Bilagsfortegnelse:

Bilag 1: Litteratursøgning

Litteratursøgning til denne kliniske retningslinje er foretaget i henhold til Metodehåndbogen, model for udarbejdelse af Nationale Kliniske Retningslinjer, Sundhedsstyrelsen, 2017.

Søgeprofil

Søgestrategien blev designet til at inkludere begge PICO-spørgsmål (**P**opulation, **I**ntervention, **C**omparison, **O**utcome) i én samlet søgning. PICO-spørgsmål:

Hvilken evidens findes der for, hvordan subkutan injektion af insulin injiceres hos voksne, så insulinen får den tilsigtede virkning og lipodystrofi forebygges?

Hvilken evidens findes for at forebygge infektion ved indstiksstedet ved subkutan insulin injektion hos voksne med diabetes?

Dette resulterede i søgninger, der omfattede følgende nøglekoncepter:

- Insulin
- Injektion
- Relevante interventioner (eksempelvis nålelængde og dosisfordeling) eller outcomes (så som infektioner og lipodystrofi)

Søgningerne blev tilrettelagt således, at kun referencer, som indeholder information om alle tre nøglekoncepter, blev identificeret. Dertil blev studier, som ikke handler om mennesker, forsøgt sorteret fra. Kun studier publiceret efter 2013 blev inkluderet, da det er det seneste hele år, som søgningen i den tidligere retningslinje fra 2015 dækkede (seneste søgning blev gennemført i september 2014).

Informationskilder og søgemetoder

Der blev gennemført søgning efter både kliniske retningslinjer/guidelines og anden sekundær (systematiske reviews) og primær litteratur.

Søgning efter kliniske retningslinjer og guidelines

Eksisterende kliniske retningslinjer og guidelines blev identificeret via søgning i generelle guidelinedatabaser og generel websøgning.

Søgning i guidelinedatabaser

I disse søgninger blev anvendt en sensitiv tilgang ved kun at søge på termen 'injection' ud fra en antagelse om, at relevante kliniske retningslinjer og guidelines indeholder netop denne term.

Database	URL	Søgning	Resultat (relevante)
Guideline Central	https://www.guidelinecentral.com/guidelines	injection	183 (0)
Guidelines International Network (GIN)	https://guidelines.ebmportal.com	injection	8 (0)
National Institute for Health and Care Excellence (NICE)	https://www.nice.org.uk/guidance/published	injection	14 (0)
Scottish Intercollegiate Guidelines Network (SIGN)	https://www.sign.ac.uk/our-guidelines	injection	0 (0)

Trip Database	https://www.tripdatabase.com	(title:injection) *+ afgrænsning til guidelines*	46 (0)
Swedish Agency for Health Technology Assessment and Assessment of Social Services (SBU)	https://www.sbu.se/en/search/?q=&p=1&s=0&c=178 (engelsk side)	injection	9 (0)
Norwegian Institute of Public Health (NIPH)	https://www.fhi.no/en (engelsk side)	injection	40 (0)
Helsedirektoratet	https://www.helsedirektoratet.no/retningslinjer	*Manuel gennemgang*	78 (0)

Generel websøgning

Medlemmer af arbejdsgruppen søgte via Google og identificerede herved fire guidelines:

- Australian Diabetes Educators Association (ADEA). Clinical Guiding Principles for Subcutaneous Injection Technique. Canberra: 2019 (35).
- Chawla R, Shunmugavelu M, Makkar B, Chawla M, Sahoo A, Majumdar S, Lodha S, Gupta S, Bhansali A. Practical guidance on insulin injection practice in diabetes self-management in the Indian setting: an expert consensus statement. Clinical Diabetology. 2019 Jun 19;8(3):176-94
- Frid AH, Kreugel G, Grassi G, Halimi S, Hicks D, Hirsch LJ, Smith MJ, Wellhoener R, Bode BW, Hirsch IB, Kalra S, Ji L, Strauss KW. New Insulin Delivery Recommendations. Mayo Clin Proc. 2016 Sep;91(9):1231-55 (3).
- The Forum for Injection Technique UK (FIT). The FIT UK Injection Technique Recommendations, 4rd Edition. 2020 (16).

Søgning efter systematiske reviews og primærlitteratur

Databasesøgninger blev udført den 6. februar 2023. Søgningerne blev udført i følgende databaser (interface angivet i parentes):

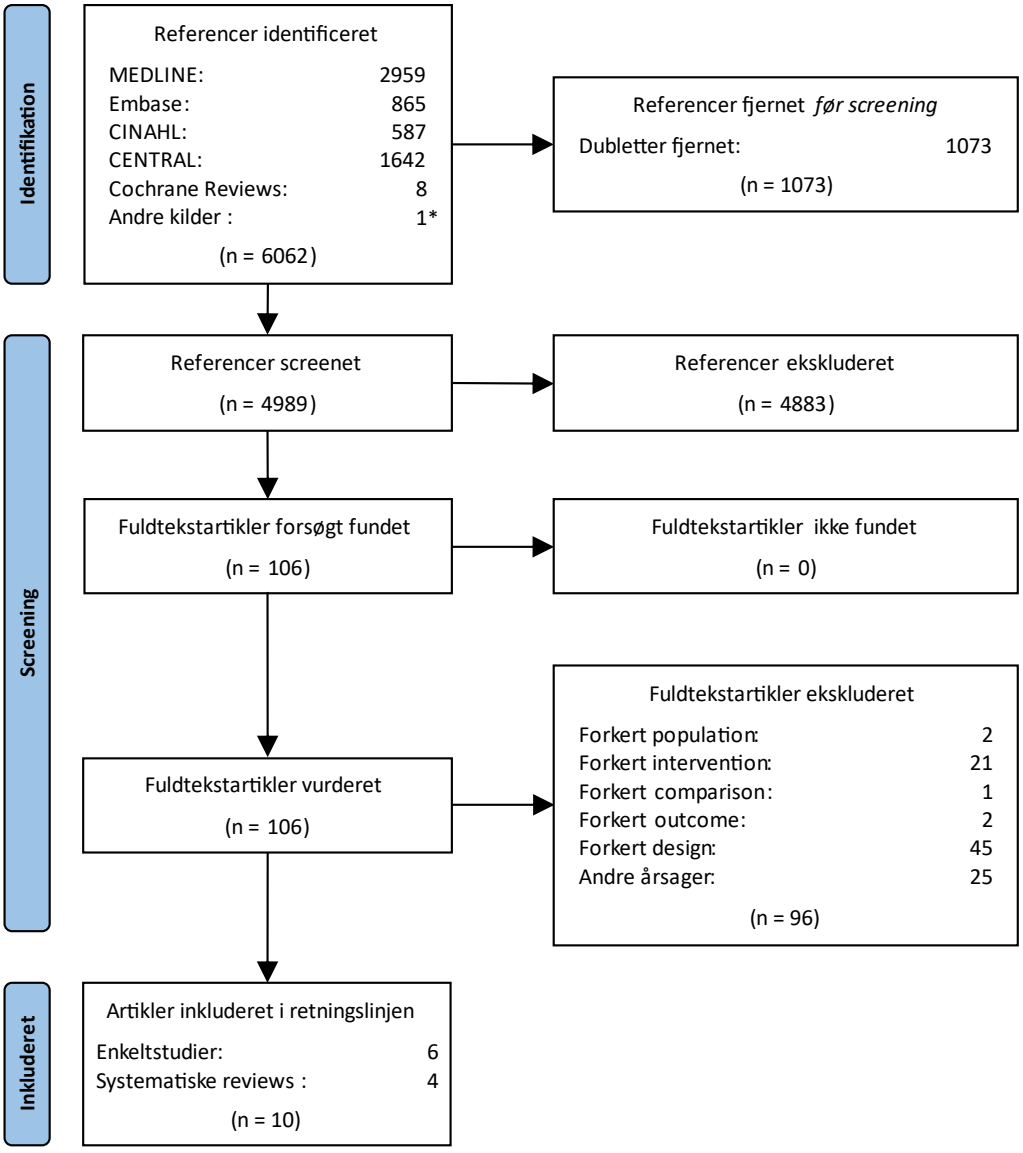
- MEDLINE (Ovid)
- Embase (Ovid)
- CINAHL (EBSCO)
- CENTRAL (Cochrane Library)
- Cochrane Database of Systematic Reviews (Cochrane Library)

Både titel/abstract- og fuldtekstscreening foregik ved, at alle referencer blev fordelt mellem arbejdsgruppens medlemmer på en måde, så alle referencer blev screenet af to personer. Uenigheder blev diskuteret mellem de to personer, som havde screenet den pågældende reference, eller af et tredje arbejdsgruppemedlem. Se figur 1 for flowdiagram for litteraturudvælgelsen.

For at identificere litteratur om patienters og sundhedsprofessionelles præferencer, jf. PICo (**P**opulation, phenomenon of **I**nterest, **Co**ntext), blev en ny søgning gennemført den 21. august 2023 i MEDLINE, Embase og CINAHL ved at tilføje publicerede søgefiltre til identifikation af patientpræferencer (både kvantitative og kvalitative studier) til den tidligere søgning. For at kunne producere en søgning, som var i overensstemmelse med den tidligere, blev den afgrænset til kun til at inkludere referencer, som var blevet tilføjet databaserne før den 6. februar 2023. Se figur 2 for flowdiagram, der viser udvælgelsen af litteratur om patienters og sundhedsprofessionelles præferencer.

Databasesøgninger
Søgningen blev udviklet i MEDLINE (Ovid) og efterfølgende oversat til de øvrige databaser. Et passende sæt af fritekstermer og kontrollerede emneord relateret til nøglekoncepterne blev anvendt. For at begrænse søgeresultaterne til studier om mennesker blev dobbeltnegationseleminering (not-not søgning) anvendt. Søgningen blev evalueret ved at lede efter et sæt af kendte nøgleartikler i de indledende MEDLINE (Ovid) søgeresultater. Alle databasesøgninger blev gennemført af Ole Nørgaard. Detaljer om alle søgninger kan findes i tabel 2.

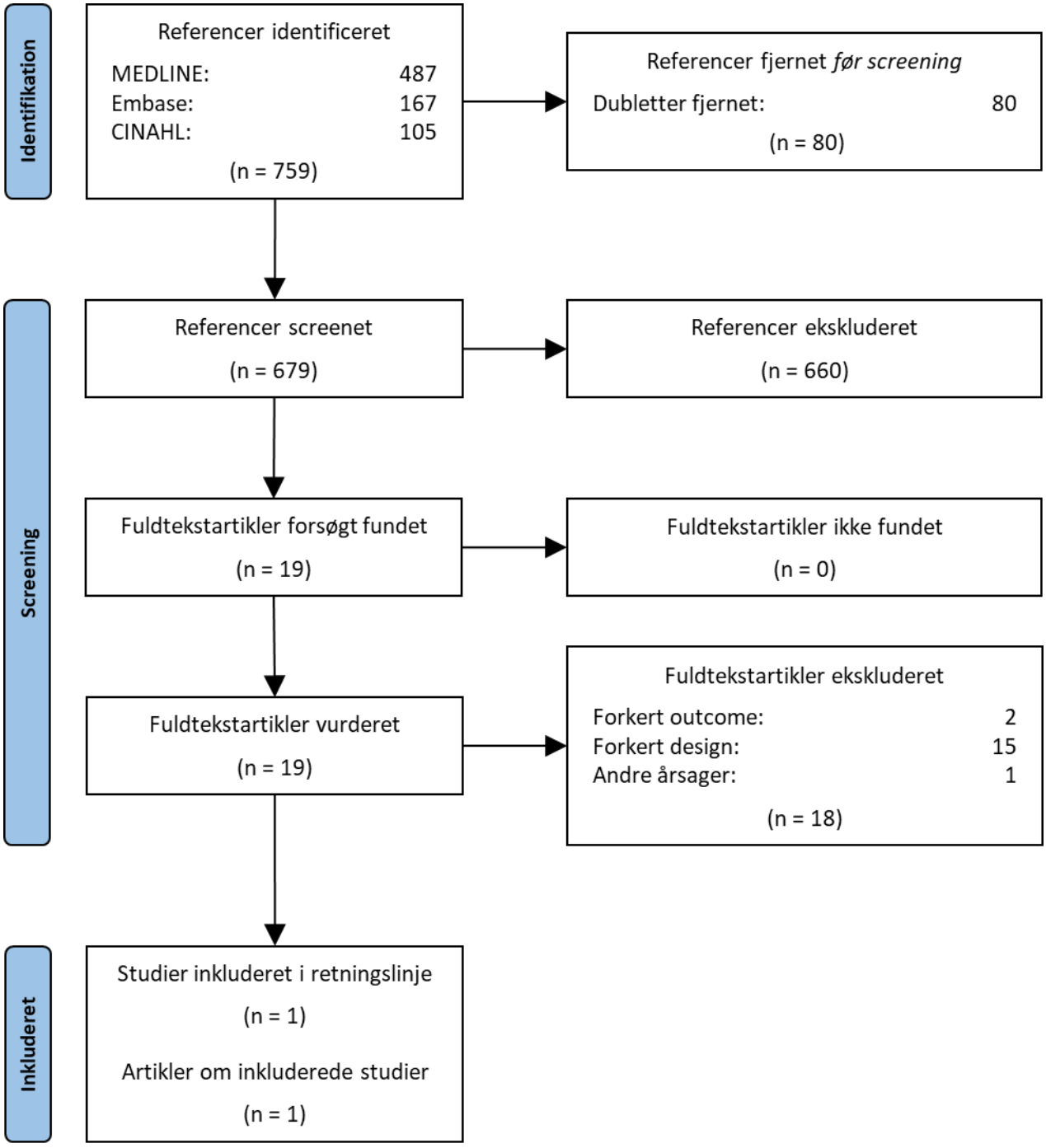
Figur 1: Flowdiagram for udvælgelse af studier om PICO



* Et systematisk review blev identificeret efter databasesøgningen af et medlem af arbejdsgruppen i forbindelse med en konference.

