Tdap/Td)								Tdap	Tdap				나)
A형간염 (HepA)								다)					
B형간염 (HepB)													
수두 (Var)									라)				
홍역/유행성 이하선염/풍진 (MMR)									라)				
대상포진 (HZV)													
수막구균 (MCV4)													
b형헤모필루스 인플루엔자(Hib)													
폴리오(IPV)													

가) 폐렴구균 위험군의 경우 가능한 임신 전 접종을 권고하나 임신 중 폐렴구균 감염예방백신이 필요시 PPSV23으로 접종 가능
나) 임신 전 접종력이 없는 경우, 임신 중 27~36주 사이 접종, 임신 중 접종하지 못한 경우 분만 후 신속하게 접종
다) 간이식 환자에서는 A형간염 접종이 필요
라) 이식한지 24개월을 초과하였고, 이식편대숙주반응이 없는 경우에 접종을 고려할 수 있음

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2014 성인예방접종 개정 권고안

01. 폐렴사슬알균 백신

〈폐렴사슬알균 백신의 권장대상과 접종 시기〉

가. 건강한 65세 이상의 고령자: 13가 단백결합 백신 또는 23가 다당류 백신을 접종한다.

나. 65세 이상 만성질환자(만성 심혈관 질환, 만성 폐질환, 당뇨병, 알코올 중독, 만성 간질환)

(그림 1)

1) 과거에 어떤 종류의 폐렴사슬알균 백신도 접종한 적이 없는 65세 이상 만성질환자: 13가 단백결합 백신을 먼저 접종하고 6–12개월이 지난 후에 23가 다당류 백신을 접종한다. 13가 단백결합 백신 접종과 23가 다당류 백신의 동시접종은 피해야 하며 최소 8주 이상 간격을 두어야 한다.

2) 과거에 13가 단백결합 백신을 접종받은 65세 이상 만성질환자: 13가 단백결합 백신의 재접종은 필요하지 않으며 23가 다당류 백신으로 1회에 한하여 추가 접종한다.

3) 과거에 13가 단백결합 백신을 접종받지 않았으나 23가 다당류 백신을 접종 받은 65세 이상 만성질환자

- 65세 이전에 23가 다당류 백신을 접종받은 경우: 13가 단백결합 백신은 과거 23가 다당류 백신 접종으로부터 1년 이상 간격을 두고 접종해야 한다. 23가 다당류 백신을 1회에 한하여 재접종하며 과거 23가 다당류 백신 접종으로부터 5년 이상, 13가 단백결합 백신 접종으로부터 6–12개월(최소 8주 이상) 간격을 두고 재접종해야 한다.
- 65세 이후에 23가 다당류 백신을 접종받은 경우: 과거 23가 다당류 백신 접종으로부터 1년 이상 간격을 두고 13가 단백결합 백신을 접종한다. 23가 다당류 백신의 추가 접종은 권고하지 않는다.

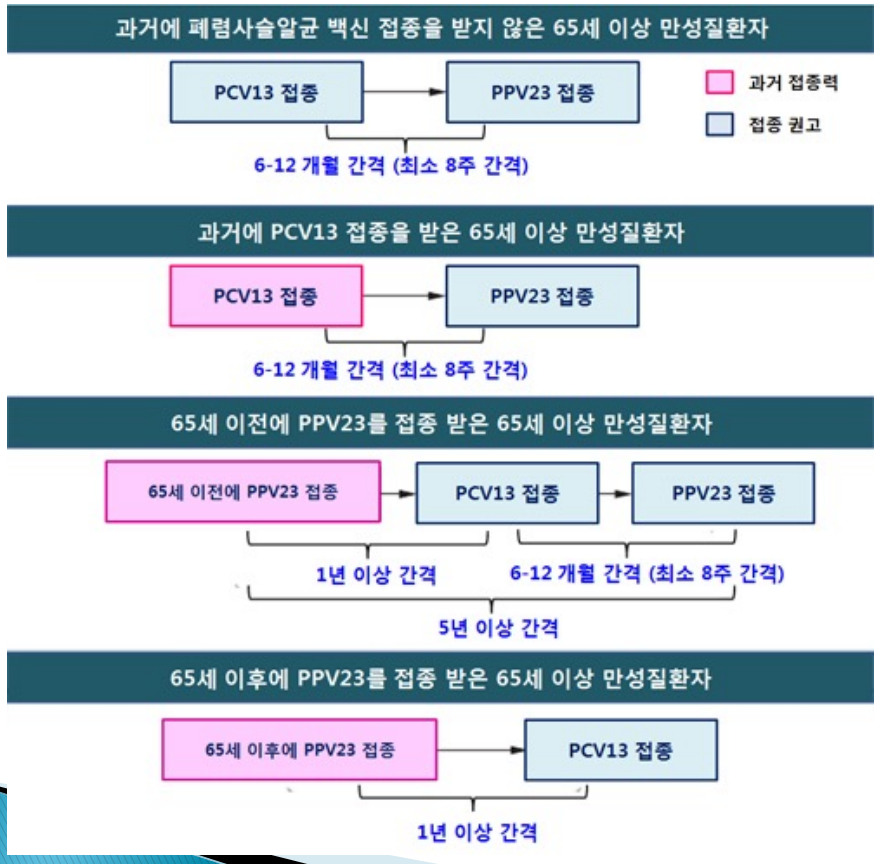
다. 18–64세 만성질환자(만성 심혈관 질환, 만성 폐질환, 당뇨병, 알코올 중독, 만성 간질환): 13가 단백결합 백신을 우선적으로 접종하고, 13가 단백결합 백신을 접종할 수 없다면 23가 다당류 백신을 접종한다.

라. 18세 이상의 면역저하환자(선천성 또는 후천성 면역 저하, HIV 감염, 만성 신부전 또는 신증후군, 백혈병, 림프종, 호지킨씨 병, 종양질환, 장기간 스테로이드를 포함하는 면역억제제를 투여하거나 방사선 치료를 받고 있는 환자, 장기 이식환자)와 기능적 또는 해부학적 무비증, 뇌척수액 누수, 인공와우를 삽입한 환자

1) 폐렴사슬알균 백신 접종력이 없는 경우: 13가 단백결합 백신을 먼저 접종하고, 최소 8주가 지난 후에 23가 다당류 백신을 접종한다.

2) 23가 다당류 백신을 1회 접종한 경우: 23가 다당류 백신 접종 후 최소 1년의 기간이 지난 후 13가 단백결합 백신을 접종한다. 13가 단백결합 백신 접종 후 최소 8주 경과하였고 23다 다당류 백신 접종 후 5년 이상 경과하였다면 23가 다당류 백신을 접종한다.

3) 23가 다당류 백신을 2회 접종한 경우: 마지막 접종 후 최소 1년이 경과한 시점에서 13가 단백결합 백신을 1회 접종한다.



02. 파상풍-디프테리아-백일해 백신

〈임산부 또는 임신 예정인 여성에 대한 파상풍-디프테리아-백일해 백신 접종 권고〉

가. 성인형 파상풍-디프테리아-백일해(Tdap) 백신의 접종력이 없는 여성은 출산 직후에, 혹은 임신 전에 1회 접종하도록 권고한다. 임신 27-36주의 임신부에게도 접종할 수 있다.

03. 대상포진 백신

〈대상포진 백신의 권장대상과 접종 시기〉

가. 60세 이상 성인은 금기사항이 없는 한 대상포진 백신의 접종을 권고한다.

나. 50-59세 성인은 개별 피접종자의 상태에 따라 대상포진 백신의 접종 여부를 결정한다.

04. 인유두종바이러스 백신

〈남성에 대한 인유두종바이러스 백신 접종 권고〉

가. 9-26세 남성은 항문암, 생식기사마귀 및 전암성 또는 이형성병변의 예방을 위해 4가 인유두종바이러스 백신 접종이 가능하다.

연령별 성인예방접종표

	만 19-29세	만 30-39세	만 40-49세	만 50-59세	만 60-64세	만 65세 이상
인플루엔자[1]						
폐렴사슬알균[2]						
파상풍-디프테리아-백일해[3]						
대상포진[4]						
A형간염[5]						
B형간염[6]						
수두[7]						
홍역-볼거리-풍진[8]						
인유두종바이러스[9]						

해당 연령군에서 면역의 증거(백신 접종력, 과거 감염력, 또는 항체 검사 양성)가 없는 경우

해당 연령군 중 고위험군(해당 기저질환이나 상황)에서 면역의 증거(백신 접종력, 과거 감염력, 또는 항체 검사 양성)가 없는 경우

고려할 필요 없음

1. **인플루엔자**: 모든 성인은 매년 10-11월에 1회 접종
2. **폐렴사슬알균**: 건강한 65세 이상 고령자는 23가 다당류백신(PPSV23)을 1회 접종하거나, 13가 단백결합백신(PCV13)과 PPSV23을 순차적으로 1회씩 접종. 65세 미만 고위험군은 PCV13과 PPSV23을 순차적으로 접종. PCV13은 1회 접종. 65세 이전에 PPSV23을 접종한 경우에는 피접종자의 상태에 따라 5년 이상의 간격을 두고 1-2회 PPSV23 재접종. PPSV23의 최초 접종 연령이 65세 미만인 만성질환자, 뇌척수액누수, 인공와우 삽입 환자는 65세 이후가 되고 이전 PPSV23 접종 후 5년 이상 경과한 경우에 1회 재접종하여 PPSV23을 총 2회 접종. PPSV23의 최초 접종 연령이 65세 미만인 면역저하자와 무비증 환자는 최초 PPSV23 접종 후 5년이 지나서 1회 재접종. PPSV23을 재접종 하는 나이가 65세가 넘으면 2회 접종으로 완료. PPSV23을 재접종 하는 나이가 65세 미만이면, 65세가 넘어 가장 최근 PPSV23 접종 후 5년이 지나 한 번 더 재접종 하여 PPSV23을 총 3회 접종. PCV13과 PPSV23을 순차적으로 접종하는 경우에 서로 간의 접종 간격은 최소 1년. 면역저하자와 뇌척수액누수, 인공와우 삽입 환자는 PCV13과 PPSV23의 접종 간격 최소 8주
3. **파상풍-디프테리아-백일해**: 소아 표준예방접종 지침에 따라 과거 소아용 디프테리아-파상풍-백일해 백신(DTP) 접종을 받은 18세 이상의 성인은 매10년마다 성인용 파상풍-디프테리아 백신(Td) 1회 접종이 필요하며, 성인용 파상풍-디프테리아-백일해 백신(Tdap)을 한 번도 접종받지 않았다면 이 중 한 번은 Td 대신 Tdap을 접종. 18세 이상의 성인에서 소아기 DTP 접종을 받지 않았거나, 기록이 분명치 않은 경우, 또는 1958년(국내 DTP 도입 시기) 이전 출생자의 경우에는 기초접종 3회를 하되, Tdap을 첫 번째로 접종하고 4-8주 후 Td, 이후 6-12개월 뒤 다시 Td를 접종함(첫 번째에 Td를 접종하였다면 이후 두 번째 혹은 세 번째 일정 중 한 번을 Tdap으로 접종). 이후 매10년마다 Td를 추가접종
4. **대상포진**: 60세 이상 성인은 생백신 1회 접종. 50-59세 성인은 개별 피접종자의 상태에 따라 대상포진이나 대상포진 후 신경통에 따른 통증에 민감하게 반영할 것으로 예상되는 경우 1회 접종
5. **A형간염**: A형간염의 고위험군은 6-18개월 간격으로 2회 접종. 국내 A형간염 유행과 역학을 고려하여 A형간염의 고위험군이 아니더라도 40세 미만에서는 항체검사결과 없이, 40세 이상에서는 항체검사 후 음성일 경우 백신 접종 권고
6. **B형간염**: B형간염백신 미접종 성인, B형간염 고위험군 중 백신 미접종자는 0, 1, 6개월의 간격으로 3회 접종
7. **수두**: 1970년 이후 출생자, 학생, 군인, 의료기관종사자, 학교 및 유치원 교사, 해외여행자, 고위험군(면역저하자)과 자주 접촉하는 사람, 가임기 여성 중 면역이 없는 사람은 4-8주 간격으로 2회 접종
8. **홍역-볼거리-풍진**: 1967년 이후 출생 성인 중 홍역에 대한 면역이 없고 건강한 일반 성인은 적어도 1회 MMR 접종. 홍역 노출 고위험군이거나 중증 합병증 발생 위험이 높은 성인이 홍역에 대한 면역 추정 증거가 없다면 최소 28일 간격을 두고 2회 MMR 접종. 볼거리에 대한 면역이 없는 일반 성인은 적어도 1회 MMR 접종. 볼거리 노출 고위험군이 볼거리에 대한 면역이 없는 경우 최소 28일 간격을 두고 2회 MMR 접종. 풍진에 대한 면역이 없는 성인은 MMR 1회 접종
9. **인유두종바이러스**: 26세 이하 성인 여성과 21세 이하 성인 남성은 3회 접종. HIV 감염인을 포함한 면역저하자, 남성 동성애자의 경우 26세까지 접종

상황별 성인예방접종표

	당뇨병	만성심혈관 질환	만성폐질환	만성신질환	만성간질환	항암 치료 중인 고형암	이식 이외 면역억제제 사용	장기이식	조혈모 세포이식	무비증	HIV 감염 CD4 < 200/mm³	HIV 감염 CD4 ≥200/mm³	임신부	의료기관 종사자
인플루엔자[1]														
폐렴사슬알균[2]														
파상풍-디프테리아-백일해[3]														
대상포진(생백신)[4]														
A형간염[5]														
B형간염[6]														
수두[7]														
홍역-볼거리-풍진[8]														
인유두종바이러스[9]														
수막알균[10]														
일본뇌염[11]														
b형 헤모필루스 인플루엔자[12]														

연령 기준에 부합하고 면역의 증거(백신 접종력, 과거 감염력, 또는 항체검사 양성)가 없는 경우, 필요성이 강조되는 백신
일반적인 권고기준에 따름
고려할 필요 없음
금기

1. **인플루엔자**: 매년 10–11월에 1회 접종. 단, 항암치료 중인 고형암, 면역억제제 사용, 장기이식, 조혈모세포이식, CD4 < 200/mm³인 HIV 감염인, 임신부는 생백신 금기. 임신부는 임신 주수에 관계없이 10–11월에 접종
2. **폐렴사슬알균**: 13가 단백결합백신(PCV13)과 23가 다당류백신(PPSV23)을 순차적으로 접종. PCV13은 1회 접종. 65세 이전에 PPSV23을 접종한 경우에는 피접종자의 상태에 따라 5년 이상의 간격을 두고 1–2회 PPSV23 재접종. PPSV23의 최초 접종 연령이 65세 미만인 만성질환자, 뇌척수액누수, 인공와우 삽입 환자는 65세 이후가 되고 이전 PPSV23 접종 후 5년 이상 경과한 경우에 1회 재접종하여 PPSV23을 총 2회 접종. PPSV23의 최초 접종 연령이 65세 미만인 면역저하자와 무비증 환자는 최초 PPSV23 접종 후 5년이 지나서 1회 재접종. PPSV23을 재접종 하는 나이가 65세가 넘으면 2회 접종으로 완료. PPSV23을 재접종 하는 나이가 65세 미만이면, 65세가 넘어 가장 최근 PPSV23 접종 후 5년이 지나 한 번 더 재접종 하여 PPSV23을 총 3회 접종. PCV13과 PPSV23을 순차적으로 접종하는 경우에 서로 간의 접종 간격은 최소 1년. 면역저하자와 뇌척수액누수, 인공와우 삽입 환자는 PCV13과 PPSV23의 접종 간격 최소 8주
3. **파상풍-디프테리아-백일해**: 소아 표준예방접종 지침에 따라 과거 소아용 디프테리아-파상풍-백일해 백신(DTP) 접종을 받은 18세 이상의 성인은 매10년마다 성인용 파상풍-디프테리아 백신(Td) 1회 접종이 필요하며, 성인용 파상풍-디프테리아-백일해 백신(Tdap)을 한 번도 접종받지 않았다면 이 중 한 번은 Td 대신 Tdap을 접종. 18세 이상의 성인에서 소아기 DTP 접종을 받지 않았거나, 기록이 분명치 않은 경우, 또는 1958년(국내 DTP 도입 시기) 이전 출생자의 경우에는 기초접종 3회를 하되, Tdap을 첫 번째로 접종하고 4–8주 후 Td, 이후 6–12개월 뒤 다시 Td를 접종함(첫 번째에 Td를 접종하였다면 이후 두 번째 혹은 세 번째 일정 중 한 번을 Tdap으로 접종). 이후 매10년마다 Td를 추가접종. 조혈모세포이식 환자는 소아용 백신(DTaP)으로 3회 기초 접종. 임신부는 매 임신 27–36주에 Tdap 접종. 임신 중 Tdap을 접종하지 않은 경우 출산 직후 접종
4. **대상포진**: 항암치료 중인 고형암, 면역억제제 사용, 장기이식, 조혈모세포이식, CD4 < 200/mm³인 HIV 감염인, 임신부는 생백신 금기
5. **A형간염**: 고위험군(A형간염 유행지역 여행자나 장기 체류자, A형간염 환자와 접촉하는 자, A형간염바이러스를 다루는 실험실 종사자, 직업적으로 노출될 위험이 있는 자, 혈액응고 질환자, 만성 간 질환자, 약물 남용자, 남성 동성애자)은 6–18개월 간격으로 2회 접종. 국내 A형간염 유행과 역학을 고려하여 A형간염의 고위험군이 아니더라도 40세 미만에서는 항체검사결과 없이, 40세 이상에서는 항체검사 후 음성일 경우 백신 접종 권고
6. **B형간염**: B형간염백신 미접종 성인, B형간염 고위험군(HBs항원 양성자의 배우자, 동성애자, 약물남용자, HBs항원 양성자의 가족 접촉자, 발달장애자 시설 근무자, 혈액 또는 혈액이 오염된 체액 노출 고위험 의료종사자, 혈액 또는 복막 투석을 포함한 말기신부전 환자, B형간염 토착지역 여행자, 만성 간 질환자, HIV 감염인) 중 백신 미접종자는 0, 1, 6개월의 간격으로 3회 접종
7. **수두**: 1970년 이후 출생자, 학생, 군인, 의료기관종사자, 학교 및 유치원 교사, 해외여행자, 고위험군(면역저하자)과 자주 접촉하는 사람, 가임기 여성 중 면역이 없는 사람은 4–8주 간격으로 2회 접종. 단, 항암치료 중인 고형암, 면역억제제 사용, 장기이식, 조혈모세포이식, CD4 < 200/mm³인 HIV 감염인, 임신부는 생백신 금기. 조혈모세포이식 환자는 이식 24개월 이후이고 면역억제제를 중지한 경우에는 접종을 고려할 수 있음
8. **홍역-볼거리-풍진**: 1967년 이후 출생 성인 중 홍역에 대한 면역이 없고 건강한 일반 성인은 적어도 1회 MMR 접종. 홍역 노출 고위험군이거나 중증 합병증 발생 위험이 높은 성인이 홍역에 대한 면역 추정 증거가 없다면 최소 28일 간격을 두고 2회 MMR 접종. 볼거리에 대한 면역이 없는 일반 성인은 적어도 1회 MMR 접종. 볼거리 노출 고위험군이 볼거리에 대한 면역이 없는 경우 최소 28일 간격을 두고 2회 MMR 접종. 풍진에 대한 면역이 없는 성인은 MMR 1회 접종. 단, 항암치료 중인 고형암, 면역억제제 사용, 장기이식, 조혈모세포이식, CD4 < 200/mm³인 HIV 감염인, 임신부는 생백신 금기. 조혈모세포이식 환자는 이식 24개월 이후이고 면역억제제를 중지한 경우에는 접종을 고려할 수 있음. 의료기관종사자는 출생연도와 무관하게 면역의 증거가 없다면 2회 MMR 접종
9. **인유두종바이러스**: 26세 이하 성인 여성과 21세 이하 성인 남성은 3회 접종. HIV 감염인을 포함한 면역저하자, 남성 동성애자의 경우 26세까지 접종
10. **수막알균**: 고위험군(무비증, 보체결핍 환자, 신입훈련병, 직업적으로 수막알균에 노출되는 실험실 근무자, 수막알균 감염증 유행지역에서 현지인과 밀접한 접촉이 예상되는 여행자 또는 체류자, 기숙사에 거주하는 대학교 신입생)은 단백결합 백신 1회 접종. 단, 무비증, 보체결핍 환자, HIV 감염인에게 접종하는 경우 2개월 간격으로 2회 접종. 수막알균 감염 위험이 지속되는 고위험군은 5년마다 재접종
11. **일본뇌염**: 고위험군(논, 돼지 축사 인근에 거주하거나 일본뇌염 전파시기에 유행지역에서 활동 예정인 성인, 비토착지역에서 이주하여 국내에 장기 거주할 면역이 없는 성인, 일본뇌염 감염 위험이 높은 해외여행자, 일본뇌염 관련 연구를 하는 실험실 근무자)은 약독화 재조합바이러스 생백신 1회 접종 또는 불활화백신 3회 접종. 단, 항암치료 중인 고형암, 면역억제제 사용, 장기이식, 조혈모세포이식, CD4 < 200/mm³인 HIV 감염인, 임신부는 생백신 금기.
12. **b형 헤모필루스 인플루엔자**: 고위험군(무비증, 보체 및 면역 결핍, 조혈모세포이식)은 1회 접종하되, 이 중 조혈모세포이식 환자는 3회 접종

01

예방접종의 일반 원칙

1

Q1. 여러 가지 백신을 같은 날 접종해도 되나요?

