Evidence-based Guidelines for the use of Stem Cell Therapy

Dermatology Conditions Supplement

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Department of Health Research
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CONTENTS

ABBREVIATIONS

AD-MSCs	:	Adipose Tissue-Derived Mesenchymal Stem Cells
ADSC	:	Adipose-Derived Stem Cell
ADSC-CM	:	Adipose-Derived Stem Cell Conditioned Media
AEs	:	Adverse Events
AGA	:	Androgenetic Alopecia
ALP	:	Alkaline Phosphatase
ALT	:	Alanine Amino Transferase
AM	:	Amniotic Membrane
AMSC-CM	:	Amniotic Membrane Stem Cell-Conditioned Media
AMSC-MP	:	Amniotic Membrane Stem Cell-Metabolite Product
ASCE	:	Adipose Derived Stem Cell Exosome
AST	:	Aspartate aminotransferase
AT-ASCs	:	Autologous Adipose tissue derived Adult Stem Cells
BMI	:	Body Mass Index
BMMNCs	:	Bone Marrow Mononuclear Cells
BM-MSCs	:	Bone Marrow derived Mesenchymal Stem/Stromal Cells
BP	:	Blood Pressure
CD34 cells	:	Cell Differentiation 34 cells
CI	:	Confidence Interval
CM	:	Conditioned Media
CO_2	:	Carbon Dioxide
CoI	:	Conflict of Interest
Cr	:	Creatinine
DALYs	:	Disability Adusted Life Years
DMEM	:	Dulbecco's Modified Eagles culture medium Medium
DP	:	Dermal Papillae
DS	:	Dermal Sheath
DSC	:	Dermal Sheath Cup
ECCA	:	échelle d'évaluation clinique des cicatrices d'acné
eCO_2	:	equivalent Carbon Dioxide
EDTA	:	Ethylenediaminetetraacetic Acid
EGF	:	Epidermal Growth Factor
EGM-2	:	Endothelial Cell Growth Medium-2
ESCs	:	Embryonic Stem Cells
FCL	:	Fractional Carbon Dioxide Laser
FPHL	:	Female Pattern Hair Loss
FxCR	:	Fractional Carbon Dioxide Laser
GDG	:	Guideline Development Group
GRADE	:	Grading of Recommendations Assessment, Development and Evaluation
HA	:	Hyaluronic Acid
HACS	:	Human Adipose tissue Stem cell-derived exosomes Containing Solution

hESC-EPC CM	:	human Embryonic Stem Cells- derived Endothelial Precursor Cells Conditioned Medium
hESC-EPCs	:	human Embryonic Stem Cell-derived Endothelial Precursor Cells
HF- MSCs	:	Hair Follicle Mesenchymal Stem Cells
HSCM	:	Human Stem Cell-Conditioned Media
HUCB-MSC	:	Human Umbilical Cord blood-derived mesenchymal stem Cells
hUC-MSCs-CM	:	human Umbilical Cord Mesenchymal Stem Cells Conditioned Media
IV	:	Intravenous
L scale	:	Ludwig scale
LTFU	:	Loss To Follow Up
MCID	:	Minimal Clinical Important Difference
MD	:	Mean Difference
MMP	:	Matrix Metalloproteinase
MN	:	Microneedling
MNC	:	Mono Nuclear Cell
MPHL	:	Male Pattern Hair Loss
MSCs	:	Mesenchymal Stem/Stromal Cells
MSCT	:	Mesenchymal stem cell transplantation
NaCL	:	Sodium Chloride
NH scale	:	Norwood–Hamilton scale
NIH	:	National Institutes of Health
NR	:	Not Reported
NRF	:	National Research Foundation of Korea
OPD	:	Out Patient Department
PBS	:	Phosphate-Buffered Saline
PHL	:	Pattern Hair Loss
PRISMA	:	Preferred Reporting Items for Systematic Reviews and Meta-Analysis
PRP	:	Platelet Rich Plasma
RCT	:	Randomized Controlled Trial
RoB 2	:	Risk of Bias 2
RR	:	Relative Risk
SAEs	:	Severe Adverse Events
SD	:	Standard Deviation
SE	:	Standard Error
SMD	:	Standardized Mean Difference
SPEC	:	Shiseido Cell Processing and Expansion Center
SR/MA	:	Systematic Review/Meta-Analysis
SRLV	:	Derma Signal Skin Rejuvenation Lyophilized Vial
SVF	:	Stromal Vascular Fraction
TBSA	:	Total Body Surface Area
TEWL	:	Trans Epidermal Water Loss
UCMSCs	:	Umbilical Cord Mesenchymal Stem Cells
USA	:	United States of America

UV	:	Ultra Violet
UVR	:	Ultra Violet Radiation
VEGF	:	Vascular Endothelial Growth Factor
VSS	:	Vancouver Scar Scale
YAG	:	Yttrium Aluminium Garnet

1. SKIN REJUVENATION

i. **Key question in PICO format**

ii. **Search strategy**

iii. **PRISMA flow diagram**

iv. **Summary of included studies**

v. **Classification of studies based on level of stem cell manipulation**

vi. **Evidence to decision framework**

vii. **Data extraction**

viii. **List of excluded studies**

i. Key Question in PICO format:

In patients requiring skin rejuvenation, what is the efficacy and safety of stem cell therapy as compared to usual care?

Population: Subjects with damaged skin, severe skin disease, aging (antiaging: wrinkles, thickness and pigmentation)
Subgroups: Gender, age, cause of damage wounds, caused by cutting or breaking of the tissue, and burns.
Intervention: Any Stem cell and product derived from stem cells
Comparator: Usual Care/ Conventional Care
Critical Outcomes: **Efficacy:** Reduction in fine lines beyond 6 months, Change in Skin thickness beyond one year, Reduction in pigmentation beyond 6 months. Safety: Serious adverse events, Any tumour formation
Important: Improvement in skin quality, Dermatological quality of life, Other adverse events.

ii. Search strategy:

An electronic search was performed in PubMed, Embase, Web of Science, and Cochrane databases to identify relevant studies. MeSH terms and keywords related to stem cells and skin rejuvenation were used to build the search strategy.

No	Search Query	Results
PubMed		
#1	"Skin Aging"[Mesh] OR "Cosmetics"[Mesh] OR "Skin Pigmentation"[Mesh] OR "Wounds and Injuries"[Mesh] OR "Burns"[Mesh] OR "Cicatrix, Hypertrophic"[Mesh] OR "Vitiligo"[Mesh] OR "Alopecia"[Mesh] OR "Wound Healing"[Mesh] OR "Skin Aging"[tiab] OR "Cosmetics"[tiab] OR "Skin Pigmentation"[tiab] OR "Wounds and Injuries"[tiab] OR "Burns"[tiab] OR "Cicatrix, Hypertrophic"[tiab] OR "Vitiligo"[tiab] OR "Alopecia"[tiab] OR "Wound Healing"[tiab] OR "skin rejuvenation"[All Fields] OR "skin renewal"[All Fields] OR "skin revitalization"[All Fields] OR "facial rejuvenation"[All Fields] OR "skin regeneration"[All Fields] OR "dermal rejuvenation"[All Fields] OR "antiaging treatments"[All Fields] OR "cosmetic skin treatments"[All Fields] OR "facial revitalization"[All Fields] OR "skin rejuvenation therapy"[All Fields] OR "skin rejuvenation treatment"[All Fields] OR "hand rejuvenation"[All Fields] OR "skin repair"[All Fields] OR "damaged skin"[All Fields] OR "wrinkles"[All Fields] OR "tissue injury"[All Fields] OR "skin burn"[All Fields] OR "skin scar"[All Fields] OR "androgenic alopecia"[All Fields]	1,290,267

#2	("Stem Cells"[Mesh] OR "Stem Cell Transplantation"[Mesh] OR "Stromal Cells"[Mesh] OR "stem cell"[tiab] OR "stem cells"[tiab] OR "mesenchymal cell" OR "mesenchymal cells" OR "mononuclear cell" OR "mononuclear cells" OR "progenitor cell" OR "progenitor cells" OR "cord blood cell" OR "cord blood cells" OR "regenerative cell" OR "regenerative cells" OR "stromal cell" OR "stromal cells")	608,130
#3	((randomized controlled trial[pt]) OR (controlled clinical trial[pt]) OR (randomized[tiab] OR randomised[tiab]) OR (placebo[tiab]) OR (drug therapy[sh]) OR (randomly[tiab]) OR (trial[tiab]) OR (groups[tiab])) NOT (animals[mh] NOT humans[mh])	5,127,598
#4	#1 AND #2 AND #3 NOT (animals[MH] NOT humans[MH])	3,114

Cochrane		
#1	(“stem cell” OR “stem cells” OR “mesenchymal cell” OR “mesenchymal cells” OR “mononuclear cell” OR “mononuclear cells” OR “progenitor cell” OR “progenitor cells”):ti,ab,kw OR (“cord blood cell” OR “cord blood cells” OR “regenerative cell” OR “regenerative cells” OR "stromal cell" OR "stromal cells" OR "stem cell transplantation"):ti,ab,kw (Word variations have been searched)	21,682
#2	MeSH descriptor: [Stem Cells] explode all trees	1,147
#3	MeSH descriptor: [Stem Cell Transplantation] explode all trees	3,184
#4	MeSH descriptor: [Stromal Cells] explode all trees	340
#5	#1 OR #2 OR #3 OR #4	21,798
#6	MeSH descriptor: [Skin] explode all trees	6,283
#7	("Skin Aging" OR "Cosmetics" OR "Skin Pigmentation" OR "Wounds and Injuries" OR Burns OR "Cicatrix, Hypertrophic" OR Vitiligo OR Alopecia OR "Wound Healing" OR "skin rejuvenation" OR "skin renewal" OR "skin revitalization" OR "facial rejuvenation" OR "skin regeneration" OR "dermal rejuvenation" OR "antiaging treatments" OR "cosmetic skin treatments" OR "facial revitalization" OR "skin rejuvenation therapy" OR "skin rejuvenation treatment" OR "hand rejuvenation" OR "skin repair" OR "damaged skin" OR wrinkles OR "tissue injury" OR "skin burn" OR "skin scar" OR "androgenic alopecia"):ti,ab,kw	30,359
#8	#6 OR #7	35,513
#9	#5 AND #8 [Trials]	594