** Tre inkluderede artikler var systematiske reviews. Referencelisten i disse er blevet gennemgået.

Figur 2: Flowdiagram for litteratur om PICo


Identifikation
Referencer identificeret
MEDLINE: 487
Embase: 167
CINAHL: 105
(n = 759)
Referencer fjernet *før screening*
Dubletter fjernet: 80
(n = 80)
Screening
Referencer screenet
(n = 679)
Referencer ekskluderet
(n = 660)
Fuldtekstartikler forsøgt fundet
(n = 19)
Fuldtekstartikler ikke fundet
(n = 0)
Fuldtekstartikler vurderet
(n = 19)
Fuldtekstartikler ekskluderet
Forkert outcome: 2
Forkert design: 15
Andre årsager: 1
(n = 18)
Inkluderet
Studier inkluderet i retningslinje
(n = 1)
Artikler om inkluderede studier
(n = 1)

Tabel 2: Databasesøgninger

#	MEDLINE (Ovid)		#	Embase (Ovid)		#	CINAHL (EBSCO)		#	CENTRAL og CDSR (Cochrane Library)		Kommentarer
Insulin												
1	exp Insulins/	204679	1	exp insulin derivative	399864	1	MH "Insulins+"	37366	1	[mh "Insulins"]	16501	Kontrollerede emneord om nøglekonceptet *insulin*.
2	insulin$.ti,ab,kf,kw.	408706	2	insulin$.ti,ab,kf,kw.	552618	2	TI (insulin*) OR AB (insulin*) OR SU (insulin*)	84701	2	(insulin*):ti,ab,kw	70235	Fritekstermer om nøglekonceptet *insulin*.
3	or/1-2	445023	3	or/1-2	654265	3	S1 OR S2	85149	3	(25-#2)	70302	Foreningsmængde af kontrollerede emneord og fritekstermer om nøglekonceptet *insulin*.
Injektion												
4	exp Injections/	296124	4	exp injection/	173842	4	MH "Injections+"	39442	4	[mh "Injections"]	24865	Kontrollerede emneord om nøglekonceptet *injektion*.
5	inject$.ti,ab,kf,kw.	25945	5	inject$.ti,ab,kf,kw.	1095697	5	TI (inject*) OR AB (inject*) OR SU (inject*)	107674	5	inject*:ti,ab,kw	117858	Fritekstermer om nøglekonceptet *injektion*.
6	or/4-5	983257	6	or/4-5	1119188	6	S4 OR S5	108039	6	(12-#5)	117916	Foreningsmængde af kontrollerede emneord og fritekstermer om nøglekonceptet *injektion*.
Interventioner og outcomes												
7	exp Absorption/	91369	7	exp absorption/	88335	7	MH "Absorption+"	2012	7	[mh "Absorption"]	3595	Kontrolleret emneord om *absorption*.
8	Disinfection/	17168	8	exp disinfection/	32344	8	MH "Sterilization and Disinfection+"	13114	8	[mh ^"Disinfection"]	445	Kontrolleret emneord om *disinfektion*.
9	exp Infections/	3031127	9	exp infection/	3945804	9	MH "Infection+"	211831	9	[mh "Infections"]	92745	Kontrollerede emneord om *infektion* og *reaktioner ved injektionsstedet.*
10	Injection Site Reaction/	354	10	exp injection site reaction/	33037				10	[mh "Injection Site Reaction"]	75	
11	exp Insulins/ad	21146	11	exp insulin derivative/ad, sc	16158	10	MH "Insulins+/AD"	9952	11	[mh "Insulins"/AD]	2896	Kontrolleret emneord om *insulin,* som samtidig er markeret med underemner, der er relateret til, hvordan medicinen gives, dvs. *Administration and dosage* (.ad i MEDLINE og CINAHL samt /AD i CENTRAL og CDSR), *drug administration* (.ad i Embase) og

															subcutaneous drug administration (.sc i Embase).
12	exp Lipodystrophy/	5133	12	exp lipodystrophy/	12134	11	MH "Lipodystrophy+"	970	12	[mh "Lipodystrophy"]	282	Kontrolleret emneord om *lipodystrofi*.
13	Needles/	17185	13	exp needle/	71213	12	MH "Needles"	5130	13	[mh ^"Needles"]	1396	Kontrolleret emneord om *nåle*.
14	(absorp$ or disinfect$ or lipoatroph$ or lipo-atroph$ or lipodystroph$ or lipo-dystroph$ or lipohypertroph$ or lipo-hypertroph$ or infect$ or needle$ or split$ or subcut$ or technique$).ti,ab,kf,kw.	4469638	14	(absorp$ or disinfect$ or lipoatroph$ or lipo-atroph$ or lipodystroph$ or lipo-dystroph$ or lipohypertroph$ or lipo-hypertroph$ or infect$ or needle$ or split$ or subcut$ or technique$).ti,ab,kf,kw.	5536446	13	TI (absorp* OR disinfect* OR lipoatroph* OR lipo-atroph* OR lipodystroph* OR lipo-dystroph* OR lipohypertroph* OR lipo-hypertroph* OR infect* OR needle* OR split* OR subcut* OR technique*) OR AB (absorp* OR disinfect* OR lipoatroph* OR lipo-atroph* OR lipodystroph* OR lipo-dystroph* OR lipohypertroph* OR lipo-hypertroph* OR infect* OR needle* OR split* OR subcut* OR technique*) OR SU (absorp* OR disinfect* OR lipoatroph* OR lipo-atroph* OR lipodystroph* OR lipo-dystroph* OR lipohypertroph* OR lipo-hypertroph* OR infect* OR needle* OR split* OR subcut* OR technique*)	889777	14	(absorp* OR disinfect* OR lipoatroph* OR lipo-atroph* OR lipodystroph* OR lipo-dystroph* OR lipohypertroph* OR lipo-hypertroph* OR infect* OR needle* OR split* OR subcut* OR technique*):ti,ab,kw	327346	Friteksttermer om nøglekonceptet *interventioner og outcomes*.
15	or/7-14	6239288	15	or/7-14	7569689	14	S7 OR S8 OR S9 OR S10 OR S11 OR S12 OR S13	954058	15	(91-#14)	359965	Foreningsmængde af kontrollerede emneord og friteksttermer om nøglekonceptet *interventioner og outcomes*.
16	and/3,6,15	11423	16	and/3,6,15	13707	15	S3 AND S6 AND S14	3263	16	(21, #6, #15)	3358	Fællesmængden for alle nøglekoncepter.
Dyrestudier												
17	exp Animals/ not Humans/	5089811	17	(exp animal/ or animal experiment/ or nonhuman/) not (exp human/ or human experiment/)	7133531	16	MH "Animals+"	105349	17	[mh "Animals"] NOT [mh ^"Humans"]	2686	Identificerer dyrestudier, der ikke samtidigt er indekseret som studier om mennesker, og ekskluderer disse fra søgeresultatet.
						17	MH "Animal Studies"	151230				
						18	TI (animal model*)	3446				
						19	S16 OR S17 OR S18	247543				
						20	MH "Human"	2651585				
						21	S19 NOT S20	213607				
18	6 not 7	8390	18	6 not 7	9783	22	S15 NOT S21	2956	18	#16 NOT #17	3354	

Afgrænsning og endeligt resultat af databasesøgning											
19	limit 18 to (da="20130101-20231231" or dt="20130101-20231231" or ez="20130101-20231231" or ed="20130101-20231231")	**2959**	19	limit 18 to (dc="20130101-20231231" or dd="20130101-20231231" or rd="20130101-20231231")	5217	23	S22 (Limiters: Published Date: 20130101-20231231)	1181	19	#18 with Cochrane Library publication date Between Jan 2013 and Jan 2023, in Cochrane Reviews	**8**
									20	#18 with Publication Year from 2013 to 2023, in Trials	**1642**
			20	limit 19 to exclude medline journals	**865**	24	S23 (Limiters: Exclude MEDLINE records)	**587**			
Kvalitative studier											
20	exp Qualitative Research/	82912	21	exp qualitative research/	117711	25	MH "Qualitative Studies+"	183286			
21	exp "Surveys and Questionnaires"/	1215118	22	exp questionnaire/	923506	26	MH Surveys+	264110			
22	exp Interview/	30722	23	exp Interview/	368194	27	MH "Interviews+"	255379			
23	exp "Interview, Psychological"/	15276									
24	exp Interviews as topic/	66832									
25	exp Focus Groups/	35958				28	MH "Focus Groups"	50681			
26	Empirical research/	4027	24	empirical research/	7400	29	MH "Empirical Research"	5245			
27	Narration/	10199	25	narrative/	21535	30	MH "Narratives+"	20732			
28	((qualitative or empirical or action or ethnographic or ethnological or ethnonursing or ethnomedicine or phenomenological or narrative or narration) adj3 (research or study or method$ or design or synthes$ or systematic study or systematic studies or meta analy$ or metaanaly$ or metaanaly$ or analy$)).ti,ab,kf,kw.	256466	26	((qualitative or empirical or action or ethnographic or ethnological or ethnonursing or ethnomedicine or phenomenological or narrative or narration) adj3 (research or study or method$ or design or synthes$ or systematic study or systematic studies or meta analy$ or metaanaly$ or metaanaly$ or analy$)).ti,ab,kf,kw.	305080	31	(((qualitative OR empirical OR action OR ethnographic OR ethnological OR ethnonursing OR ethnomedicine OR phenomenological OR narrative OR narration) N3 (research or study or method* OR design OR synthes* OR systematic study OR systematic studies OR meta analy* OR metaanaly* OR metaanaly* OR analy*)	258351			
29	(metasynthes$ or meta-synthes$ or meta synthes$ or metaethnograph$ or meta-ethnograph$ or meta ethnograph$).ti,ab,kf,kw.	2735	27	(metasynthes$ or meta-synthes$ or meta synthes$ or metaethnograph$ or meta-ethnograph$ or meta ethnograph$).ti,ab,kf,kw.	3030	32	metasynthes* OR meta-synthes" OR meta synthes* OR metaethnograph* OR meta-ethnograph* OR meta ethnograph*	3283			

Begrænser resultaterne til en periode, der dækker fra den 1. januar 2013 og frem til søgedatoen.	
Afgrænser resultatet til ikke at inkludere referencer fra MEDLINE.	
Søgefilter adapteret fra Sundhedsstyrelsens anbefalinger for udarbejdelse af nationale kliniske anbefalinger (NKA): https://www.sst.dk/-/media/Viden/Sundhedsv%C3%A6sen/NKR/sogefiltre-SST-07062323.ashx	

30	(("semi-structured" or semistructured or semi structured or unstructured or informal or "in-depth" or indepth or "face-to-face" or individual$ or structured or guide$ or tailored or one-to-one or telephone or internet or doodle or oral or written or diagnostic or psychodiagnostic or intake or recorded or group$) adj3 (interview$ or discussion$ or questionnaire$ or survey$)).ti,ab,kf,kw.	307180	28	(("semi-structured" or semistructured or semi structured or unstructured or informal or "in-depth" or indepth or "face-to-face" or individual$ or structured or guide$ or tailored or one-to-one or telephone or internet or doodle or oral or written or diagnostic or psychodiagnostic or intake or recorded or group$) adj3 (interview$ or discussion$ or questionnaire$ or survey$)).ti,ab,kf,kw.	407555	33	(((("semi-structured" OR semistructured OR semi structured OR unstructured OR informal OR "in-depth" OR indepth OR "face-to-face" OR individual* OR structured OR guide* OR tailored OR one-to-one OR telephone OR internet OR doodle OR oral OR written OR diagnostic OR psychodiagnostic OR intake OR recorded OR group*) N3 (interview* OR discussion* OR questionnaire* OR survey*)))	248838			
31	(focus group$ or focus-group$ or focusgroup$).ti,ab,kf,kw.	64593	29	(focus group$ or focus-group$ or focusgroup$).ti,ab,kf,kw.	80115	34	focus group* OR focus-group" OR focusgroup*	62805		
32	(field work or fieldwork or field-work or key informant$ or ground work or groundwork or narration or narrative$).ti,ab,kf,kw.	101244	30	(field work or fieldwork or field-work or key informant$ or ground work or groundwork or narration or narrative$).ti,ab,kf,kw.	112247	35	field work OR fieldwork OR field-work OR key informant* OR ground work OR groundwork OR narration OR narrative*	70727		
33	(evidence synthes$ or realist synthes$).ti,ab,kf,kw.	7922	31	(evidence synthes$ or realist synthes$).ti,ab,kf,kw.	8812	36	evidence synthes* OR realist synthes*	23359		
34	(grounded theory or naturalistic inquiry).ti,ab,kf,kw.	15405	32	(grounded theory or naturalistic inquiry).ti,ab,kf,kw.	19072	37	grounded theory OR naturalistic inquiry	1694		
35	or/20-34	1758437	33	or/21-32	1684133	38	S25 OR S26 OR S27 OR S28 OR S29 OR S30 OR S31 OR S32 OR S33 OR S34 OR S35 OR S36 OR S37	753857		
Patientpræferencer										
36	exp *Attitude to Health/	245549	34	exp *attitude to health/	64025	39	(MM "Attitude to Health+")	88448		Søgefilter adapteret fra Selva A, Solà I, Zhang Y, Pardo-Hernandez H, Haynes RB, Martínez García L, Navarro T, Schünemann H, Alonso-Coello P. Development and use of a content search strategy for retrieving studies on patients' views and preferences. Health Qual Life Outcomes. 2017 Aug 30;15(1):126. doi: 10.1186/s12955-017-0698-5.
37	exp *Patient Participation/	16692	35	exp *patient participation/	11332	40	(MM "Consumer Participation")	14032		
38	*Patient Preference/	6476	36	*patient preference/	6581	41	(MM "Patient Preference")	1335		
39	exp *Decision Making/ and (patient$ or user$ or men or women).ti.	10192	37	exp *decision making/ and (patient$ or user$ or men or women).ti.	13709	42	(MM "Decision Making+") AND (TI (patient* OR user* OR men OR women))	12514		
40	(choice$ or valuation$ or value$).ti.	239743	38	(choice$ or valuation$ or value$).ti.	275802	43	TI (choice* OR valuation* OR value*)	71819		
41	(acceptab$ or attitude$ or (discrete adj choice$) or (decision adj (aid$ or analy$ or board$ or support or tool$)) or ((decision$	1726906	39	(acceptab$ or attitude$ or (discrete adj choice$) or (decision adj (aid$ or analy$ or board$ or support or tool$)) or	220490	44	TI ((acceptab* OR attitude* OR (discrete W1 choice*) OR (decision W1 (aid* OR analy* OR board* OR support OR tool*)) OR ((decision*	551616		

	adj mak$) and (patient$ or user$ or men or women)) or expectation$ or health state values or ((health or patient$ or user$) adj (participation or perce$ or perspective$ or view$)) or knowledge or point of view or preference$).ti,ab,kf,kw.			((decision$ adj mak$) and (patient$ or user$ or men or women)) or expectation$ or health state values or ((health or patient$ or user$) adj (participation or perce$ or perspective$ or view$)) or knowledge or point of view or preference$).ti,ab,kf,kw.			W1 mak*) AND (patient* OR user* OR men OR women)) OR expectation* OR health state values OR ((health OR patient* OR user*) W1 (participation OR perce* OR perspective* OR view*)) OR knowledge OR point OR view OR preference*)) OR AB ((acceptab* OR attitude* OR (discrete W1 choice*) OR decision W1 (aid* OR analy* OR board* OR support OR tool*)) OR ((decision* W1 mak*) AND (patient* OR user* OR men OR women)) OR expectation* OR health state values OR ((health OR patient* OR user*) W1 (participation OR perce* OR perspective* OR view*)) OR knowledge OR point of view OR preference*))			
42	or/36-41	209157	40	or/34-39	2489273	45	S39 OR S40 OR S41 OR S42 OR S43 OR S44	685879			
43	or/35,42	3456058	41	or/33,40	3744344	46	S38 OR S45	1248758			
44	and/19,43	504	42	and/20,41	182	47	S24 AND S46	107			
45	limit 44 to (da="20130101-20230206" or dt="20130101-20230206" or ez="20130101-20230206" or ed="20130101-20230206")	**487**	43	limit 42 to (dc="20130101-20230206" or dd="20130101-20230206" or rd="20130101-20230206")	**167**	48	S47 (Limiters: Published Date: 20130101-2023023)	**105**			

Bilag 2: Beskrivelse af anvendt metode for denne kliniske retningslinje

Denne retningslinje er udarbejdet på baggrund af evidensgrundlaget og konsensusbeslutninger fra eksperter fra et eksisterende sæt internationale retningslinjer udgivet i 2016 af Mayo Foundation for Medical Education and Research "New Insulin Delivery Recommendations" (3) og tilpasset danske forhold, hvor det har været relevant og muligt. Alle anbefalinger er formuleret efter opnåelse af konsensus i arbejdsgruppen til denne kliniske retningslinje.