일반적으로 대부분의 백신은 동시접종(같은 날에 2개 이상의 백신을 서로 다른 부위에 접종하는 것)을 하더라도 예방효과가 감소하거나 이상반응이 증가하지 않는 것으로 알려져 있습니다. 따라서 같은 날 여러 가지 백신을 동시에 접종하는 것은 가능합니다. 단, 여러 가지 백신을 접종할 때, 각 백신을 한 개의 주사기에 넣어서 혼합하여 투여하면 안 됩니다. 또한 같은 사지에 두 가지 이상의 백신을 접종하는 경우에는 국소 이상반응을 구분할 수 있도록 1인치(2.5 ㎝) 이상 떨어뜨려서 접종해야 합니다. 만약 동시접종을 하지 못해서 서로 다른 날짜에 접종해야 하는 경우, 생백신과 불활화 백신, 불활화 백신과 불활화 백신 사이에는 접종 간격의 특별한 제한은 없으나, 생백신과 생백신 사이에는 4주 이상의 간격이 필요합니다.

Q2. 같은 날 동시에 접종하면 안 되는 백신이 있나요?

주사용 불활화 콜레라 백신과 황열 백신의 동시접종은 금기로 되어 있습니다. 이는 두 백신을 동시에 접종하는 경우 황열 백신에 대한 면역반응이 감소하기 때문입니다. 대상포진 백신의 제품설명서에는 23가 다당질 폐렴사슬알균 백신과 대상포진 백신의 동시접종은 금지하는 것으로 설명되어 있습니다. 이는 이전 연구에서 대상포진 백신과 다당질 폐렴사슬알균 백신을 동시에 접종한 경우, 1개월 간격을 두고 접종한 경우에 비해 대상포진 백신 접종 후 항체가가 낮게 측정되었기 때문입니다. 그러나 그 이후 연구들에서 근거 없음이 확인되었고 미국 예방접종자문위원회(Advisory Committee on Immunization Practices, ACIP) 에서도 동시접종에 문제가 없음을 발표하였습니다.

2

Q7. 2회 이상 접종해야 하는 백신의 경우, 서로 다른 회사의 제품으로 접종해도 되나요?

같은 제조사의 백신을 접종하는 게 바람직합니다. 다만, b형 헤모필루스 인플루엔자 백신, B형간염 백신, A형간염 백신의 경우 제조사가 다른 제품으로 교차접종을 하더라도 항체 양전률이나 면역원성에 영향을 미치지 않습니다. 그러나 DTaP, 로타바이러스 백신, 인유두종바이러스 백신의 경우 효율성, 독성 및 안전성에 대한 표준화가 이루어지지 않았으며 교차접종에 대한 연구 결과가 제한적이어서 교차접종은 권고하지 않습니다.

단, 이전 제조사의 백신을 구할 수 없거나 이전에 접종 받았던 백신의 종류를 알 수 없는 경우에는 교차접종이 가능합니다.

Q8. 2회 이상 접종해야 하는 백신의 경우, 차기 백신 접종 예정일이 지났다면 처음부터 다시 접종해야 하나요?

일반적으로 권고되는 기간보다 접종 간격이 길어졌다고 해서 처음부터 다시 시작하거나 부가적인 접종을 할 필요는 없으며 남은 차수만 접종하면 됩니다.

단, 경구용 장티푸스 백신의 경우는 예외로, 일부 전문가들은 총 4회의 접종 일정이 3주가 초과되게 미루어졌을 때에는 접종을 처음부터 다시 시작하도록 권고하고 있습니다.

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Q9. 2회 이상 접종해야 하는 백신의 경우, 차기 백신 접종 예정일보다 당겨서 접종하면 어떻게 되나요?

권장되는 접종 간격을 지켰을 때 가장 적절한 예방효과를 기대할 수 있으며 효과가 가장 좋습니다. 다만, 불가피하게 백신 접종간격을 짧게 접종해야 하는 경우에는 최소 접종간격을 이용한 가속접종 계획(accelerated schedule)을 이용할 수 있습니다. 그러나 평상시에는 가속접종 계획을 사용해서는 안 됩니다.

만약 최소 접종간격보다 5일 이상 앞당겨서 접종되었다면 해당 차수의 백신 접종은 무효로 간주하고 다시 접종해야 합니다. 재접종 시에는 부적절한 접종 시점으로부터 최소 접종간격을 지켜서 다시 접종해야 합니다.

Q10. 임신부나 수유부도 예방접종이 가능한가요?

임신부에게 생백신은 금기이며 불활화 백신은 필요에 따라 접종할 수 있습니다. 생백신은 태아에게 바이러스가 전달될 수 있다는 이론적인 위험성 때문에 임신부에게 투여하지 않습니다. 이에 비해 불활화 백신은 체내에서 증식하지 않기 때문에 태아에게 감염을 일으키지 않으므로 필요에 따라 임신부에게 접종 가능합니다.

임신부는 인플루엔자에 걸릴 경우 합병증이 발생할 위험이 높은 고위험군입니다. 따라서 불활화 백신 중에서도 인플루엔자 백신은 인플루엔자 유행 시기에 임신 계획이 있거나 임신 중인 여성은 모두 접종 받아야 합니다.

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Q11. 성인에게 소아용 백신을 접종해서 원래 투여되어야 하는 용량보다 절반만 들어갔습니다. 이 경우 재접종을 해야 하나요?

적정량의 백신이 접종되지 않은 경우 충분한 면역반응이 유발되지 않을 가능성이 있으므로 재접종 하는 것이 바람직합니다. 단, 불활화 백신의 경우 간격에 상관없이 재접종 할 수 있으나 생백신의 경우 4주 이상의 간격을 두고 재접종 해야 합니다.

Q12. 성인에게 둔부나 대퇴부에 백신을 접종해도 되나요?

백신 접종 부위는 연령에 따른 근육발달에 맞추어 권고하게 됩니다. 성인의 경우 피하 접종 시 상완 상부 외측, 근육접종이나 피내접종 시에는 상완의 삼각근 부위를 이용하도록 되어 있습니다. 만약 성인에게 둔부나 대퇴부에 백신을 접종하는 경우 적절한 부위에 백신이 투여되지 않아 충분한 면역반응을 유도하지 못하거나 이상반응이 증가할 수 있으며 좌골신경 손상 등의 문제가 발생할 수 있습니다. 따라서 성인은 불가피한 상황이 아니라면 상완에 백신을 접종해야 합니다.

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Q13. 피하접종 해야 하는 백신을 근육주사 한 경우 어떻게 해야 하나요?

피하접종 해야 하는 백신을 근육주사 하게 되면 충분한 면역반응을 유도하지 못하거나 이상반응이 증가할 수 있습니다. 그러나 피하접종 해야 하는 백신을 실수로 근육주사 했더라도 재접종 하는 것은 권고되지 않습니다. 단, 백신 접종 후 이상반응이 발생하지 않는지 주의 깊게 관찰할 필요가 있습니다.

Q14. 계란을 먹으면 가벼운 발진이 생기는 사람에게 백신을 접종해도 되나요?

계란에 대한 아나필락시스 또는 아나필락시스양 알레르기 반응이 생기는 사람은 계란 단백이 함유될 가능성이 있는 백신(예: 인플루엔자, 황열)은 접종 받으면 안 됩니다. 그러나 아나필락시스나 아나필락시스양 반응이 아니라면 백신 접종의 금기 사항이 아닙니다. 일반적으로 계란 또는 계란 함유 제품을 먹을 수 있는 사람이라면 계란 단백이 함유될 가능성이 있는 백신이라도 접종 가능합니다.

Q15. 계란은 아니지만 다른 음식에 알레르기가 있는 사람에게 백신을 접종해도 되나요?

백신에 포함되지 않은 성분에 대한 알레르기가 있는 사람은 백신 접종의 금기가 아닙니다. 따라서 백신 접종이 가능합니다.

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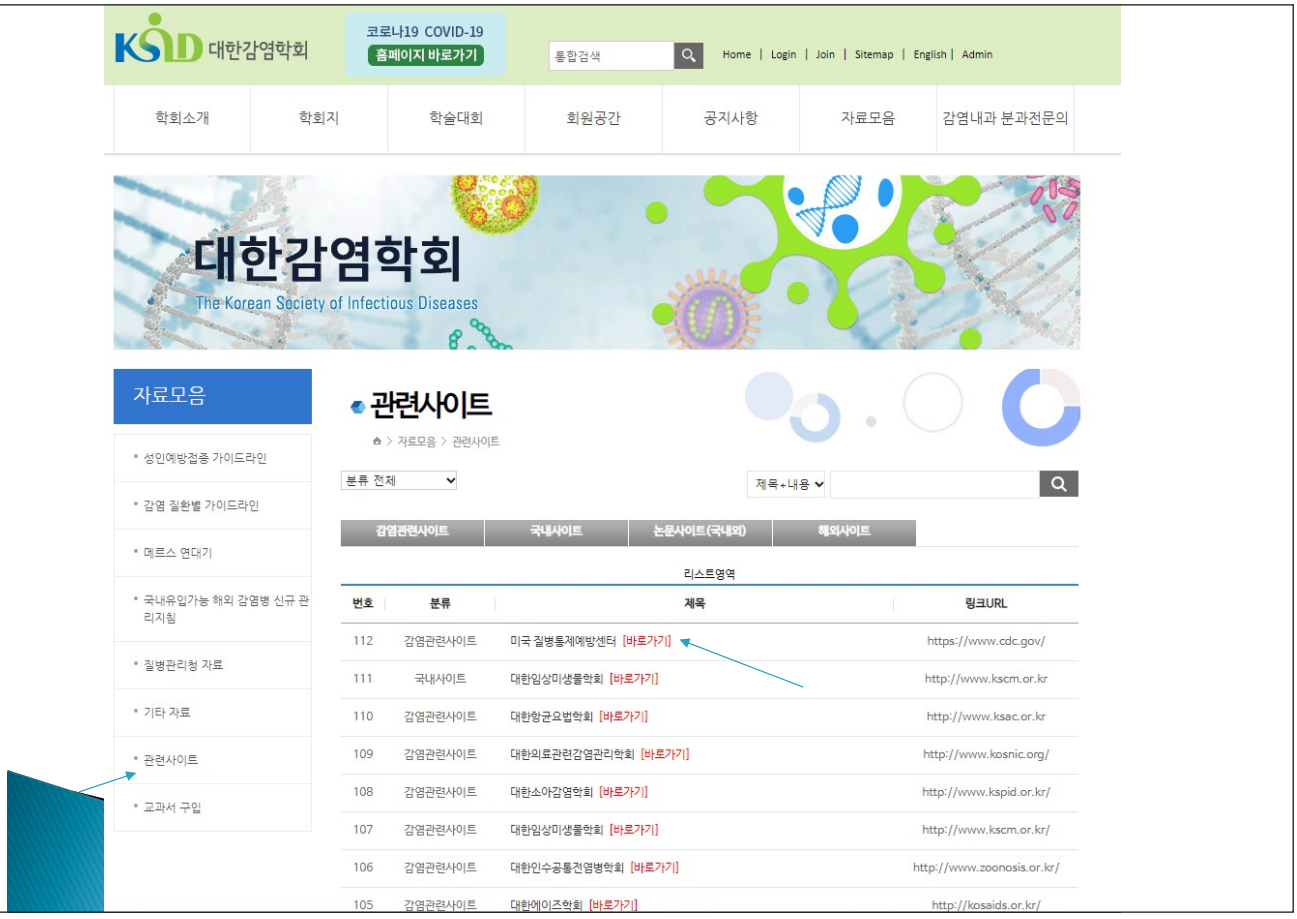

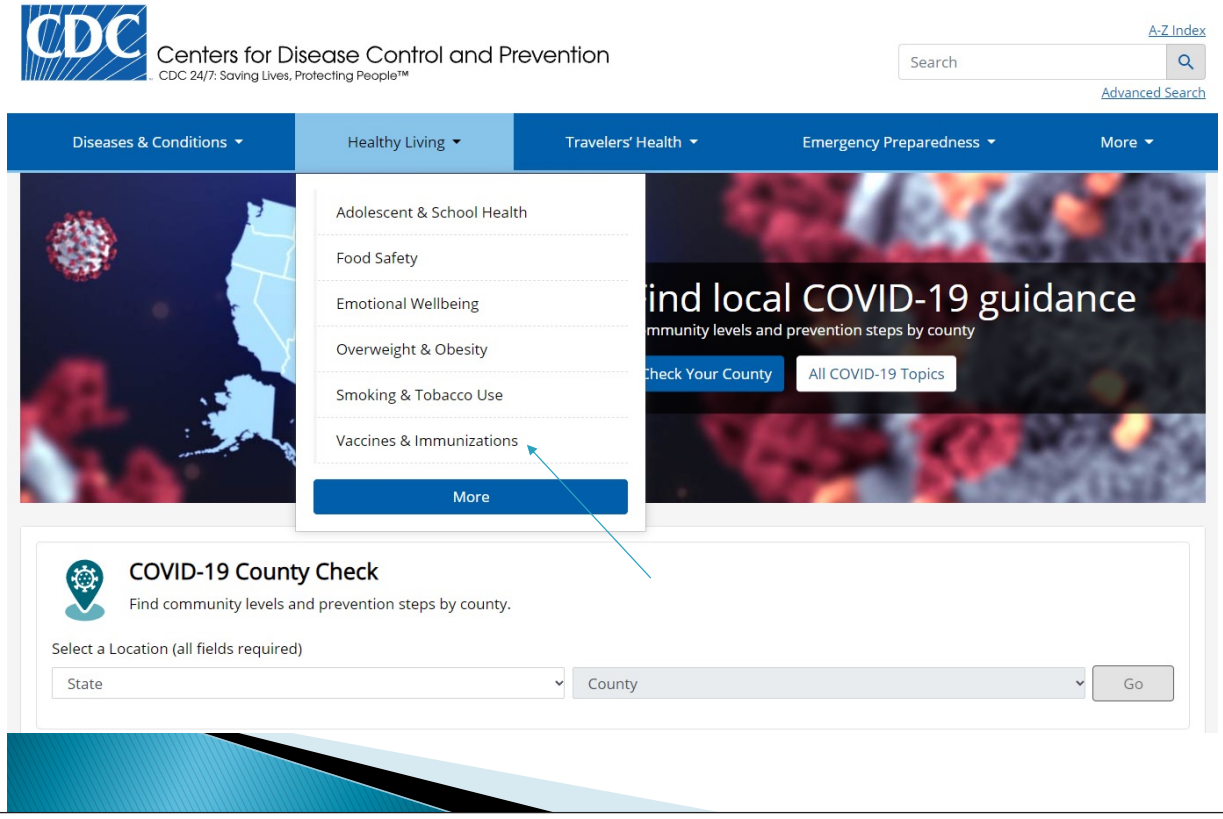
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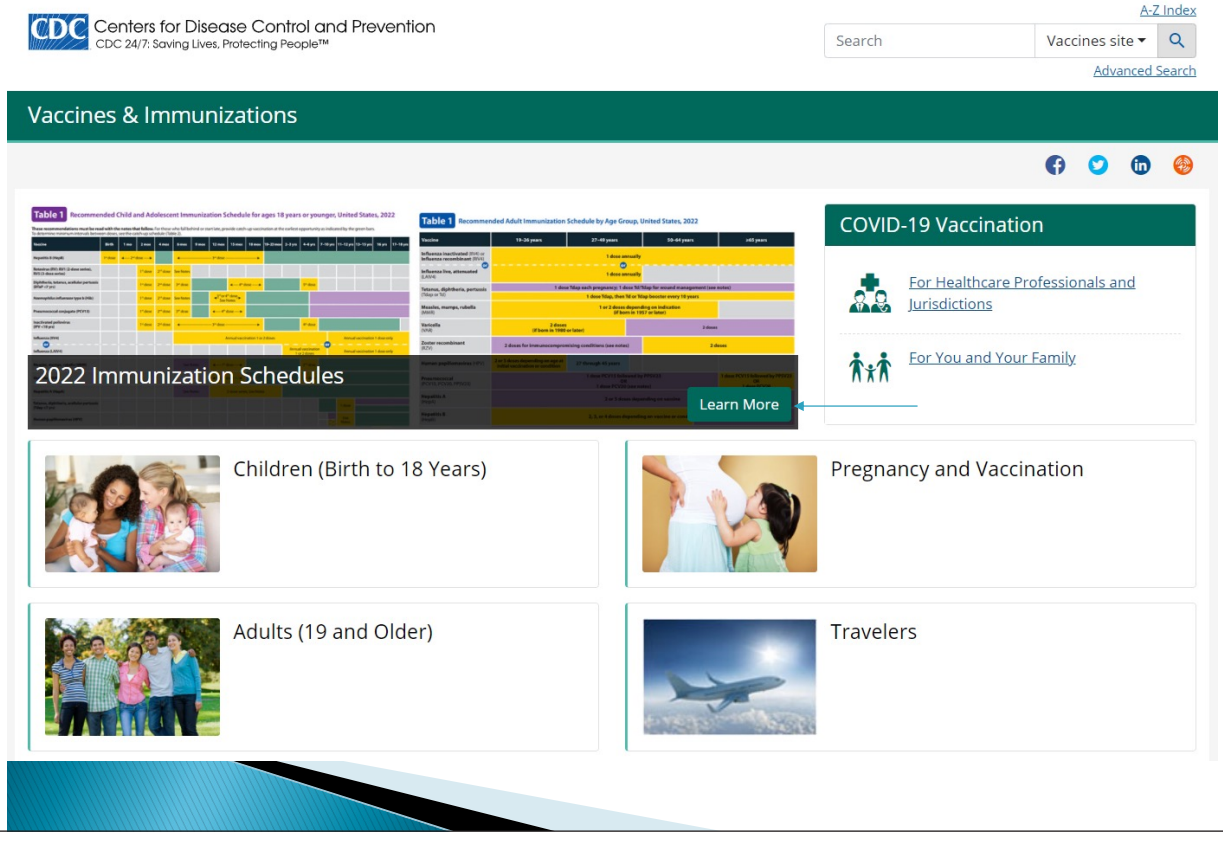
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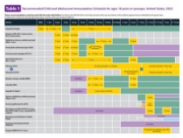
Immunization Schedules

For Healthcare Providers

Child and Adolescent Schedule
Recommended vaccination schedule for ages 18 years or younger
Birth to 18 Years



Adult Schedule
Recommended vaccination schedule for ages 19 years or older
19 Years or Older

Clinical Vaccination Resources
Download Schedule App for Healthcare Providers
Vaccination Resources for Healthcare Providers

Interim COVID-19 Immunization Schedule for Ages 5+
Guidance for COVID-19 vaccination schedules based on age and medical condition
COVID-19 Vaccination Schedule

For You and Your Family

Table 1 Recommended Child and Adolescent Immunization Schedule for ages 18 years or younger, United States, 2022

These recommendations must be read with the notes that follow. For those who fall behind or start late, provide catch-up vaccination at the earliest opportunity as indicated by the green bars.
To determine minimum intervals between doses, see the catch-up schedule (Table 2).