EMBASE		
#1	‘stem cell'/exp OR 'stem cell transplantation'/exp OR 'stroma cell'/exp OR 'fetus blood'/exp OR 'mesenchyme cell'/exp OR 'stem cell':ti,ab,kw OR 'stem cells':ti,ab,kw OR 'mesenchymal cell':ti,ab,kw OR 'mesenchymal cells':ti,ab,kw OR 'mononuclear cell':ti,ab,kw OR 'mononuclear cells':ti,ab,kw OR 'progenitor cell':ti,ab,kw OR 'progenitor cells':ti,ab,kw OR 'cord blood cell':ti,ab,kw OR 'cord blood cells':ti,ab,kw OR 'cord blood':ti,ab,kw OR 'regenerative cell':ti,ab,kw OR 'regenerative cells':ti,ab,kw OR 'stromal cell':ti,ab,kw OR 'stromal cells':ti,ab,kw	939,435

#2	**'skin aging'** OR **'cosmetic'**/exp OR **cosmetic** OR **'skin pigmentation'**/exp OR **'skin pigmentation'** OR **'wound'**/exp OR **wound** OR **'skin injury'**/exp OR **'skin injury'** OR **'burn'**/exp OR **burn** OR **'hypertrophic skin disease'**/exp OR **'hypertrophic skin disease'** OR **'vitiligo'**/exp OR **vitiligo** OR **'alopecia'**/exp OR **alopecia** OR **'wound healing'**/exp OR **'wound healing'** OR **'skin rejuvenation'**/exp OR **'skin rejuvenation'** OR **'skin revitalization'** OR ((**'skin'**/exp OR **skin**) AND **revitalization**) OR **'skin renewal'** OR ((**'skin'**/exp OR **skin**) AND **renewal**) OR **'facial rejuvenation'**/exp OR **'facial rejuvenation'** OR **'skin regeneration'**/exp OR **'skin regeneration'** OR **'dermal rejuvenation'** OR (**dermal** AND (**'rejuvenation'**/exp OR **rejuvenation**)) OR **'antiaging activity'**/exp OR **'antiaging activity'** OR **'facial revitalization'** OR (**facial** AND **revitalization**) OR **'hand rejuvenation'**/exp OR **'hand rejuvenation'** OR **'skin repair'**/exp OR **'skin repair'** OR **'skin defect'**/exp OR **'skin defect'** OR **'wrinkle'**/exp OR **wrinkle** OR **'tissue injury'**/exp OR **'tissue injury'** OR **'skin scar'**/exp OR **'skin scar'**	1,174,134
#3	(**'randomized controlled trial'**/exp OR **'controlled clinical trial'**/de OR **random***:ti,ab,tt OR **'randomization'**/de OR **'intermethod comparison'**/de OR **placebo**:ti,ab,tt OR **compare**:ti,tt OR **compared**:ti,tt OR **comparison**:ti,tt OR ((**evaluated**:ab OR **evaluate**:ab OR **evaluating**:ab OR **assessed**:ab OR **assess**:ab) AND (**compare**:ab OR **compared**:ab OR **comparing**:ab OR **comparison**:ab)) OR ((**open** NEXT/1 **label**):ti,ab,tt) OR (((**double** OR **single** OR **doubly** OR **singly**) NEXT/1 (**blind** OR **blinded** OR **blindly**)):ti,ab,tt) OR **'double blind procedure'**/de OR ((**parallel** NEXT/1 **group***):ti,ab,tt) OR **crossover**:ti,ab,tt OR **'cross over'**:ti,ab,tt OR (((**assign*** OR **match** OR **matched** OR **allocation**) NEAR/6 (**alternate** OR **group** OR **groups** OR **intervention** OR **interventions** OR **patient** OR **patients** OR **subject** OR **subjects**OR **participant** OR **participants**)):ti,ab,tt) OR **assigned**:ti,ab,tt OR **allocated**:ti,ab,tt OR ((**controlled** NEAR/8 (**study** OR **design** OR **trial**)):ti,ab,tt) OR **volunteer**:ti,ab,tt OR **volunteers**:ti,ab,tt OR **'human experiment'**/de OR **trial**:ti,tt) NOT (((**random*** NEXT/1 **sampl*** NEAR/8 (**'cross section*'** OR **questionnaire*** OR **survey** OR **surveys** OR **database** OR **databases**)):ti,ab,tt) NOT (**'comparative study'**/de OR **'controlled study'**/de OR **'randomised controlled'**:ti,ab,tt OR **'randomized controlled'**:ti,ab,tt OR **'randomly assigned'**:ti,ab,tt) OR (**'cross-sectional study'** NOT (**'randomized controlled trial'**/exp OR **'controlled clinical trial'**/de OR **'controlled study'**/de OR **'randomised controlled'**:ti,ab,tt OR **'randomized controlled'**:ti,ab,tt OR **'control group'**:ti,ab,tt OR **'control groups'**:ti,ab,tt)) OR (**'case control*'**:ti,ab,tt AND **random***:ti,ab,tt NOT (**'randomised controlled'**:ti,ab,tt OR **'randomized controlled'**:ti,ab,tt)) OR (**'systematic review'**:ti,tt NOT (**trial**:ti,tt OR **study**:ti,tt)) OR (**nonrandom***:ti,ab,tt NOT **random***:ti,ab,tt) OR **'random field*'**:ti,ab,tt OR ((**'random cluster'** NEAR/4 **sampl***):ti,ab,tt) OR (**review**:ab AND **review**:it NOT **trial**:ti,tt) OR (**'we searched'**:ab AND (**review**:ti,tt OR **review**:it)) OR **'update review'**:ab OR ((**databases** NEAR/5 **searched**):ab) OR ((**rat**:ti,tt OR **rats**:ti,tt OR **mouse**:ti,tt OR **mice**:ti,tt OR **swine**:ti,tt OR **porcine**:ti,tt OR **murine**:ti,tt OR **sheep**:ti,tt OR **lambs**:ti,tt OR **pigs**:ti,tt OR **piglets**:ti,tt OR **rabbit**:ti,tt OR **rabbits**:ti,tt OR **cat**:ti,tt OR **cats**:ti,tt OR **dog**:ti,tt OR **dogs**:ti,tt OR **cattle**:ti,tt OR **bovine**:ti,tt OR **monkey**:ti,tt OR **monkeys**:ti,tt OR **trout**:ti,tt OR **marmoset***:ti,tt) AND **'animal experiment'**/de) OR	5,629,297

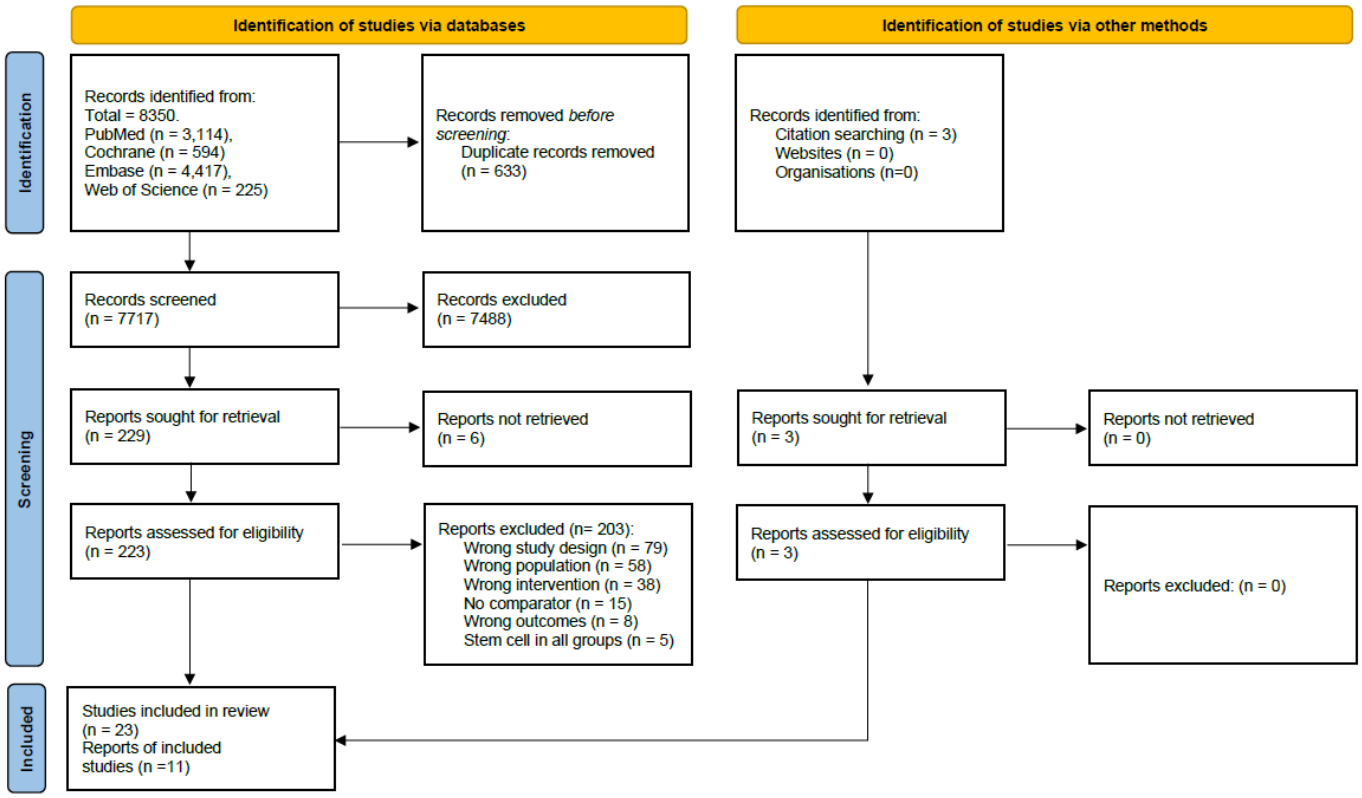
	('**animal experiment**'/de NOT ('**human experiment**'/de OR '**human**'/de)))	
#4	('animal'/exp OR 'invertebrate'/exp OR 'animal experiment'/de OR 'animal model'/de OR 'animal tissue'/de OR 'animal cell'/de OR 'nonhuman'/de) NOT (('animal'/exp OR 'invertebrate'/exp OR 'animal experiment'/de OR 'animal model'/de OR 'animal tissue'/de OR 'animal cell'/de OR 'nonhuman'/de) AND ('human'/de OR 'normal human'/de OR 'human cell'/de))	7,840,807
#5	(#1 AND #2 AND #3) NOT #4	4,417