Anbefalingerne fra Frid et al, er baseret på en stor international undersøgelse af daværende praksis og blev skrevet og undersøgt af 183 diabeteseksperter fra 54 lande ved Forum for Injection Technique og Terapi: Expert Recommendations (FITTER) workshop afholdt i Rom, Italien, i 2015. Der er lavet en litteratursøgning i MEDLINE, Embase, PubMed og Cochrane Library for at identificere publikationer til at understøtte anbefalingerne. Søgningen blev foretaget i perioden mellem januar 2008 og december 2015. Studierne som understøtter anbefalingerne er ikke kritisk vurderet med checklister, men panelet brugte en tidligere anvendt skala til at klassificere styrken af hver anbefaling. Følgende klassificering blev brugt: A = anbefales stærkt, B = anbefales, og C = uløst problem. Til klassificering af graden af videnskabelig støtte til hver anbefaling brugte de følgende skala: 1 = mindst en stringent udført undersøgelse, der er peer-reviewed og publiceret (ekskluderer observationsstudier); 2 = mindst en observationel, epidemiologisk eller befolkningsbaseret offentliggjort undersøgelse; og 3 = ekspertkonsensus med udtalelse baseret på bred patientoplevelse.

Anbefalingerne fra 2016 er metodisk kvalitetsvurderet med AGREE II instrumentet af to personer fra Center for Kliniske Retningslinjer, med en samlet score på 5. Bedømmelsen af de enkelte domæner blev vurderet til: Samlet bedømmelse af domæne 1 på 89 %, domæne 2 på 61%, domæne 3 på 60%, domæne 4 på 92 %, domæne 5 på 35%, og domæne 6 på 92% og fundet anvendelige.

Arbejdsgruppen for denne kliniske retningslinje har foretaget en ny omfattende litteratursøgning fra 2013 til august 2023 (se bilag med litteratursøgning), hvor anbefalinger fra Frid et al. 2016 (3) blev identificeret, yderligere to systematiske reviews (73, 80) hvoraf det ene kun blev brugt til at gennemgå referencer og fem relevante primære studier (52, 53, 57-59) for de udarbejdede PICOs blev identificeret. De systematiske reviews er kritisk vurderet ud fra AMSTAR 2, og primærstudierne er kritisk vurderet med relevante checklister fra JBI, og der er lavet extractions på relevante områder. Der er af arbejdsgruppen yderligere identificeret et systematisk review fra 2024, som også er kritisk vurderet (47).

De outcomes, der er valgt i anbefalinger af Frid et al. (3) er blevet diskuteret i forhold til relevans for danske forhold og i forhold til PICO-spørgsmål i denne retningslinje. Det er vurderet, om hvert enkelt outcome er kritisk eller vigtigt outcome for at kunne formulere en anbefaling. Arbejdsgruppen har formuleret PICO-spørgsmål på baggrund af tidligere udarbejdet klinisk retningslinje (13) og det adapterede evidensgrundlag, og har efterfølgende foretaget deres egen vurdering af tiltroen til estimaterne. Evidensen er gennemgået, og der er udarbejdet nye anbefalinger, tilpasset danske forhold. For hver anbefaling er de gavnlige og skadelige virkninger, kvaliteten af evidensen og, hvor det er muligt, evidenstabeller samt patientpræferencer blevet diskuteret. Herefter blev der taget stilling til, hvorledes anbefalingen skulle lyde, og hvilke praktiske oplysninger, det var vigtigt at formidle.

Bilag 3: Sammenfatning af resultater fra spørgeskemaundersøgelser, der belyser patientperspektivet

Der blev identificeret i alt seks studier, der anvender spørgeskemaer med selvrapporterede data. Studierne belyser patientperspektivet i forhold til længde af penkanyle relateret til oplevelse af smerte og generel anvendelighed. Resultaterne omhandlende patientperspektivet sammenfattes herunder.

I et prospektiv, multicenter, randomiseret, open label crossover-studie fra USA af Bergenstal et al. viser resultaterne, at overvægtige patienter med type 1- og 2-diabetes foretrækker at anvende penkanyler på 4 mm, da den opleves mindre smertefuld og mere anvendelig sammenlignet med 8 og 12,7 mm penkanyler (63).

Miwa et al. har undersøgt patienters oplevelser med 4 og 6 mm penkanyler hos 41 patienter med enten type 1- eller type 2-diabetes i Japan. De konkluderer, at patienterne oplever signifikant mindre smerte målt ved VAS ved anvendelse af en 4 mm penkanyle. Eneste parameter, hvor 6 mm penkanylen scorer højere, er i forhold til, hvor stabil penkanylen opleves, når den er injiceret (60).

I endnu et japansk studie sammenligner Nagai et al. to forskellige penkanyler i forhold smerteoplevelse, anvendelighed og generel præference blandt 84 patienter med enten type 1- eller type 2-diabetes. 4 mm penkanyle med et lige lumen sammenlignes med en 5 mm penkanyle med et tilspidset lumen. Det konkluderes, at anvendelse af 4 mm penkanyle er mindre smertefuld for patienterne og vurderes mere anvendelig (62).

I et canadisk studie Berad et al. er patientpræference i forhold til anvendelse af hhv. 5 og 8 mm penkanyler undersøgt blandt 66 overvægtige patienter med type 2-diabetes. Resultaterne viser, at 41,8 % af deltagerne foretrækker 5 mm penkanyle, og 27,9 % foretrækker 8 mm penkanyle. 30,3 % har ingen præference. På alle øvrige parametre om anvendelighed, komfort og mindst smerte scorer 5 mm penkanyle højest (68).

Et hollandsk studie af Kreugel et al. (67) sammenligner de ligeledes patientpræferencer og smerteoplevelse i forhold til brug af hhv. 8 og 5 mm penkanyle. I dette studie findes der ingen forskel i overordnet præference mellem de to penkanyler. 46 % af patienterne foretrak 5 mm penkanyle, og 41 % foretrak 8 mm penkanyle. 13 % af patienterne rapporterede ingen præference. Der kunne heller ikke identificeres forskel i smerteoplevelse målt på VAS. Patienterne oplevede mindre blødning ved brug af 5 mm penkanyle, men oftere lækage af insulin efter injektion sammenlignet med 8 mm penkanyle (67).

I et studie af Hirsch et al. udført i USA blev smerte og lækage efter injektion af insulin blandt 173 både overvægtige og normalvægtige patienter med type 1- og type 2-diabetes undersøgt. Studiet konkluderer, at patienterne oplevede mindre smerte, når de anvendte 4 mm penkanyle, undtagen de ikke-overvægtige, der sammenlignede 4 og 5 mm penkanyler. Ligeledes var der færre indberetninger om lækage ved anvendelse af 4 mm penkanyle. Der var en tendens til, at gruppen af overvægtige oftere rapporterede lækage (66).

Bilag 4: De kliniske spørgsmål (fokuserede spørgsmål)

PICO 1: Tilsigtet absorption og virkning af insulin herunder forebyggelse af lipodystrofi

Hvilken evidens findes der for, hvordan subkutan injektion af insulin injiceres hos voksne, så insulinen får den tilsigtede virkning og lipodystrofi forebygges?

Bør der foretages systematisk skift af injektionssted inden for samme anatomiske region?

Bør henholdsvis human og analog insulin injiceres subkutant i en bestemt anatomisk region på kroppen for at sikre den tilsigtede virkning?

Hvilken penkanyle længde bør anvendes til at injicere insulin subkutant?

Bør der foretages skift af penkanyle ved hver ny insulininjektion?

Bør insulindosis deles i flere injektioner?

Bør injektion af insulin foretages i løftet hudfold?

Tabel 2: Fokuseret spørgsmål (PICO 1)

Population/Setting	**I**ntervention	**C**omparator	**O**utcome
Voksne (18+) med diabetes i insulinbehandling, som enten selv varetager injektion, eller som har behov for hjælp fra pårørende, sundhedsprofessionelle eller andre faggrupper i både primær og sekundær sundhedssektor	Systematisk skift af injektionsområde ved hver ny insulininjektion Injektion af insulin s.c. i abdomen Injektion af insulin s.c. i abdomen Injektion af insulin s.c. i lårets laterale del Injektion af insulin s.c. i lårets laterale del Injektion af insulin s.c. i overarmen	Injicerer insulin inden for det samme anatomiske områder mere én gang Inden for en måned Injektion af insulin s.c. i lårets laterale del Injektion af insulin s.c. i overarmen Injektion af insulin s.c. i abdomen Injektion af insulin s.c. i overarmen	**Kritiske:** Absorption af insulin (glukosevariabilitet) Lipodystrofi (atrofi og hypertrofi)

	Injektion af insulin s.c. i overarmen Injektion af insulin med 4 mm penkanyle s.c. Injektion af insulin med 5 mm penkanyle s.c. Injektion af insulin med 6 mm penkanyle s.c. Skift af penkanyle ved hver ny insulininjektion Deling af insulindosis ordineret til et givet tidspunkt i to eller flere injektioner Insulininjektion i løftet hudfold	Injektion af insulin s.c. i abdomen Injektion af insulin s.c. i lårets laterale del Injektion af insulin med 5 og 6 mm penkanyle s.c. Injektion af insulin med 4 og 6 mm penkanyle s.c. Injektion af insulin med 4 og mm penkanyle s.c. Anvendelse af penkanyle mere end én gang Injektion af den ordinerede insulindosis til et givet tidspunkt i én injektion Insulininjektion uden løftet hudfold	

Baggrund for valg af spørgsmål
Absorption af insulin efter insulininjektion har betydning for, at insulin får den tilsigtede virkning hos personen med diabetes. Forekomst af lipodystrofi er én af de faktorer som kan medføre variationer i optagelsen af insulin og føre til uforklarlige variationer i blodglukose med risiko for hypo- og hyperglykæmiske episoder.

PICO 2: Forebyggelse af infektion

Hvilken evidens findes for at forebygge infektion ved indstiksstedet ved subkutan insulin injektion hos voksne med diabetes?

Bør der foretages skift af penkanyle ved hver ny insulininjektion?

Bør der foretages huddesinfektion forud for injektion af insulin på hospitaler, i borgerens eget hjem eller på bosteder og plejehjem?

Tabel 3: Fokuseret spørgsmål (PICO 2)

Population/Setting	**I**ntervention	**C**omparator	**O**utcome
Voksne (18+) med diabetes i insulinbehandling, som enten selv varetager injektion, eller som har behov for hjælp fra pårørende, sundhedsprofessionelle eller andre faggrupper i både primær og sekundær sundhedssektor	Skift af penkanyle ved hver ny insulininjektion Huddesinfektion forud for injektion af insulin i borgerens eget hjem Huddesinfektion forud for injektion af insulin på hospital bosteder og plejehjem	Anvende samme penkanyle til mere end én insulininjektion Undlade huddesinfektion forud for injektion af insulin i borgerens eget hjem Undlade huddesinfektion forud for injektion af insulin på hospital, bosteder og plejehjem	**Kritiske:** Infektion

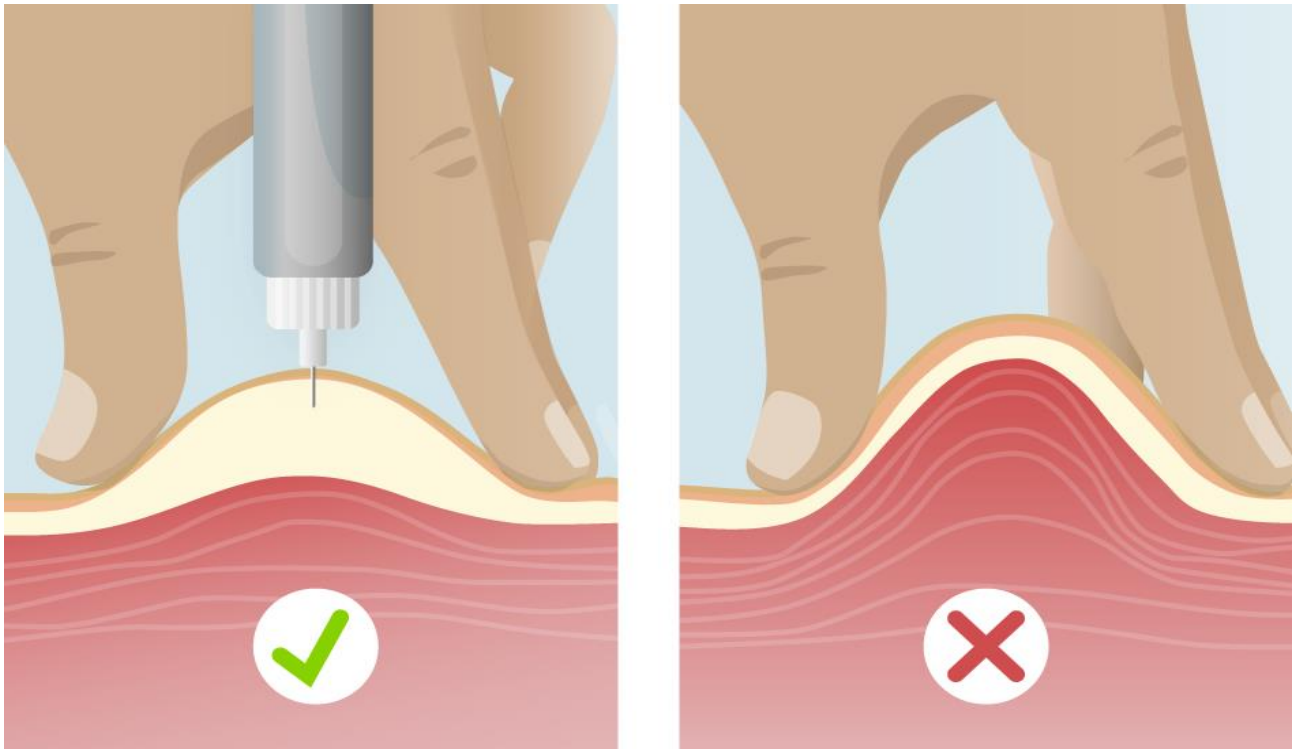
Baggrund for valg af spørgsmål
På hospitalerne har det været procedure at foretage huddesinfektion forud for injektion af insulin. I primær sektor er sundhedsprofessionelle derimod ofte i tvivl om, hvorvidt de skal foretage huddesinfektion hos voksne med diabetes i eget hjem eller på bosteder og plejehjem. Hidtil har praksis været at anbefale personer med diabetes udelukkende at udføre håndhygiejne forud for injektion af insulin i eget hjem.