Vaccine	Birth	1 mo	2 mos	4 mos	6 mos	9 mos	12 mos	15 mos	18 mos	19–23 mos	2–3 yrs	4–6 yrs	7–10 yrs	11–12 yrs	13–15 yrs	16 yrs	17–18 yrs
Hepatitis B (HepB)	1st dose	◄— 2nd dose —►			◄— 3rd dose —►												
Rotavirus (RV): RV1 (2-dose series), RV5 (3-dose series)			1st dose	2nd dose	See Notes												
Diphtheria, tetanus, acellular pertussis (DTaP <7 yrs)			1st dose	2nd dose	3rd dose		◄— 4th dose —►					5th dose					
Haemophilus influenzae type b (Hib)			1st dose	2nd dose	See Notes		◄— 3rd or 4th dose, See Notes —►										
Pneumococcal conjugate (PCV13)			1st dose	2nd dose	3rd dose		◄— 4th dose —►										
Inactivated poliovirus (IPV <18 yrs)			1st dose	2nd dose	◄— 3rd dose —►							4th dose					
Influenza (IIV4)					Annual vaccination 1 or 2 doses									Annual vaccination 1 dose only			
or													or				
Influenza (LAIV4)											Annual vaccination 1 or 2 doses			Annual vaccination 1 dose only			
Measles, mumps, rubella (MMR)					See Notes		◄— 1st dose —►					2nd dose					
Varicella (VAR)							◄— 1st dose —►					2nd dose					
Hepatitis A (HepA)					See Notes		2-dose series, See Notes										
Tetanus, diphtheria, acellular pertussis (Tdap ≥7 yrs)														1 dose			
Human papillomavirus (HPV)														See Notes			
Meningococcal (MenACWY-D ≥9 mos, MenACWY-CRM ≥2 mos, MenACWY-TT ≥2years)			See Notes											1st dose		2nd dose	
Meningococcal B (MenB-4C, MenB-FHbp)														See Notes			
Pneumococcal polysaccharide (PPSV23)											See Notes						
Dengue (DEN4CYD; 9-16 yrs)														Seropositive in endemic areas only (See Notes)			

Range of recommended ages for all children
Range of recommended ages for catch-up vaccination
Range of recommended ages for certain high-risk groups
Recommended vaccination can begin in this age group
Recommended vaccination based on shared clinical decision-making
No recommendation/ not applicable

Table 2 Recommended Catch-up Immunization Schedule for Children and Adolescents Who Start Late or Who Are More than 1 Month Behind, United States, 2022

The table below provides catch-up schedules and minimum intervals between doses for children whose vaccinations have been delayed. A vaccine series does not need to be restarted, regardless of the time that has elapsed between doses. Use the section appropriate for the child's age. **Always use this table in conjunction with Table 1 and the Notes that follow.**

Vaccine	Minimum Age for Dose 1	Minimum Interval Between Doses			
		Dose 1 to Dose 2	Dose 2 to Dose 3	Dose 3 to Dose 4	Dose 4 to Dose 5
Children age 4 months through 6 years					
Hepatitis B	Birth	**4 weeks**	**8 weeks *and* at least 16 weeks after first dose** minimum age for the final dose is 24 weeks		
Rotavirus	6 weeks Maximum age for first dose is 14 weeks, 6 days.	**4 weeks**	**4 weeks** maximum age for final dose is 8 months, 0 days		
Diphtheria, tetanus, and acellular pertussis	6 weeks	**4 weeks**	**4 weeks**	**6 months**	**6 months**
Haemophilus influenzae type b	6 weeks	**No further doses needed** if first dose was administered at age 15 months or older. **4 weeks** if first dose was administered before the 1st birthday. **8 weeks (as final dose)** if first dose was administered at age 12 through 14 months.	**No further doses needed** if previous dose was administered at age 15 months or older **4 weeks** if current age is younger than 12 months ***and*** first dose was administered at younger than age 7 months ***and*** at least 1 previous dose was PRP-T (ActHib®, Pentacel®, Hiberix®), Vaxelis® or unknown **8 weeks *and* age 12 through 59 months (as final dose)** if current age is younger than 12 months ***and*** first dose was administered at age 7 through 11 months; OR if current age is 12 through 59 months ***and*** first dose was administered before the 1st birthday ***and*** second dose was administered at younger than 15 months; OR if both doses were PedvaxHIB® and were administered before the 1st birthday	**8 weeks (as final dose)** This dose only necessary for children age 12 through 59 months who received 3 doses before the 1st birthday.	
Pneumococcal conjugate	6 weeks	**No further doses needed** for healthy children if first dose was administered at age 24 months or older **4 weeks** if first dose was administered before the 1st birthday **8 weeks (as final dose for healthy children)** if first dose was administered at the 1st birthday or after	**No further doses needed** for healthy children if previous dose was administered at age 24 months or older **4 weeks** if current age is younger than 12 months and previous dose was administered at <7 months old **8 weeks (as final dose for healthy children)** if previous dose was administered between 7–11 months (wait until at least 12 months old); OR if current age is 12 months or older and at least 1 dose was administered before age 12 months	**8 weeks (as final dose)** This dose only necessary for children age 12 through 59 months who received 3 doses before age 12 months or for children at high risk who received 3 doses at any age.	
Inactivated poliovirus	6 weeks	**4 weeks**	**4 weeks** if current age is <4 years **6 months (as final dose)** if current age is 4 years or older	**6 months (minimum age 4 years for final dose)**	
Measles, mumps, rubella	12 months	**4 weeks**			
Varicella	12 months	**3 months**			
Hepatitis A	12 months	**6 months**			
Meningococcal ACWY	2 months MenACWY-CRM 9 months MenACWY-D 2 years MenACWY-TT	**8 weeks**	See Notes	See Notes	
Children and adolescents age 7 through 18 years					
Meningococcal ACWY	Not applicable (N/A)	**8 weeks**			
Tetanus, diphtheria; tetanus, diphtheria, and acellular pertussis	7 years	**4 weeks**	**4 weeks** if first dose of DTaP/DT was administered before the 1st birthday **6 months (as final dose)** if first dose of DTaP/DT or Tdap/Td was administered at or after the 1st birthday	**6 months** if first dose of DTaP/DT was administered before the 1st birthday	
Human papillomavirus	9 years	**Routine dosing intervals are recommended.**			
Hepatitis A	N/A	**6 months**			
Hepatitis B	N/A	**4 weeks**	**8 weeks *and* at least 16 weeks after first dose**		
Inactivated poliovirus	N/A	**4 weeks**	**6 months** A fourth dose is not necessary if the third dose was administered at age 4 years or older and at least 6 months after the previous dose.	A fourth dose of IPV is indicated if all previous doses were administered at <4 years or if the third dose was administered <6 months after the second dose.	
Measles, mumps, rubella	N/A	**4 weeks**			
Varicella	N/A	**3 months** if younger than age 13 years. **4 weeks** if age 13 years or older			
Dengue	9 years	**6 months**	6 months		

Table 3 Recommended Child and Adolescent Immunization Schedule by Medical Indication, United States, 2022

Always use this table in conjunction with Table 1 and the Notes that follow.

VACCINE	INDICATION									
	Pregnancy	Immunocompromised status (excluding HIV infection)	HIV infection CD4+ count[1]		Kidney failure, end-stage renal disease, or on hemodialysis	Heart disease or chronic lung disease	CSF leak or cochlear implant	Asplenia or persistent complement component deficiencies	Chronic liver disease	Diabetes
			<15% or total CD4 cell count of <200/mm³	≥15% and total CD4 cell count of ≥200/mm³						
Hepatitis B										
Rotavirus		SCID[2]								
Diphtheria, tetanus, and acellular pertussis (DTaP)										
Haemophilus influenzae type b										
Pneumococcal conjugate										
Inactivated poliovirus										
Influenza (IIV4)										
or										
Influenza (LAIV4)						Asthma, wheezing: 2–4yrs[3]				
Measles, mumps, rubella	*									
Varicella	*									
Hepatitis A										
Tetanus, diphtheria, and acellular pertussis (Tdap)										
Human papillomavirus	*									
Meningococcal ACWY										
Meningococcal B										
Pneumococcal polysaccharide										
Dengue										

Vaccination according to the routine schedule recommended

Recommended for persons with an additional risk factor for which the vaccine would be indicated

Vaccination is recommended, and additional doses may be necessary based on medical condition or vaccine. See Notes.

Precaution—vaccine might be indicated if benefit of protection outweighs risk of adverse reaction

Contraindicated or not recommended—vaccine should not be administered

*Vaccinate after pregnancy

No recommendation/not applicable

1 For additional information regarding HIV laboratory parameters and use of live vaccines, see the *General Best Practice Guidelines for Immunization*, "Altered Immunocompetence," at www.cdc.gov/vaccines/hcp/acip-recs/general-recs/immunocompetence.html and Table 4-1 (footnote J) at www.cdc.gov/vaccines/hcp/acip-recs/general-recs/contraindications.html.
2 Severe Combined Immunodeficiency
3 LAIV4 contraindicated for children 2–4 years of age with asthma or wheezing during the preceding 12 months

Recommended Adult Immunization Schedule for ages 19 years or older

UNITED STATES 2022

How to use the adult immunization schedule

1. Determine recommended vaccinations by age **(Table 1)**
2. Assess need for additional recommended vaccinations by medical condition or other indication **(Table 2)**
3. Review vaccine types, frequencies, intervals, and considerations for special situations **(Notes)**
4. Review contraindications and precautions for vaccine types **(Appendix)**

Vaccines in the Adult Immunization Schedule*

Vaccine	Abbreviation(s)	Trade name(s)
Haemophilus influenzae type b vaccine	Hib	ActHIB® Hiberix® PedvaxHIB®
Hepatitis A vaccine	HepA	Havrix® Vaqta®
Hepatitis A and hepatitis B vaccine	HepA-HepB	Twinrix®
Hepatitis B vaccine	HepB	Engerix-B® Recombivax HB® Heplisav-B®
Human papillomavirus vaccine	HPV	Gardasil 9®
Influenza vaccine (inactivated)	IIV4	Many brands
Influenza vaccine (live, attenuated)	LAIV4	FluMist® Quadrivalent
Influenza vaccine (recombinant)	RIV4	Flublok® Quadrivalent
Measles, mumps, and rubella vaccine	MMR	M-M-R II®
Meningococcal serogroups A, C, W, Y vaccine	MenACWY-D MenACWY-CRM MenACWY-TT	Menactra® Menveo® MenQuadfi®
Meningococcal serogroup B vaccine	MenB-4C MenB-FHbp	Bexsero® Trumenba®
Pneumococcal 15-valent conjugate vaccine	PCV15	Vaxneuvance™
Pneumococcal 20-valent conjugate vaccine	PCV20	Prevnar 20™
Pneumococcal 23-valent polysaccharide vaccine	PPSV23	Pneumovax 23®
Tetanus and diphtheria toxoids	Td	Tenivac® Tdvax™
Tetanus and diphtheria toxoids and acellular pertussis vaccine	Tdap	Adacel® Boostrix®
Varicella vaccine	VAR	Varivax®
Zoster vaccine, recombinant	RZV	Shingrix

*Administer recommended vaccines if vaccination history is incomplete or unknown. Do not restart or add doses to vaccine series if there are extended intervals between doses. The use of trade names is for identification purposes only and does not imply endorsement by the ACIP or CDC.

Recommended by the Advisory Committee on Immunization Practices (www.cdc.gov/vaccines/acip) and approved by the Centers for Disease Control and Prevention (www.cdc.gov), American College of Physicians (www.acponline.org), American Academy of Family Physicians (www.aafp.org), American College of Obstetricians and Gynecologists (www.acog.org), American College of Nurse-Midwives (www.midwife.org), and American Academy of Physician Associates (www.aapa.org), and Society for Healthcare Epidemiology of America (www.shea-online.org).

Report

- Suspected cases of reportable vaccine-preventable diseases or outbreaks to the local or state health department
- Clinically significant postvaccination reactions to the Vaccine Adverse Event Reporting System at www.vaers.hhs.gov or 800-822-7967

Injury claims

All vaccines included in the adult immunization schedule except pneumococcal 23-valent polysaccharide (PPSV23) and zoster (RZV) vaccines are covered by the Vaccine Injury Compensation Program. Information on how to file a vaccine injury claim is available at www.hrsa.gov/vaccinecompensation.

Questions or comments

Contact www.cdc.gov/cdc-info or 800-CDC-INFO (800-232-4636), in English or Spanish, 8 a.m.–8 p.m. ET, Monday through Friday, excluding holidays.

Download the CDC Vaccine Schedules app for providers at www.cdc.gov/vaccines/schedules/hcp/schedule-app.html.

Helpful information

- Complete Advisory Committee on Immunization Practices (ACIP) recommendations: www.cdc.gov/vaccines/hcp/acip-recs/index.html
- *General Best Practice Guidelines for Immunization* (including contraindications and precautions): www.cdc.gov/vaccines/hcp/acip-recs/general-recs/index.html
- Vaccine information statements: www.cdc.gov/vaccines/hcp/vis/index.html
- Manual for the Surveillance of Vaccine-Preventable Diseases (including case identification and outbreak response): www.cdc.gov/vaccines/pubs/surv-manual
- Travel vaccine recommendations: www.cdc.gov/travel
- Recommended Child and Adolescent Immunization Schedule, United States, 2022: www.cdc.gov/vaccines/schedules/hcp/child-adolescent.html
- ACIP Shared Clinical Decision-Making Recommendations: www.cdc.gov/vaccines/acip/acip-scdm-faqs.html

U.S. Department of Health and Human Services
Centers for Disease Control and Prevention

Scan QR code for access to online schedule

CS310021-A

Table 1 Recommended Adult Immunization Schedule by Age Group, United States, 2022

Vaccine	19–26 years	27–49 years	50–64 years	≥65 years
Influenza inactivated (IIV4) or **Influenza recombinant** (RIV4)	1 dose annually			
or	or			
Influenza live, attenuated (LAIV4)	1 dose annually			
Tetanus, diphtheria, pertussis (Tdap or Td)	1 dose Tdap each pregnancy; 1 dose Td/Tdap for wound management (see notes)			
	1 dose Tdap, then Td or Tdap booster every 10 years			
Measles, mumps, rubella (MMR)	1 or 2 doses depending on indication (if born in 1957 or later)			
Varicella (VAR)	2 doses (if born in 1980 or later)	2 doses		
Zoster recombinant (RZV)	2 doses for immunocompromising conditions (see notes)		2 doses	
Human papillomavirus (HPV)	2 or 3 doses depending on age at initial vaccination or condition	27 through 45 years		
Pneumococcal (PCV15, PCV20, PPSV23)	1 dose PCV15 followed by PPSV23 OR 1 dose PCV20 (see notes)			1 dose PCV15 followed by PPSV23 OR 1 dose PCV20
Hepatitis A (HepA)	2 or 3 doses depending on vaccine			
Hepatitis B (HepB)	2, 3, or 4 doses depending on vaccine or condition			
Meningococcal A, C, W, Y (MenACWY)	1 or 2 doses depending on indication, see notes for booster recommendations			
Meningococcal B (MenB)	2 or 3 doses depending on vaccine and indication, see notes for booster recommendations			
	19 through 23 years			
***Haemophilus influenzae* type b** (Hib)	1 or 3 doses depending on indication			

Recommended vaccination for adults who meet age requirement, lack documentation of vaccination, or lack evidence of past infection

Recommended vaccination for adults with an additional risk factor or another indication

Recommended vaccination based on shared clinical decision-making

No recommendation/ Not applicable

Table 2 Recommended Adult Immunization Schedule by Medical Condition or Other Indication, United States, 2022

Vaccine	Pregnancy	Immuno-compromised (excluding HIV infection)	HIV infection CD4 percentage and count: <15% or <200 mm³	HIV infection CD4 percentage and count: ≥15% and ≥200 mm³	Asplenia, complement deficiencies	End-stage renal disease, or on hemodialysis	Heart or lung disease; alcoholism[1]	Chronic liver disease	Diabetes	Health care personnel[2]	Men who have sex with men
IIV4 or RIV4	1 dose annually										
or										or	
LAIV4	Contraindicated					Precaution				1 dose annually	
Tdap or Td	1 dose Tdap each pregnancy	1 dose Tdap, then Td or Tdap booster every 10 years									
MMR	Contraindicated*	Contraindicated	1 or 2 doses depending on indication								
VAR	Contraindicated*	Contraindicated		2 doses							
RZV		2 doses at age ≥19 years		2 doses at age ≥50 years							
HPV	Not Recommended*	3 doses through age 26 years		2 or 3 doses through age 26 years depending on age at initial vaccination or condition							
Pneumococcal (PCV15, PCV20, PPSV23)		1 dose PCV15 followed by PPSV23 OR 1 dose PCV20 (see notes)									
HepA	2 or 3 doses depending on vaccine										
HepB	3 doses (see notes)	2, 3, or 4 doses depending on vaccine or condition									
MenACWY	1 or 2 doses depending on indication, see notes for booster recommendations										
MenB	Precaution	2 or 3 doses depending on vaccine and indication, see notes for booster recommendations									
Hib		3 doses HSCT[3] recipients only			1 dose						

Recommended vaccination for adults who meet age requirement, lack documentation of vaccination, or lack evidence of past infection

Recommended vaccination for adults with an additional risk factor or another indication

Recommended vaccination based on shared clinical decision-making

Precaution—vaccination might be indicated if benefit of protection outweighs risk of adverse reaction

Contraindicated or not recommended—vaccine should not be administered.

*Vaccinate after pregnancy.

No recommendation/ Not applicable

1. Precaution for LAIV4 does not apply to alcoholism. **2.** See notes for influenza; hepatitis B; measles, mumps, and rubella; and varicella vaccinations. **3.** Hematopoietic stem cell transplant.

Notes Recommended Adult Immunization Schedule, United States, 2022

- **Pregnancy:** Delay MenB until after pregnancy unless at increased risk and vaccination benefits outweigh potential risks
- For MenB **booster dose recommendations** for groups listed under "Special situations" and in an outbreak setting (e.g., in community or organizational settings and among men who have sex with men) and additional meningococcal vaccination information, see www.cdc.gov/mmwr/volumes/69/rr/rr6909a1.htm

Note: MenB vaccines may be administered simultaneously with MenACWY vaccines if indicated, but at a different anatomic site, if feasible.

Pneumococcal vaccination

Routine vaccination

- **Age 65 years or older** who have not previously received a pneumococcal conjugate vaccine or whose previous vaccination history is unknown: 1 dose PCV15 or 1 dose PCV20. If PCV15 is used, this should be followed by a dose of PPSV23 given at least 1 year after the PCV15 dose. A minimum interval of 8 weeks between PCV15 and PPSV23 can be considered for adults with an immunocompromising condition,* cochlear implant, or cerebrospinal fluid leak to minimize the risk of invasive pneumococcal disease caused by serotypes unique to PPSV23 in these vulnerable groups.
- For guidance for patients who have already received a previous dose of PCV13 and/or PPSV23, see www.cdc.gov/mmwr/volumes/71/wr/mm7104a1.htm.

Special situations

- **Age 19–64 years** with certain underlying medical conditions or other risk factors** who have not previously received a pneumococcal conjugate vaccine or whose previous vaccination history is unknown: 1 dose PCV15 or 1 dose PCV20. If PCV15 is used, this should be followed by a dose of PPSV23 given at least 1 year after the PCV15 dose. A minimum interval of 8 weeks between PCV15 and PPSV23 can be considered for adults with an immunocompromising condition,* cochlear implant, or cerebrospinal fluid leak to minimize the risk of invasive pneumococcal disease caused by serotypes unique to PPSV23 in these vulnerable groups.
- For guidance for patients who have already received a previous dose of PCV13 and/or PPSV23, see www.cdc.gov/mmwr/volumes/71/wr/mm7104a1.htm.

***Note:** Immunocompromising conditions include chronic renal failure, nephrotic syndrome, immunodeficiency, iatrogenic immunosuppression, generalized malignancy, human immunodeficiency virus, Hodgkin disease, leukemia, lymphoma, multiple myeloma, solid organ transplants, congenital or acquired asplenia, sickle cell disease, or other hemoglobinopathies.

****Note:** Underlying medical conditions or other risk factors include alcoholism, chronic heart/liver/lung disease, chronic renal failure, cigarette smoking, cochlear implant, congenital or acquired asplenia, CSF leak, diabetes mellitus, generalized malignancy, HIV, Hodgkin disease, immunodeficiency, iatrogenic immunosuppression, leukemia, lymphoma, multiple myeloma, nephrotic syndrome, solid organ transplants, or sickle cell disease or other hemoglobinopathies.