Web of Science		
#1	(TI="Skin Aging" OR AB="Skin Aging") OR (TI=Cosmetics OR AB=Cosmetics) OR (TI="Skin Pigmentation" OR AB="Skin Pigmentation") OR (TI="Wounds and Injuries" OR AB="Wounds and Injuries") OR (TI=Burns OR AB=Burns) OR (TI="Cicatrix, Hypertrophic" OR AB="Cicatrix, Hypertrophic") OR (TI=Vitiligo OR AB=Vitiligo) OR (TI=Alopecia OR AB=Alopecia) OR (TI="Wound Healing" OR AB="Wound Healing") OR ALL="skin rejuvenation" OR ALL="skin renewal" OR ALL="skin revitalization" OR ALL="facial rejuvenation" OR ALL="skin regeneration" OR ALL="dermal rejuvenation" OR ALL="antiaging treatments" OR ALL="cosmetic skin treatments" OR ALL="facial revitalization" OR ALL="skin rejuvenation therapy" OR ALL="skin rejuvenation treatment" OR ALL="hand rejuvenation" OR ALL="skin repair" OR ALL="damaged skin" OR ALL=wrinkles OR ALL="tissue injury" OR ALL="skin burn" OR ALL="skin scar" OR ALL="androgenic alopecia"	366,138
#2	((TI="stem cell" OR AB="stem cell") OR (TI="stem cells" OR AB="stem cells") OR (TI="mesenchymal cell" OR AB="mesenchymal cell") OR (TI="mesenchymal cells" OR AB="mesenchymal cells") OR (TI="mononuclear cell" OR AB="mononuclear cell") OR (TI="mononuclear cells" OR AB="mononuclear cells") OR (TI="progenitor cell" OR AB="progenitor cell") OR (TI="progenitor cells" OR AB="progenitor cells") OR (TI="cord blood cell" OR AB="cord blood cell") OR (TI="cord blood cells" OR AB="cord blood cells") OR (TI="regenerative cell" OR AB="regenerative cell") OR (TI="regenerative cells" OR AB="regenerative cells") OR (TI="stromal cell" OR AB="stromal cell") OR (TI="stromal cells" OR AB="stromal cells"))	5,60,296
#3	TS=(randomised OR randomized OR randomisation OR randomisation OR placebo* OR (random* AND (allocat* OR assign*)) OR (blind* AND (single OR double OR treble OR triple))) NOT TS=(animal or animals or pisces or fish or fishes or catfish or catfishes or sheatfish or silurus or arius or heteropneustes or clarias or gariepinus or fathead minnow or fathead minnows or pimephales or promelas or cichlidae or trout or trouts or char or chars or salvelinus or salmo or oncorhynchus or guppy or guppies or millionfish or poecilia or goldfish or goldfishes or carassius or auratus or mullet or mullets or mugil or curema or shark or sharks or cod or cods or gadus or morhua or carp or carps or cyprinus or carpio or killifish or eel or eels or anguilla or zander or sander or lucioperca or stizostedion or turbot or turbots or psetta or flatfish or flatfishes or plaice or pleuronectes or platessa or tilapia or tilapias or oreochromis or sarotherodon or common sole or dover sole or solea or zebrafish or zebrafishes or danio or rerio or seabass or dicentrarchus or labrax or morone or lamprey or lampreys or petromyzon or pumpkinseed or	

	pumpkinseeds or lepomis or gibbosus or herring or clupea or harengus or amphibia or amphibian or amphibians or anura or salientia or frog or frogs or rana or toad or toads or bufo or xenopus or laevis or bombina or epidalea or calamita or salamander or salamanders or newt or newts or triturus or reptilia or reptile or reptiles or bearded dragon or pogona or vitticeps or iguana or iguanas or lizard or lizards or anguis fragilis or turtle or turtles or snakes or snake or aves or bird or birds or quail or quails or coturnix or bobwhite or colinus or virginianus or poultry or poultries or fowl or fowls or chicken or chickens or gallus or zebra finch or taeniopygia or guttata or canary or canaries or serinus or canaria or parakeet or parakeets or grasskeet or parrot or parrots or psittacine or psittacines or shelduck or tadorna or goose or geese or branta or leucopsis or woodlark or lullula or flycatcher or ficedula or hypoleuca or dove or doves or geopelia or cuneata or duck or ducks or greylag or graylag or anser or harrier or circus pygargus or red knot or great knot or calidris or canutus or godwit or limosa or lapponica or meleagris or gallopavo or jackdaw or corvus or monedula or ruff or philomachus or pugnax or lapwing or peewit or plover or vanellus or swan or cygnus or columbianus or bewickii or gull or chroicocephalus or ridibundus or albifrons or great tit or parus or aythya or fuligula or streptopelia or risoria or spoonbill or platalea or leucorodia or blackbird or turdus or merula or blue tit or cyanistes or pigeon or pigeons or columba or pintail or anas or starling or sturnus or owl or athene noctua or pochard or ferina or cockatiel or nymphicus or hollandicus or skylark or alauda or tern or sterna or teal or crecca or oystercatcher or haematopus or ostralegus or shrew or shrews or sorex or araneus or crocidura or russula or european mole or talpa or chiroptera or bat or bats or eptesicus or serotinus or myotis or dasycneme or daubentonii or pipistrelle or pipistrellus or cat or cats or felis or catus or feline or dog or dogs or canis or canine or canines or otter or otters or lutra or badger or badgers or meles or fitchew or fitch or foumart or foulmart or ferrets or ferret or polecat or polecats or mustela or putorius or weasel or weasels or fox or foxes or vulpes or common seal or phoca or vitulina or grey seal or halichoerus or horse or horses or equus or equine or equidae or donkey or donkeys or mule or mules or pig or pigs or swine or swines or hog or hogs or boar or boars or porcine or piglet or piglets or sus or scrofa or llama or llamas or lama or glama or deer or deers or cervus or elaphus or cow or cows or bos taurus or bos indicus or bovine or bull or bulls or cattle or bison or bisons or sheep or sheeps or ovis aries or ovine or lamb or lambs or mouflon or mouflons or goat or goats or capra or caprine or chamois or rupicapra or leporidae or lagomorpha or lagomorph or rabbit or rabbits or oryctolagus or cuniculus or laprine or hares or lepus or rodentia or rodent or rodents or murinae or mouse or mice or mus or musculus or murine or woodmouse or apodemus or rat or rats or rattus or norvegicus or guinea pig or guinea pigs or cavia or porcellus or hamster or hamsters or mesocricetus or cricetulus or cricetus or gerbil or gerbils or jird or jirds or meriones or unguiculatus or jerboa or jerboas or jaculus or chinchilla or chinchillas or beaver or beavers or castor fiber or castor canadensis or sciuridae or squirrel or squirrels or sciurus or chipmunk or chipmunks or marmot or marmots or marmota or suslik or susliks or spermophilus or cynomys or cottonrat or cottonrats or sigmodon or vole or voles or microtus or myodes or glareolus or primate or primates or prosimian or prosimians or lemur or lemurs or	

	lemuridae or loris or bush baby or bush babies or bushbaby or bushbabies or galago or galagos or anthropoidea or anthropoids or simian or simians or monkey or monkeys or marmoset or marmosets or callithrix or cebuella or tamarin or tamarins or saguinus or leontopithecus or squirrel monkey or squirrel monkeys or saimiri or night monkey or night monkeys or owl monkey or owl monkeys or douroucoulis or aotus or spider monkey or spider monkeys or ateles or baboon or baboons or papio or rhesus monkey or macaque or macaca or mulatta or cynomolgus or fascicularis or green monkey or green monkeys or chlorocebus or vervet or vervets or pygerythrus or hominoidea or ape or apes or hylobatidae or gibbon or gibbons or siamang or siamangs or nomascus or symphalangus or hominidae or orangutan or orangutans or pongo or chimpanzee or chimpanzees or pan troglodytes or bonobo or bonobos or pan paniscus or gorilla or gorillas or troglodytes)	
#4	#1 AND #2 AND #3	225

iii. PRISMA Flow Diagram:



iv. Summary of included studies:

Rejuvenation of skin in ageing

S.No.	Study	Population	Intervention	Comparator	Outcome
1.	Lee et al. 2014[1], South korea	Participants were 41~64 years old (mean, 51.6 years) and had Fitzpatrick Skin Type III or IV. 25 participants were randomly assigned to left and right sides of the face of treatment with microneedling alone (control) or microneedling plus hESC-EPC CM computer generated random list. LTFU: nil Exclusion criteria: Use of bleaching creams, history of any skin rejuvenation treatment within 6 months, history of keloids, and active eczema.	Microneedling plus Conditioned medium of human embryonic stem cells- derived Endothelial precursor cells (hESC-EPC CM) 1.5 ml of hESC-EPC CM was painted on the face and 2 passes of micro needling with dermarollers received 5 treatments at 2-week intervals.	Microneedling alone	Overall satisfaction score, global assessments for pigmentation, global assessments for wrinkle, Pigmentation improvement from baseline (Melanin Index), Erythema improvement from baseline (Erythema index), Maximum roughness, Average roughness (R3) wrinkle index
2.	Liang et al. 2022[2], China	Volunteers with facial photo-aging (Fitzpatrick III, IV) 41 (6.54) as mean (SD). 30 patients were randomized by random number table created by the computer software. If the number was odd, the left side was used as the intervention side. If the number was even, the right side was used as the intervention side. LTFU: 2	hUC-MSCs-CM and dermaroller MN treatment 1.0 ml of saline or hUC-MSCs-CM was painted, and the remaining 1.0 ml was added locally after dermaroller MN treatment. For one side, 1.0 ml of saline or hUC-MSCs-CM was painted and the remaining 1.0 ml was added locally after dermaroller MN treatment, which was performed in eight rows, with a total of	Saline and dermaroller MN treatment	Adverse events, Erythema, pigmentation improvement from baseline (Melanin Index), erythema improvement from baseline (Erythema index), wrinkle index, uv spots, Red Spots, Pores, Elasticity change hydration change TEWL change melanin