Indsat outcomes i tabel:

Outcomes	**Kritisk/Vigtigt**
Absorption	Kritisk
Lipodystrofi	Kritisk

Infektion omkring indstikssted	Vigtigt

Bilag 5: Illustration korrekt løftet hudfold



Sørg for ikke at have muskelvæv med, når du løfter en hudfold

Kilde: 'Illustration: Steno Diabetes Center Copenhagen, Marianne Larsen

Bilag 6: Ekstraktion af data og kvalitetsvurdering af inkluderede studier

Extractions Klinisk retningslinje Injektion af insulin:

<table>
<tr><th>Author/year/ country</th><th>Population</th><th>Design</th><th>Intervention</th><th>Outcomes</th><th>Results</th><th>P value/CI</th></tr>
<tr>
<td>Bergenstal et al. 2015
US</td>
<td>Adult patients with T1DM and T2DM aged 18 to 80 years with a BMI of 30 or greater and an HbA1c level of 5.5% to 9.5% (37-80 mmol/mol)
Using pen needles (PN) and following a stable insulin regimen for the past to month.

The mean patient age was nearly 57 years,
the mean BMI was 37.0 (range, 29.1-59.9),
and the mean HbA1c level was 7.5% (58 mmol/mol).

92% had T2DM, and more than two-thirds normally used an 8-mm PN.
Average total daily insulin dose (TDD) exceeded 78 U, (range,
6-350 U)</td>
<td>Prospective, multicenter, randomized, open-label, 2-period, crossover, equivalence, home-based study

The patients inserted the insulin injection without supervision at home</td>
<td>N = 274 patients were randomized into the study to either the
4-mm 32-gauge - vs 8-mm 31-gaugue PN group (n= 139)
or the
4-mm 32-gauge vs 12.7-mm 29-gauge PN group (n= 135)

They used one PN for 12 weeks and then crossed over to use the second PN for 12 weeks. The order of PN use was controlled.

They were instructed to insert the 4-mm PN straight in with no pinch-up and to pinch up when inserting the 8-mm PN into the abdomen or thigh.
Patients were instructed to insert the 12.7-mm PN at 45° or to pinch up and inject at a 90° angle.</td>
<td><u>Primary outcome:</u>
Mean HbA1c (%) level after each 12-week study period

<u>Secondary outcomes:</u>
Relative injection pain Visual analog scale scores ranged from -75 mm (“much less painful”) to +75 mm (“much more painful”), with 0 mm (scale midpoint) meaning “as painful as the previous needle.

Leakage rates and volume of insulin.
Leakage was based on patient diary entries.
Leakage droplet charts were provided for estimating skin leakage volume, quantified on a scale from 1 to 6 depending on droplet size.

Needle preference
Overall preference
Ease of use
Ease of insertion
Ease of performing injection
Overall comfort
Needle anxiety</td>
<td>Results
N = 226 completed the trial

4-mm - vs 8-mm PN group (n= 113)
<table><tr><th>Study-arm</th><th>Baseline</th><th>Cross-over</th><th>End of study</th></tr><tr><td>4 to 8 mm</td><td>7,59 %</td><td>7,63 %</td><td>7,78 %</td></tr><tr><td>8 to 4 mm</td><td>7,46 %</td><td>7,59 %</td><td>7,59 %</td></tr></table>
4-mm vs 12.7-mm PN group (n=113)
<table><tr><th>Study-arm</th><th>Baseline</th><th>Cross-over</th><th>End of study</th></tr><tr><td>4 to 12,7 mm</td><td>7,57 %</td><td>7,58 %</td><td>7,73 %</td></tr><tr><td>12,7 to 4mm</td><td>7,45 %</td><td>7,54 %</td><td>7,51 %</td></tr></table>
4-mm PN was 12,4 mm lower than 8-mm PN

4-mm PN was 30,8 mm lower than 12,7 mm PN

Leakage rates
4 mm PN: 2748/65,096 (4.2)
8 mm PN: 1331/32,125 (4.1)
12.7 mm PN: 1422/33,448 (4.3)
Leakage volume
4 mm PN: 1.3±0.6 and 8 mm PN: 1.4±0.7 vs.
12.7 mm PN: 1.8±1.0

4 -mm - vs 8-mm PN (%) 4-mm - vs 12,7-mm PN (%)
<table><tr><td>46,0</td><td>36,3</td><td>59,6</td><td>29,8</td></tr></table></td>
<td>95 % CI

(−0.21, 0.06)

(−0.19, 0.00)

(95% lower bound = 0.4 mm)

(95% lower bound = 18.54 mm)

P value:
0,77

<0,05</td>
</tr>
</table>

				Were assessed using a 6-point Likert scale questionnaire.	59,8 | 40,2 | 61,4 | 38,6 63,5 | 37,5 | 69,3 | 30,3 58,0 | 42,0 | 60,5 | 39,5 55,4 | 44,6 | 65,8 | 34,2 60,7 | 39,3 | 71,1 | 28,9	>0,5 | <0,5 0,05 | 0,02 0,01 | <0,001 0,11 | 0,03 0,3 | <0,001 0,03 | <0,001

Author/year/ country	**Population**	**Design**	**Intervention**	**Outcomes**	**32G x 4-mm needle /needle size**	**33G tip (28 G base) x 5mm needle mm/needle size**	**P vaue/CI**
Nagai, Y., et al., 2013, Japan	84 patients with diabetes – 79 completed. Male or female patients with type 1 (n = 9) or type 2 diabetes (n = 75) receiving insulin therapy were eligible if they had used the TR33T5 needle at least twice daily for more than 12 months, were 20 years of age or older, and had stable glycemic control. Women who were pregnant or intended to become pregnant during the study period were excluded	Single-center study. randomized, open-label crossover trial To compare efficacy (glycaemic control (GA)) and patient preference for two types of needle	N=79 The patients injected their usual insulin dosage with one type of needle for 4 weeks and then switched to the other type for the next 4 weeks. Started with BD32S4 and switched to TR33T5 Twenty-five patients did not use the skinfold technique while using the TR33T5 needle. Group 2: N=79 The patients injected their usual insulin dosage with one type of needle for 4 weeks and then switched to the other type for the	The serum glycated albumin level was measured before and after each 4-week period Each patient assessed pain during injection on a 150-mm visual analog scale (VAS). Needle preference, perceptions of handling, and acceptance were assessed by the patients, who completed a questionnaire after	20.5 – 4.7%. 60.3%	20.2 – 4.4%. The Mean difference VAS score was - 14.5mm 19.2%	P = 0.865 95% confidence interval -20.9 to -8.0 mm. P<0.0001). <0.0001

	Female 35 Male 49 Age (years) 64 +/– 11 BMI (kg/m2) 24.8 +/- – 3.7 Duration of diabetes (years) 14 +/- 10 Duration of insulin therapy (years) 7+/- 7		next 4 weeks. This group started with TR33T5 and switched to BD32S4	using each type of needle for 4 weeks. Bleeding Dribbling from skin site Dribbling from needle tip Needle bending Needle breakage	2.2% (147/6,735) 2.4% (160/6,735) 4.3% (288/6,735) 0.06% (4/6,735) 0.01% (1/6,735)	3.7% (239/6,485) 3.9% (251/6,485) 6.3% (408/6,485) 0.2% (14/6,485) 0.05% (3/6,485)	<0.0001 <0.0001 <0.0001 <0.05 0.366

Author/year/ country	**Population**	**Design**	**Intervention**	**Outcomes**	**32G x 4-mm needle /needle size**	**32G x 6-mm needle size**	**32G x 8-mm needle/needle size**	**Pvalue/CI**
Hirose, T. et al, 2013, Japan	12 healthy Japanese adult males. Aged 20-40 years Further inclusion criteria included weight 55-80 kg, BMI 18,5-25 kg/m2, body fat percentage 15-20%, systolic blood pressure 90-140 mmHg, diastolic blood pressure <90 mmHg, pulse rate 40-100 b.p.m, glycated hemoglobin <5,2%, fasting blood glucose <110 mg/dL and blood glucose <140 mg/dL at 2 h	A three-way, randomized, cross-over, single-center study. The participant were randomized to one of six groups using a computer-generated randomization list. Compare the blood insulin pharmacokinetic properties of three different insulin pen needles. A total of 12 participants were randomized to six groups. (Figure 1)	**n=12** each patient attended the institute four times, one screening visit and 3 test visits. The order of needles to be used differed between each group to minimize possible bias (Figure 1) All injections were administered into the abdomen, after	The new 32G x 4 needle was bioequivalent to two widely used needles, namely the 32G x 6 and 31G x 8 mm needles in terms of the peak insulin concentration (Cmax) and total insulin exposure (AUC0–∞). The 32G x 4 needle was also bioequivalent to the 32G x 6 needle, but not the 31G x 8 mm needle, for the time to reach peak insulin concentration (Tmax),	Tmax 4mm 39.39 ±9.26 Cmax: 16.99± 4.17 1420 ± 255 9.65 ± 2.79 795 ± 104	6mm 39.76 ±6.02 16.95± 3.22 1506 ± 259 9.69 ± 2.41 845 ± 115	8 mm 43.01 ±8.03 17.19 ±4.08 1539 ± 279 9.70 ± 2.45 860 ± 101	The comparison of T max were not statically significant (P = 0,9098 and P =0,3177, respectively) Similarly the comparison were not significant (P= 0.9823 and P=0.9059, respectively) Were not statically significant (P= 0.4212 and P=0.2843, respectively) The type of needle and the needle

	after 75-g glucose lead Compare the new 32-G x 4 mm needle with two other available needles with lengths of 6 mm (32G) and 8 mm (31G) in terms of insulin pharmacokinetics in healthy Japanese adult males.	Statistical analyses were carried out using prism version 5.04	using a alcohol gauzeswab, the insulin was injected without lifting a skinfold for the 4 mm needle, and with a lifted skinfold for the 8 and 6 mm neddles to reduce the risk of i.m injection and standardize injection depth. All test were carried out in a single-blind manner, with the participants blinded to which needle was being used at each test.	which was longer in the latter needle than in the 32G x 4 and 32G x 6 mm needles. The study believe the use of a 4-mm needle does not adversely affect the pharmacokinetic properties of insulin compared with longer needles, when injected subcutaneously in adults. The results can be generalized into other ethnicities, age-groups or even obese people, as even the shortest needle penetrates through the skin. However, differences in the subcutaneous tissue thickness, subcutaneous vascularity and adiposity between common injection sites (e.g. thigh, buttocks and abdomen) might influence the resulting insulin pharmacokinetic profiles, and the risk of i.m injection, highlighting the importance of good injection technique.				order did not affect any off the measured (P= 0.1309, P=0.8025 and P= 0.8318

Author/year/ country	Population	Design	Intervention	Outcomes	32G x 4-mm needle /needle size	32G x 6-mm needle mm/needle size	P value/CI
Miwa, T. et al, 2012, Japan	41 insulin-treated patients with type I or type 2 diabetes, who had been used an insulin pen for at least one year. Additional inclu-sion criteria included insulin injection of two or more times per day, a glycated hemoglobin level in the range of 5.9-8.9% and a body mass index of less than 35 kg/m2. Tue mean body mass index of all the randomized subjects was 23.2 kg/m^2, 36 (88%) had type 2 diabetes, 28 (68%) were male, and the mean age was 64 years old (Table 2).	Prospective, randomized, open-label, cross-over study	**n=19** Group 1 (the 32-gauge x 4-mm PN was used during Study Period 1, then the 32- gauge x 6-mm PN was used during Study Period 2) **n=19** Group 2 (the order for using the pen needles (PNs) was reversed).	Any differences in glycated albumin (GA) levels at the ends of the two study periods. Mean diff Adverse events during injection in the two study periods Bleeding Leakage from skin Leakage from needle point Needle bending Needle breakage Perceived pain in the use of the two types of PNs was assessed using a validated 150-mm visual analog scale (VAS) – (We calculated the degrees of perceived pain when using the two PNs by measuring the gap in the VAS. A calculated value of 0 means no difference in pain. Positive values indicate that the PN used in Study Period 2 was more painful, and negative values mean that it was less painful.)	Number not reported 48.8% n= 19.5% 31.7% 7.2% 0.0% - 7.3 mm Numbers not reported Afrapporter fra figure 4 I studiet	Number not reported 39% 12.2% 26.8% 4.9% 2.4% -26. o mm	CI 95 % 3.67-7.69 0.505 0.547 0.809 1.000 1.000 =0.0009

Author/year/ country	Population	Design	Intervention	Outcomes	32G x 5-mm needle /needle size	32G x 8-mm needle mm/needle size	P vaue/CI
Kreugel G. et al 2011	Total of 130 insulin-treated type 1 and type 2 diabetes patients with a body mass index ≥30 kg/m2 were randomized 126 patients completed the study.	Multicenter, open-label crossover study. Aim: to determine the influence of needle length for insulin administration on metabolic control and patient preference in	Insulin pen needles of two different lengths (5mm and 8mm) were compared. Patients started using the 5-mm needle for 3 months, after which they switched to injecting insulin with the 8-mm needle for another 3 months, or vice versa.	Hemoglobin A1c (A1C), fructosamine 1,5-anhydroglucitol Self-reported side effects Patient preference When all 126 patients were pooled: Baseline mean A1C Efter 3 mdr mean A1C Concentrations of serum fructosamine 1,5-AG There were no significant differences in self-reported hypoglycemic Events during both periods Bleeding Insulin backflow with the 8-mm needle Bruising	 7.63±1.0% 7.47±0.9% 256±50 mmol/l 10.6±6.5 mg/L Not reported	 7.63±1.0% 7.59±1.0% 267±48 mmol/l 10.4±6.5 mg/L Not reported	No within-group changes were observed with respect to A1C, serum fructosamine, 1,5-anhydroglucitol, hypoglycemic events, bruising, and pain. . Patients reported less bleeding (P¼0.04) with the 5-mm needle and less insulin backflow with the 8-mm needle (P¼0.01), but no difference in bruising. p=0.02 NS NS P=0.04 Patients reported less bleeding with the 5-mm needle.