Tetanus, diphtheria, and pertussis vaccination

Routine vaccination

- **Previously did not receive Tdap at or after age 11 years:** 1 dose Tdap, then Td or Tdap every 10 years

Special situations

- **Previously did not receive primary vaccination series for tetanus, diphtheria, or pertussis:** 1 dose Tdap followed by 1 dose Td or Tdap at least 4 weeks after Tdap and another dose Td or Tdap 6–12 months after last Td or Tdap (Tdap can be substituted for any Td dose, but preferred as first dose), Td or Tdap every 10 years thereafter
- **Pregnancy:** 1 dose Tdap during each pregnancy, preferably in early part of gestational weeks 27–36
- **Wound management:** Persons with 3 or more doses of tetanus-toxoid-containing vaccine: For clean and minor wounds, administer Tdap or Td if more than 10 years since last dose of tetanus-toxoid-containing vaccine; for all other wounds, administer Tdap or Td if more than 5 years since last dose of tetanus-toxoid-containing vaccine. Tdap is preferred for persons who have not previously received Tdap or whose Tdap history is unknown. If a tetanus-toxoid-containing vaccine is indicated for a pregnant woman, use Tdap. For detailed information, see www.cdc.gov/mmwr/volumes/69/wr/mm6903a5.htm

Varicella vaccination

Routine vaccination

- **No evidence of immunity to varicella:** 2-dose series 4–8 weeks apart if previously did not receive varicella-containing vaccine (VAR or MMRV [measles-mumps-rubella-varicella vaccine] for children); if previously received 1 dose varicella-containing vaccine, 1 dose at least 4 weeks after first dose
- Evidence of immunity: U.S.-born before 1980 (except for pregnant women and health care personnel [see below]), documentation of 2 doses varicella-containing vaccine at least 4 weeks apart, diagnosis or verification of history of varicella or herpes zoster by a health care provider, laboratory evidence of immunity or disease

Special situations

- **Pregnancy with no evidence of immunity to varicella:** VAR contraindicated during pregnancy; after pregnancy (before discharge from health care facility), 1 dose if previously received 1 dose varicella-containing vaccine or dose 1 of 2-dose series (dose 2: 4–8 weeks later) if previously did not receive any varicella-containing vaccine, regardless of whether U.S.-born before 1980
- **Health care personnel with no evidence of immunity to varicella:** 1 dose if previously received 1 dose varicella-containing vaccine; 2-dose series 4–8 weeks apart if previously did not receive any varicella-containing vaccine, regardless of whether U.S.-born before 1980
- **HIV infection with CD4 percentages ≥15% and CD4 count ≥200 cells/mm³ with no evidence of immunity:** Vaccination may be considered (2 doses 3 months apart); VAR contraindicated for HIV infection with CD4 percentage <15% or CD4 count <200 cells/mm³
- **Severe immunocompromising conditions:** VAR contraindicated

Zoster vaccination

Routine vaccination

- **Age 50 years or older:** 2-dose series RZV (Shingrix) 2–6 months apart (minimum interval: 4 weeks; repeat dose if administered too soon), regardless of previous herpes zoster or history of zoster vaccine live (ZVL, Zostavax) vaccination (administer RZV at least 2 months after ZVL)

Special situations

- **Pregnancy:** There is currently no ACIP recommendation for RZV use in pregnancy. Consider delaying RZV until after pregnancy.
- **Immunocompromising conditions (including HIV):** RZV recommended for use in persons age 19 years or older who are or will be immunodeficient or immunosuppressed because of disease or therapy. For detailed information, see www.cdc.gov/mmwr/volumes/71/wr/mm7103a2.htm.

Morbidity and Mortality Weekly Report (*MMWR*)

CDC

Use of 15-Valent Pneumococcal Conjugate Vaccine and 20-Valent Pneumococcal Conjugate Vaccine Among U.S. Adults: Updated Recommendations of the Advisory Committee on Immunization Practices — United States, 2022

Weekly / January 28, 2022 / 71(4);109–117

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View suggested citation

Summary

What is already known about this topic?

Currently, the 13-valent pneumococcal conjugate vaccine (PCV) (PCV13) and the 23-valent pneumococcal polysaccharide vaccine (PPSV23) are recommended for U.S. adults. Recommendations vary by age and risk groups.

What is added by this report?

On October 20, 2021, the Advisory Committee on Immunization Practices recommended 15-valent PCV (PCV15) or 20-valent PCV (PCV20) for PCV–naïve adults who are either aged ≥65 years or aged 19–64 years with certain underlying conditions. When PCV15 is used, it should be followed by a dose of PPSV23, typically ≥1 year later.

What are the implications for public health practice?

Pneumococcal vaccination recommendations were simplified across age and risk group. Eligible adults may receive either PCV15 in series with PPSV23 or PCV20 alone.

TABLE 1. Recommendations for use of 15-valent pneumococcal conjugate vaccine in series with 23-valent pneumococcal polysaccharide vaccine or 20-valent pneumococcal conjugate vaccine in pneumococcal conjugate vaccine-naïve adults aged ≥19 years — United States, 2022

Medical indication group	Specific underlying medical condition	Age group, yrs	
		19–64	≥65
None	None	None	1 dose of PCV20 or 1 dose of PCV15 followed by a dose of PPSV23 ≥1 years later*
Underlying medical conditions or other risk factors	Alcoholism Chronic heart disease† Chronic liver disease Chronic lung disease¶ Cigarette smoking Diabetes mellitus Cochlear implant CSF leak Congenital or acquired asplenia Sickle cell disease or other hemoglobinopathies Chronic renal failure** Congenital or acquired immunodeficiencies**,†† Generalized malignancy** HIV infection** Hodgkin disease** Iatrogenic immunosuppression**,§§ Leukemia** Lymphoma** Multiple myeloma** Nephrotic syndrome** Solid organ transplant**	1 dose of PCV20 or 1 dose of PCV15 followed by a dose of PPSV23 ≥1 years later§	1 dose of PCV20 or 1 dose of PCV15 followed by a dose of PPSV23 ≥1 years later*

Abbreviations: CSF = cerebrospinal fluid; PCV15 = 15-valent pneumococcal conjugate vaccine; PCV20 = 20-valent pneumococcal conjugate vaccine; PPSV23 = 23-valent pneumococcal polysaccharide vaccine.

* Adults with immunocompromising conditions, cochlear implant, or CSF leak might benefit from shorter intervals such as ≥8 weeks. These vaccine doses do not need to be repeated if given before age 65 years.
† Includes congestive heart failure and cardiomyopathies.
§ Adults with immunocompromising conditions, cochlear implant, or CSF leak might benefit from shorter intervals such as ≥8 weeks.
¶ Includes chronic obstructive pulmonary disease, emphysema, and asthma.
** Indicates immunocompromising conditions.
†† Includes B- (humoral) or T-lymphocyte deficiency, complement deficiencies (particularly C1, C2, C3, and C4 deficiencies), and phagocytic disorders (excluding chronic granulomatous disease).
§§ Diseases requiring treatment with immunosuppressive drugs, including long-term systemic corticosteroids and radiation therapy.

Vaccines & Preventable Diseases Home

Vaccines by Disease
- Chickenpox (Varicella)
- Dengue
- Diphtheria
- Flu (Influenza)
- Hepatitis A
- Hepatitis B
- Hib
- Human Papillomavirus (HPV)
- Measles
- Meningococcal
- Mumps
- Pneumococcal
  - What Everyone Should Know
  - For Healthcare Professionals
- Polio
- Rotavirus
- Rubella
- Shingles

Pneumococcal Vaccine Recommendations

Below are summaries of recommendations from CDC's Advisory Committee on Immunization Practices (ACIP). For the full text of the recommendations, see Pneumococcal ACIP Vaccine Recommendations.

Vaccination of Infants, Children, and Adults 65 Years or Older

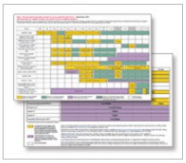
CDC recommends routine administration of pneumococcal conjugate vaccine (PCV13) for all children younger than 2 years of age:

- Give PCV13 to infants as a series of 4 doses, one dose at each of these ages: 2 months, 4 months, 6 months, and 12 through 15 months.
- Children who miss their shots or start the series later should still get the vaccine. The number of doses recommended and the intervals between doses will depend on the child's age when vaccination begins.

CDC recommends routine administration of pneumococcal conjugate vaccine (PCV15 or PCV20) for all adults 65 years or older who have never received any pneumococcal conjugate vaccine or whose previous vaccination history is unknown:

- If PCV15 is used, this should be followed by a dose of PPSV23 one year later. The minimum interval is 8 weeks and can be considered in adults with an immunocompromising condition†, cochlear implant, or cerebrospinal fluid leak.
- If PCV20 is used, a dose of PPSV23 is NOT indicated.
- See Pneumococcal Vaccination: Summary of Who and When to Vaccinate for CDC guidance on vaccination options for adults who have previously received a pneumococcal conjugate vaccine.

Immunization Schedules



View current schedules for children, teens, and adults.

Footnote

† Immunocompromising conditions include chronic renal failure, congenital or acquired asplenia, generalized malignancy, HIV infection, Hodgkin disease, iatrogenic immunosuppression, leukemia, lymphoma, multiple myeloma, nephrotic syndrome, sickle cell disease or other hemoglobinopathies, and solid organ transplant.

https://www.cdc.gov/vaccines/vpd/index.html

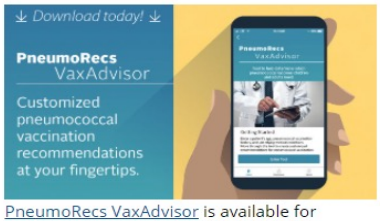
Vaccination of Older Children and Adults with Certain Indications

In certain situations, children 2 years or older and adults younger than age 65 should also receive pneumococcal vaccines. See Pneumococcal Vaccination: Summary of Who and When to Vaccinate for all pneumococcal vaccine recommendations by vaccine and age.

Catch-up Guidance for Children 4 Months through 18 Years

The following "job-aid" provides catch-up guidance for PCV13 for children 4 months through 18 years of age. It includes detailed scenarios by age group and previous number of doses received. This should assist clinicians in interpreting Figure 2 of the Childhood/Adolescent Immunization Catch-up Schedule.

- Pneumococcal Conjugate Vaccine (PCV) Catch-Up Guidance for Children 4 Months through 18 Years of Age [3 pages]



PneumoRecs VaxAdvisor is available for download on iOS and Android mobile devices.

Contraindications and Precautions

Do not administer a pneumococcal conjugate vaccine to:

- A person who has ever had a severe allergic reaction (e.g., anaphylaxis) after a previous dose of PCV7, PCV13, PCV15, or PCV20, or to any vaccine containing diphtheria toxoid
- A person with a severe allergy to any component of these vaccines

Do not administer PPSV23 to:

- A person who has ever had a severe allergic reaction (e.g., anaphylaxis) after a previous dose
- A person with a severe allergy to any component of this vaccine

Clinicians may administer pneumococcal vaccines, if the provider and parent or patient deems the benefits of vaccination to outweigh the risks, to:

- A person who has a moderate or severe acute illness with or without fever

https://www.cdc.gov/vaccines/vpd/index.html

Appendix Recommended Adult Immunization Schedule, United States, 2022

Guide to Contraindications and Precautions to Commonly Used Vaccines

Adapted from Table 4-1 in Advisory Committee on Immunization Practices (ACIP) General Best Practice Guidelines for Immunization: Contraindication and Precautions available at www.cdc.gov/vaccines/hcp/acip-recs/general-recs/contraindications.html and ACIP's Recommendations for the Prevention and Control of 2021-22 Seasonal Influenza with Vaccines available at www.cdc.gov/mmwr/volumes/70/rr/rr7005a1.htm

Interim clinical considerations for use of COVID-19 vaccines including contraindications and precautions can be found at www.cdc.gov/vaccines/covid-19/clinical-considerations/covid-19-vaccines-us.html

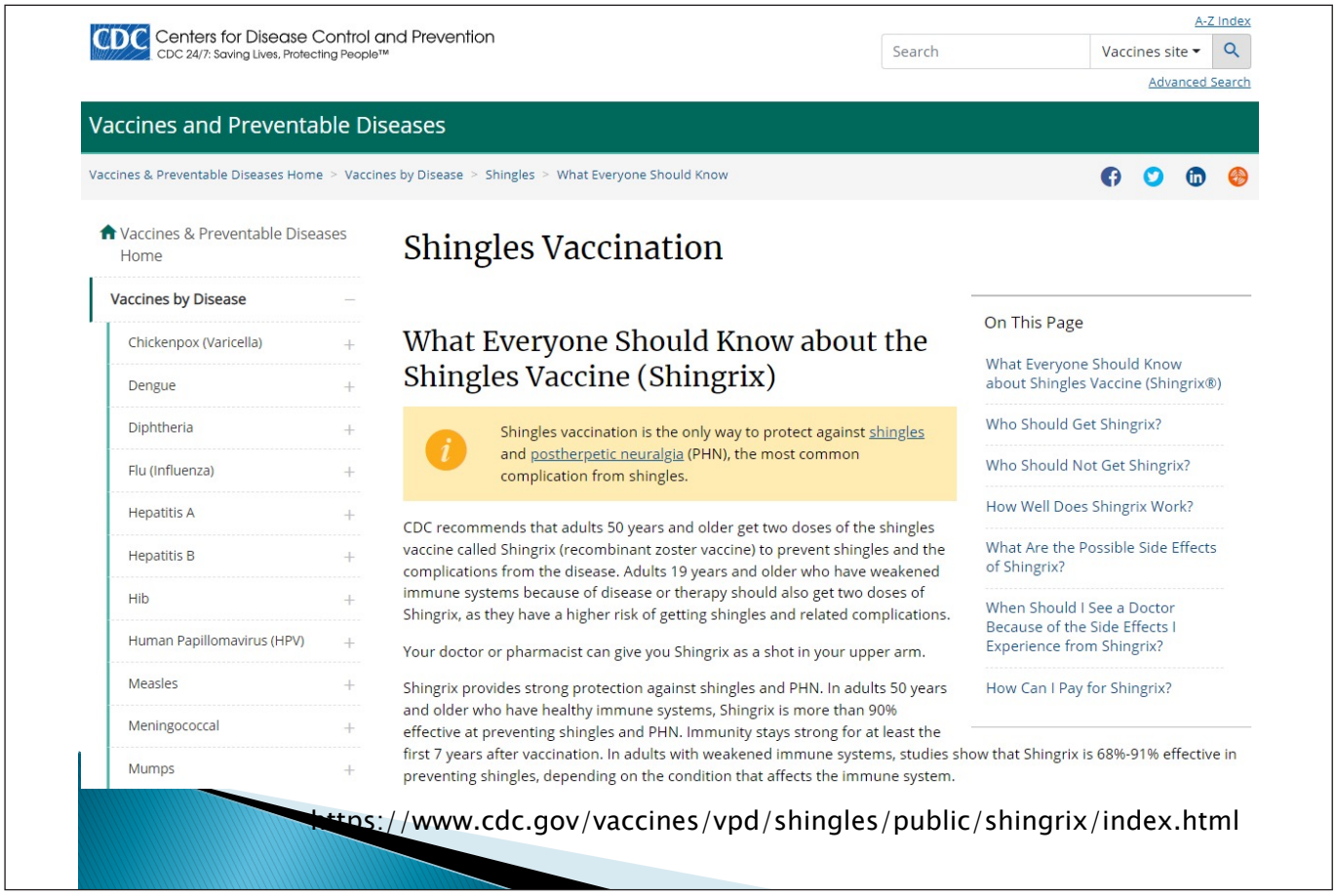
Vaccine	Contraindications[1]	Precautions[2]
Influenza, egg-based, inactivated injectable (IIV4)	• Severe allergic reaction (e.g., anaphylaxis) after previous dose of any influenza vaccine (i.e., any egg-based IIV, ccIIV, RIV, or LAIV of any valency) • Severe allergic reaction (e.g., anaphylaxis) to any vaccine component[3] (excluding egg)	• Guillain-Barré syndrome (GBS) within 6 weeks after a previous dose of any type of influenza vaccine • Persons with egg allergy with symptoms other than hives (e.g., angioedema, respiratory distress) or required epinephrine or another emergency medical intervention: Any influenza vaccine appropriate for age and health status may be administered. If using egg-based IIV4, administer in medical setting under supervision of health care provider who can recognize and manage severe allergic reactions. May consult an allergist. • Moderate or severe acute illness with or without fever
Influenza, cell culture-based inactivated injectable [(ccIIV4), Flucelvax® Quadrivalent]	• Severe allergic reaction (e.g., anaphylaxis) to any ccIIV of any valency, or to any component[3] of ccIIV4	• Guillain-Barré syndrome (GBS) within 6 weeks after a previous dose of any type of influenza vaccine • Persons with a history of severe allergic reaction (e.g., anaphylaxis) after a previous dose of any egg-based IIV, RIV, or LAIV of any valency. If using ccIV4, administer in medical setting under supervision of health care provider who can recognize and manage severe allergic reactions. May consult an allergist. • Moderate or severe acute illness with or without fever
Influenza, recombinant injectable [(RIV4), Flublok® Quadrivalent]	• Severe allergic reaction (e.g., anaphylaxis) to any RIV of any valency, or to any component[3] of RIV4	• Guillain-Barré syndrome (GBS) within 6 weeks after a previous dose of any type of influenza vaccine • Persons with a history of severe allergic reaction (e.g., anaphylaxis) after a previous dose of any egg-based IIV, ccIIV, or LAIV of any valency. If using RIV4, administer in medical setting under supervision of health care provider who can recognize and manage severe allergic reactions. May consult an allergist. • Moderate or severe acute illness with or without fever
Influenza, live attenuated [LAIV4, Flumist® Quadrivalent]	• Severe allergic reaction (e.g., anaphylaxis) after previous dose of any influenza vaccine (i.e., any egg-based IIV, ccIIV, RIV, or LAIV of any valency) • Severe allergic reaction (e.g., anaphylaxis) to any vaccine component[3] (excluding egg) • Adults age 50 years or older • Anatomic or functional asplenia • Immunocompromised due to any cause including, but not limited to, medications and HIV infection • Close contacts or caregivers of severely immunosuppressed persons who require a protected environment • Pregnancy • Cochlear implant • Active communication between the cerebrospinal fluid (CSF) and the oropharynx, nasopharynx, nose, ear, or any other cranial CSF leak • Received influenza antiviral medications oseltamivir or zanamivir within the previous 48 hours, peramivir within the previous 5 days, or baloxavir within the previous 17 days.	• Guillain-Barré syndrome (GBS) within 6 weeks after a previous dose of any type of influenza vaccine • Asthma in persons aged 5 years old or older • Persons with egg allergy with symptoms other than hives (e.g., angioedema, respiratory distress) or required epinephrine or another emergency medical intervention: Any influenza vaccine appropriate for age and health status may be administered. If using LAIV4 (which is egg based), administer in medical setting under supervision of health care provider who can recognize and manage severe allergic reactions. May consult an allergist. • Persons with underlying medical conditions (other than those listed under contraindications) that might predispose to complications after wild-type influenza virus infection [e.g., chronic pulmonary, cardiovascular (except isolated hypertension), renal, hepatic, neurologic, hematologic, or metabolic disorders (including diabetes mellitus)] • Moderate or severe acute illness with or without fever

1. When a contraindication is present, a vaccine should NOT be administered. Kroger A, Bahta L, Hunter P. ACIP General Best Practice Guidelines for Immunization. www.cdc.gov/vaccines/hcp/acip-recs/general-recs/contraindications.html
2. When a precaution is present, vaccination should generally be deferred but might be indicated if the benefit of protection from the vaccine outweighs the risk for an adverse reaction. Kroger A, Bahta L, Hunter P. ACIP General Best Practice Guidelines for Immunization. www.cdc.gov/vaccines/hcp/acip-recs/general-recs/contraindications.html
3. Vaccination providers should check FDA-approved prescribing information for the most complete and updated information, including contraindications, warnings, and precautions. Package inserts for U.S.-licensed vaccines are available at www.fda.gov/vaccines-blood-biologics/approved-products/vaccines-licensed-use-united-states.