			192 needles, 0.5 mm in length. The participants received 5 sessions of treatment at 2-week intervals for a total of 10 weeks		
3.	Widianingsih et al. 2019[3], Indonesia	Healthy individual, 40 to 60 years of age showing clinical signs of photoaging. Mean age: 49.78±6.01. 9 females face was randomly allocated to AMSC-MP or saline, immediately after fractional laser procedure. LTFU: nil	Topical amniotic membrane stem cell (AMSC)-metabolite product (MP) after fractional laser procedure. 1.0×10^6 mL All participants received 3 sessions of treatment with 4-weeks intervals.	Saline solution after fractional laser procedure	Adverse events, Erythema, Mild pain, global assessments for pigmentation, global assessments for wrinkle, uv spots, Pores
4.	Prakoeswa et al. 2018[4], Indonesia	Subjects were 41–60 years old, willing to participate this study and signed the informed consent, has received or willing to receive priming with 0.025% tretinoin cream for two weeks. Mean of age of 50.31 ± 5.095 years 48 women were randomised into two groups; 24 women AMSC-CM and the other 24 women received NS. LTFU: nil	Microneedling plus AMSC-CM Intervention group received treatment with microneedling plus 3 mL of AMSC-CM. Progression of photoaging was evaluated on weeks 0, 4 and 8, as well as the side effects	Microneedling plus saline	Global assessments for pigmentation, wrinkle index, UV spots, Pores, spot
5.	Charles-de-Sá et al. 2020[5], Brazil	Subjects with a smoking habit, with hematologic or hemodynamic disorders, autoimmune diseases, connective tissue diseases, diabetes	ADSC skin therapy 2×10^6 cells in 0.4 ml PBS The expanded ADSCs were conditioned in 1	PRP skin therapy	-

		type I or II, other metabolic diseases, and chronic use of corticosteroids, and those that had been submitted to recent dermatological or surgical face treatments (e.g., facial peeling) were not included.	ml syringes attached to 30 G needle, containing 2×10^6 cells in 0.4 ml PBS. The ADSCs were injected into the patient's subdermal skin, in an area of 1 cm in the left preauricular region, 1 cm distally forward the tragus.		
6.	Park et al. 2023[6], Republic of Korea	Subjects aged ≥40 years with facial skin aging Mean age-54.0 ± 7.8 Male 8, Female 20 28 patients, each half face was randomly allocated using block randomization with block size of four LTFU: nil	Human adipose tissue stem cell-derived exosomes containing solution (HACS) and microneedling. HACS was topically applied to the one-half face, followed by microneedling at a depth of 1 mm. The other half face was treated with 2 mL normal saline solution followed by microneedling The individuals underwent three treatment sessions every 3 weeks and were followed up for 6 weeks after the last intervention.	Saline solution and microneedling	% percentage reduction in skin wrinkle Ra, % percentage reduction in skin wrinkle Rt, % percentage reduction in skin wrinkle Rz, % percentage improvement skin elasticity, % percentage improvement skin hydration, % percentage improvement skin pigmentation
7.	Wu et al. 2017[7], California	20 female subjects over the age of 18 with moderate-to-severe facial wrinkling were enrolled. 10 subjects were randomized to receive MSC conditioned growth factor formulation to the right side of the face and human fibroblast-conditioned growth factor formulation to the left side of the face, and 10 were randomized in opposite fashion LTFU: nil	MSC- conditioned growth factor formulation products were applied twice daily for a period of three months, with follow-up visits conducted at 1, 2, and 3 months	Human fibroblast-conditioned growth factor formulation	% percentage reduction in skin wrinkle Ra, percentage improvement in skin texture, percentage improvement in skin firmness

8.	Zhou et al. 2016[8], China	All patients had deterioration in expanded skin texture and thin/papery skin overlying the expander that did not improve after a 2 weeks' suspension of expansion, had elevated pressures in the tissue expander for at least 2 weeks, and needed further skin expansion to complete reconstruction. Age in years, mean (SD): Study group: 34.32 (12.73), control: 34.89 (12.86) male: Study group: 15, control: 14 38 patients were randomized as 19 to MNC group, 19 to control group LTFU: nil	Autologous Bone Marrow Mononuclear cell (BMMNCs) 2.4–12.5 × 10^7 cells were adjusted to a final volume of 6–20 ml with saline.	Saline	Epidermal thickness, dermal thickness skin texture
9.	Claudio-da-silva et al. 2009[9], Brazil	Female volenteers with facial rhytides 4 Mean age-5.8 + 7.48. All females Randomly distributed into 3 groups: Hyaluronic acid (HA), MSC, HA+MSC. 15 were randomized into HA-4, MSC-6, HA+MSC-5 LTFU: No information	MSC, MSC+HA 0.6 ml On day of application, cells dissociated with trypsin at ratio of 1:2	HA	-

Androgenetic Alopecia

	Study	Population	Intervention	Comparator	Outcome
10.	Butt et al. 2019[10], Pakistan	Male and female patients with androgenetic alopecia 15 y or older.	SVF + PRP 3 mL at 20 µL/100,000 cells	PRP	Hair density, Reduction in pull test Safety outcomes

		Active hair loss within last 12 months Hamilton score III to VI in male patients and Ludwig score I-III in female patients. 22 patients randomized into 11 in intervention group and 11 in control group. There were 77.27% males and 22.73% females in the study.	Each patient underwent two sessions (of injections/transplantations) each after 4 weeks and was followed up for 6 months after the last session		
11.	Gan et al. 2023[11], China	The patients were 25-45 years old, with an average age of 32± 1.24 years. These included 25 female patients and 25 male patients, all of whom were Chinese. The Norwood grade for male hair loss was II-V, and the Ludwig grade for female hair loss was I-III 25 Male 25 Female 50 patients were randomized into two hair loss areas on the left and right, of the midline of each patient's head were designated as intervention and control groups respectively. LTFU: nil	HF- MSC 100 micro litre, cell volume was 10^5 Interval of 0.5 cm between each injected point	Normal saline	Hair Diameter Proportion of terminal hair Mean follicular unit. Safety outcomes
12.	Lee et al. 2020[12], Korea	Patient with MPHL OR FPHL Mean Age - experimental - 45 +/- 3.19 control - 45.3+/- 2.45 Male:female ratio- experimental - 7/8, control - 7/7 30 patients randomized	Human adipose derived mesenchymal stem cells A subcutaneous (hypodermis) scalp injection of either 0.1 ml/cm^2 of Puregraft purified autologous fat or saline (no-fat control) using a blunt-	Normal saline	Hair density, global improvement score

		into 15 in intervention side and 15 in control group LTFU: nil	tip cannula		
13.	Tak et al. 2020[13], South Korea	38 patients (29 men) with AGA were assigned to an intervention group, with twice-daily self-application of intervention solution over the scalp with fingers, or to a control group. LTFU:4 (1 in ADSC, 3 in Placebo)	2 ml of ADSC in the subjects were given a 130-mL bottle containing the topical solution, which was colorless and odorless. They wereinstructed to apply 2 mL of this solution to the hair loss area, twice every day for 16 weeks.	Placebo (distilled water)	Hair count, hair diameter, global improvement score
14.	Gentile et al. 2020[14], Italy	Patients, 17 males showed AGA grades 2–5 as controlled by the NH scale and 10 females showed AGA grades 1-2 as dictated by the L scale. 17 male, female- 10 27 patients randomized where intervention drug was applied on frontal scalp, while control drug were infused in the parietal areas in patients with thinning confined to the frontal and parietal areas. LTFU: nil	Autologous Micrografts from Scalp Tissue 0.2 mL/cm^2 Micrograft's suspension interfollicular infusions (0.2 mL/cm^2) were performed to the targeted area (TA) at 5 mm depth utilizing a mesotherapy medical device outfitted with a 10mL Luer-Lock syringe (Sup-plemental Material) with a 30-gauge needle, in three sessions spaced 45 days apart.	Placebo	Hair count, hair density Safety outcome
15.	Han et al. 2019[15], Korea	30 healthy adults aged 20~60 with a diagnosis of mild-to-moderate patterned hair loss (men: modified Norwood-Hamilton classification types II, IIa, IIv, IIIa, or IIIv and women. 30 patients were	HUCB-MSC Patients from both groups were instructed to apply the tonic twice daily for 16 weeks (day and night, 1 mL/dose) and massage the scalp for 1~2 min during	Alcohol	Hair density Hair circumference Safety outcomes

		randomised as 15 in intervention group and 15 in Alcohol group LTFU: nil	application		
16 (A)	Legiawati et al. (A) 2023[16], Indonesia	Male AGA patients between the ages of 25 and 59 years old whose clinical presentation met Hamilton-Norwood criteria grades II to VI. All male 37 patients were randomized into group A and B. In group A, scalp of 17 patients were divided into intervention side and control side LTFU: nil	Non- Concentrated ADSC-CM with minoxidil 2ml of ADSC-CM. Intradermal injection of 2 ml of non - concentrated ADSC-CM in intervention side. 2 ml of NaCl 0.9% in control side. Over 6 weeks, this regimen was administered intradermally every 2 weeks.	0.9% NaCl with Minoxidil	Hair count, Hair density, Vellus rate, Terminal rate, Mean hair thickness, Total follicular units and their changes from baseline.
16 (B)	Legiawati et al. (B) 2023[16], Indonesia	Male AGA patients between the ages of 25 and 59 years old whose clinical presentation met Hamilton-Norwood criteria grades II to VI. All male 37 patients were randomized into group A and B. In group A, scalp of 17 patients were divided into intervention side and control side. In group B, 20 patients were allocated to control side. LTFU: nil	Concentrated ADSC-CM with minoxidil. 2 ml of ADSC-CM Intradermal injection of 2 ml of concentrated ADSC-CM in intervention side. 2 ml of NaCl 0.9% in control side. Over 6 weeks, this regimen was administered intradermally every 2 weeks	0.9% NaCl with Minoxidil	Hair count, Hair density, Vellus rate, Terminal rate, lean hair thickness, Total follicular units and their changes from baseline.
17.	Tsuboi et al. 2020[17], Japan	Eligible male and female subjects were aged over 20 years with MPHL in males classified as type III-vertex, IV, V and VI	Three concentrations of DSC cell suspensions ($7.5x10^6$, $1.5x10^6$, and $3.0x10^5$ cells) and a placebo (each in a	Placebo	Total hair density and cumulative hair diameter

		using the Norwood-Hamilton classification 9, and FPHL in females classified as grades 3-6 using the Shiseido classification 65 participants (50 men and 15 women, with a mean age ± standard deviation of 51.1±7.0 years). Four circular injection sites (each approximately 2 cm^2) for each participant were fixed inside the hair-loss areas. LTFU: 3	volume of 1 mL) were injected separately into 4 randomly allocated injection sites.		