				Pain perception median VAS score	7mm (interquartile range, 0–22)	9mm (interquartile range, 0–23)	P=0.01, Less Insulin backflow with the 8-mm needle. NS NS

Author/year/ country	**Population**	**Design**	**Intervention**	**Outcomes**	**4 mm x 32G PNs and 5mm x 31G PNs**	**4 mm x 32G PNs and or 8 mm x 31G PNs**	**Pvalue/ CI**
Hirsch,L et al, 2010, USA	173 included, 168 completed, 163 included in the fructosamine analyses. Baseline HbA1c in all subjects was 7.5—————— 1.0% (SD) and fructosamine 301—— 55.1 mmol/L. Subjects were either 'low dose' or 'regular dose' users (highest single insulin dose _ 20 units and 21–40 units, respectively). Subjects using an insulin pen at least once per day for two months or more. 56% male, mean 52.6 yrs, 63% type 2 78% were Caucasian mean age nearly 53 years (range 18 to 76)	Randomized non-inferiority cross-over trial, at four U.S. Centers.	N= 83, 47 low dose (under or =20 units), 36 regular dose (21-40 units), 4 mm x 32G PNs and 5mm x 31G PNs (4/5 mm) in two, 3-week treatment periods N= 80, 45 low dose,□35 regular dose 4 mm x 32G PNs and or 8 mm x 31G PNs (4/8 mm) in two, 3-week treatment periods	Percent absolute change in serum fructosamine (% |_ Fru|) unexplained, severe hypoglycemia % (table 5) hyperglycemia % (table 5) Leakage at injection sites, mean number of events reported (table 3) pain measured by visual analog scale	mean% D Fru 4.9% 67.5% of fructosamine changes were within +/- 5%, and 89.2% within +/-10%. 4 mm (N=173): 9 (5,2) 4 mm: 0(0) 4 mm: (n=164): 9,0 Mean difference (mm): - 11.91 SD 46,27 SEM: 5,61	mean% fru 5.5% 51.9% of fructosamine changes were within+/-5%, and 86.4% within +/-10% 5 mm (N=89) 5 (5.6) 8 mm (N=84): 4 (4.8) 5 mm: 2 (2.2) 8 mm (N=84): 1 (1.2) 5 mm (n=83): 12,3 8 mm (n=81): 7,9 Mean difference (mm): -23,26 SD: 35,25	4/5: 95% CI 3.8, 6.0 4/8 95% CI: 4.3, 6.4

	BMI 18–49 kg/m2, mean 31. 52% of subjects were obese Most subjects (65%) had been diagnosed with diabetes for 10 years and 58% were treated with insulin for 6 years; only 7% had used insulin51 year. In addition to insulin, 68 (42%) subjects were treated with oral hypoglycemic agents and/or pramlintide or exenatide: 63% (65 of 103) of the type 2 subjects were treated with oral hypoglycemic agents and 12% were injecting pramlintide or exenatide. SE TABEL 1 Exclusion criteria were physical conditions which would make them unable to perform study procedures, recent history of unstable diabetes including ketoacidosis or hypoglycemic unawareness, bleeding disorders, or pregnancy.					SEM: 4,24	95% upper bound 4/5: -2,55 p-værdi: 0.019 95% upper bound 4/8: -16,18 p-værdi: <0.001

Author/year/ country	Population	Design	Intervention	Outcomes	4 mm x 32G PNs and 5mm x 31G PNs	4 mm x 32G PNs and or 8 mm x 31G PNs	Pvalue/ CI
Hirsch, L, et al, 2012, USA	173 subjects randomized, 168 completed the study, and five were excluded. Adult with Type 1 or type 2 diabetes HbA1c 5.5 – 9,5 % mean BMI was 31.0 kg/m2 (range, 20 to 49 kg/m2) used an insulin pen for > 2 months were recruited (table 1)	Prospective, randomized, open label, two-period cross-over This report explores injection depth and the impact for subjects with different BMIs. It provides results of a secondary, post hoc analysis comparing the outcomes between obese (BMI <30 kg/m2) and non-obese (BMI >30 kg/m2) subjects	N = 89 Pen needles (PN) 4 mm x 32 G vs. 5 mm x 31 G N = 84 Pen needles (PN) 4 mm x 32 G vs. 8 mm x 31 G	The primary study objectives were to show equivalent glycemic control (fructosamine) within the 4/5 mm and 4/8 mm study groups. Reports of insulin leakage and comparisons of pain between the study pen needles, the latter via a 150 mm pain visual analogue scale (VAS), were also assessed. Specific endpoints assessed are change in fructosamine, pain perception, and leakage of insulin from the skin in the 4/5 mm and 4/8 mm groups.	Glycemic control: There was no suggestion of any trend in directional change in blood glucose levels with the new PN. Change in fructosamine: 4 vs 5 mm 4 vs 8 mm Pain was significantly less for the 4 mm than 5 and 8 mm PNs PAIN: Study group 4 vs 5 mm 4 vs 8 mm the number of reported leakage events was lower for the 4 mm needle, and it was preferred overall LEAKAGE: Needle type 4 mm (72) 5 mm (39) 8 mm (45) Total 106	BMI Mean(%) BMI < 30 4.7% BMI > 30 5,1% BMI < 30 5.6% BMI > 30 5,3% BMI (kg/m2) Mean (mm) BMI<30 -7.24 BMI > 30 - 13,82 BMI<30 -18,86 BMI > 30 -29,09 Events BMI<30 BMI>30 650 272 378 481 192 291	Cl 3,5, 7,1% 4,4, 7,3% 3,8, 7,6% 4,0, 7,1% Cl P-value 6,84 0,195 -0,85 0,040 -8,3 0,002 -19,36 <0,001

						357 148 209 1488 610 878		
Author/year/ country	**Population**	**Design**	**Intervention**	**Control**	**Outcomes**	**Intervention resultater**	**Kontrol resultater**	**P value/CI**
Santosa, A. et al 2018, Indonesia	The population were patients with diabetes mellitus type 2 in dr. Moewardi Hospital Solo, Indonesia, 55% of the respondents was male and 45% was female. All respondents were ≥ 40 years old, most of the respondents were in normal body weight and they have suffered the illness >10 years. patients with complications (neuropathy diabetic, retinopathy diabetic, nephropathy diabetic); hyper osmolality ketoacidosis were part of exclusion criteria	Experimental with Randomized Complete Block Design (RCBD).	60 respondents taken from simple random sampling. Injection used was Rapid-acting insulin with the dosage prescribed by the doctor. Injection was done in four (4) locations; abdomen, deltoid, Thigh gluteus. The administration were: 0 minutes (along with meals), 10 minutes before meal,	Deltoid Thigh Gluteus Abdomen Thigh Gluteus Abdomen Deltoid Gluteus Abdomen Deltoid Thigh 10 Minutes 20 Minutes 30 Minutes 0 Minute 20 Minutes 30 Minutes 0 Minute 10 Minutes 30 Minutes 0 Minute 10 Minutes	Two hour postprandial glucose levels were measured using a Glucometer (mg/dl). Mean difference	Numbers not reported Mean difference -18.22 -44.22 -60.62 18.22 -26.00 -42.40 44.22 26.00 -16.40 60.62 42.40 16.62 -9.1 -35.58 -60.03 9.1 -26.48 -50.93 35. 58 26.48 -24.45 60.03 50.93	Numbers not reported Mean difference	 P value: 0.002 P value: 0.000 P value: 0.000 P value: 0.002 P value: 0.000 P value: 0.000 P value: 0.000 P value: 0.000 P value: 0.008 P value: 0.000 P value: 0.000 P value: 0.008 P value: 0.003 P value: 0.000 P value: 0.000 P value: 0.003 P value: 0.000 P value: 0.000 P value: 0.000 P value: 0.000 P value: 0.000 P value: 0.000 P value: 0.000

			20 minutes before meal 30 minutes before meal. Effect of Insulin Injection Site and Time Interval Administration for the Postprandial Glucose Control (mg/dl): Abdomen Deltoid Thigh Gluteus	20 Minutes Time interval: 0 10 20 30 0 10 20 30 0 10 20 30 0 10 20 30		24.45 Numbers: 240 133.2 141.4 166.5 183.8 151.3 161.5 184.8 200.1 172.8 179.2 205.6 244.1 186.0 197.5 228.6 255.3		P value: 0.000 P value: 0.004

Author/year/ country	**Population**	**Design**	**Intervention**	**Control**	**Outcomes**	**Intervention resultater**	**Pvalue/CI**
Hôvelmann, U et al, 2017, Germany	21 healthy male. Aged 18–64 years	randomised, open-label, five-period, crossover trial	N= 21 were exposed to faster aspart		Pharmacokinetics:	N= 19 subjects completed the trial	95% Cl

	Body mass index of 20.0–28.0 kg/m2 Fasting plasma glucose ≤ 5.6 mmol/L. Subject characteristics are shown in Table 1	the primary objective of comparing total exposure between administration in the abdomen, upper arm and thigh	To investigate the pharmacokinetics, including the absolute bioavailability, of faster aspart administered subcutaneously in the abdomen, upper arm or thigh in healthy subjects. Subjects received faster aspart single-dosing at five visits: 0.2 U/kg subcutaneously in the abdomen (lifted skin fold of the lower abdominal wall above the inguinal area), upper arm (lifted skin fold of the outer aspect of the upper arm) and thigh (lifted skin fold of the anterior surface of the thigh), 0.2 U/kg intramuscularly in the thigh and 0.02 U/kg intravenously (1-min injection through a catheter inserted into a hand or forearm vein). For subcutaneous and intramuscular administration, blood was		**Onset of exposure** Abdomen Upper arm Thigh **Total exposure:** Abdomen Upper arm Thigh Upper arm/abdomen Thigh/abdomen Thigh/upper arm **Maximum concentration (Cmax)** Abdomen Upper arm Thigh Upper arm/abdomen Thigh/abdomen Thigh/upper arm Safety: Faster aspart was well tolerated with no safety issues identified during the trial.	Onset of appearance (min) 2,8 (1.3-5.0) 2,3 (1.1-5.3) 3,4 (1,8-5,9) LS mean (pmol_h/L) 1000,9 921,9 926,5 Treatment ratio 0,92 0,93 1,00 LS mean (pmol_h/L) 394,6 363,8 275,7 Treatment ratio 0,92 0,70 0,76	P value Cl 0,070 (0.84–1.01) 0,092 (0.85–1.01) 0,907 (0.92–1.09) P value Cl 0,447 (0.74–1.14) 0,002 (0.56–0.87) 0,016 (0.61–0.95)

			sampled for pharmacokinetics within 2 min predose, then every 2 min from dosing until 20 min post-dose, every 5 min until 80 min, every 10 min until 2 h, every 15 min until 3 h, and then at 3.5, 4, 5, 6, 7, 8, 10 and 12 h postdose. For intravenous administration, the same schedule applied until 2.5 h, followed by sampling at 3, 4, 6 and 8 h post-dose.				

Author/year/ country	**Population**	**Design**	**Intervention/control**	**Outcomes**	**Results**	**P value/CI**
Lesek Nosek et al. 2014 Germany	Study subjects were healthy males or females aged 18–55 years, with a body mass index (BMI) of 18.0–27.0 kg/m2 and fasting plasma glucose concentrations of B 6.0 mmol/L Twenty subjects (17 males and three females) were randomised, and 19 subjects	Randomised, open-label, five-period, single-centre crossover trial Only data from the SC dosing arms (three period) are reported in the article	**N= 20** The study subjects received single SC doses of IDeg (0.4 U/kg; separated by 13–21 days) in the thigh, abdomen, and deltoid. Each dose was followed by a 24-h euglycaemic clamp and 120-h pharmacokinetic blood sampling. The study subjects received the single doses of IDec SC in	**Pharmacokinetic endpoints** (Table 1) IDeg serum concentration after a single dose given SC administration in the thigh, abdomen, or deltoid area. (AUCIDeg,0–120h, SD) Maximum insulin degludec serum concentration after a single dose	**AUCIDeg,0–120h, SD** Deltoid vs. thigh Abdomen vs. thigh Abdomen vs. deltoid **Cmax,IDeg,SD** Deltoid vs. thigh Abdomen vs. thigh Abdomen vs. deltoid **AUCIDeg,τ, SS** Abdomen and deltoid vs. thigh	**Mean ratio [95 % CI]** 1,06 [1.01 – 1.10] 1,07 [1.03 – 1.11] 1,01 [0.96 – 1.06] 1.27 [1.08–1.49] 1.23 [1.07–1.42] 0.97 [0.84–1.12] 1.08 [NA]

	completed the trial. One subject completed only the deltoid and the abdomen period The mean [standard deviation (SD)] age of subjects who were randomised to dosing sequences was 37.4 (9.5) years, the mean (SD) BW was 76.4 (12.0) kg and the mean (SD) BMI was 24.1 (2.4) kg/m2. The majority of subjects (17/20) were caucasian, two were African American and one was Asian non-Indian.		random order in the thigh, abdomen, and deltoid during three different visits. Subjects attended dosing visits in a fasted state, and each subject remained in the clinic for 48 h after dosing, during which blood samples for pharmacokinetic analysis and blood glucose concentrations were taken. IDeg was provided in 3 mL Penfill cartridges (100 U/mL). For dosing and administered (using a syringe and needle) into a lifted skinfold in either the anterior surface of the thigh, the lower abdominal wall (above the inguinal area) or the outer aspect of the deltoid area. Only Insulin Decludec is investigated	(Cmax,IDeg,SD) *Simulation-based once-daily steady-state values:* Area under the insulin degludec serum concentration–time curve at steady state, (AUCIDeg,τ, SS) Maximum insulin degludec serum concentration at steady state, (Cmax,IDeg,SS) **Pharmacodynamic endpoints** (Table 2) Glucose-lowering effect of insulin degludec following a single subcutaneous injection in the thigh, abdomen, or deltoid area. Area under the glucose infusion rate (GIR) curve 0–24 h after a single dose (AUCGIR,0–24h, SD) Maximum GIR after a single dose, (GIRmax,SD)	**Cmax,IDeg,SS** Abdomen and deltoid vs. thigh **AUCGIR,0–24h, SD** Thigh Abdomen Deltoid **GIRmax,SD** Thigh Abdomen Deltoid **AUCGIR,τ, SS** Thigh Abdomen and deltoid **GIRmax,SS** Thigh Abdomen and deltoid	1.10 [NA] **Mean estimate + CV (coefficient of variation)** 2,572 38 2,833 42 2,960 43 2.7 32 3.0 37 3.0 42 4.719 5.005 3.5 3.8