Appendix Recommended Adult Immunization Schedule, United States, 2022

Vaccine	Contraindications[1]	Precautions[2]
Haemophilus influenzae type b (Hib)	• Severe allergic reaction (e.g., anaphylaxis) after a previous dose or to a vaccine component[3] • For Hiberix, ActHib, and PedvaxHIB only: History of severe allergic reaction to dry natural latex	• Moderate or severe acute illness with or without fever
Hepatitis A (HepA)	• Severe allergic reaction (e.g., anaphylaxis) after a previous dose or to a vaccine component[3] including neomycin	• Moderate or severe acute illness with or without fever
Hepatitis B (HepB)	• Severe allergic reaction (e.g., anaphylaxis) after a previous dose or to a vaccine component[3] including yeast • For Heplisav-B only: Pregnancy	• Moderate or severe acute illness with or without fever
Hepatitis A- Hepatitis B vaccine [HepA-HepB, (Twinrix®)]	• Severe allergic reaction (e.g., anaphylaxis) after a previous dose or to a vaccine component[3] including neomycin and yeast	• Moderate or severe acute illness with or without fever
Human papillomavirus (HPV)	• Severe allergic reaction (e.g., anaphylaxis) after a previous dose or to a vaccine component[3]	• Moderate or severe acute illness with or without fever
Measles, mumps, rubella (MMR)	• Severe allergic reaction (e.g., anaphylaxis) after a previous dose or to a vaccine component[3] • Severe immunodeficiency (e.g., hematologic and solid tumors, receipt of chemotherapy, congenital immunodeficiency, long-term immunosuppressive therapy or patients with HIV infection who are severely immunocompromised) • Pregnancy • Family history of altered immunocompetence, unless verified clinically or by laboratory testing as immunocompetent	• Recent (≤11 months) receipt of antibody-containing blood product (specific interval depends on product) • History of thrombocytopenia or thrombocytopenic purpura • Need for tuberculin skin testing or interferon-gamma release assay (IGRA) testing • Moderate or severe acute illness with or without fever
Meningococcal ACWY (MenACWY) [MenACWY-CRM (Menveo®); MenACWY-D (Menactra®); MenACWY-TT (MenQuadfi®)]	• Severe allergic reaction (e.g., anaphylaxis) after a previous dose or to a vaccine component[3] • For MenACWY-D and Men ACWY-CRM only: severe allergic reaction to any diphtheria toxoid– or CRM197–containing vaccine • For MenACWY-TT only: severe allergic reaction to a tetanus toxoid-containing vaccine	• Moderate or severe acute illness with or without fever
Meningococcal B (MenB) [MenB-4C (Bexsero); MenB-FHbp (Trumenba)]	• Severe allergic reaction (e.g., anaphylaxis) after a previous dose or to a vaccine component[3]	• Pregnancy • For MenB-4C only: Latex sensitivity • Moderate or severe acute illness with or without fever
Pneumococcal conjugate (PCV15)	• Severe allergic reaction (e.g., anaphylaxis) after a previous dose or to a vaccine component[3] • Severe allergic reaction (e.g., anaphylaxis) to any diphtheria-toxoid–containing vaccine or to its vaccine component[3]	• Moderate or severe acute illness with or without fever
Pneumococcal conjugate (PCV20)	• Severe allergic reaction (e.g., anaphylaxis) after a previous dose or to a vaccine component[3] • Severe allergic reaction (e.g., anaphylaxis) to any diphtheria-toxoid– containing vaccine or to its vaccine component[3]	• Moderate or severe acute illness with or without fever
Pneumococcal polysaccharide (PPSV23)	• Severe allergic reaction (e.g., anaphylaxis) after a previous dose or to a vaccine component[3]	• Moderate or severe acute illness with or without fever
Tetanus, diphtheria, and acellular pertussis (Tdap) Tetanus, diphtheria (Td)	• Severe allergic reaction (e.g., anaphylaxis) after a previous dose or to a vaccine component[3] • For Tdap only: Encephalopathy (e.g., coma, decreased level of consciousness, prolonged seizures), not attributable to another identifiable cause, within 7 days of administration of previous dose of DTP, DTaP, or Tdap	• Guillain-Barré syndrome (GBS) within 6 weeks after a previous dose of tetanus-toxoid–containing vaccine • History of Arthus-type hypersensitivity reactions after a previous dose of diphtheria-toxoid—containing or tetanus-toxoid– containing vaccine; defer vaccination until at least 10 years have elapsed since the last tetanus-toxoid–containing vaccine • Moderate or severe acute illness with or without fever • For Tdap only: Progressive or unstable neurological disorder, uncontrolled seizures, or progressive encephalopathy until a treatment regimen has been established and the condition has stabilized
Varicella (VAR)	• Severe allergic reaction (e.g., anaphylaxis) after a previous dose or to a vaccine component[3] • Severe immunodeficiency (e.g., hematologic and solid tumors, receipt of chemotherapy, congenital immunodeficiency, long- term immunosuppressive therapy or patients with HIV infection who are severely immunocompromised) • Pregnancy • Family history of altered immunocompetence, unless verified clinically or by laboratory testing as immunocompetent	• Recent (≤11 months) receipt of antibody-containing blood product (specific interval depends on product) • Receipt of specific antiviral drugs (acyclovir, famciclovir, or valacyclovir) 24 hours before vaccination (avoid use of these antiviral drugs for 14 days after vaccination) • Use of aspirin or aspirin-containing products • Moderate or severe acute illness with or without fever
Zoster recombinant vaccine (RZV)	• Severe allergic reaction (e.g., anaphylaxis) after a previous dose or to a vaccine component[3]	• Moderate or severe acute illness with or without fever • Current herpes zoster infection

1. When a contraindication is present, a vaccine should NOT be administered. Kroger A, Bahta L, Hunter P. ACIP General Best Practice Guidelines for Immunization. www.cdc.gov/vaccines/hcp/acip-recs/general-recs/contraindications.html
2. When a precaution is present, vaccination should generally be deferred but might be indicated if the benefit of protection from the vaccine outweighs the risk for an adverse reaction. Kroger A, Bahta L, Hunter P. ACIP General Best Practice Guidelines for Immunization. www.cdc.gov/vaccines/hcp/acip-recs/general-recs/contraindications.html
3. Vaccination providers should check FDA-approved prescribing information for the most complete and updated information, including contraindications, warnings, and precautions. Package inserts for U.S.-licensed vaccines are available at www.fda.gov/vaccines-blood-biologics/approved-products/vaccines-licensed-use-united-states.


CDC Centers for Disease Control and Prevention
CDC 24/7: Saving Lives, Protecting People™
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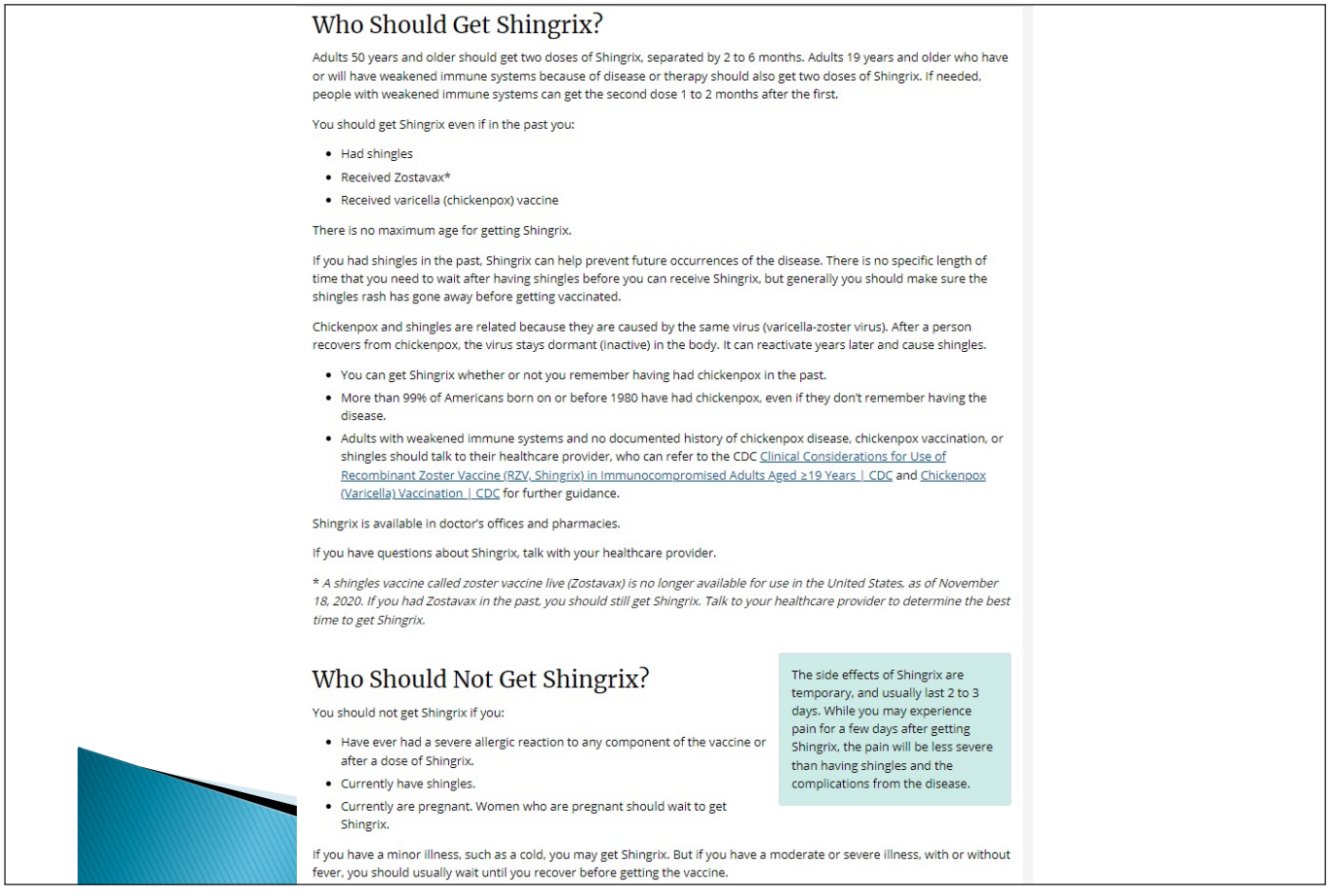
Advanced Search
Vaccines and Preventable Diseases
Vaccines & Preventable Diseases Home > Vaccines by Disease > Shingles > What Everyone Should Know
Vaccines & Preventable Diseases Home
Vaccines by Disease
Chickenpox (Varicella)
Dengue
Diphtheria
Flu (Influenza)
Hepatitis A
Hepatitis B
Hib
Human Papillomavirus (HPV)
Measles
Meningococcal
Mumps
Shingles Vaccination
What Everyone Should Know about the Shingles Vaccine (Shingrix)
Shingles vaccination is the only way to protect against shingles and postherpetic neuralgia (PHN), the most common complication from shingles.
CDC recommends that adults 50 years and older get two doses of the shingles vaccine called Shingrix (recombinant zoster vaccine) to prevent shingles and the complications from the disease. Adults 19 years and older who have weakened immune systems because of disease or therapy should also get two doses of Shingrix, as they have a higher risk of getting shingles and related complications.
Your doctor or pharmacist can give you Shingrix as a shot in your upper arm.
Shingrix provides strong protection against shingles and PHN. In adults 50 years and older who have healthy immune systems, Shingrix is more than 90% effective at preventing shingles and PHN. Immunity stays strong for at least the first 7 years after vaccination. In adults with weakened immune systems, studies show that Shingrix is 68%-91% effective in preventing shingles, depending on the condition that affects the immune system.
On This Page
What Everyone Should Know about Shingles Vaccine (Shingrix®)
Who Should Get Shingrix?
Who Should Not Get Shingrix?
How Well Does Shingrix Work?
What Are the Possible Side Effects of Shingrix?
When Should I See a Doctor Because of the Side Effects I Experience from Shingrix?
How Can I Pay for Shingrix?
https://www.cdc.gov/vaccines/vpd/shingles/public/shingrix/index.html


Who Should Get Shingrix?
Adults 50 years and older should get two doses of Shingrix, separated by 2 to 6 months. Adults 19 years and older who have or will have weakened immune systems because of disease or therapy should also get two doses of Shingrix. If needed, people with weakened immune systems can get the second dose 1 to 2 months after the first.
You should get Shingrix even if in the past you:
Had shingles
Received Zostavax*
Received varicella (chickenpox) vaccine
There is no maximum age for getting Shingrix.
If you had shingles in the past, Shingrix can help prevent future occurrences of the disease. There is no specific length of time that you need to wait after having shingles before you can receive Shingrix, but generally you should make sure the shingles rash has gone away before getting vaccinated.
Chickenpox and shingles are related because they are caused by the same virus (varicella-zoster virus). After a person recovers from chickenpox, the virus stays dormant (inactive) in the body. It can reactivate years later and cause shingles.
You can get Shingrix whether or not you remember having had chickenpox in the past.
More than 99% of Americans born on or before 1980 have had chickenpox, even if they don't remember having the disease.
Adults with weakened immune systems and no documented history of chickenpox disease, chickenpox vaccination, or shingles should talk to their healthcare provider, who can refer to the CDC Clinical Considerations for Use of Recombinant Zoster Vaccine (RZV, Shingrix) in Immunocompromised Adults Aged ≥19 Years | CDC and Chickenpox (Varicella) Vaccination | CDC for further guidance.
Shingrix is available in doctor's offices and pharmacies.
If you have questions about Shingrix, talk with your healthcare provider.
* A shingles vaccine called zoster vaccine live (Zostavax) is no longer available for use in the United States, as of November 18, 2020. If you had Zostavax in the past, you should still get Shingrix. Talk to your healthcare provider to determine the best time to get Shingrix.
Who Should Not Get Shingrix?
You should not get Shingrix if you:
Have ever had a severe allergic reaction to any component of the vaccine or after a dose of Shingrix.
Currently have shingles.
Currently are pregnant. Women who are pregnant should wait to get Shingrix.
If you have a minor illness, such as a cold, you may get Shingrix. But if you have a moderate or severe illness, with or without fever, you should usually wait until you recover before getting the vaccine.
The side effects of Shingrix are temporary, and usually last 2 to 3 days. While you may experience pain for a few days after getting Shingrix, the pain will be less severe than having shingles and the complications from the disease.

How Well Does Shingrix Work?

Two doses of Shingrix provide strong protection against shingles and postherpetic neuralgia (PHN), the most common complication of shingles.

- In adults 50 to 69 years old with healthy immune systems, Shingrix was 97% effective in preventing shingles; in adults 70 years and older, Shingrix was 91% effective.
- In adults 50 years and older, Shingrix was 91% effective in preventing PHN; in adults 70 years and older, Shingrix was 89% effective.
- In adults with weakened immune systems, Shingrix was between 68% and 91% effective in preventing shingles, depending on their underlying immunocompromising condition.

In people 70 years and older who had healthy immune systems, Shingrix immunity remained high throughout 7 years following vaccination.

What Are the Possible Side Effects of Shingrix?

Studies show that Shingrix is safe. The vaccine helps your body create a strong defense against shingles. As a result, you are likely to have temporary side effects from getting the shots. The side effects might affect your ability to do normal daily activities for 2 to 3 days.

Most people got a sore arm with mild or moderate pain after getting Shingrix, and some also had redness and swelling where they got the shot. Some people felt tired, had muscle pain, a headache, shivering, fever, stomach pain, or nausea. Some people who got Shingrix experienced side effects that prevented them from doing regular activities. Symptoms went away on their own in about 2 to 3 days. Side effects were more common in younger people.

You might have a reaction to the first or second dose of Shingrix, or both doses. If you experience side effects, you may choose to take over-the-counter pain medicine such as ibuprofen or acetaminophen.

Guillain-Barré syndrome (GBS), a serious nervous system disorder, has been reported very rarely after Shingrix. There is also a very small increased risk of GBS after having shingles.

If you experience side effects from Shingrix, you should report them to the Vaccine Adverse Event Reporting System (VAERS). Your doctor might file this report, or you can do it yourself through the VAERS website, or by calling 1-800-822-7967.

If you have any questions about side effects from Shingrix, talk with your doctor.

When Should I See a Doctor Because of the Side Effects I Experience from Shingrix?

Shingrix causes a strong response in your immune system, so it may produce short-term side effects. These side effects can be uncomfortable, but they are expected and usually go away on their own in 2 or 3 days. You may choose to take over-the-counter pain medicine such as ibuprofen or acetaminophen. Contact your healthcare provider if the symptoms are not improving or if they are getting worse.

In clinical trials, Shingrix was not associated with serious adverse events. In fact, serious side effects from vaccines are extremely rare. For example, for every 1 million doses of a vaccine given, only one or two people might have a severe allergic reaction. Signs of an allergic reaction happen within minutes or hours after vaccination and include hives, swelling of the face and throat, difficulty breathing, a fast heartbeat, dizziness, or weakness. If you experience these or any other life-threatening symptoms, see a doctor right away.

경청해주셔서 감사합니다.

고려대학교 의과대학 가정의학교실

2022 연수강좌

일차의료에서 흔히 사용하는 영양수액 총정리

신고은
고려의대 가정의학과

<영양치료 전 가능한 검사는? >

영양치료 전 가능한 검사

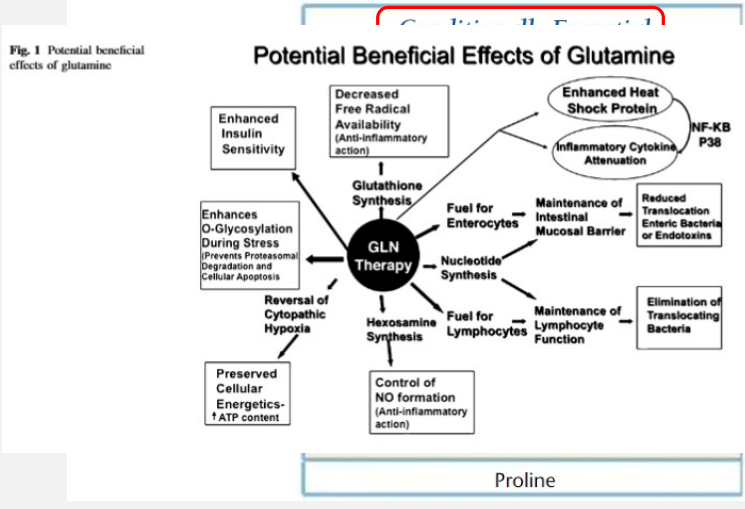
- 혈액검사: CBC, TFT, BUN, Cr., LFT 등의 일반적인 혈액검사, Cortisol, s-DHEA, Estradiol, FSH, Testosterone, NK cell
- Body Composition Analysis(In Body & Body Insight): 부종, 근육 량, 미토콘드리아 기능(phase angle)
- Heart rate variability test (HRV): TP, SDNN, RMSSD, LF/HF, SNS/PNS 지표 확인, 스트레스, 면역 상태, 교감 신경 형, 부교감 신경 형 파악
- 소변 유기산 검사: 영양소 대사(지방산, 탄수화물, 에너지 생성), 비타민 B군 지표(단백질 대사), 메틸화 조효소, 신경전달물질, 산화손상 및 항 산화, 해독 지표, 장내미생물 대사
- 타액 호르몬 검사: Cortisol, DHEA, Testosterone, Estradiol, Progesterone
- 모발 중금속/미네랄 검사: 중금속 오염, 미네랄 불균형

<흔히 사용하는 수액제제 알아보기
:면역 기능 중심>

- Glutamine
- Thymosin-alpa 1

GLUTAMINE

- Immune enhancer
- Maintains muscle
- Nitrogen transporter
- Carbon supply for gluconeogenesis
- Genesis of Glutathione



Laboratory Evaluations for Integrative and Functional Medicine
Glutamine as indispensable nutrient in oncology: Experimental and clinical evidence Eur J Nutr (2010) 49:197–210

GLUTAMINE

Category	Examples
Severe catabolic illness	Burns
	Multiple trauma
	Bone marrow supplementation
	Acute/chronic infection
	Other critical illness
Intestinal dysfunction	Inflammatory bowel disease
	Infectious enteritis
	Necrotizing enterocolitis or intestinal immaturity
	Short-bowel syndrome
	Mucosal damage following chemotherapy
	Radiation or critical disease
	Surgical gastrointestinal patients
Immunodeficiency syndromes	Immune system dysfunction associated with critical illness or bone marrow transplantation
	Acquired immunodeficiency syndrome
Advanced malignant disease	Cancer cachexia
Low-birth-weight babies	Premature infants

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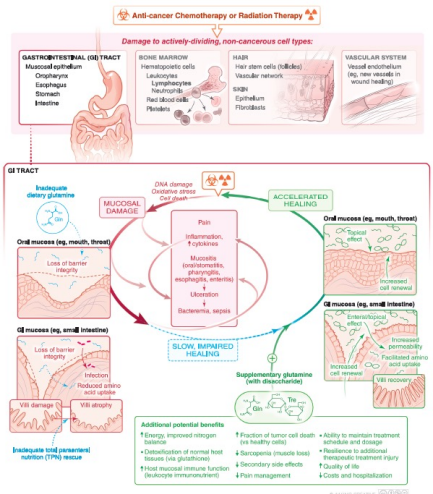

Laboratory Evaluations for Integrative and Functional Medicine

Glutamine for Amelioration of Radiation and Chemotherapy Associated Mucositis during Cancer Therapy 2020 Jun 4;12(6):1675.doi: 10.3390/nu12061675

nutrients

Review

Glutamine for Amel Chemotherapy Asso Cancer Therapy

Peter M. Anderson [1,*] and Rajesh

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Abstract: Glutamine is a major di healing tissues damaged by chemo (enteral) glutamine to reduce symp patients. Benefits include not only b stomatitis, pharyngitis, esophagitis, a (10 grams/day) + disaccharides, suc glutamine uptake by mucosal cells. T and ulceration associated with chem stomach and small intestine. Topic amino acid to promote mucosal heal

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SPECIAL ARTICLE

Systematic review of natura for the management of oral practice guidelines—part 1: supplements

Noam Yarom [1,2] · Allan Hovan [3] · Paolo Hanan Saca-Hazboun [9] · Abhishek kandwa Narmin Mohammed Nasr [13] · Tanya Roule Vinisha Ranna [19] · Anusha Vaddi [20] · Karis behalf of The Mucositis Study Group of th Society of Oral Oncology (MASCC/ISOO)