Burns and Wounds

	Study	**Population**	**Intervention**	**Comparator**	**Outcome**
18.	Abouzaid et al. 2021[18], Egypt	Newly admitted burn patients aged between 14 and 45 years, any gender, stable general condition, total body surface area (TBSA) affected between 10% and 25%, with the depth of the superficial or deep dermal burns. Mean age - Intervention group: 24 (13–45) Median (Min–Max), Control group: 27 (16 – 45) 30 Male, 20 Female in number on intervention group, 28 Male, 22 Female in control group 50 patients randomized in to 25 in intervention group and 25 in control group LTFU: 5 in intervention	Group A consisted of 50 patients treated with a single injection of autologous fat grafting in the affected area along with topical nanofat application, and then the wounds were dressed with nano fat 1 cc fat over 10 cm long line is applied to avoid lumps and pumps, injection is done while the injection cannula is withdrawn in retrograde motion.	Conventional methods of serial dressings with 1% silver Sulphadiazine, mafenide and/ or others	Hyper pigmentation, hypo pigmentation contracture scar, hypertrophic scar, hospitalization

		group, 10 in control group Discontinued intervention: 5 in intervention group, 5 in control group			

Scars and Keloids

	Study	Population	Intervention	Comparator	Outcome
19.	Abou Eitta et al. 2019[19], Egypt	Patient with bilateral involvement of both halves of the face with post-acne scarring. 10 patients were recruited and subjected to split-face Mean age- 20 to 45 years old (mean 33.20 ± 6.51). LTFU: nil	Adipose tissue derived adult stem cells (AT-ASCs) Patients received one single treatment of intradermal injection of AT-ASCs on the right side of the face and three sessions of FxCR with 1-month interval for the left side.	Fractional carbon dioxide laser (FxCR).	No useful outcome
20.	Roohaninasab et al. 2023[20], Iran	Patients with skin types 1 to 4 who had burn scars at more than one site that had been present for at least three months and were between 25 and 50 years of age. Mean age- 31.00 ± 9.67 3 male, 7 female 10 patients' randomization method was used for randomization. In this way, two scar areas were into intervention and control group LTFU: nil	This research was supported by the Skin and Stem Cell Research Center, Tehran University of Medical Sciences 20 × 10^6 cells/mL from aspirated 100 cc of fat tissue In all patients, CO_2 laser alone (together with injection of normal saline as placebo) was performed in one part of the burn scar, and the combination of CO_2 laser and SVF injection was performed in the other lesion	Fractional CO_2 laser	-
21.	Fan et al. 2020[21] China	Primiparous women receiving elective cesarean delivery Ages between 21-35 years Gestation ages ≥37	Low dose- umbilical cord mesenchymal stem cellslow-dose (3 × 10^6) High Dose- umbilical	Placebo hydrogel	Vancouver Scar Scale (VSS)

		weeks and < 42 weeks. Mean age-28.04 ± 3.39 90 females randomly assigned in a 1:1:1 ratio, by means of a computer algorithm, to allocate placebo, low-dose (3×10^6), or high-dose (6×10^6) groups. LTFU: nil	cord mesenchymal stem cellslow-dose (6×10^6)		
22.	Kwon et al. 2020[22], South Korea	Patients whose échelle d'évaluation clinique des cicatrices d'acné (ECCA) scores were 50 or higher were eligible for inclusion Mean age- 35.6 ± 8.2 (19–54) 18 male, 7 female 25 patients were randomized as split face. LTFU: nil	Adipose tissue stem cell-derived exosomes 9.78×10^{10} particles/ml (for the day of FCL treatment) or 1.63×10^{10} particles/ml (for days subsequent to FCL treatment) patient was treated with 10,600-nm FCL	Control gel	ECCA scores reduction
23.	Park et al. 2019[23], South Korea	Patients with preexisting skin con ditions, with skin infections, retinoids intakes, those with photosensitive dermatoses and severe systemic disease, frequently smoking tobacco, with allergies to topical anesthetic cream, and those who were pregnant, or lactating have all been excluded.	Fractional eCO2 laser followed by Human adipose-derived stem cells-conditioned media with HA. Initially 100% HSCM, followed by 80% HSCM for next 6 days. Atrophic scar sites were initially treated with an energy of 20–30 mJ at a density of 400 per 120 mm spot under static mode.	Fractional eCO2 laser followed by normal saline, later HA	Reduction in volume of atrophic acne scar, Reduction in area of scar

v. Classification of studies on the basis of level of manipulation of the stem cell/ Stem cell derived product use *(interpreted by the Secretariat as defined by CDSCO* and the information provided in the trial itself):*

S. No.	Trial Details	Intervention	Level of manipulation	Information extracted from trial
A	**Rejuvenation of skin in ageing**			
1.	Lee et al. 2014[1]	Microneedling + Human Stem Cell Conditioned Medium	More	"Used commercially available CM of hESC-EPCs…Endothelial growth medium-2 (EGM-2; Lonza, Walkersville, ML, USA) was used as control medium."
2.	Widianingsih et al. 2019[3]	Fractional erbium YAG laser plus + topical application of amniotic membrane stem cell (AMSC)- metabolite product (MP)	More	"AMSC are collected from epithelial layer of the amnion and expanded in culture medium."
3.	Prakoeswa et al. 2018[4]	Amniotic membrane stem cell (AMSC)-conditioned media	More	"The procedures for obtaining amniotic membrane from the donor, culture process of AMSCs and separation of the AMSC-CM from the AMSCs were performed"
B	**Androgenetic Alopecia**			
4.	Butt et al. 2019[10]	Stromal vascular fraction (SVF) + platelet-rich plasma (PRP)	Less	"Adipose tissue was harvested using a handheld cannula…processed within 2 hours under sterilized conditions to obtain SVF. Briefly, adipose tissue was washed repeatedly…then digested by adding an equal volume of collagenase type IV for 30 minutes at 37°C with periodic agitation. The digested tissue was passed through a 70 μm strainer and centrifuged at 650 g for 15 minutes, supernatant was discarded, and SVF was obtained as cell pellet that was mixed in 5 mL of PBS and centrifuged at 650 g for 5 minutes. In this cell pellet, PRP was added before injection in the affected areas of the scalp of AGA patients."
5.	Lee et al. 2020[12]	Adipose tissue-derived stem cells (ADSCs)	More	"ADSCs were cultured with hydrogel for 72 hours in serum-free DMEM/F12…To produce the final product, a solution with Cutripeptide, pyridoxine hydrochloride, panthenol, and biotin was prepared in water for injection, and stem cell conditioned medium was added to the solution."

6.	Tak et al. 2020[13]	Adipose tissue-derived stem cells (ADSCs)	More	"Repeated subculturing was performed using serum-free medium. Thereafter, the culture medium was removed and trypsin/EDTA was added for separating the stem cells, which were then washed several times with PBS to obtain pure ADSCs."
C	**Burns and Wounds**			
7.	Abouzaid et al 2021[18]	Autologous fat grafting (AFG)	Less	"Lipoaspiration cannula 4 mm in diameter and lipoaspiration syringe are used in order not to apply high pressure, to have more viable fat…Fat is left to be separated from fluids by gravity. After a few minutes, the fluids are discarded and then the purified fat is transferred to 20 cc or 10 cc syringes, which will be used for the fat grafting process according to Coleman's technique."
D	**Scars and Keloids**			
8.	Abou Eitta et al. 2019[19]		Less	"The cannula was then moved back and forth while gently drawing fat into the syringe and then lipo-aspirate was evacuated into a sterile tube and immediately transferred to the stem cells laboratory…After digestion, the infranatant containing the stromal vascular fraction (SVF) was aspirated into sterile 15 ml sterile falcon centrifuge tubes, and equal volume of complete media was added to each tube to inactivate the collagenase and then centrifuged for 10 minutes at 300g to collect the SVF as a pellet…Pellet was then washed twice using PBS and then re-suspended in 1 ml PBS and delivered in a sterile eppendorf for injection."
9.	Roohaninasab et al. 2023[20]	Fractional CO2 laser + stromal vascular fraction (SVF)	Less	"100 cc of fat was removed from the thigh area of each patient…The adipose tissue was digested with collagenase type I…Enzyme digestion was prevented by washing with DMEM 10% FBS, and floating and lysed fat cells were discarded. SVF cells were pelleted by centrifugation at 500g for 10 min. The pellet was resuspended in PBS, and an erythrocyte lysis buffer (Sigma-Aldrich Corp, St. Louis, USA) was added and incubated at 37 °C for 10 min. This cell suspension was centrifuged (500g, 5 min), and SVF cells were counted using an automatic cell counter."
10.	Fan et al. 2020[21]	Umbilical Cord-Derived Mesenchymal Stem Cells (UC-MSCs)	More	"The digested mixture was then passed through a 100-μm filter to obtain cell suspensions. The cells were plated at a density of 1×10^6 cells/cm^2 in non-coated T-25 or T-75 cell culture flasks. Growth

				medium consisted of Dulbecco's modified Eagle's medium with low glucose…Cell cultures were maintained in a humidified atmosphere with 5% CO_2 at 37 °C. After 3 days of culture, the medium was replaced and non-adherent cells were removed. The medium was then changed twice weekly thereafter until 60–80% confluence had been reached."
11.	Kwon et al. 2020[22]	Fractional CO2 laser + adipose tissue stem cell- derived exosomes	More	"Exosomes in this study were acquired from human ASC-CM by ExoSCRT™ technology…Briefly, CM was collected from ASCs cultured with serum-free Dulbecco's Modified Eagle's Medium in a 5% CO_2 atmosphere at 37°C. Collected CM was filtered through a 0.2-μm filter to remove non-exosomal particles. Exosomes were further concentrated and purified by tangential-flow filtration with a 500-kDa molecular weight cut-off filter membrane cartridge."

* as defined by CDSCO in Annexure- I of the guideline document.

vi. Evidence to Decision Framework:

QUESTION

In patients requiring skin rejuvenation, what is the efficacy and safety of stem cell therapy as compared to usual care?	
POPULATION:	Skin rejuvenation
INTERVENTION:	Stem cell transplantation
COMPARISON:	Usual care
MAIN OUTCOMES:	Efficacy: Reduction in fine lines beyond 6 months, Change in skin thickness beyond one year, Reduction in pigmentation beyond 6 months; Safety: Serious adverse events, Any tumour formation; Important: Improvement in skin quality, Dermatological quality of life, Other adverse events
SETTING:	Hospital
PERSPECTIVE:	Health Systems/Population

BACKGROUND:	Skin ageing is a complex phenomenon that results in changes to the epidermis and dermis due to both intrinsic processes (age, genetic background) and external stimuli (photodamage from UV exposure). Androgenetic Alopecia (AGA), is a common genetic condition caused by over-sensitivity to androgens, affecting upto 50% of both males and females.[24] The condition is strongly associated with genetic predisposition and androgen-mediated signalling, leading to reduced hair density. In an Indian cohort, the prevalence of AGA among males aged 30–50 years was reported to be 58%.[25] Cutaneous scarring, including hypertrophic scars, keloids, and atrophic scars, represents an aberrant fibroproliferative response that may arise following severe burns, blunt trauma, surgical interventions, or wound infections. Keloids, in particular, result from dysregulated extracellular matrix remodeling characterized by excessive collagen synthesis coupled with impaired degradation. Burn injuries remain another critical care challenge, frequently caused by exposure to high temperatures, electricity, radiation, friction, or chemical agents, and are associated with long-term morbidity and healthcare burden.[26]
CONFLICT OF INTERESTS:	None

ASSESSMENT

Problem Is the problem a priority?		
JUDGEMENT	**RESEARCH EVIDENCE**	**ADDITIONAL CONSIDERATIONS**
○ No ○ Probably no ○ Probably yes ● Yes ○ Varies ○ Don't know	Over the past few decades, the prevalence of dermatological disorders has increased substantially, contributing to a significant global burden on healthcare systems. In 2021, skin and subcutaneous diseases accounted for 4.7 billion incident cases, 2.0 billion prevalent cases, 119,129 deaths, and 41.9 million disability-adjusted life years (DALYs) globally.[27] The broad term skin rejuvenation includes rejuvenation of skin in ageing, alopecia, scars, keloids and burn injuries represent significant concerns, adversely affecting both physical health and psychosocial well-being.	