				Simulation-based once-daily steady-state values Area under the GIR curve at steady state (AUCGIR,τ, SS) Maximum GIR at steady state (GIRmax,SS)		

Author/year/ country	**Population**	**Design**	**Intervention/control**	**Outcomes**	**Results intervention**	**Results control**	**P value/CI**
Trimble LE and Meneilly, GS 2014	Twenty elderly insulin-naive subjects (age 80±1 years; 7 female, 13 male; BMI 29±1 kg/m2; diabetes duration 11±2 years; A1C 7.1 ±0.2% [54±2 mmol/mol])	Objectives: To determine the rate of insulin absorption from different anatomic sites in diabetic patients over the age of 70. To determine the best practice for subcutaneous injection in older adults. Research Method: Measurement of serial glucose and insulin levels using 360 minute euglycemic clamp studies. The study was blinded to the investigators.	Subjects underwent three 360-min euglycemic glucose clamp studies in random order. In each, 0.1 units/kg of insulin lispro (Humalog; Eli Lilly, Indianapolis, IN) was administered subcutaneously using a 5-mm needle. In two studies, insulin was given 6.0 cm from the umbilicus using either a skin lift or no skin lift. In the third, insulin was injected into the upper arm without skin lift	Pain of injection (using a visual analog scale Samples were taken regularly to measure glucose and insulin	Not reported Not reported There was a significant study/ time interaction among studies in insulin values (F = 2.5, P <0.05), implying that injection into the abdominal site resulted in higher peak insulin values, but the difference was not clinically significant.	Not reported Not reported	Pain was minimal with injection and did not differ among sites. There was no significant difference in glucose values or infusion rates (data not shown). We conclude that the abdomen without a skin lift is the preferred site and technique for older adults. Health care professionals may use either the outer aspect of the arm or the abdomen without a skin lift.

					Our study suggests that insulin is equally well absorbed from the outer aspect of the arm and the abdomen in elderly patients with diabetes, and absorption is not modified by technique.		

Author/year/ country	Population	Design	Intervention/control	Outcomes	Results	P value/CI
Beckley 2013, Israel	Patients were considered for inclusion if they had type 2 diabetes mellitus requiring insulin therapy, were using insulin for at least 12 months, used the same dose for the past 30 days, and had a glycosylated hemoglobin (HbA1c) level of level of 6.5–9% at the immediate past evaluation.	A cross-over study.without randomization and blinding. The aim was to measure blood glucose level in different injection sites.	N=9 Enrolled patients were counseled on the proper insulin injection technique and asked to inject all insulin doses in their abdomen for the next 14 days and continue to selfmonitor and record blood glucose values at the same frequency as previously directed. Patients then returned to the medical clinic and were instructed to choose either their upper arm or thigh to inject for the next 14 days and continue monitoring as before. Patients returned once more to return completed self-	The mean ± S.D. absolute Difference in Daily blood glucose concentrations between the abdomen and any other injection site at the same frequency as previously directed	Between the abdomen and any other injection site : 23.6 ± 19.8 mg/dL For patients who chose to inject in their upper arm for the second 14-day period, the mean ± S.D. absolute difference between injection sites was 39.5 ± 11.3 mg/dL. For those who chose to inject in their thigh, the mean ± S.D. absolute difference was 15.6 ± 18.7 mg/dL When patients changed from the abdomen to another injection site, their blood glucose concentrations decreased as much as 51 mg/dL or increased as much as 46.9 mg/dL. It was unclear if these fluctuations were due to pharmacokinetic alterations, injection technique, short observation time, or another unaccounted reason.	

			monitoring blood glucose records and complete a follow-up survey about injection-site preferences.			

Author/year/ country	**Population**	**Design**	**Intervention/control**	**Outcomes**	**Results intervention**	**Results control**	**P value/CI**
Warenham-Mathiassen, S. et al, 2022, Denmark	50 participants with diabetes and 50 controls recruited through a Danish volunteer recruitment website and by word-of-mouth	The study has an experimental design with several components, including both laboratory analyzes and simulations. It includes both observational elements (sampling of skin and units) and analytical elements (biomolecular analyzes and mathematical modelling). It is comparative with the use of control groups (people without diabetes) to provide a basis of comparison for the results.. The study aimed to characterize skin microflora at injection sites and establish microbial contamination of used pen injectors and needles. The second objective was	N = 100 Intervention: 50 participants with diabetes - sampled through tape strips and skin swabs on the abdomen and thigh for skin microflora. Used pen injectors and needles were collected after in-home use and from the hospital after drug administration by health care professionals. Samples were analyzed by conventional culture, matrix assisted laser desorption/ionization-time of flight, mass spectrometry, confocal laser scanning microscopy and 16S/ITS high throughput sequencing. A mathematical model simulated the risk of needle contamination during injections.	Microbiological contamination of insulin pens during intended and repeated use.	**Intervention** A mathematical model simulated the risk of needle contamination during injections. Injection site populations were in 102 cells/cm2 order, with increased viable bacteria and anaerobic bacteria on the skin in persons with diabetes Participants with diabetes had significantly more anaerobic bacteria as well as more bacteria on thigh compared with controls Injection site analysis through sampling and microscopy exposed scarce and inconsistently distributes microflora dominated by		p = 0,05

		to evaluate the risk of injections during typical and repeated subcutaneous injections sampled through tape strips and skin swabs on the abdomen and thigh for skin microflora.	Control: 50 participants		interpersonal variation The mathematical model confirmed the heterogeneous distribution of penetrating a colony during subcutaneous injections.		

Author/year/ country	**Population**	**Design**	**Intervention/control**	**Outcomes**	**Results intervention**	**Results control**	**P value**
Misnikova, iv et al. 2011, Rusland	45 hospitalized patients with diabetes mellitus type 1 and 2; over 18 years of ages on a regimen of three injections of short or rapidacting insulin a day. Median age 48, 62% female. Patients with changes in skin and/or subcutaneous adipose tissue at the site of insulin injection (e.g. lipohypertrophy, lipoatrophy, and infection, scaring), poor eyesight, or a history of mental illness were excluded from the study.	The aim of the study was to assess the complications of repeated use of BD Micro-Fine Plus insulin pen needles. Blinded RCT study. the medical staff changed the needles to maintain the blinding.	The patients were randomized into 3 groups with 15 patients in each group. The first group used their needle once only, the second group used a single needle for 4 days (12 injections), and the third group used a single needle for 7 days (21 injections). Change of needles was carried out by the medical staff. The duration of observation for all groups was 7 days.	contamination of needles with bacterial microflora, The intensity of pain The presence of local reaction at the site of insulin injection.	Not reported	Not reported	Growth of microbe flora (Staphylococcus epidermidis - (Hly +) was found in 26,6 % of the patients, who used a needle once only. The maximum number of needles contaminated by microflora was found in the 3rd group (33.3 %) Staphylococcus epidermidis - (Hly +) and Gram+ bacilli. The intensity of pain was significantly higher in the 2nd group than in 1st one (p=0,045) on the fourth day of study, and in the 3rd group pain was considerably more intense than in 1st group (p=0.03) on day 7 of the study. Hyperemic foci at injection sites on day 4 and 7 of the study were found only in the 2nd and 3d groups

							(13.3 and 26,6 %, correspondingly). After a single use microbe contamination can be detected on insulin needles. Repeated use of needles amplifies the risk of needle contami-nation. Patients using insulin needles several times have more pain at injection site.
Heise, t et al. 2014, Tyskland/Danmark	82 adults aged 54±11.9 years with type 1 or type 2 diabetes receiving daily injections of insulin or glucagon-like peptide-1 (GLP-1) agonists. BMI 26.4±2.6 39% female	The aim of this study was to assess pain associated with subcutaneous injection into the abdomen and thigh of different combinations of injection speeds and volumes. Single-centre, one-visit, double-blinded, randomized controlled trial. Crossover study	Participants received 17 subcutaneous injections (12 in abdomen, 5 in thigh) of saline at different injection speeds (150, 300 and 450 µl/s), with different volumes (400, 800, 1200 and 1600 µl), and two needle insertions without any injection.	Pain was evaluated on a 100-mm visual analogue scale (VAS) (0 mm no pain, 100 mm worst pain) and on a yes/no scale for pain acceptability.	Injection of larger volumes caused significantly more pain VAS least square mean differences: 1600 µl 1600 µl 1200 µl 1200 µl,	 400 µl 800 µl 400 µl 800 µl,	Injection speed had no impact on injection pain (p = 0.833). 7·2 mm (95% confidence interval – CI; 4.6–9.7; p < 0.0001) 7.2 mm (4.4–10.0; p < 0.0001); 3.5 mm (0.4–6.6; p = 0.025) 3.6 mm (0.4–6.7; p = 0.027)

Quality assessment standard for a cross-over study. (Checklist)

Question 1	Appropriate cross-over design	Three points are considered: (1) the condition of the patients should be chronic and stable; (2) the intervention should not provide permanent change, but rather temporary relief; (3) the effect of the first intervention should not last into the second treatment period.	Low: all the three points are absolutely correct; Unclear: it hard to judge because some information was missing or ambiguous; High: one or more points are incorrect.
Question 2	Randomized treatment order	The order of receiving treatments should be randomized adequately.	Low: the method is appropriate and clearly described; Unclear: it is described as "randomized", but it is hard to judge whether the implementation was adequate because some information (method, etc.) was not provided; High: the method is inappropriate, or no randomization is applied.
Question 3	Carry-over effect	The authors should evaluate the carry-over effect and provide relevant information clearly.	Low: carry-over effect was evaluated and the results showed no carryover effect; Unclear: carry-over effect was not evaluated, and it is hard for evaluators to judge; High: carry-over effect was evaluated and the results showed apparent carry-over effect, or indicated evidently from some other provided information.
Question 4	Unbiased data	That only first-period data are available is considered a risk of bias.	Low: data for every period are provided; Unclear: data are unavailable for part of outcomes, or only analytical results are provided and it is hard to judge whether the results are analyzed based only on data from the first-period or every period. High: only first-period data are available.
Question 5	Allocation concealment	The study should apply appropriate approaches to ensure the allocation sequence is concealed.	Low: allocation sequence was concealed adequately by appropriate methods. Unclear: concealment approaches were not described, or relevant information was ambiguous;

			High: no approaches to allocation concealment were used or concealed inadequately.
Question 6	Blinding	The study should apply a proper blinding method to prevent performance and detection bias. Those involved in blinding (participants, doctors, measurers, or analysts) depends on the particularity of the studies.	Low: appropriate blinding method was applied; No blinding, but the outcome and the outcome measurement are not likely to be influenced by lack of blinding; Unclear: relevant information was not provided; High: no blinding method was applied, or applied incorrectly, or ineffectively, which very likely affected the outcome.
Question 7	Incomplete outcome data	The authors should provide relevant information about the completeness of outcome data, including the level of incomepleteness, reasons, and analytic method to tackle these data shortcomings, etc.	Low: no missing outcome data, or the reason is acceptable, or missing outcome data were appropriate analyzed; Unclear: it is hard to judge because some information was not provided; High: missing outcome data existed and the reasons were unacceptable, and the analytic method was inappropriate.
Question 8	Selective outcome reporting	The authors should report all the outcomes fully. Selective reporting of part of outcomes or data for an outcome or subsets of the data or analyses using the same data and etc. should be avoided.	Low: fully reported; Unclear: it is hard to judge due to the unavailability of some original information; High: the reports of the study suggest a high risk of selective outcome reporting.
Question 9	Other bias	Any other potential risk of bias that may affect the quality of cross-over studies.	Low: the study is apparently free of other problems; Unclear: whether certain problems existed and led to a risk of bias is uncertain; High: alvorlig risiko for bias existed due to evident problems.

NOTE: the standard was summarized from the Cochrane Collaboration's tool for assessing risk of bias and the Cochrane handbook`s suggestions for assessing risk of bias in cross-over studies. The assessment of some items, especially items 5–8, are almost the same as that described in Cochrane Collaboration's tool for assessing the risk of bias.

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Citation	Q1	Q2	Q3	Q4	Q5	Q6	Q7	Q8	Q9
Miwa, T.et al. 2012	L	U	U	L	U	H	L	L	L

Nosek, L. et al.2014	H Raske patienter	U	L	H	U	H	L	L	H Raske patienter
Bergenstal, RM, et al. 2015	L	U	U	L	U	H	L	L	L
Nagai, Y. et al 2013	L	L	U	L	L	H	U	L	U To forskellige mtoder til udformning af kanyler
Hirose, T et al.2012	H Raske patienter	L	L	L	L	H	L	L	H Raske patienter
Beckley, JA, et al. 2013	L	H	U	L	H	H	H	U	H Meget lille sample sixe
Hirsch, L.J. et al. 2010, USA	L	L	U	L	L	H	L	L	L
Hirsch LJ, et al. 2012, USA	L	L	U	L	L	H	L	L	H Sample size lille– sub group analyser fra tidligere studie
Kreugel,G. et al. 2010, Netherlands	U	U	U	L	H	H	L	L	U Recall bias – Smerte vurderet retrospektivt
Hövelmann, U. 2017	H Raske deltagere	U Metode ikke beskrevet	L	L	U	H	U	L	H Alle deltagere var mænd. Pharmacodynamics Ikke vurderet (healthy subjects)
Heise, T. et al. 2014	L	L	N/A	L	L	L	L	L	H

									Alle injektioner både hastighed og volumen blev ikke injiceret i låret

L= lav risiko for biaslav risiko for bias, U = unclear, H = alvorlig risiko for bias

Kritisk vurdering af RCT- studier

Citation	Q1	Q2	Q3	Q4	Q5	Q6	Q7	Q8	Q9	Q10	Q11	Q12	Q13
Santosa, A. 2018	U	U	U	Y	N	U	Y	Y	N	Y	Y	Y	Y
Misnikova, IV et al 2011	Y	N	Y	Y	N	N	Y	U	U	Y	Y	Y	Y
%													

Note: Y=yes N=no U= unclear

JBI critical appraisal checklist for randomized controlled trials: *Tufanaru C, Munn Z, Aromataris E, Campbell J, Hopp L. Chapter 3:* Systematic *reviews of effectiveness. In: Aromataris E, Munn Z (Editors). JBI Manual for Evidence Synthesis.* JBI, 2020. Available from **https://synthesismanual.jbi.global**

Q1 Was true randomization used for assignment of participants to treatment groups?