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Abstract
Purpose To update the clinical practice guic treatment of oral mucositis (OM).
Methods A systematic review was conducted in Cancer / International Society of Oral Onc treatment setting, was assigned an evidence l ISOO clinical practice guidelines. Based on Suggestion, and No Guideline Possible.
Results A total of 78 papers were identified w analyzed with 27 previously reviewed studies and neck (H&N) cancer patients receiving rad the use of parenteral glutamine for the preve established. A previous Suggestion for zinc radiotherapy was reversed to No Guideline P
Conclusions Of the vitamins, minerals, and n Recommendation against parenteral glutamin patients for the management of OM.

nutrients

MDPI

Article

Impact of Parenteral Glutamine Supplement on Oncologic Outcomes in Patients with Nasopharyngeal Cancer Treated with Concurrent Chemoradiotherapy

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Abstract: Background: Oral mucositis (OM) is a common toxic side effect in nasopharyngeal carcinoma (NPC) patients receiving concurrent chemoradiotherapy (CCRT) that has a negative impact on treatment outcomes and patients' survival. Our study aimed to evaluate the impact of parenteral glutamine supplement (dipeptiven) on oncologic outcomes in patients with NPC treated with CCRT. Methods: Patients who were diagnosed with pathologically proved NPC and treated with CCRT were enrolled into our study. Patients were classified as dipeptiven (+) and dipeptiven (–). Oncologic outcomes were measured, and multivariate regression analysis was performed. Grade 3–4 treatment related toxicities were also documented. Results: A total of 144 patients with NPC were recruited in this study to evaluate oncologic outcomes, with 41 dipeptiven (+) and 103 dipeptiven (–). CCRT interruption rate and severe adverse effect (SAE) rate were significant lower in the dipeptiven (+) group than in the dipeptiven (–) group. The median overall survival (OS) was not mature yet in the dipeptiven (+) group and 30 months in the dipeptiven (–) group ($p < 0.01$). Multivariate analysis demonstrated that dipeptiven supplementation and CCRT interruption were independent predictors associated with better survival. The OS was longest in patients with a dipeptiven supplement and patients who had CCRT interruption had significantly worst OS. As for safety profiles, grade 3 to 4 adverse effects were fewer in dipeptiven (+) than in dipeptiven (–). Conclusion: Dipeptiven supplementation is crucial in NPC patients treated with CCRT, which can ameliorate treatment-related toxicity and augment treatment efficacy. Further prospective clinical trials are warranted to validate our results.

check for updates

Citation: Wang, C.-C.; Hwang, T.-Z.; Yang, C.-C.; Lien, C.-F.; Wang, C.-C.; Shih, Y.-C.; Yeh, S.-A.; Hsieh, M.-C. Impact of Parenteral Glutamine Supplement on Oncologic Outcomes in Patients with Nasopharyngeal Cancer Treated with Concurrent Chemoradiotherapy. *Nutrients* **2022**, *14*, 997. https://doi.org/10.3390/nu14050997

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GLUTAMINE

제품명	디펩티벤주 Dipeptiven Inj.
성분 / 함량	N(2)-L-Alanyl-L-glutamine N(2)-엘알라닐-엘글루타민 동일성분 의약품 20g/100mL

■ 효능 · 효과

정맥영양요법을 실시하는 경우 아미노산 수액이나 아미노산 함유 수액에 보충하여 글루타민 보급

■ 용법 · 용량

성인 N(2)-L-알라닐-L-글루타민은 전체 아미노산 섭취량의 약 30%이상을 초과하지 않는 범위에서 1일 체중 kg당 0.3-0.5g를 아미노산 수액 또는 아미노산 함유 수액에 첨가하여 점적 정맥주사한다.
보통 성인의 아미노산 총 투여량은 1일 체중 kg당 2 g을 초과하지 않는다.
투여속도는 시간당 0.1 g 아미노산/kg 체중을 초과하지 않는다.
이 약의 투여는 3주를 넘지 않도록 한다.

50ml
(비급여)

100ml
(급여)

- PH: 5.4-6.0
- Osmolarity: 0.921mosm/L
- 임상적용:
  -점막 재생이 필요한 enteritis, IBS 환자
  -장점막 및 구강점막 재생이 필요한 chemotherapy를 받는 암환자
- 기본수액: NS or Amino Acids
- 주의 사항: severe renal insufficiency, hepatic insufficiency, metabolic acidosis, hypersensitivity

TABLE 1 | Pre-clinical and clinical studies with Tα1 in cancer and chronic hepatitis B and C.

Pathology	Study	Treatment	Efficacy	References
Melanoma	Pre-clinical	Tα1 monotherapy	Evidence of treatment efficacy	(15, 30)
			No significant evidence of treatment efficacy	(17–19, 31, 33–35)
		Tα1 in combination therapy with:		
		αβ-IFN	Evidence of treatment efficacy	(17–19)
		IL-2	Evidence of treatment efficacy	(19)
		Cy and αβ-IFN	Evidence of treatment efficacy	(20)
		anti-PD-1 Ab	Evidence of treatment efficacy	(30)
		Tα1 fusion proteins:		
		- concatemer	Evidence of treatment efficacy	(31)
		- thymopentin	Evidence of treatment efficacy	(32)
		- RGDR	Evidence of treatment efficacy	(33)
		- iRGD	Evidence of treatment efficacy	(34)
		- Fc	Evidence of treatment efficacy	(35)
	Clinical	Tα1 in combination therapy with:		
		- dacarbazine and IL-2	Evidence of treatment efficacy	(25)
		- dacarbazine and IFNα	Evidence of treatment efficacy	(26)
		- dacarbazine and IFNα	Evidence of treatment efficacy	(27, 29)
		- dacarbazine	Evidence of treatment efficacy	(28, 29)
Chronic hepatitis B	Clinical	Tα1 monotherapy	Evidence of treatment efficacy	(40, 42–44)
			No evidence of treatment efficacy	(46, 47)
		Tα1 in combination therapy with:		
		- IFNα	Evidence of treatment efficacy	(48–51)
		- pegylated IFNα	No evidence of treatment efficacy	(52)
		- famciclovir	Evidence of treatment efficacy	(62)
		- lamivudine	Evidence of treatment efficacy	(63)
		- entecavir	Evidence of treatment efficacy	(64)
			No evidence in HBV-related compensated cirrhosis	(65)
Chronic hepatitis C	Clinical	Tα1 monotherapy	No evidence of treatment efficacy	(54, 55)
		Tα1 in combination therapy with:		
		- IFNα	Evidence of treatment efficacy	(53, 56–58)
		- IFN and ribavirin	Evidence of treatment efficacy	(66–69)
			No evidence in on-treatment viral response	(70)
HCC	Clinical	Tα1 monotherapy	Evidence of treatment efficacy	(71, 72)
		Tα1 in combination therapy with:		
		- TACE	Evidence of treatment efficacy	(73–75)
		- lamivudine	Evidence of treatment efficacy	(76)
		- sorafenib	Evidence of treatment efficacy	(77)
Lung cancer	Pre-clinical	Tα1 monotherapy	Evidence of treatment efficacy	(19, 85–87, 89)
			No significant evidence of treatment efficacy	(17, 24, 34, 80, 84)
		Tα1 in combination therapy with:		
		- αβ-IFN	Evidence of treatment efficacy	(17, 19)
		- Cy and αβ-IFN	Evidence of treatment efficacy	(90)
		- Cy and IL-2	Evidence of treatment efficacy	(24)
		- gemcitabine	Evidence of treatment efficacy	(84)
		Tα1 fusion protein:	Evidence of treatment efficacy	(34)
		- iRGD		
	Clinical	Tα1 monotherapy	Evidence of treatment efficacy	(79)
		Tα1 in combination therapy with:		
		- cisplatin, etoposide, IFNα2a	Evidence of treatment efficacy	(81)
		- ifosfamide, IFNα	Trend toward treatment efficacy	(82)
		- cisplatin, vinorelbine or gemcitabine	Evidence of treatment efficacy	(83)

THYMOSIN-ALPHA 1

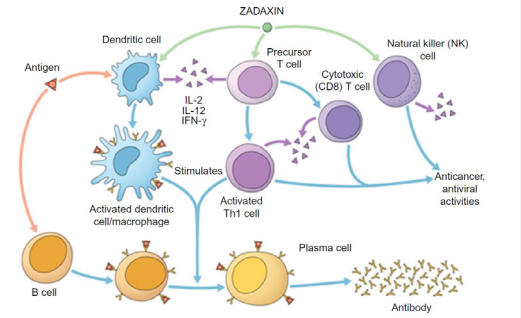


Fig. 1 Immune-stimulating mechanism of action of Ta1.

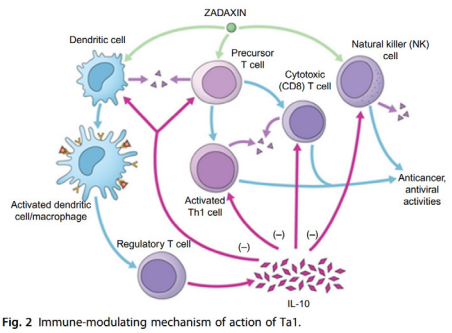


Fig. 2 Immune-modulating mechanism of action of Ta1.

- Immune stimulating effect
  - -Increase NK cell activity
  - -Increase the activity of dendritic cell
  - -Increase secretion of cytokines(IL-2, IFN-γ)
  - -Increase the level of cytotoxic T cell
- Immune modulating effect
- Direct acting effect

Vitamins and Hormone volume 102, 2016,Pages 151-178: Immune Modulation with Thymosin Alpha 1 Treatment

THYMOSIN-ALPHA 1

제품명	자닥신주 Zadaxin Injection	
성분 / 함량	Thymosin-α1 싸이모신알파1 1.6mg	동일성분 의약품

▪ 효능 · 효과

면역기능이 저하된 고령 환자의 인플루엔자 백신접종시의 보조요법

▪ 용법 · 용량

이 약 900ug/m²(1바이알)을 백신접종 첫 주부터 4주간 주 2회씩 피하 또는 근육 주사 한다.
투여 직전, 첨부된 용제에 녹여 주사한다.

- 임상적용:
  - -암환자, 암 경험자 면역 보조
  - -반복되는 바이러스 질환(감기, 대상포진 등)
  - -NK cell 낮은 환자
- 면역치료 목적에서의 용법:
  - -주 1회 혹은 주2회 피하 또는 근육주사/ 기본 8회 투약
- 금기 : 면역 억제제를 투약중인 장기 이식 환자

<흔히 사용하는 수액제제 알아보기
:비타민 제제 중심으로 >

- Vitamin C
- Vitamin B1, B5, B6, B12

VITAMIN C

Table 22-1. Vitamin C may be useful for preventing and/or treating the following conditions

Cardiovascular
Atherosclerosis/ischemic heart disease
Hypertension
Thrombophlebitis

Dermatological
Furuncles
Herpes simplex
Herpes zoster
Immune thrombocytopenic purpura
Prickly heat
Sunburn
Wrinkles, photoaging

Ear, nose, and throat
Allergic rhinitis
Sinusitis

Gastrointestinal
Constipation
Gallstones
Gastritis
Peptic ulcer

Infectious disease
Acquired immunodeficiency syndrome
Colds
Diphtheria
Influenza
Leprosy
Measles
Infectious mononucleosis
Tuberculosis
Urinary tract infection

Musculoskeletal
Herniated disc
Muscle cramps
Osteogenesis imperfecta
Paget's disease (osteitis deformans)
Complex regional pain syndrome

Obstetrical and gynecological
Dysfunctional uterine bleeding
Leg cramps of pregnancy
Premature rupture of membranes

Ophthalmological
Conjunctivitis
Glaucoma
Uveitis

Psychiatric
Depression
Schizophrenia

Other
Asthma
Burns
Cancer
Critical illness
Diabetes
Gingivitis
Hepatitis
Hypoadrenalism
Infertility
Obesity
Opioid addiction
Post-exercise muscle soreness

VITAMIN C THERAPY 의 역사와 논쟁 1

- Irwin Stone
- Linus Pauling & Cameron
  - Linus Pauling: 화학자, 노벨 화학상과 노벨 평화상을 수상
  - Cameron: 외과의사로 라이너스 폴링의 임상시험을 대신 해줄 의사를 찾으면서 만나게 됨.
  - 1976년 비타민 C와 암 치료에 대한 임상연구에 긍정적인 결과를 얻게 됨
  - 1978년 라이너스 폴링과 유안 카메론은 매일 10g 이상의 고용량 비타민 C 투약이 생존기간을 대조군에 비해 4.2배 증가시키고 삶의 질도 개선 시킨다고 연구를 발표
- Linus Pauling은 미국 국립 암 연구소에 임상실험 지원을 요청, Mayo Clinic의 Moertel 교수가 임상 시험 시작
- Mayo Clinic의 Moertel 연구팀, 두 차례의 RCT 연구는 모두 실패: 경구로 10g/day을 사용
- Mark Levin 교수 연구팀 PO 제제는 혈중 농도를 올리지 못하고 IV 형태를 사용해야 함을 밝혀냄
  - Annal of internal medicine. 2004:4: Vitamin C Pharmacokinetics: Implication for Oral and Intravenous Use

VITAMIN C THERAPY 의 역사와 논쟁 2

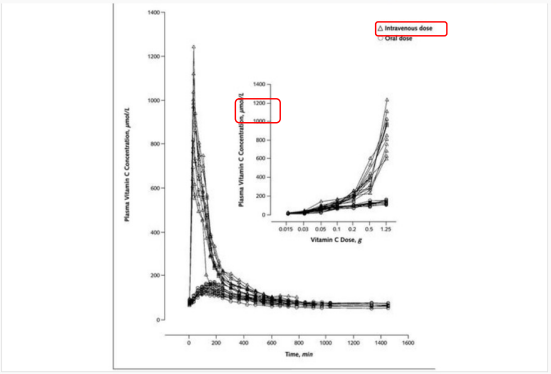


Figure 1. Plasma vitamin C concentrations in healthy volunteers after intravenous or oral administration of vitamin C.

Plasma vitamin C concentrations are shown as a function of time after the 1.25-g oral or intravenous dose administered at steady state for that dose in 12 persons (3 men, 9 women). *Inset:* Peak plasma vitamin C concentrations as a function of dose after oral or intravenous administration of vitamin C. Seventeen persons (7 men, 10 women) received doses from 0.015 to 0.1 g, 16 persons (6 men, 10 women) received the 0.2-g dose, 14 persons (6 men, 8 women) received the 0.5-g dose, and 12 persons (3 men, 9 women) received the 1.25-g dose. Persons received each dose while at steady state for that dose.

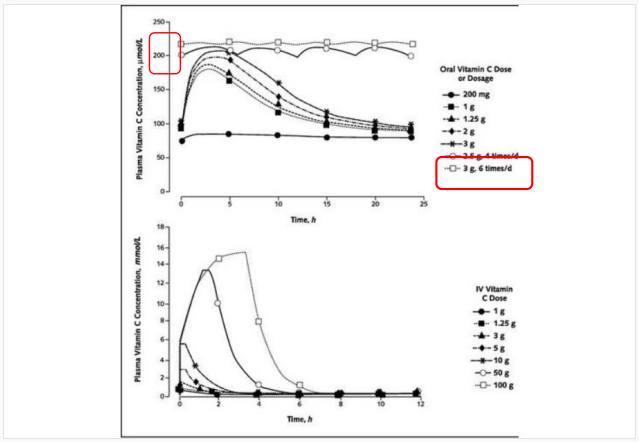
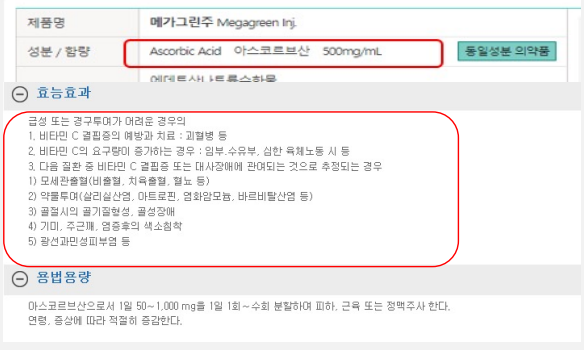


Figure 2. Predicted plasma vitamin C concentrations in healthy persons after oral (*top*) **or intravenous (***IV*) (*bottom*) **administration of vitamin C.**

VITAMIN C

- Antioxidant
  - Protect indispensable molecules(proteins, lipids, carbohydrates, and DNA/RNA) in the body from damage by free radicals and reactive oxygen species(ROS)
- Enzyme cofactor
  - Biosynthesis of collagen, carnitine, and neuropeptide
  - Regulation of gene expression

VITAMIN C



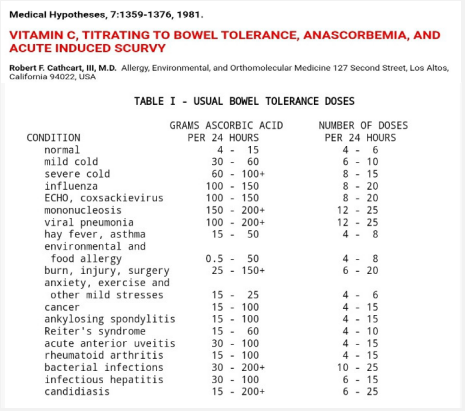
- PH 6.61
- Osmolarity: 5.32 mosm/mL
- RDA: 여성 75mg, 남성 90mg (흡연자는 하루 35mg을 추가)(UL: 2000mg)
- 임상 적용: 항산화, 항염증, 항 바이러스, 면역력 증진, 중금속 해독, 항암
- 기본 수액: NS, 5% DW, SW(항암 목적 고용량 투여 시)

VITAMIN C-주의해야 할 사항은?

- 신장결석을 진단 받은 환자
- Decreased renal function , ascites, CHF 등이 있는 환자
- G6PD 결핍 환자
- 고용량 투여 시 hypocalcemia 주의 (Calcium Gluconate IV)
- 높은 오스몰 농도, 혈관 통 주의

VITAMIN C-어떻게 , 얼마나?

- IV or P.O?
  - To reduce common chemotherapy-related symptoms and improve quality of life
  - To treat cancer
- IV 용량
  - 항암 목적: 50-100g (혈중농도 350-400mg/dL)
  - 건강증진: 10g-20g
- P.O제제 복용 시 용량
  - Food and nutrition board upper intake level: 2000mg
  - Bowel tolerance까지 복용가능
  - 건강한 사람은 3g-6g을 하루 3-4회 분복
  - 만성 질환 등 소모성 질환이 있을 경우 bowel tolerance까지 분복



Medical Hypotheses, 7:1359-1376, 1981.