Desirable Effects How substantial are the desirable anticipated effects?		
○ Trivial ○ Small ○ Moderate ○ Large ○ Varies ● Don't know	**Rejuvenation of skin in ageing:** **Melanin index:** One trial with a total of 25 participants (Lee et al. 2014-split face study) reported the melanin index at 12 weeks. The mean difference was -23 units (95% CI: -29.90 to -16.10) between the stem cell arm and the usual care arm, which was statistically significant. **UV spots:** One trial with a total of 48 participants reported the UV spots at the end of 8 weeks. The mean difference was -0.58 (95% CI: -4.50 to 3.34) between the stem cell arm and usual care arm, which was statistically non-significant. Another trial with a total of 9 participants (Wildianingsih et al. 2019-split face study) reported the UV spots at the end of 12 weeks. The mean difference was -1.00 (95% CI: -4.36 to 2.36) between the stem cell arm and usual care arm, which was statistically non-significant. **Overall satisfaction score (post score):** One trial with a total of 25 participants (Lee et al. 2014-split face study), reported the overall satisfaction score (post score) at the end of 12 weeks. The mean difference was 0.53 (95% CI: -0.22 to 1.28) between the stem cell arm and the usual care arm, which was statistically non-significant. **Global assessment for pigmentation (post score):** One trial with a total of 25 participants (Lee et al. 2014-split face study), reported the global assessment for pigmentation (post score) based on photographs at the end of 12 weeks. The mean difference was 0.22 (95% CI: -0.11 to 0.55) between the stem cell arm and the usual care arm, which was statistically non-significant. **Global Assessment for Wrinkle (post score):** One trial with a total of 25 participants (Lee et al. 2014-split face study), reported the global assessment for wrinkle (post score) based on photographs at the end of 12 weeks. The mean difference was 0.43 (95% CI: 0.18 to 0.68) between the stem cell arm and the usual care arm. The difference was statistically significant but clinically	

	unimportant as it was less than the MCID of one grade improvement. **Wrinkle Improvement (post score):** One trial with a total of 25 participants (Lee et al. 2014-split face study), reported the wrinkle improvement (post score) in context of R2 (maximum roughness) and R3 (average roughness) values measured by Visiometer. The mean difference of R2 value two weeks after final session was -0.04 (95% CI: -0.09 to 0.01) and of the R3 value was -0.03 (95% CI: -0.08 to 0.02) between the stem cell arm and usual care arm, which were statistically non-significant. **Wrinkle (post score):** One trial with a total of 48 participants reported the wrinkle (post score) at the end of 8 weeks. The mean difference was -2.38 (95% CI: -5.43 to 0.67) between the stem cell arm and usual care arm, which was statistically non-significant. Another trial with a total of 9 participants (Wildianingsih et al. 2019-split face study) reported the wrinkle (post score) at the end of 12 weeks. The mean difference was 6.89 (95% CI: -9.83 to 23.60) between the stem cell arm and usual care arm, which was statistically non-significant. **Androgenetic alopecia** **Hair density post scores:** One trial with 29 participants reported the hair density (hair/cm^2) post score at the end of 3 months. The mean difference was 12.80 (95% CI: 1.87 to 23.73) between the stem cell arm and usual care arm. The difference was statistically significant but clinically unimportant as it was less than the MCID of 17.86. Another trial with 22 participants reported the hair density (hair/cm^2) post score at the end of 6 months. The mean difference was -6.61 (95% CI: -14.89 to 1.67) between the stem cell arm and usual care arm, which was statistically non-significant. **Hair density change score:** One trial with 38 participants reported the hair density (number/cm^2) change score at the end of 4 months. The mean difference was 2.47 (95% CI: 0.86 to 4.08) between the stem cell arm and usual care arm. The difference was statistically significant and clinically important as it was more than the MCID of 0.24.	

	Hair diameter change score: One trial with 38 participants reported the hair diameter (µm) change score at the end of 4 months. The mean difference was 5.00 (95% CI: 1.37 to 8.63) between the stem cell arm and usual care arm. The difference was statistically significant and clinically important as it was more than the MCID of 0.6. **Treatment assessment score:** Evidence from two trials with a total of 63 participants reported the treatment assessment score using 7-point evaluation (+3 -extremely favorable to -3 -extremely unfavorable) at the end of 3-4 months. The pooled mean difference was 0.65 (95% CI: 0.28 to 1.01) between the stem cell arm and usual care arm, which was statistically significant. **Scar and Keloid** **Area of scar (Post scores):** Evidence from one trial with 10 participants (Abou Eitta et al. 2019-Split face study) reported the area of scar (post score) in area percentage at the end of 3 months using NIH ImageJ image analysis software. The mean difference was 0.09 (95% CI: -0.78 to 0.96) between the stem cell arm and usual care arm, which was statistically non- significant. Evidence from another trial (Fan et al. 2020) with 60 participants reported the area of scar (post score) in mm^2 at the end of 6 months. The mean difference was -28.29 (95% CI: -84.76 to 28.18) between the stem cell arm and usual care arm, which was statistically non-significant. **Volume of scar (Post scores):** One trial with 60 participants reported the volume of scar (post score) in mm^3 at the end of 6 months. The mean difference was -165 (95% CI: -359.39 to 29.39) between the stem cell arm and usual care arm, which was statistically non- significant. **Treatment satisfaction (Post scores)** **Patients reported treatment satisfaction (Post score):** One trial with 10 participants (Roohaninasib et al. 2023- split face study) reported the treatment satisfaction (post score) by patients at the end of 2 months. The mean difference	

	was 1.10 (95% CI: 0.37 to 1.83) between the stem cell and usual care arm, which was statistically significant. Another trial with 60 participants reported the treatment satisfaction (post score) by patients at the end of 6 months. The mean difference was 0.23 (95% CI: -0.02 to 0.48) between the stem cell and usual care arm, which was statistically non-significant. **Physicians reported treatment satisfaction (Post score):** One trial with 10 participants (Roohaninasib et al. 2023- split face study) reported the treatment satisfaction (post score) by physicians at the end of 2 months. The mean difference was 1.20 (95% CI: 0.79 to 1.61) between the stem cell and usual care arm, which was statistically significant. **Vancouver Scar Scale (Post scores):** One trial with 10 participants (Roohaninasib et al. 2023- split face study) reported the Vancouver Scar Scale (Post score) at the end of 2 months. The mean difference was -1.10 (95% CI: -2.48 to 0.28) between the stem cell arm and usual care arm, which was statistically non-significant. Another trial with 60 participants (Fan et al. 2020) reported the Vancouver Scar Scale (Post score) at the end of 6 months. The mean difference was -1.72 (95% CI: -3.02 to -0.42) between the stem cell arm and usual care arm, which was statistically significant. **échelle d'évaluation clinique des cicatrices d'acné-ECCA (Change scores):** One trial with 25 participants (Kwon et al. 2020- split face study) reported the ECCA (change score) at the end of 3 months. The difference was -12.49 (95% CI: -19.93 to -5.05) between the stem cell arm and usual care arm, which was statistically significant. **Burns and wounds** **Area percentage of collagen (post score):** One trial with 100 participants reported the area percentage of collagen (post score) at the end of 3 months. The mean difference was -20.55 (95% CI: -21.67 to -19.43) between the stem cell arm and usual care arm, which was statistically significant.	

Undesirable Effects How substantial are the undesirable anticipated effects?		
JUDGEMENT	**RESEARCH EVIDENCE**	**ADDITIONAL CONSIDERATIONS**
○ Trivial ○ Small ○ Moderate ○ Large ○ Varies ● Don't know	No serious adverse events were reported in the included studies.	
Certainty of evidence What is the overall certainty of the evidence of effects?		
JUDGEMENT	**RESEARCH EVIDENCE**	**ADDITIONAL CONSIDERATIONS**
● Very low ○ Low ○ Moderate ○ High ○ No included studies	The evidence in this review is of very low quality due to high risk of bias, inconsistency and imprecision in the effect shown by stem cell therapy.	
Values Is there important uncertainty about or variability in how much people value the main outcomes?		
JUDGEMENT	**RESEARCH EVIDENCE**	**ADDITIONAL CONSIDERATIONS**

○ Important uncertainty or variability ○ Possibly important uncertainty or variability ● Probably no important uncertainty or variability ○ No important uncertainty or variability	No research evidence was identified.	Main outcomes are clinical improvement in the form of improved wrinkles, pigmentation, increased hair density and hair diameter, reduced scarring and decreased pain (for burns and wounds), which is likely to be highly valued by most patients.
Balance of effects Does the balance between desirable and undesirable effects favor the intervention or the comparison?		
JUDGEMENT	**RESEARCH EVIDENCE**	**ADDITIONAL CONSIDERATIONS**
○ Favors the comparison ○ Probably favors the comparison ○ Does not favor either the intervention or the comparison ○ Probably favors the intervention ○ Favors the intervention ○ Varies ● Don't know	It is less clear if benefits of stem cell intervention outweigh the harms, based on limited evidence.	

Resources required How large are the resource requirements (costs)?		
JUDGEMENT	**RESEARCH EVIDENCE**	**ADDITIONAL CONSIDERATIONS**
● Large costs ○ Moderate costs ○ Negligible costs and savings ○ Moderate savings ○ Large savings ○ Varies ○ Don't know	No direct evidence of the resources required was identified.	The costs of the intervention may be high depending on the procedures used.
Certainty of evidence of required resources What is the certainty of the evidence of resource requirements (costs)?		
JUDGEMENT	**RESEARCH EVIDENCE**	**ADDITIONAL CONSIDERATIONS**
○ Very low ○ Low ● Moderate ○ High ○ No included studies	No research evidence was identified.	The GDG members were fairly certain that stem cell therapy requires large resources.
Cost effectiveness Does the cost-effectiveness of the intervention favor the intervention or the comparison?		
JUDGEMENT	**RESEARCH EVIDENCE**	**ADDITIONAL CONSIDERATIONS**

○ Favors the comparison ● Probably favors the comparison Does not favor either the intervention or the comparison ○ Probably favors the intervention ○ Favors the intervention ○ Varies ○ No included studies	No research evidence was identified.	The intervention was not found to be effective and hence the committee deferred to comment on cost effectiveness.
Equity What would be the impact on health equity?		
JUDGEMENT	**RESEARCH EVIDENCE**	**ADDITIONAL CONSIDERATIONS**
○ Reduced ● Probably reduced ○ Probably no impact ○ Probably increased ○ Increased ○ Varies ○ Don't know	No research evidence was identified.	As stem cell therapy is an expensive treatment offered only at tertiary centers, it is likely to reduce equity.
Acceptability Is the intervention acceptable to key stakeholders?		
JUDGEMENT	**RESEARCH EVIDENCE**	**ADDITIONAL CONSIDERATIONS**

○ No ○ Probably no ● Probably yes ○ Yes ○ Varies ○ Don't know	No research evidence was identified.	Despite uncertainty regarding the medical risks and benefits associated with stem cell injections, patients requiring skin rejuvenation have very high expectations from stem cell therapy
Feasibility Is the intervention feasible to implement?		
JUDGEMENT	**RESEARCH EVIDENCE**	**ADDITIONAL CONSIDERATIONS**
○ No ○ Probably no ● Probably yes ○ Yes ○ Varies ○ Don't know	No research evidence was identified.	Stem cell transplantation can be performed in tertiary care centres so feasibility in lesser equipped hospitals and clinics is not possible.