Q2 Was allocation to treatment groups concealed?

Q3 Were treatment groups similar at the baseline?

Q4 Were participants blind to treatment assignment?

Q5 Were those delivering treatment blind to treatment assignment?

Q6 Were outcomes assessors blind to treatment assignment?

Q7 Were treatment groups treated identically other than the intervention of interest?

Q8 Was follow up complete and if not, were differences between groups in terms of their follow up adequately described and analyzed?

Q9 Were participants analyzed in the groups to which they were randomized?

Q10 Were outcomes measured in the same way for treatment groups?

Q11 Were outcomes measured in a reliable way?

Q12 Was appropriate statistical analysis used?

Q13 Was the trial design appropriate, and any deviations from the standard RCT design (individual randomization, parallel groups) accounted for in the conduct and analysis of the trial?

Overall appraisal: Include □ Exclude □ Seek further info □

Kritisk vurdering af Non-RCT studier

Citation	Q1	Q2	Q3	Q4	Q5	Q6	Q7	Q8	Q9
Wareham-S. Mathiassen, et al., 2022, Denmark	Y	Y	Y	Y	Y	Y U	Y	Y	Y
Trimble, LA et al. 2014, Canada	Y	U	Y	N	Y	N/A	Y	U	U
%									

Note: Y=yes N=no U= unclear

Q1 Is it clear in the study what is the 'cause' and what is the 'effect' (i.e., there is no confusion about which variable comes first)
Q2 Were the participants included in any comparisons similar?
Q3 Were the participants included in any comparisons receiving similar treatment/care, other than the exposure or intervention of interest?
Q4 Was there a control group?
Q5 Were there multiple measurements of the outcome both pre and post the intervention/exposure?
Q6 Was follow up complete and if not, were differences between groups in terms of their follow up adequately described and analysed?
Q7 Were the outcomes of participants included in any comparisons measured in the same way?
Q8 Were outcomes measured in a reliable way?
Q9 Was appropriate statistical analysis used?

Overall appraisal: Include □ Exclude □ Seek further info□

Kritisk vurdering af kvalitativt studie

Citation	**Q1**	**Q2**	**Q3**	**Q4**	**Q5**	**Q6**	**Q7**	**Q8**	**Q9**	**Q10**
Krall et al 2000	U	U	U	U	U	N	N	U	Y	U

Note: Y=yes N=no U= unclear

Lockwood C, Munn Z, Porritt K. Qualitative research synthesis: methodological guidance for systematic reviewers utilizing meta-aggregation. Int J Evid Based Healthc. 2015;13(3):179–187

1. Is there congruity between the stated philosophical perspective and the research methodology?
2. Is there congruity between the research methodology and the research question or objectives?
3. Is there congruity between the research methodology and the methods used to collect data?
4. Is there congruity between the research methodology and the representation and analysis of data?
5. Is there congruity between the research methodology and the interpretation of results?
6. Is there a statement locating the researcher culturally or theoretically?
7. Is the influence of the researcher on the research, and vice- versa, addressed?
8. Are participants, and their voices, adequately represented?
9. Is the research ethical according to current criteria or, for recent studies, and is there evidence of ethical approval by an appropriate body?
10. Do the conclusions drawn in the research report flow from the analysis, or interpretation, of the data?

Vurdering af kliniske retningslinjer AGREE II

1. **Titel: Frid, AH et al New Insulin Delivery Recommendations, Mayo Clin Proc. 2016**

Dato for bedømmelse: 27/6-2023

Fra Agree II manualen:

III. Rating Scale and User's Manual Sections Each of the AGREE II items and the two global rating items are rated on a 7-point scale (1– strongly disagree to 7–strongly agree). The User's Manual provides guidance on how to rate each item using the rating scale and also includes 3 additional sections to further facilitate the user's assessment. The sections include User's Manual Description, Where to Look, and How to Rate. i)

Rating Scale All AGREE II items are rated on the following 7-point scale: 1 Strongly Disagree 2 3 4 5 6 7 Strongly Agree Score of 1 (Strongly Disagree). A score of 1 should be given when there is no information that is relevant to the AGREE II item, if the concept is very poorly reported, or if the authors state explicitly that criteria were not met. Score of 7 (Strongly Agree). A score of 7 should be given if the quality of reporting is exceptional and where the full criteria and considerations articulated in the User's Manual have been met.

Scores between 2 and 6. A score between 2 and 6 is assigned when the reporting of the AGREE II item does not meet the full criteria or considerations. A score is assigned depending on the completeness and quality of reporting. Scores increase as more criteria are met and considerations addressed. The "How to Rate" section for each item includes details about assessment criteria and considerations specific to the item.

Spørgsmål fra AGREE-Instrumentet	Score	Kommentarer – gerne på dansk
Afgrænsning og formål		
1. The overall objective(s) of the guideline is (are) specifically described.	6	
2. The health question(s) covered by the guideline is (are) specifically described.	7	
3. The population (patients, public, etc.) to whom the guideline is meant to apply is specifically described.	7	
Inddragelse af interessenter		
4. The guideline development group includes individuals from all relevant professional groups.	7	One drafted the guidelines – several experts reviewed and 183 diabetes experts from54 countries participated and reviewed the reccommendations
5. The views and preferences of the target population (patients, public, etc.) have been sought.	1	

6. The target users of the guideline are clearly defined.	7	
Stringens i udarbejdelsen		
7. Systematic methods were used to search for evidence.	5	
8. The criteria for selecting the evidence are clearly described	2	
9. The strengths and limitations of the body of evidence are clearly described	3	
10. The methods for formulating the recommendations are clearly described	6	One drafted the recommendations – several experts reviewed and 183 diabetes experts from54 countries participated and reviewed the recommendations
11. The health benefits, side effects, and risks have been considered in formulating the recommendations.	7	
12. There is an explicit link between the recommendations and the supporting evidence.	6	
13. The guideline has been externally reviewed by experts prior to its publication.	6	
14. A procedure for updating the guideline is provided.	1	
Klarhed og præsentation		
15. The recommendations are specific and unambiguous.	7	
16. The different options for management of the condition or health issue are clearly presented.	7	
17. Key recommendations are easily identifiable.	7	
Anvendelighed		
18. The guideline describes facilitators and barriers to its application.	3	
19. The guideline provides advice and/or tools on how the recommendations can be put into practice.	7	
20. The potential resource implications of applying the recommendations have been considered.	1	

21. The guideline presents monitoring and/or auditing criteria.	1	
Redaktionel uafhængighed		
22. The views of the funding body have not influenced the content of the guideline.	7	
23. Competing interests of guideline development group members have been recorded and addressed.	7	
Rate the overall quality of this guideline	5	

Samlet bedømmelse: En samlet score på 5. Bedømmelsen af de enkelte domæner blev vurderet til: Samlet bedømmelse af domæne 1 på 89 %, domæne 2 på 61%, domæne 3 på 60%, domæne 4 på 92 %, domæne 5 på 35%, og domæne 6 på 92%.

Samlet vurdering: vil du anbefale at den kliniske retningslinje anvendes i praksis? (sæt kryds)

Anbefales:

Anbefales (med forbehold eller ændringer): Ja

Anbefales ikke at blive publiceret:

Yderligere kommentarer kan skrives her:

Vurdering af systematiske reviews

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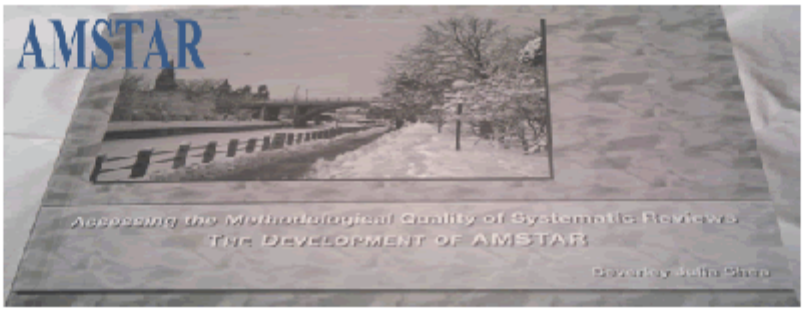

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AMSTAR Checklist

Printer Friendly Version

Article Name:
Ting et al 2015

1. Did the research questions and inclusion criteria for the review include the components of PICO?

For Yes:
- ☑ Population
- ☑ Intervention
- ☑ Comparator group
- ☑ Outcome

Optional (recommended)
- ☐ Timeframe for follow up

- ☑ Yes
- ☐ No

2. Did the report of the review contain an explicit statement that the review methods were established prior to the conduct of the review and did the report justify any significant deviations from the protocol?

For Partial Yes:
The authors state that they had a written protocol or guide that included ALL the following:
- ☐ review question(s)
- ☐ a search strategy
- ☐ inclusion/exclusion criteria
- ☐ a risk of bias assessment

For Yes:
As for partial yes, plus the protocol should be registered and should also have specified:
- ☐ a meta-analysis/synthesis plan, if appropriate, and
- ☐ a plan for investigating causes of heterogeneity
- ☐ a plan for investigating causes of heterogeneity

- ☐ Yes
- ☐ Partial Yes
- ☑ No

3. Did the review authors explain their selection of the study designs for inclusion in the review?

For Yes, the review should satisfy ONE of the following:

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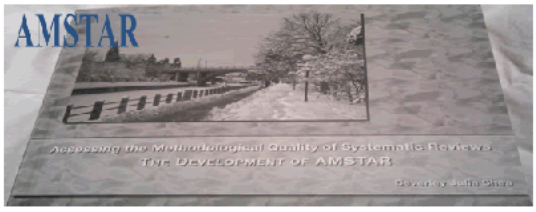

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AMSTAR Checklist

Printer Friendly Version

Article Name:
Mader et al 2024

1. Did the research questions and inclusion criteria for the review include the components of PICO?

For Yes:	Optional (recommended)	
☑ Population	☐ Timeframe for follow up	☑ Yes
☑ Intervention		☐ No
☑ Comparator group		
☑ Outcome		

2. Did the report of the review contain an explicit statement that the review methods were established prior to the conduct of the review and did the report justify any significant deviations from the protocol?

For Partial Yes: The authors state that they had a written protocol or guide that included ALL the following:	For Yes: As for partial yes, plus the protocol should be registered and should also have specified:	
☑ review question(s)	☑ a meta-analysis/synthesis plan, if appropriate, and	☐ Yes
☑ a search strategy	☐ a plan for investigating causes of heterogeneity	☑ Partial Yes
☑ inclusion/exclusion criteria	☐ a plan for investigating causes of heterogeneity	☐ No
☑ a risk of bias assessment		

3. Did the review authors explain their selection of the study designs for inclusion in the review?

For Yes, the review should satisfy ONE of the following:

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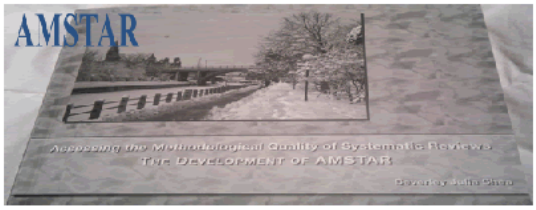

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AMSTAR Checklist

Printer Friendly Version

Article Name:

Zabaleta-del-Olmo et al. 2016: Safety of the reuse of needles

1. Did the research questions and inclusion criteria for the review include the components of PICO?

For Yes: Optional (recommended)

- [x] Population
- [x] Intervention
- [x] Comparator group
- [x] Outcome
- [ ] Timeframe for follow up

- [x] Yes
- [ ] No

2. Did the report of the review contain an explicit statement that the review methods were established prior to the conduct of the review and did the report justify any significant deviations from the protocol?

For Partial Yes: The authors state that they had a written protocol or guide that included ALL the following:

- [x] review question(s)
- [x] a search strategy
- [x] inclusion/exclusion criteria
- [x] a risk of bias assessment

For Yes: As for partial yes, plus the protocol should be registered and should also have specified:

- [x] a meta-analysis/synthesis plan, if appropriate, and
- [x] a plan for investigating causes of heterogeneity
- [ ] a plan for investigating causes of heterogeneity

- [x] Yes
- [ ] Partial Yes
- [ ] No

3. Did the review authors explain their selection of the study designs for inclusion in the review?

For Yes, the review should satisfy ONE of the following:

Bilag 7: Implementering

Anbefalingerne i den kliniske retningslinje er kun værdifulde i det omfang, de implementeres i den kliniske hverdag.

De faglige selskaber er vigtige aktører i forhold til at sikre udbredelse af kendskab til den kliniske retningslinje.

Arbejdsgruppen foreslår, at retningslinjen omtales på hjemmesiderne for Fagligt Selskab for Diabetessygeplejersker (FSDS), Faglig Selskab for Konsultation- og Infirmerisygeplejersker (FSKIS), Dansk Sygepleje Selskab (DASYS), Sygeplejersker i Kommunerne (FSSK), Forbundet af Offentligt Ansatte (FOA), Børne- og Ungdomspædagogernes Landsforbund (BUPL), Socialpædagogerne (SL), Endokrinologisk Selskab(DES) og Dansk Selskab for Almen Medicin (DSAM) med orientering om, hvad den indebærer for det pågældende fagområde og med et link til den fulde version af retningslinjen.

Information kan også formidles via medlemsblade, elektroniske nyhedsbreve samt faglige sociale medier.

Der skal indsendes orientering om retningslinjen til Sygeplejersken samt sygeplejevidenskab.dk med henblik på note i medlemsbladet.

Desuden er hjemmesiden for Fagligt Selskab for Diabetessygeplejersker oplagt til udbredelse af retningslinjens anbefalinger. Ydermere er Diabetesforeningen, Type1 Tænketank for Diabetes og Videncenter for Diabetes fora, hvor der er mulighed for at komme ud til personen med diabetes og udbrede kendskabet til anbefalingerne.

For at understøtte retningslinjens anvendelse lokalt i regioner og kommuner er det hensigtsmæssigt, at den kliniske retningslinje integreres i de forløbsbeskrivelser, instrukser og vejledninger, som allerede anvendes i praksis. Regioner og kommuner bør således sikre, at de anbefalinger, som må være relevante indarbejdes i instrukser og vejledninger.