VITAMIN C, TITRATING TO BOWEL TOLERANCE, ANASCORBEMIA, AND ACUTE INDUCED SCURVY

Robert F. Cathcart, III, M.D. Allergy, Environmental, and Orthomolecular Medicine 127 Second Street, Los Altos, California 94022, USA

TABLE I - USUAL BOWEL TOLERANCE DOSES

CONDITION	GRAMS ASCORBIC ACID PER 24 HOURS	NUMBER OF DOSES PER 24 HOURS
normal	4 - 15	4 - 6
mild cold	30 - 60	6 - 10
severe cold	60 - 100+	8 - 15
influenza	100 - 150	8 - 20
ECHO, coxsackievirus	100 - 150	8 - 20
mononucleosis	150 - 200+	12 - 25
viral pneumonia	100 - 200+	12 - 25
hay fever, asthma	15 - 50	4 - 8
environmental and food allergy	0.5 - 50	4 - 8
burn, injury, surgery	25 - 150+	6 - 20
anxiety, exercise and other mild stresses	15 - 25	4 - 6
cancer	15 - 100	4 - 15
ankylosing spondylitis	15 - 100	4 - 15
Reiter's syndrome	15 - 60	4 - 10
acute anterior uveitis	30 - 100	4 - 15
rheumatoid arthritis	15 - 100	4 - 15
bacterial infections	30 - 200+	10 - 25
infectious hepatitis	30 - 100	6 - 15
candidiasis	15 - 200+	6 - 25

VITAMIN B

Energy production:

- Tiredness
- Exhaustion
- Chronic fatigue
- Impaired physical performance
- Weakness

Nerves:

- Unpleasent physical sensations (numbness, tingling),
- Neuropathies, paralysis
- Loss of control, palsey

Cell division/DNA synthesis:

- Skin, hair and nail problems
- Anaemia
- Inflammation
- Problems with mucous membranes (in the mouth or genetalia)
- Inflamed tounge or mouth ulcers
- Torn corners of the mouth
- Chronic diarrhoea

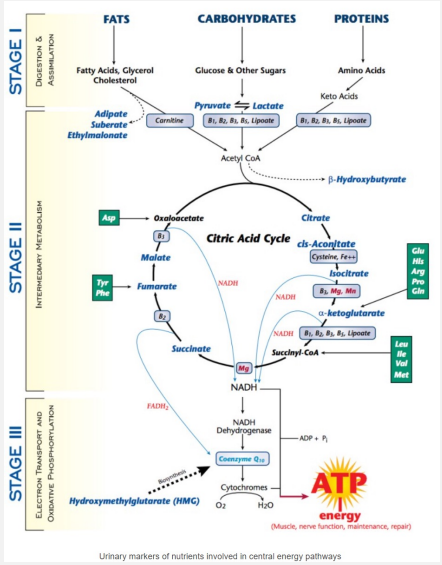
Psychology/neurotransmitters:

- Depression
- Insomnia
- Migranes
- Schizophrenia, psychoses
- Dementia, cognitive decline
- Concentration difficulties
- Confusion, mental "fogginess"

Immune system:

- High susceptibility to infections
- Chronic infection
- Chronic inflammation

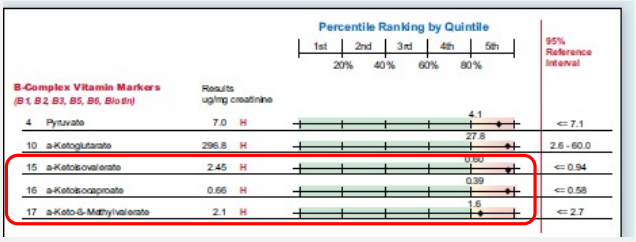
VITAMIN B



Urinary markers of nutrients involved in central energy pathways

Laboratory Evaluations for Integrative and Functional Medicine

VITAMI



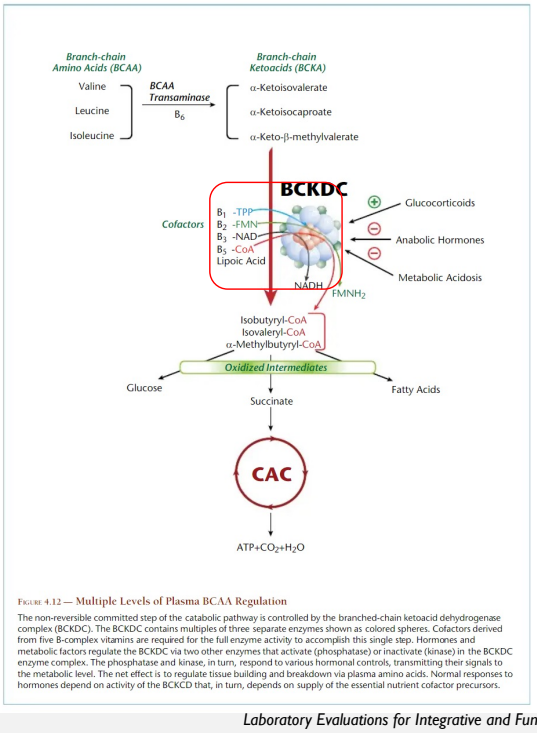


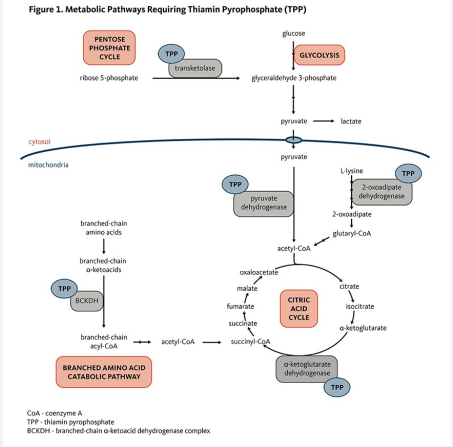
FIGURE 4.12 — Multiple Levels of Plasma BCAA Regulation

The non-reversible committed step of the catabolic pathway is controlled by the branched-chain ketoacid dehydrogenase complex (BCKDC). The BCKDC contains multiples of three separate enzymes shown as colored spheres. Cofactors derived from five B-complex vitamins are required for the full enzyme activity to accomplish this single step. Hormones and metabolic factors regulate the BCKDC via two other enzymes that activate (phosphatase) or inactivate (kinase) in the BCKDC enzyme complex. The phosphatase and kinase, in turn, respond to various hormonal controls, transmitting their signals to the metabolic level. The net effect is to regulate tissue building and breakdown via plasma amino acids. Normal responses to hormones depend on activity of the BCKCD that, in turn, depends on supply of the essential nutrient cofactor precursors.

Laboratory Evaluations for Integrative and Functional Medicine

VITAMIN B1

- Involved in several enzyme functions
  - Associated with the metabolism of carbohydrate, BCCA, and fatty acids



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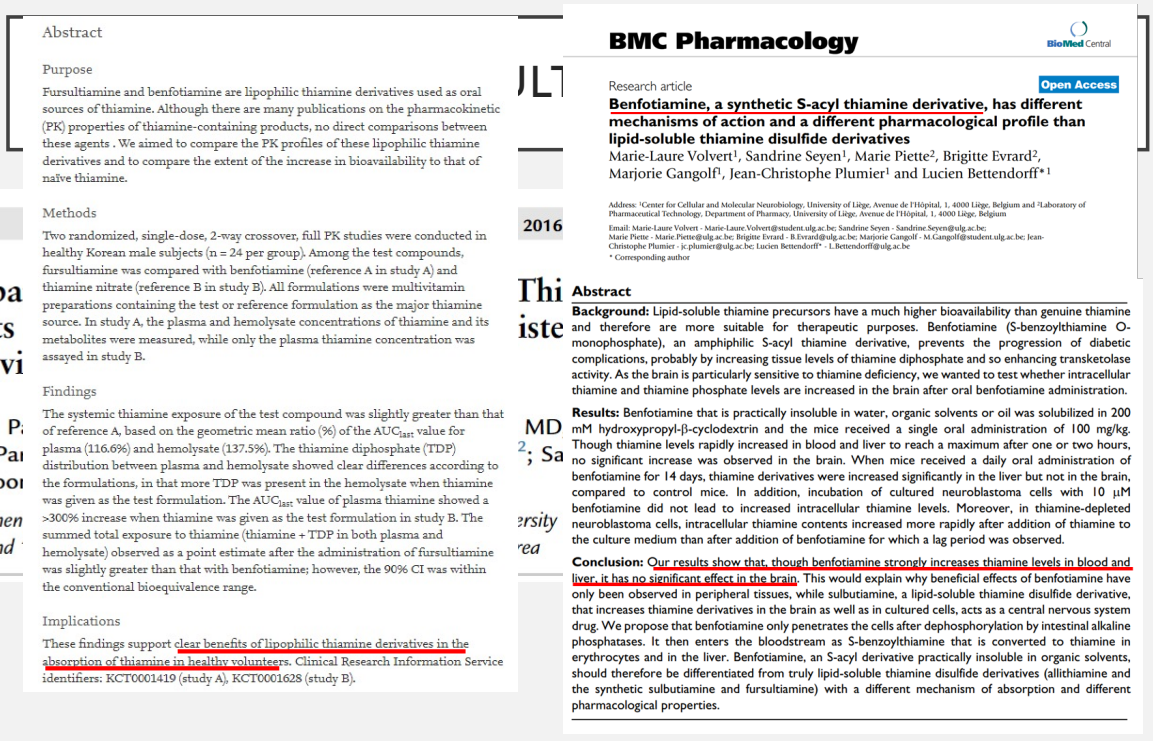

Abstract

Purpose

Fursultiamine and benfotiamine are lipophilic thiamine derivatives used as oral sources of thiamine. Although there are many publications on the pharmacokinetic (PK) properties of thiamine-containing products, no direct comparisons between these agents . We aimed to compare the PK profiles of these lipophilic thiamine derivatives and to compare the extent of the increase in bioavailability to that of naïve thiamine.

Methods

Two randomized, single-dose, 2-way crossover, full PK studies were conducted in healthy Korean male subjects (n = 24 per group). Among the test compounds, fursultiamine was compared with benfotiamine (reference A in study A) and thiamine nitrate (reference B in study B). All formulations were multivitamin preparations containing the test or reference formulation as the major thiamine source. In study A, the plasma and hemolysate concentrations of thiamine and its metabolites were measured, while only the plasma thiamine concentration was assayed in study B.

Findings

The systemic thiamine exposure of the test compound was slightly greater than that of reference A, based on the geometric mean ratio (%) of the AUC_{last} value for plasma (116.6%) and hemolysate (137.5%). The thiamine diphosphate (TDP) distribution between plasma and hemolysate showed clear differences according to the formulations, in that more TDP was present in the hemolysate when thiamine was given as the test formulation. The AUC_{last} value of plasma thiamine showed a >300% increase when thiamine was given as the test formulation in study B. The summed total exposure to thiamine (thiamine + TDP in both plasma and hemolysate) observed as a point estimate after the administration of fursultiamine was slightly greater than that with benfotiamine; however, the 90% CI was within the conventional bioequivalence range.

Implications

These findings support clear benefits of lipophilic thiamine derivatives in the absorption of thiamine in healthy volunteers. Clinical Research Information Service identifiers: KCT0001419 (study A), KCT0001628 (study B).

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BMC Pharmacology

BioMed Central

Research article

Open Access

Benfotiamine, a synthetic S-acyl thiamine derivative, has different mechanisms of action and a different pharmacological profile than lipid-soluble thiamine disulfide derivatives

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* Corresponding author

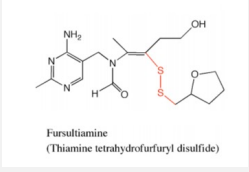
Abstract

Background: Lipid-soluble thiamine precursors have a much higher bioavailability than genuine thiamine and therefore are more suitable for therapeutic purposes. Benfotiamine (S-benzoylthiamine O-monophosphate), an amphiphilic S-acyl thiamine derivative, prevents the progression of diabetic complications, probably by increasing tissue levels of thiamine diphosphate and so enhancing transketolase activity. As the brain is particularly sensitive to thiamine deficiency, we wanted to test whether intracellular thiamine and thiamine phosphate levels are increased in the brain after oral benfotiamine administration.

Results: Benfotiamine that is practically insoluble in water, organic solvents or oil was solubilized in 200 mM hydroxypropyl-β-cyclodextrin and the mice received a single oral administration of 100 mg/kg. Though thiamine levels rapidly increased in blood and liver to reach a maximum after one or two hours, no significant increase was observed in the brain. When mice received a daily oral administration of benfotiamine for 14 days, thiamine derivatives were increased significantly in the liver but not in the brain, compared to control mice. In addition, incubation of cultured neuroblastoma cells with 10 μM benfotiamine did not lead to increased intracellular thiamine levels. Moreover, in thiamine-depleted neuroblastoma cells, intracellular thiamine contents increased more rapidly after addition of thiamine to the culture medium than after addition of benfotiamine for which a lag period was observed.

Conclusion: Our results show that, though benfotiamine strongly increases thiamine levels in blood and liver, it has no significant effect in the brain. This would explain why beneficial effects of benfotiamine have only been observed in peripheral tissues, while sulbutiamine, a lipid-soluble thiamine disulfide derivative, that increases thiamine derivatives in the brain as well as in cultured cells, acts as a central nervous system drug. We propose that benfotiamine only penetrates the cells after dephosphorylation by intestinal alkaline phosphatases. It then enters the bloodstream as S-benzoylthiamine that is converted to thiamine in erythrocytes and in the liver. Benfotiamine, an S-acyl derivative practically insoluble in organic solvents, should therefore be differentiated from truly lipid-soluble thiamine disulfide derivatives (allithiamine and the synthetic sulbutiamine and fursultiamine) with a different mechanism of absorption and different pharmacological properties.

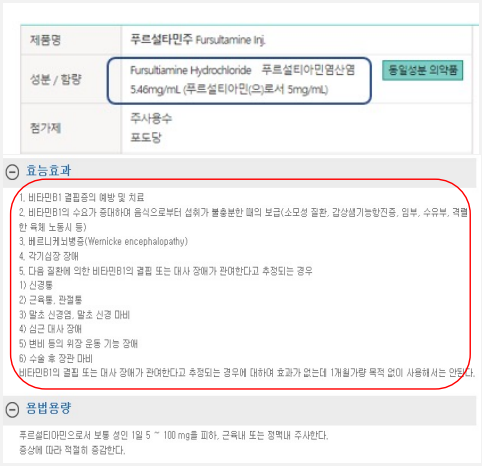
VITAMIN B1-FURSULTIAMINE



Fursultiamine
(Thiamine tetrahydrofurfuryl disulfide)

- 항 산화 작용
  - 유황 화합물이 체내 활성산소제거
- 에너지대사 촉진
  - 조효소로 TCA 회로를 활성화시켜 에너지 생성 촉진, 근육 내 피로 물질인 lactic acid 생성 억제, 피로를 회복시키는 역할
- 신경기능 장애 개선
  - 신경세포 증식 촉진, 신경재생 촉진, 근 골격 계 활동전위를 증가 시킴
- 심근대사 장애 개선
  - Thiamine에 비해 심근세포 내로 들어가는 양이 많음, 심근대사 장애 개선
  - 심박수 억제와 심근 수축력 강화를 가져옴

VITAMIN B1-FURSULTIAMINE



제품명	푸르설타민주 Fursultamine Inj.	
성분 / 함량	Fursultiamine Hydrochloride 푸르설티아민염산염 546mg/mL (푸르설티아민(오)로서 5mg/mL)	동일성분 의약품
첨가제	주사용수 포도당	

⊖ 효능효과

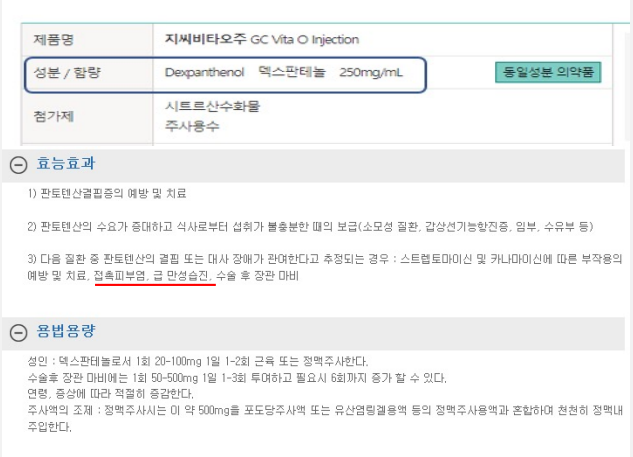
1. 비타민B1 결핍증의 예방 및 치료
2. 비타민B1의 수요가 증대하여 음식으로부터 섭취가 불충분한 때의 보급(소모성 질환, 갑상샘기능항진증, 임부, 수유부, 격렬한 육체 노동시 등)
3. 베르니케뇌병증(Wernicke encephalopathy)
4. 각기심장 장애
5. 다음 질환에 의한 비타민B1의 결핍 또는 대사 장애가 관여한다고 추정되는 경우
1) 신경통
2) 근육통, 관절통
3) 말초 신경염, 말초 신경 마비
4) 심근 대사 장애
5) 변비 등의 위장 운동 기능 장애
6) 수술 후 장관 마비
비타민B1의 결핍 또는 대사 장애가 관여한다고 추정되는 경우에 대하여 효과가 없는데 1개월가량 특적 없이 사용해서는 안된다.

⊖ 용법용량

푸르설티아민으로서 보통 성인 1일 5 ~ 100 mg을 피하, 근육내 또는 정맥내 주사한다.
증상에 따라 적절히 증감한다.

- PH: 3.65
- Osmolarity: 2.22mosm/mL
- RDA: 1.0-1.5mg/UL:NA
- 임상 적용: 피로회복, 통증, 음주 후, 말초 신경 염, 운동 후 회복
- 주의사항: 과민 반응
- 기본 수액: NS, 5%DW

VITAMIN B5-PANTOTHENIC ACID



제품명	지씨비타오주 GC Vita O Injection	
성분 / 함량	Dexpanthenol 덱스판테놀 250mg/mL	동일성분 의약품
첨가제	시트르산수화물 주사용수	

⊖ 효능효과

1) 판토텐산결핍증의 예방 및 치료

2) 판토텐산의 수요가 증대하고 식사로부터 섭취가 불충분한 때의 보급(소모성 질환, 갑상선기능항진증, 임부, 수유부 등)

3) 다음 질환 중 판토텐산의 결핍 또는 대사 장애가 관여한다고 추정되는 경우 : 스트렙토마이신 및 카나마이신에 따른 부작용의 예방 및 치료, 접촉피부염, 급 만성습진, 수술 후 장관 마비

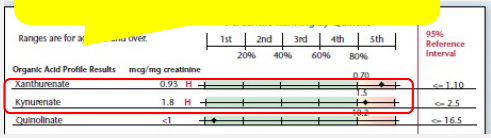
⊖ 용법용량

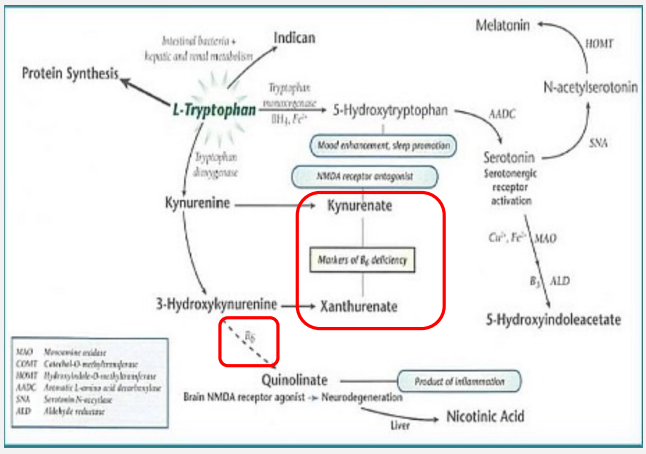
성인 : 덱스판테놀로서 1회 20-100mg 1일 1-2회 근육 또는 정맥주사한다.
수술후 장관 마비에는 1회 50-500mg 1일 1-3회 투여하고 필요시 6회까지 증가 할 수 있다.
연령, 증상에 따라 적절히 증감한다.
주사액의 조제 : 정맥주사시는 이 약 500mg을 포도당주사액 또는 유산염링겔용액 등의 정맥주사용액과 혼합하여 천천히 정맥내 주입한다.

- PH: 5.48
- Osmolarity: 1.931mosm/mL
- RDA: 5mg/d (UL: NA)
- 기능: Coenzyme A의 precursor, 에너지 대사, 콜레스테롤, 성호르몬 합성, 지방산 합성에 관여
- 임상 적용: 피부질환, 부신 피로(코티솔 분해 억제) 완화, 비만 치료
- 기본 수액: NS, 5%DW

VITAMINB6-PYRIDOXINE

Vitamin B6 결핍 시 증가





Laboratory Evaluations for Integrative and Functional Medicine

VITAMINB6-PYRIDOXINE

- Tryptophan metabolism
- Homocysteine metabolism
- Hemoglobin synthesis and function
- Neurotransmitter synthesis
- Protein metabolism

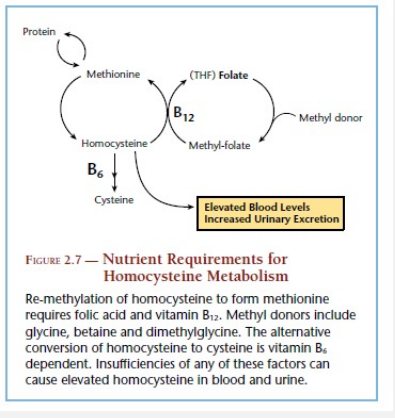


FIGURE 2.7 — **Nutrient Requirements for Homocysteine Metabolism**

Re-methylation of homocysteine to form methionine requires folic acid and vitamin B_{12}. Methyl donors include glycine, betaine and dimethylglycine. The alternative conversion of homocysteine to cysteine is vitamin B_6 dependent. Insufficiencies of any of these factors can cause elevated homocysteine in blood and urine.

Laboratory Evaluations for Integrative and Functional Medicine

VITAMINB6-PYRIDOXINE

제품명	메가비타식스주 Megavitasix Injection
성분 / 함량	Pyridoxine Hydrochloride 피리독신염산염 50mg/mL 동일성분 의약품
첨가제	주사용수

효능효과

1. 비타민 B6 결핍증의 예방 및 치료
약물투여(예: 이소니아지드, 하이드랄라진, 페니실라민)로 인한 경우 포함

2. 비타민B6의 수요가 증대하여, 식사로부터의 섭취가 불충분할 경우
소모성 질환, 임부 · 수유부, 에스트로겐제제(예: 경구피임제) 복용자 등

3. 비타민 B6 의존증
비타민 B6 반응성 빈혈 등

4. 다음 질환 중 비타민 B6의 결핍 또는 대사장애가 관여한다고 추정되는 경우
1) 구각염, 구순염, 구내염, 설염
2) 급 · 만성 습진, 지루성 습진, 접촉성 피부염
3) 말초신경염
4) 방사선장애(숙취, 宿醉)

용법용량

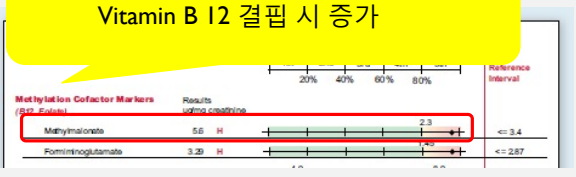
경구복용이 어려울 경우
○ 성인 : 피리독신염산염으로서 1일 10~100 mg을 1~2회 분할하여 근육, 피하 또는 정맥주사 한다.
- 비타민 B6 의존증인 경우에는 고용량을 투여할 수 있다.