SUMMARY OF JUDGEMENTS

	JUDGEMENT						
PROBLEM	No	Probably no	Probably yes	**Yes**		Varies	Don't know
DESIRABLE EFFECTS	**Trivial**	**Small**	Moderate	Large		Varies	**Don't know**
UNDESIRABLE EFFECTS	Trivial	**Small**	Moderate	Large		**Varies**	**Don't know**
CERTAINTY OF EVIDENCE	**Very low**	Low	Moderate	High			No included studies
VALUES	Important uncertainty or variability	Possibly important uncertainty or variability	**Probably no important uncertainty or variability**	No important uncertainty or variability			
BALANCE OF EFFECTS	Favors the comparison	Probably favors the comparison	Does not favor either the intervention or the comparison	Probably favors the intervention	Favors the intervention	Varies	**Don't know**
RESOURCES REQUIRED	**Large costs**	Moderate costs	Negligible costs and savings	Moderate savings	Large savings	Varies	Don't know
CERTAINTY OF EVIDENCE OF REQUIRED RESOURCES	**Very low**	Low	**Moderate**	High			No included studies
COST EFFECTIVENESS	Favors the comparison	**Probably favors the comparison**	Does not favor either the intervention or the comparison	Probably favors the intervention	Favors the intervention	Varies	No included studies
EQUITY	Reduced	**Probably reduced**	Probably no impact	Probably increased	Increased	Varies	Don't know
ACCEPTABILITY	No	Probably no	**Probably yes**	Yes		Varies	Don't know
FEASIBILITY	No	Probably no	**Probably yes**	Yes		Varies	Don't know

TYPE OF RECOMMENDATION

Strong recommendation against the intervention	Conditional recommendation against the intervention	Use only in the context of rigorously conducted randomized controlled trials	Conditional recommendation for either the intervention or the comparison	Conditional recommendation for the intervention	Strong recommendation for the intervention
○	○	●	○	○	○

CONCLUSIONS

Recommendation

Stem cell therapy is **not recommended** in routine clinical practice for the treatment of Skin Rejuvenation (rejuvenation of skin in ageing, androgenetic alopecia, scars and keloid, burn and wounds conditions). It may be used only in the context of rigorously conducted randomized controlled trials.

Justification

This recommendation has been made as the evidence is inadequate in quality and quantity to determine the safety and efficacy of stem cell therapy for skin rejuvenation. Results should be interpreted with caution, in view of various study limitations like high risk of bias, small number of participants and/or events in the included studies, different sources of stem cell and limited period of follow-up.

vii. Data Extraction:

Two review authors independently screened the articles retrieved from the searches, using the Rayyan online screening tool and determined eligibility by reading the abstract of each study. Studies that clearly did not satisfy inclusion criteria, were eliminated and the remaining studies were retrieved for full text screening. The selected studies were read independently by two review authors, and in the event of disagreement, a third author adjudicated. A Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) flow chart was included in the full review, illustrating the status of identified studies. Studies were included in the review irrespective of whether measured outcome data were reported in a 'usable' way. Two review authors independently extracted data using a standard format and checked for agreement before entry into Review Manager. Multiple reports of the same study were collated, ensuring that each study, rather than each report, was the unit of interest in the review. Characteristics of the included studies were collected in sufficient detail to populate a table of 'Characteristics of included studies' in the full review.

A fixed-effect or random-effects model was used to estimate the overall direction, size, and consistency of an effect. For dichotomous variables, treatment effects as risk ratios (RR) with 95% confidence intervals (CI) were computed. For continuous data, mean differences (MD) with 95% CI were measured. In studies, where the results obtained were measured on different scales, standardized mean differences (SMD) were calculated. In cases where there was insufficient information available to calculate standard deviations for the changes, they were imputed.

Dealing with missing data

In case of missing, incomplete, or inconsistent data with RCT protocols, the authors/manufacturers were contacted for further information. They were contacted by email in cases, where studies did not report the outcome measures of interest, or did not describe randomization, or intention-to-treat analysis, or had missing data.

Assessment of heterogeneity

Clinical heterogeneity was assessed using the Chi^2 test (p value < 0.1 for statistical significance) and I^2 statistic was employed to quantify heterogeneity. Considerable heterogeneity was considered if I^2 was more than 75%, substantial if it was between 50% and 90%, moderate if it was between 30% and 60%, and mild if less than 40%. In the presence of statistical heterogeneity (I^2 greater than or equal to 50%), possible causes were explored through prespecified subgroup analysis and a random-effects model was applied.

Subgroup analysis

Subgroup analyses were planned for the type of stem cell therapy, source of stem cell, and comparator (active or placebo) provided adequate data was available. These analyses considered gender, age, cause of damaged wounds, cause of skin aging, and were based on skin diseases and other diseases. However, due to inadequate number of studies in each outcome based on similar duration of follow-up, subgroup analysis was not performed.

Assessment of reporting biases

For 10 or more included studies, a funnel plot test was conducted for asymmetry to assess any evidence of reporting bias. Additionally, possible sources of asymmetry in a funnel plot were explored.

Data synthesis

A meta-analysis was done only when participants, interventions, comparisons, and outcomes were judged to be sufficiently similar to ensure a clinically meaningful and relevant answer. For the analysis, RevMan 5.4 software, the statistical package provided by the Cochrane Collaboration, or R v4.3.023 with meta v6.5.024, metafor v4.2.025, metasens v1.5.226, and brms v2.20.127 packages were used.

Data Extraction Sheet:

1. Study	**Lee et al. 2014[1]**
Study type	Prospective randomized controlled observer-blinded split-face study.
Number of participants	25 (split face study)
Countries, setting and Funding	South Korea: CHA University; Grant of the Korean Health Technology R&D Project, Ministry of Health & Welfare, Republic of Korea
Duration of study Follow up (post intervention)	2 weeks after final treatment (12 weeks)
Subgroup analysis within study	NA
Inclusion criteria	Participants were 41~64 years old (mean, 51.6 years) and had Fitzpatrick Skin Type III or IV
Exclusion criteria	Use of bleaching creams, history of any skin rejuvenation treatment within 6 months, history of keloids, and active eczema.
Recruitment/selection of patients	Twenty-five participants were recruited for this prospective randomized controlled observer-blinded split-face study. The left and right sides of the face of each participant were randomly assigned to treatment with microneedling alone (control) or microneedling plus hESC-EPC CM.
Intervention: Source and Type of stem cells	Commercially available, Conditioned medium of endothelial precursor cells differentiated from human embryonic stem cells (hESC-EPCs)
Comparator	
Intervention: Method of their characterization	Microneedling plus Conditioned medium of human embryonic stem cells- derived Endothelial precursor cells (hESC-EPC CM). To collect the lipoaspirate, asepsis and antisepsis followed by the infiltration of 50 cc of 0.25% lidocaine solution with adrenaline 1:500,000 in demarcated locations in the infra-umbilical region. The material was aspirated using syringes with 3 mm cannulas

	diameter, which were subsequently sealed and placed in a decanter for 30 minutes to remove the contents serosanguineous. 10 cc of antibiotic solution was added to the collected adipose tissue and the material was transported in a refrigerated environment to the processing unit.
Intervention: Route of administration	Topical application
Intervention: Dose	In study group: 1.5 ml of hESC-EPCs CM was painted on the face and 2 passes of micro needling with dermarollers were performed. Participants received 5 treatments at 2-week intervals.
Intervention: Dose - If the trial has taken multiple doses, then which dose values has been used for MA	In study group: 1.5 ml of hESC-EPCs CM was painted on the face and 2 passes of micro needling with dermarollers were performed. Participants received 5 treatments at 2-week intervals.
Efficacy Outcomes reported with time points	Melanin Index, Global assessment for pigmentation, Global assessment for wrinkle, Wrinkle improvement, overall satisfaction score.
Safety Outcomes reported with time points- Serious AEs	No serious adverse events reported.
Safety Outcomes reported with time points- Other Adverse Events	Mild pain and temporary erythema during and after treatments were tolerable in all participants. The only minimal adverse event reported in one participant was mild desquamation, which resolved spontaneously within 1 week.

2. Study	**Liang et al. 2014[2]**
Study type	Randomized controlled split-face study.
Number of participants	30
Countries, setting and Funding	China, hospital, Beijing Natural Science Foundation
Duration of study Follow up (post intervention)	2 weeks
Subgroup analysis within study	-
Inclusion criteria	Volunteers with facial photo-aging (Fitzpatrick III, IV)
Exclusion criteria	Obvious inflammation, ulcer or effusion on the face, and previous skin rejuvenation treatment in the past 3 months.
Recruitment/selection of patients	A total of 30 volunteers with facial photo-aging (Fitzpatrick III 20, IV 10) were included for the present study. Two participants were withdrawn from the study due to job-related factors. The remaining 28 volunteers completed the study. These volunteers were within 35–60 years old, with a mean (SD) age of 41 (6.54) years old.

Intervention: Source and Type of stem cells	human umbilical cord-derived mesenchymal stem cells conditioned media (hUC-MSCs-CM)
Comparator	Saline
Intervention: Method of their characterization	hUC-MSCs-CM and dermaroller MN treatment
Intervention: Route of administration	Topical
Intervention: Dose	1.0 ml of saline or hUC-MSCs-CM was painted and the remaining 1.0 ml was added locally after dermaroller MN treatment. Five sessions were performed for each volunteer at 2-week intervals.
Intervention: Dose - If the trial has taken multiple doses, then which dose values has been used for MA	1.0 ml of saline or hUC-MSCs-CM was painted and the remaining 1.0 ml was added locally after dermaroller MN treatment. Five sessions were performed for each volunteer at 2-week intervals.
Efficacy Outcomes reported with time points	Melanin index, UV spots, pores, Brown spots, Erythema Index, Wrinkles, Pores, Elasticity
Safety Outcomes reported with time points- Serious AEs	No severe side effects were reported during the whole study
Safety Outcomes reported with time points- Other Adverse Events	Two participants in MN plus hUC-MSCs-CM group reported dry skin and one reported erythema. Three patients reported dry skin and two patients reported erythema in MN alone group, respectively.