For udbredelse af kendskab til retningslinjen i klinisk praksis foreslås at Center for Kliniske Retningslinjer afholder et webinar sammen med arbejdsgruppen for udarbejdelsen af denne retningslinje. Webinaret optages og lægges på dennes hjemmeside sammen med retningslinjen. Endvidere kan webinaret tilbydes til uddannelsesinstitutioner, der uddanner sygeplejersker og SOSU'er, under titlen "Fra forskning til praksis – injektion af insulin til voksne med diabetes".

Derudover foreslås det, at der laves en eller flere podcasts, hvor målgruppen både kan være sundhedsprofessionelle eller personer med diabetes.

Man ved, at indikatorer fra landsdækkende kliniske databaser har den fordel, at de kan bruges til benchmarking og til at følge egen kvalitet over tid. Der findes dog ikke egnede landsdækkende indikatorer i forhold til implementering af den kliniske retningslinje, og det er derfor nødvendigt at etablere lokal måling med dataindsamling og indikatorberegning. Data kan hentes fra f.eks. lokale IT-systemer, data fra journaler eller ved journalaudit. Der henvises til Sundhedsstyrelsens implementeringshåndbog..

Bilag 8: Monitorering

Sundhedsprofessionelle, der arbejder med voksne med diabetes, bør være opmærksomme på og kontinuerligt overveje, hvordan korrekt subkutan injektion af insulin sikres. Dette inkluderer opmærksomhed på injektionsteknik, anatomisk region for injektion af insulin, registrering af injektion i det anatomiske område, observation af huden, valg af penkanylelængde, anvendelse af ny penkanyle før hver injektion af insulin, og om løftet hudfold er påkrævet.

.

Desuden skal barrierer, der påvirker livskvaliteten for voksne med diabetes, der skal foretage injektion med insulin, adresseres, herunder smerter – angst og behov for information og undervisning.

I Danmark er der nedsat en styregruppe, som har ansvar for at definere og beslutte indikatorer og population for diabetes i Dansk Diabetes Database (DDD) (kilde Dokumentation - RKKP). DDD er en videreførelse og udbygning af Dansk Voksen Diabetes Database (DVDD) (92).

DDD muliggør en ensartet national monitorering af kvaliteten i diabetesbehandling og læring på tværs af landet. I øjeblikket fokuserer styregruppen primært på at forebygge invaliderende og potentielt dødelige komplikationer fra øjne, nyrer, nervebaner, fødder samt hjerte-kredsløb.

Arbejdsgruppen har undersøgt, om der er findes regionale kliniske databaser, der inkluderer indikatorer i overensstemmelse med denne kliniske retningslinje. For nuværende findes der ikke indikatorer, men kliniske databaser og patientens elektroniske journal inkluderer data i forskelligt omfang.

Arbejdsgruppen foreslår følgende indikatorer til vurdering af retningslinjens implementering:

1. Indikator: Andelen af voksne med diabetes, der foretager skift af injektionssted inden for samme anatomiske region.

2. indikator: Andelen af voksne med diabetes, der foretager skift af penkanyle før hver insulininjektion.

3. indikator: Andelen af voksne med diabetes, som systematisk undersøges for lipodystrofi.

4. indikator: Andelen af voksne med diabetes, der anvender 4 mm penkanyle.

Bilag 9: Arbejdsgruppe, høring og bedømmelses proces

Arbejdsgruppens medlemmer:

Susanne Myrup Houe, Diabetessygeplejerske, Master i sundhedspædagogik og sundhedsfremme, Afdeling for Vidensformidling og Kompetenceudvikling, Steno Diabetes Center Copenhagen

Solveig May-Britt Jansen, Diabetessygeplejerske. BA, Afdeling for Diabetesbehandling, Steno Diabetes Center Copenhagen

Lisa Holm Rasmussen, Klinisk sygeplejespecialist og diabeteskoordinator, cand.cur., Steno Diabetes Center Odense

Charlotte Engell Barfoed, Klinisk sygeplejespecialist og diabetessygeplejerske, Master i sundhedspædagogik og sundhedsfremme, Steno Diabetes Center Copenhagen

Charlotte Schiøtz, Sygeplejerske, MPH, Sygeplejen, Ældre og Sundhed, Langeland Kommune

Anne-Mette Veber Tønder, Klinisk sygeplejespecialist og diabetessygeplejerske, MCN, Medicinsk Afdeling M/FAM, Endokrinologisk ambulatorium, OUH Svendborg Sygehus

Marianne Wetendorff Nørgaard, Lektor, Ph.d., Leder af Center for Kliniske Retningslinjer, Klinisk Institut, Aalborg Universitet

Britt Laugesen, Lektor i Klinisk Sygepleje, Ph.d., Forskningsenhed for Klinisk Sygepleje, Aalborg Universitetshospital & Center for Kliniske Retningslinjer, Klinisk Institut, Aalborg Universitet

Konsulenter:

Ole Nørgaard, Informationsspecialist, cand.scient.san.publ., Videncenter for Diabetes, Afdeling for Vidensformidling og Kompetenceudvikling, Steno Diabetes Center Copenhagen

Jørgen Rungby, Overlæge, professor, Steno Diabetes Center Copenhagen

Peer review og høring:

Den kliniske retningslinje for injektion af insulin til voksne (+18 år) med diabetes har forud for udgivelsen været i høring blandt følgende høringsparter:

Dansk Selskab for Almen Medicin

Dansk Endokrinologisk selskab

DASYS, herunder Fagligt Selskab for kommunalt ansatte, Fagligt Selskab for nefrologi, Fagligt Selskab for cardiologi, Fagligt selskab for konsultationssygeplejersker, fagligt Selskab for Diabetessygeplejersker

Diabetesforeningen

Steno centrene

Kommunernes Landsforening

Danske regioner

Type 1 tænketanken

Center For Kliniske Retningslinjer
Oktober 2024

Dansk Diabetes Database (DDiD)

Retningslinjen er peer reviewet af:

Intern bedømmelse:

Preben Ulrich Pedersen, RN, Phd

Professor Emeritus Aalborg Universitet

Ekstern bedømmelse:

Signe Stelling Risom, RN, Phd,

Seniorforsker, Afdeling for hjertesygdomme, Herlev og Gentofte Hospital

Docent, Institut for sygepleje og ernæring, Københavns Professionshøjskole

Lektor, Institut for Klinisk Medicin, Københavns Universitet

Bilag 10: Fondsstøtte

Der er ikke modtaget fondsstøtte til dette arbejde. Fagligt Selskab for Diabetessygeplejersker har støttet gruppen med transportudgifter og forplejning.

Arbejdsgruppens medlemmer er ansat på Steno Diabetes Center Copenhagen, Steno Diabetes Center Odense, i Langeland Kommune og på Odense Universitetshospital Svendborg. Arbejdsstederne har bidraget med ressourcer i form af arbejdstid.

Bilag 11: Habilitetsforhold

Der vurderes ikke at være interessekonflikter hos arbejdsgruppens medlem Susanne Myrup Houe, der har kunnet påvirke habiliteten ved udarbejdelsen af retningslinjen.

Arbejdsgruppens medlem Solveig May-Britt Jansen har aktier i Novo Nordisk, men det vurderes ikke at være interessekonflikter hos Solveig, som har kunnet påvirke habiliteten ved udarbejdelsen af retningslinjen.

Der vurderes ikke at være interessekonflikter hos arbejdsgruppens medlem Lisa Holm Rasmussen, der har kunnet påvirke habiliteten ved udarbejdelsen af retningslinjen.

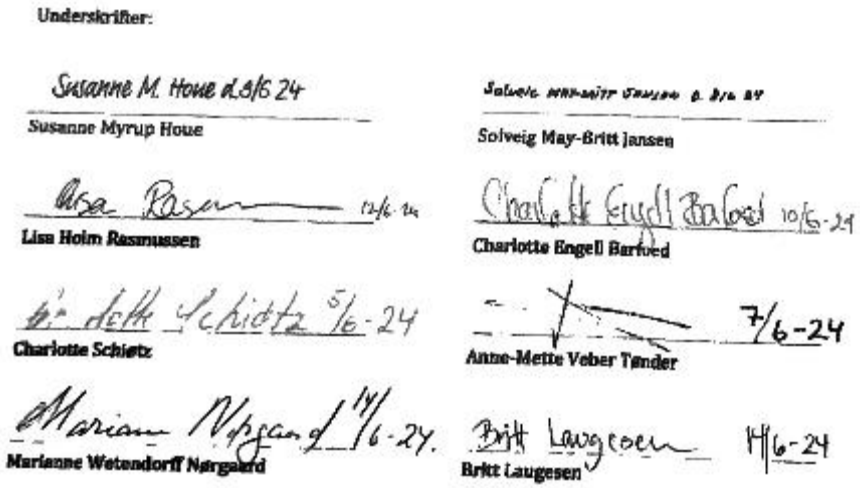
Der vurderes ikke at være interessekonflikter hos arbejdsgruppens medlem Charlotte Engell Barfoed, der har kunnet påvirke habiliteten ved udarbejdelsen af retningslinjen.

Der vurderes ikke at være interessekonflikter hos arbejdsgruppens medlem Charlotte Schiøtz, der har kunnet påvirke habiliteten ved udarbejdelsen af retningslinjen.

Der vurderes ikke at være interessekonflikter hos arbejdsgruppens medlem Anne-Mette Veber Tønder, der har kunnet påvirke habiliteten ved udarbejdelsen af retningslinjen.

Der vurderes ikke at være interessekonflikter hos arbejdsgruppens medlem Marianne Wetendorff Nørgaard, Lektor, Phd, Leder af Center for Kliniske Retningslinjer, Klinisk Institut, Aalborg Universitet

Der vurderes ikke at være interessekonflikter hos arbejdsgruppens medlem Britt Laugesen, Lektor i Klinisk Sygepleje, Forskningsenhed for Klinisk Sygepleje, Aalborg Universitetshospital & Center for Kliniske Retningslinjer, Klinisk Institut, Aalborg Universitet.



Bilag 12: Nyt siden sidst

Målgruppen:

I denne kliniske retningslinje er målgruppen bredere defineret, idet den henvender sig til sundhedsprofessionelle i primær- og sekundær sektor, som varetager pleje og behandling af voksne med diabetes eller vejleder i subkutan injektion af insulin til voksne med diabetes, pårørende eller kollegaer.

Derudover nævnes alle ansatte, der i deres arbejde har kontakt til personer med diabetes med behov for hjælp til injektion af insulin eller vejledning heri. Dette gælder uanset profession.

Desuden nævnes patienter, pårørende og andre, der ønsker information om subkutan injektion af insulin til voksne kan søge viden i retningslinjen.

Anbefaling i relation til de enkelte PICO spørgsmål:

Denne kliniske retningslinje er udarbejdet på grundlag af eksisterende anbefalinger fra 2016 udgivet af Mayo Foundation for Medical Education and Research" New Insulin Delivery Recommendations" (3) og tilpasset danske forhold samt øvrigt identificeret litteratur.

Anbefaling i relation til besvarelse af PICO spørgsmål gennemgås og er opdelt i følgende:

- Graden af anbefalingen
- Rationale for anbefaling
- Gavnlige og skadelige virkninger
- Kvaliteten af evidensen
- Sammenfatning af evidens

Nyt fokuseret spørgsmål:
PICO 2

Forebyggelse af infektion:

Hvilken evidens findes for at forebygge infektion ved indstiksstedet ved subkutan insulin injektion hos voksne med diabetes?

↑Svag anbefaling: Bør der foretages skift af penkanyle ved hver ny insulininjektion?

Overvej at anbefale skift af penkanyle ved hver insulininjektion for at forebygge og undgå infektion.

Bør der foretages huddesinfektion forud for subkutan injektion af insulin i borgerens eget hjem eller bosted?

Konsensusanbefaling:
Det er god praksis at overveje, at der foretages huddesinfektion forud for injektion af insulin, når det foregår på hospitaler da det sandsynligvis reducerer risikoen for indføring af bakterier i vævet i underhuden.
Det er ligeledes god praksis at foretage huddesinfektion forud for injektion af insulin i borgeres eget hjem eller på bosteder og plejehjem da det sandsynligvis reducerer risikoen for indføring af bakterier i vævet i underhuden, selv om de infektionsfremkaldende mikroorganismer ofte stammer fra borgerens normalflora og derfor udgør en mindre risiko. Hvis personen med diabetes selv injicerer insulin, er anbefalingen, at *det ikke er god praksis rutinemæssigt* at desinficere før injektion

PICo:

Patientperspektivet undersøges mht. skift af penkanyle, længde på penkanyle, huddesinfektion, deling af insulindosis og løftet hudfold.

Sundhedsprofessionelles perspektiv mht. til skift af penkanyle, længde på penkanyle, huddesinfektion, deling af insulindosis og løftet hudfold undersøges.

Litteratur- og evidensgennemgang
Foretaget ny litteratursøgning, fra 2013 - august 2023.

Evidensen er gennemgået, og der er udarbejdet nye anbefalinger, tilpasset danske forhold.

Forfattere:

Nye forfattere, CFKR og Videncenter for diabetes Steno Diabetes Center Copenhagen har medvirket i opdateringen af denne kliniske retningslinje.

Bilag:
Alle bilag er opdaterede eller nye.

Bilag 13: Opdatering og fremtidig forskning

Der vil blive taget stilling til behov for opdatering hvert fjerde år med mindre ny evidens eller den teknologiske udvikling på området tilsiger andet.

Fremtidig forskningsindsats

Den meget begrænsede evidens der er fremkommet i forbindelse med udarbejdelsen af den kliniske retningslinje peger på, at der mangler forskning på flere områder.

Lipodystrofi bør undersøges i større studier, hvor risikofaktorer bør undersøges nærmere, evt. i større observationelle studier, hvis ikke RCT studier er muligt.

De inkluderede studier i denne kliniske retningslinje er alle med meget få deltagere, af mindre god kvalitet, med manglende blinding – flere RCT crossover studier er udført med raske personer, hvor der kan være risiko for manglende generaliserbarhed. Der er behov for større randomiserede studier, med inklusion af personer med diabetes, evt. multicenterstudier.

Der mangler større randomiserede studier, hvor desinfektion af huden før injektion af insulin undersøges i forhold til infektion.

Der mangler ligeledes kvalitative studier, inden for de områder der er undersøgt i denne kliniske retningslinje, hvor patienters og sundhedsprofessionelles præferencer undersøges.

Kun et enkelt studie havde undersøgt patientens perspektiv. Kvaliteten af studiet var lav. Det er således relevant at medtænke patientperspektivet i kommende studier. Generelt er det vigtigt at få meget mere viden om patientperspektivet. Der er behov for flere større og bedre studier, hvor patienternes præferencer undersøges, samt studier som beskriver de sundhedsprofessionelles perspektiv.