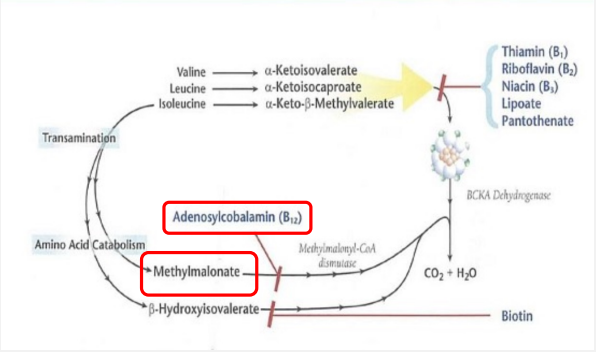
연령, 증상에 따라 적절히 증감한다.

- PH 4.21
- Osmolarity: 0.47mosm/mL
- RDA: 1.2-1.8mg/d (UL: 100mg/d)
- 임상 적용: 피로 회복,통증, 말초 신경 염, 임신성 구토(tryptophan 대사를 증가), 월경 전 증후군
- 기본 수액: NS, 5%DW

VITAMIN B12-COBALAMIN

Vitamin B 12 결핍 시 증가





Laboratory Evaluations for Integrative and Functional Medicine

VITAMIN B12-COBALAMIN

- Homocysteine metabolism
- DNA synthesis
  - Poor vitamin B_{12} status has been linked to increased risk of breast cancer
- Preservation of the myelin sheath around neurons and neurotransmitters synthesis
- Folate metabolism and synthesis of citric acid cycle intermediate, succinyl-CoA

Drug Category	Name	Nutrient	Effect on Nutrient Status or Function	Human Studies [1]	Risk Factors	References
Acid-Suppressing Drugs	Proton Pump Inhibitors	Vitamin B12 Vitamin C Iron CalciumMagnesium Zinc β-Carotene	Decrease Decrease Decrease Decrease Decrease Decrease Decrease	5 observational 5 intervention 1 observation 4 intervention 2 case reports 1 observational 2 intervention >10 observational 4 intervention 30 case reports 2 intervention 1 intervention	Advanced age *H. pylori* infection Genetics (slow metabolizers Low dietary intake (vegetarians) *H. pylori* infection Pre-existing iron deficiency Vegetarians Advanced age Women Advanced age Duration of drug use Women Undetermined	[10–17] [18–22] [23] [24–28] [29–31] – –
Hypercholesterolemics	Statins	Coenzyme Q10 Vitamin D Vitamin E/β-Carotene	Decrease Increase/Decrease Increase/Decrease	7 observational >10 intervention >10 observational 4 intervention 1 observational 6 intervention	Dose Advanced age Statin-associated myopathy Heart disease Vitamin D deficiency Statin-associated myopathy Undetermined	[104–114] [115–128] –
Hypoglycemics	Biguanides (Metformin) Thiazolidinediones	Vitamin B12 Calcium/Vitamin D	Decrease Decrease	>10 observational >10 intervention 3 observational >10 intervention	Dose/duration of drug use Advanced age Vegetarians Advanced age Women Low calcium/vitamin D intake	[129–140] [141–145]
Corticosteroids	Glucocorticosds (oral)	Calcium/Vitamin D Sodium/Potassium Chromium	Decrease Increase (sodium) Decrease (potassium) Decrease	>80 observational >10 intervention ~5 case reports/observational 1 intervention 1 intervention	Low calcium/vitamin D intake At risk for bone fracture/loss Undetermined Undetermined	[146–154] – –
Bronchodilators	Corticosteroids (inhaled)	Calcium/Vitamin D	Decrease	>10 observational >10 intervention	Presence of COPDSmoking At risk for bone fracture/loss Low calcium/vitamin D intake	[155–159]
Antidepressants	Selective Serotonin Reuptake Inhibitors	Folate [3] Calcium/Vitamin D	Increase [3] Decrease	5 observational 2 intervention >10 observational	Low folate intake Genetics (MTHFR variants) Alcoholism At risk for bone fracture/loss Low calcium/vitamin D intake	[160–167] [168–171]
Oral Contraceptives	Estrogen and/or Progesterone	Vitamin B6 Vitamin B12/Folate Calcium Magnesium Vitamin C/Vitamin E	Decrease Decrease Increase/decrease Decrease Decrease	>10 observational 5 intervention 4 case reports >30 observational 5 intervention 7 observational 6 intervention >20 observational >10 observational 2 intervention	Undetermined Vegetarians Low folate intake Genetics (folate) Duration of drug use Duration of drug use Physical activity level Low calcium intake Age at first use Race Type of combined OC used Undetermined	– [172–183] [184–193] [194–200] –

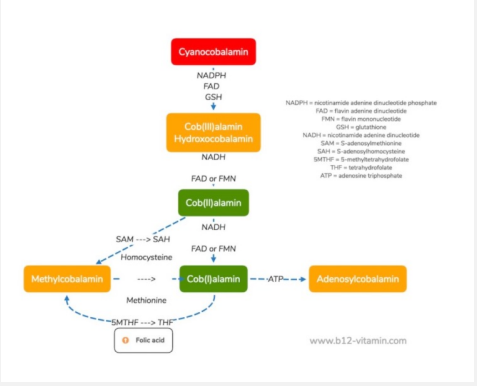
[1] Total number of studies that have investigated the potential drug–nutrient interaction (includes both significant and null results); [2] Nutrient effect on drug side effect; [3] Effect of nutrient on drug efficacy.

Evidence of Drug–Nutrient Interactions with Chronic Use of Commonly Prescribed Medications: An Update . 2018 Mar 20;10(1):36. doi: 10.3390/pharmaceutics10010036.

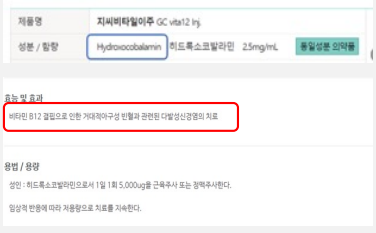
TYPES OF VITAMIN B12

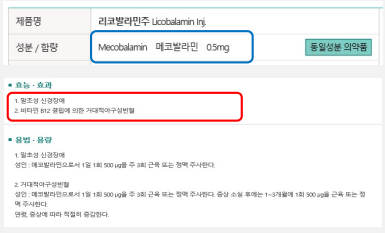
Types of Vitamin B12 Compared

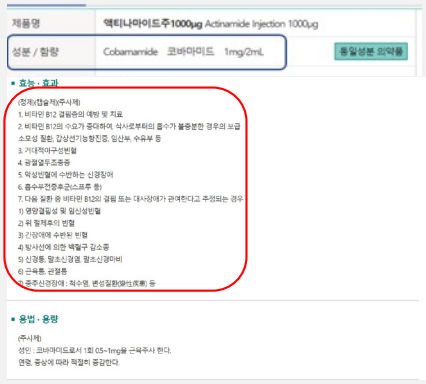
Cobalamin	Natural Form?	Bioactive Coenzyme?	Conversion steps necessary	Sustained Release	Special Effect
Cyanocobalamin 'the synthetic B12'	no	no	4	average to poor	No particular effect
Hydroxocobalamin 'the long lasting B12'	yes	no	3	very good	Detoxification of cyanide & NO
Methylcobalamin 'the DNA & nerves B12'	yes	yes	0	average	DNA, brain, nerves, blood, detoxification
Adenosylcobalamin 'the energy B12'	yes	yes	0	average	Energy, muscles, brain, DNA



VITAMIN B12-COBALAMIN







- PH: 4.58
- Osmolarity: 0.182mosm/ml
- RDA: 2.4 μg/d(UL: NA)
- 임상 적용: 통증, 말초 신경 염, 인지기능 개선
- 기본 수액: NS, 5% DW

<흔히 사용하는 수액제제 알아보기
:부신 기능 중심 >

- Vitamin B
- Glycyrrhizine(감초주사)
- Magnesium

SALIVARY HORMONE TEST

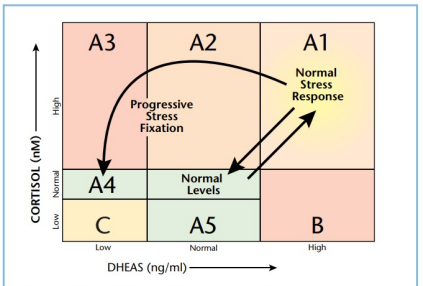
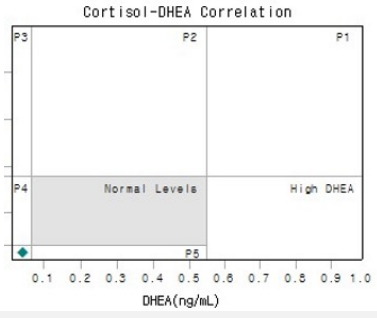


FIGURE 10.4 — Stress Responses of Cortisol and DHEA

The values that are plotted are the average of noon and 5 p.m. levels for salivary cortisol and DHEA. The quadrants represent normal and abnormal patterns, with A1 to A4 representing progressive failure of the normal ACTH response.

Reference Range	Units
3,1 ~ 24,0	nM
2,0 ~ 10,0	nM
1,5 ~ 8,7	nM
0,9 ~ 4,0	nM
8,0 ~ 46,7	nM
0,06 ~ 0,54	ng/mL

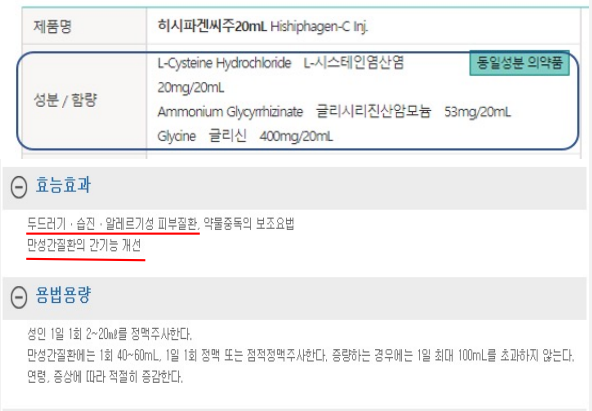


Laboratory Evaluations for Integrative and Functional Medicine

감초주사의 작용

- Glycyrrhizin(40mg)
  - 항염과 항알레르기
  - 11-beta hydroxysteroid dehydrogenase를 억제해서 채내 cortisol level 상승, steroid로 비슷한 효과를 줌
  - 면역증강과 항 바이러스
  - 인터페론 생성을 유도, 바이러스 복제를 억제
- Cystein (20mg)
  - Glutathione의 구성 성분으로 간 해독과정에 중요한 역할을 함
  - 콜라겐 형성과 피부 탄력 유지
- Glycin(400mg)
  - Glycyrrhizin의 알도스테론 효과를 예방해주는 역할
  - 간 해독 phase Ⅱ에서 아미노산 결합

GLYCYRRHIZIN(감초주사)



제품명	히시파겐씨주20mL Hishiphagen-C Inj.
성분 / 함량	L-Cysteine Hydrochloride L-시스테인염산염 20mg/20mL (동일성분 의약품) Ammonium Glycyrrhizinate 글리시리진산암모늄 53mg/20mL Glycine 글리신 400mg/20mL

⊖ 효능효과

두드러기 · 습진 · 알레르기성 피부질환, 약물중독의 보조요법
만성간질환의 간기능 개선

⊖ 용법용량

성인 1일 1회 2~20㎖를 정맥주사한다.
만성간질환에는 1회 40~60mL, 1일 1회 정맥 또는 점적정맥주사한다. 증량하는 경우에는 1일 최대 100mL를 초과하지 않는다.
연령, 증상에 따라 적절히 증감한다.

- PH 6.9
- Osmolarity: 0.298mosm/ml
- 임상 적용: 만성 피로(코티솔 분해 억제), 항 바이러스, 항 염증, 항 산화, 간 기능 개선, 피부질환
- 주의사항: 과민반응, 혈압이 높은 환자 및 가성 알도스테론증 주의 필요
- 기본수액: NS, 5%DW

MAGNESIUM

- Energy Production
  - plays a key role in more than 350 enzymes
- DNA & RNA synthesis
- Protein, carbohydrate and fatty acid metabolism
- Key cofactor in both methylation and sulfur amino acid metabolism
- Formation of active cofactors from vitamins B1, B2, B3, B6 and pantothenic acid

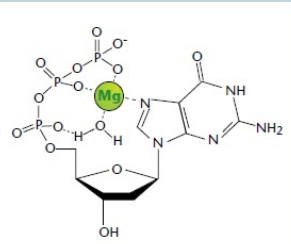


FIGURE 3.7 — **The Magnesium-ATP Complex**

The Mg-ATP complex is a tetradentate ligand, where four of the six coordination positions of magnesium are bound to three ATP oxygen atoms and one ring nitrogen atom. The binding to the first phosphate group is mediated through a water molecule interposed between it and the Mg^{2+} ion.

Laboratory Evaluations for Integrative and Functional Medicine

MAGNESIUM

제품명	**메가네슘주10%** Meganessium Injection 10%
성분 / 함량	Magnesium Sulfate Hydrate 황산마그네슘수화물 0.1g 동일성분 의약품

효능효과

저마그네슘혈증에 의한 경련, 자간증의 발작, 자궁경직 방지, 전해질보급(저마그네슘혈증)

용법용량

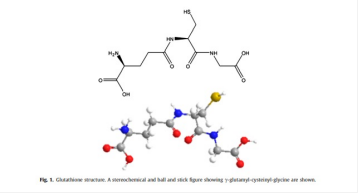
○ 저마그네슘혈증에 의한 경련 : 마그네슘황산염으로서 1 ~ 2 g을 정맥주사한다(4.05 ~ 8.1 mmol).
○ 자간증의 발작 : 이 약으로서 4 ~ 5 g을 10분간 정맥주사 한다(16.2 ~ 20.25 mmol)
○ 자궁경직 방지 : 이 약으로서 초기 4 g을 정맥주사한다(16.2 mmol), 이후 1 g을 투여할 수 있다.
○ 전해질보급(저마그네슘혈증) : 이 약으로서 1 g을 6시간마다 4회 근육주사한다. 또는 이 약 5 g을 5 % 포도당주사액이나 0.9 % 생리식염 주사액에 첨가하여 3시간동안 정맥내투여를 할 수 있다. 결핍증 치료시 환자의 신장배출기능을 잘 살펴야 한다.
○ 소아 : 이 약의 안전성은 시험된 바 없다.

- PH: 6.8
- Osmolarity: 0.424mosm/mL
- RDA: 400mg
- 임상 적용: 만성피로(부신 피로) , 근육통, 혈관 통, 편두통 완화, 월경 전 증후군
- 주의사항: 저혈압 환자, hypocalcemia (Calcium Gluconate IV), 신기능 저하 환자
- 기본수액: NS, 5%DW

< 흔히 사용하는 수액제제 알아보기
: 항산화 기능 중심>

- Glutathione
- Alpha-lipoic Acid

GLUTATHIONE



- Help synthesize & repair DNA
- Direct chemical neutralization of singlet oxygen, hydroxyl radicals, and superoxide radicals
- Cofactor for several antioxidant enzymes
- Regeneration of vitamin C and E
- Vital to mitochondrial function

Glutathione: Overview of its protective roles, measurement, and biosynthesis Feb-Apr 2009;30(1-2):1-12. doi: 10.1016/j.mam.2008.08.006.

GLUTATHIONE (백옥주사)

제품명	루치온주 Luthione Injection
성분 / 함량	■ 1바이알 중 동일성분 의약품 Glutathione(Reduced) 글루타티온(환원형) 600mg

■ 효능·효과

시스플라틴 또는 유사계열 화학요법에 의한 신경성질환의 예방

■ 용법·용량

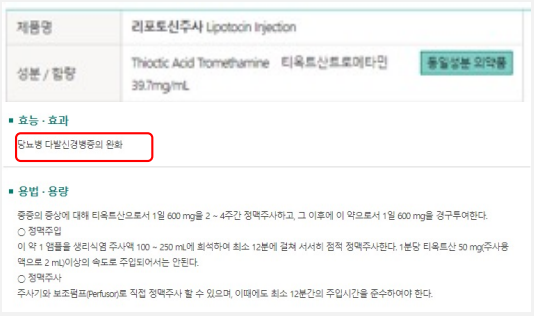
중증의 경우 1일 600~1200 mg을 근육 주사 또는 점적 정맥 주사한다.
수일에 걸쳐 치료하는 경우 또는 경미한 경우에는 1일 300~600 mg을 근육 주사 또는 점적 정맥 주사한다.

- 임상 적용: 항산화, 해독, 면역 증강
- 기본수액: NS
- 주의사항:강력한 항산화제로 IVNT시 다른 제제와 섞지 않고 단독으로 빠른 시간에 투여한다.
  (side shooting or NS 100 mix full drop)

ALPHA-LIPOIC ACID(THIOCTIC ACID)

- Recycle antioxidant(vitamin C, Coenzyme Q 10, glutathione)
- Co-factor of mitochondrial enzymes
- Suppress hypothalamic AMPK activity
- Increase insulin sensitivity

ALPHA-LIPOIC ACID(THIOCTIC ACID)



제품명	리포토신주사 Lipotocin Injection
성분 / 함량	Thioctic Acid Tromethamine 티옥트산트로메타민 39.7mg/mL

동일성분 의약품

■ 효능 · 효과

당뇨병 다발신경병증의 완화

■ 용법 · 용량

중증의 증상에 대해 티옥트산으로서 1일 600 mg을 2 ~ 4주간 정맥주사하고, 그 이후에 이 약으로서 1일 600 mg을 경구투여한다.
○ 정맥주입
이 약 1 앰플을 생리식염 주사액 100 ~ 250 mL에 희석하여 최소 12분에 걸쳐 서서히 점적 정맥주사한다. 1분당 티옥트산 50 mg(주사용액으로 2 mL)이상의 속도로 주입되어서는 안된다.
○ 정맥주사
주사기와 보조펌프(Perfusor)로 직접 정맥주사 할 수 있으며, 이때에도 최소 12분간의 주입시간을 준수하여야 한다.

- 임상 적용: 항 산화, 체중 조절 (AMPK 작용억제), 당 대사 개선, 당뇨병성 말초 신경 염 증상 개선
- 기본수액: 5% DW (당뇨환자, 암환자 제외)
- 주의 사항: 항산화제로 다른 영양소와 mix 하지 않고 단독으로 빠르게 투약, vitamin B1의 결핍을 유발할 수 있어 보충 필요, 고용량 투약 시 저 혈당 발생 가능

<IVNT시 주의 사항 >

IVNT시 주의 사항

- 수액 전, 후 혈압측정
- 큰 혈관 사용 :Ante-cubital fossa area
- Osmolarity 교정
  - Ideally 250-600 mosm 유지, 1000-1200 mosm 넘지 않도록
- PH 교정: 자주 사용하는 수액 PH 알아 두기
- 기본 수액
  - NS, 5% DW
  - SW (고용량 Vit C 투약시에 사용)
- 혼합 시 주의 사항
  - 기본 수액은 NS, 5% DW
  - Trace mineral은 아미노산에 mix를 기본으로 함 : PH 조절 목적으로 일반적으로 amino acid 에 mix
    - 비타민 C, 히스파겐씨 주, 탄산수소 나트륨과 mix시 침전물 생성 가능성
    - Lipid 포함 TPN 제제 mix 시 Trace mineral의 낮은 PH로 인한 산화 가능성 주의
  - Glutathione, Alpha-lipoic acid, Selenium는 NS 혹은 5%DW에 mix 하여 단독 투여
- 수액 속도 조절
- 수액 별 이상반응 미리 숙지
  - Vit C, 멀티미네랄: 혈관 통
  - Vit B1, 히스파겐씨 주 : 과민반응
  - Mg: 저혈압
  - Alpha-lipoic acid: 저혈당

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- *www. b12-vitamin.com/forms/*
- https://lpi.oregonstate.edu/mic
- *www.health.kr*
- *비타민 치료 제4판*
- www.ksnm.or.kr(한국영양의학회)

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