3. Study	**Widianingsih et al. 2019[3]**
Study type	Controlled split face study
Number of participants	9 (split face)
Countries, setting and Funding	Indonesia, Surabaya Skin Centre Clinic, No information
Duration of study Follow up (post intervention)	12 weeks
Subgroup analysis within study	-
Inclusion criteria	Healthy nonsmoking individual, 40 to 60 years of age showing clinical signs of photoaging
Exclusion criteria	No information
Recruitment/selection of patients	Face of 9 patients were randomized to study side and control side
Intervention: Source and Type of stem cells	Amniotic membrane stem cell
Comparator	Fractional erbium YAG (yttrium aluminum garnet) laser plus saline solution,

Intervention: Method of their characterization	Topical amniotic membrane stem cell (AMSC)-metabolite product (MP) after fractional laser procedure. Amniotic epithelial cells or amniotic mem- brane stem cells (AMSCs) can be collected from different fetal annexes (amnion, chorion, amniotic fluid, Wharton jelly) and have to be safe, easy to collect, and devoid of immunogenic and tumorigenic properties. AMSC are collected from epithelial layer of the amnion which derives directly from the epiblast as it retains some ESCs (embryonic stem cells) characteristic.
Intervention: Route of administration	Topical
Intervention: Dose	Dose not mentioned. All participants received 3 sessions of treatment were repeated at 4-week intervals.
Intervention: Dose - If the trial has taken multiple doses, then which dose values has been used for MA	Dose not mentioned. All participants received 3 sessions of treatment were repeated at 4-week intervals.
Efficacy Outcomes reported with time points	UV spots, pores, skin tone, acne, mild pain
Safety Outcomes reported with time points- Serious AEs	No serious side effects
Safety Outcomes reported with time points- Other Adverse Events	All patient have mild erythema and subsided in a few days up to 2 weeks without any intervention treatment. Seven participant felt mild pain but can still withhold without any treatment added. The crust peels off in 5-7 days after laser treatment. No post-inflammatory hyperpigmentation found.

4. Study	**Prakoeswa et al 2018[4]**
Study type	Controlled and prospective study
Number of participants	48
Countries, setting and Funding	Indonesia, Dermato Venereology outpatient clinic of Dr. Soetomo General Hospital Surabaya, No information on funding
Duration of study Follow up (post intervention)	8 weeks
Subgroup analysis within study	-
Inclusion criteria	Subjects were 41–60 years old, willing to participate this study and signed the informed consent, has received or willing to receive priming with 0.025% tretinoin cream for two weeks
Exclusion criteria	Wound on the face, had a history of herpes simplex, Suffered from diabetes mellitus
Recruitment/selection of	48 women were randomised into two groups; 24 women received

patients	amniotic membrane stem cell conditioned medium (AMSC-CM) and the other 24 women received normal saline (NS)
Intervention: Source and Type of stem cells	Allogenic, amniotic membrane stem cell
Comparator	Normal Saline
Intervention: Method of their characterization	Microneedling plus AMSC-CM. AMSC-CM was obtained from the stem cell laboratory at the Institute of Tropical Diseases, Universitas Airlangga. The procedures for obtaining amniotic membrane from the donor, culture process of AMSCs and separation of the AMSC-CM from the AMSCs were performed legally in accordance with the international standards for tissue donor and stem cell culture from humans.
Intervention: Route of administration	Topical
Intervention: Dose	Intervention group received treatment with microneedling plus 3 mL of AMSC-CM. Control group received treatment with microneedling plus 3 mL of NS. Drug was applied for 3 times with an interval of 2 weeks.
Intervention: Dose - If the trial has taken multiple doses, then which dose values has been used for MA	Intervention group received treatment with microneedling plus 3 mL of AMSC-CM. Control group received treatment with microneedling plus 3 mL of NS. Drug was applied for 3 times with an interval of 2 weeks.
Efficacy Outcomes reported with time points	UV spots, pores, wrinkles, spot polarized, skin tone
Safety Outcomes reported with time points- Serious AEs	Not mentioned
Safety Outcomes reported with time points- Other Adverse Events	Not mentioned

5. Study	**Charles-de-Sá et al. 2020[5]**
Study type	Prospective clinical, randomized and comparative study
Number of participants	20 (4 males and 16 females)
Countries, setting and Funding	Brazil, Carlos Chagas Filho Institute of Biophysics, Federal University of Rio de Janeiro-Brazil, at the Excellion Services Biomedical SA® lab oratory in Rio de Janeiro-Brazil, at the Center for Anatomy and Histology at the University of Verona-Italy and at Per forma Ltda clinic, in Natal, RN, Brazil, No information
Duration of study Follow up (post intervention)	Four months after the subdermal PRP and ADSC injection until the skin removal has been done.
Subgroup analysis within	-

study	
Inclusion criteria	Healthy individuals of both genders, with ages ranging from 45 to 65 years, presenting photoaging skin variables, different skin color phototypes (Fitzpatrick) and cervicofacial sagging.
Exclusion criteria	Subjects with a smoking habit, with hematologic or hemodynamic disorders, autoimmune diseases, connective tissue diseases, diabetes type I or II, other metabolic diseases, and chronic use of corticosteroids, and those that had been submitted to recent dermatological or surgical face treatments (e.g., facial peeling) were not included.
Recruitment/selection of patients	20 patients were randomized into 10 in study group and 10 in control group
Intervention: Source and Type of stem cells	Autologous, Adipose Derived Mesenchymal Stem Cells
Comparator	Platelet-Rich Plasma (PRP)
Intervention: Method of their characterization	Under local anesthesia with 0.5% xylocaine and 1,500,000 U epinephrine, 10cc of adipose tissue from the infra-abdominal region was manually harvested by liposuction, using a 10 ml syringe (Luer Lock; BD®) coupled to a liposuction cannula of 3mm diameter, 15cm long, containing 3 distal holes (Tulip®, USA), with manual vacuum. The lipoaspirate was transferred to a glass vial containing RPMI culture medium and antibiotics (amphotericin and ciprofloxacin). It was transported under refrigeration to the laboratory to be processed accordingly to the specific protocol to isolate and expand ADSC.
Intervention: Route of administration	Subdermal plane in the left retroauricular skin in an area of 1cm [2], 1cm behind the auricular conchal.
Intervention: Dose	2×10^6 cells in 0.4 ml PBS
Intervention: Dose - If the trial has taken multiple doses, then which dose values has been used for MA	Included only in systematic review, not included in meta-analysis
Efficacy Outcomes reported with time points	Histological analysis, Structural analysis of the deep layer of the dermis, Immunohistochemical analysis.
Safety Outcomes reported with time points- Serious AEs	Not mentioned
Safety Outcomes reported with time points- Other Adverse Events	No abnormal skin reactions were observed, such as persisting inflammation, necrosis, hyperplasic or abnormal cell growth, tumor development, or any other adverse events such as vasculitis or hypertrophic scars

6. Study	**Park et al. 2023[6]**

Study type	Prospective, randomized, split-face comparative study
Number of participants	28
Countries, setting and Funding	South Korea National Research Foundation of Korea (NRF) grant funded by the Korea government
Duration of study Follow up (post intervention)	6 weeks after the last study
Subgroup analysis within study	-
Inclusion criteria	Subjects aged ≥ 40 years with facial skin aging
Exclusion criteria	Pregnancy, history of keloid scarring, and acute inflammatory or infectious conditions on the face. concurrent use of treatments that may affect the evaluation of effects, such as chemical and mechanical resurfacing, photo rejuvenation, and filler injection, was prohibited during the study period.
Recruitment/selection of patients	Twenty- eight subjects with facial skin aging were enrolled in this study.
Intervention: Source and Type of stem cells	Adipose tissue stem cell- derived exosome-containing solution.
Comparator	Saline solution and microneedling
Intervention: Method of their characterization	Human adipose tissue stem cell-derived exosomes containing solution (HACS) and microneedling. 2 mL normal saline solution was mixed with a vial of Adipose tissue stem cell-derived exosomes + Derma Signal Skin Rejuvenation Lyophilized Vial (SRLV)-S (ExoCoBio Inc) to prepare a HACS.
Intervention: Route of administration	Topical
Intervention: Dose	2 mL normal saline solution was mixed with a vial of ASCE to prepare a HACS. HACS was topically applied to the one-half face, followed by microneedling at a depth of 1 mm. The other half face was treated with 2 mL normal saline solution followed by microneedling. The individuals underwent three treatment sessions every 3 weeks and were followed up for 6 weeks after the last intervention.
Intervention: Dose - If the trial has taken multiple doses, then which dose values has been used for MA	Included only in systematic review, not included in meta-analysis
Efficacy Outcomes reported with time points	Global Aesthetic Improvement Scale score, clinical improvements in skin wrinkles, elasticity, hydration, and pigmentation, histopathological evaluation, serious adverse events
Safety Outcomes reported with time points- Serious	No serious adverse events reported.

AEs	
Safety Outcomes reported with time points- Other Adverse Events	Transient erythema, edema, and petechiae were observed during and after the treatment. However, these were mild symptoms and resolved spontaneously within 1 week. No permanent skin changes or scar formation was observed in any participant.

7. Study	**Wu et al. 2017[7]**
Study type	Prospective, randomized, double-blind, split-face trial
Number of participants	20
Countries, setting and Funding	California, Funded by Nuderm
Duration of study Follow up (post intervention)	Follow-up visits conducted at 1, 2, and 3 months of treatment.
Subgroup analysis within study	-
Inclusion criteria	20 female subjects over the age of 18 with moderate-to- severe facial wrinkling were enrolled.
Exclusion criteria	Pregnant or breastfeeding; had treatment with any neuromodulator, energy device, chemical peel, or soft tissue filler within the previous six months; had applied any topical products containing vitamins A, C, or E derivatives, alpha- hydroxy acids, or salicylic acids within the previous two weeks or at any time during the trial; or had any pre-existing dermatological condition in the facial region.
Recruitment/selection of patients	Total 20 participants. Ten subjects were randomized to receive MSC conditioned growth factor formulation to the right side of the face and human fibroblast-conditioned growth factor formulation to the left side of the face, and 10 were randomized in opposite fashion.
Intervention: Source and Type of stem cells	Commercially available mesenchymal stem cells (MSCs)
Comparator	human fibroblast-conditioned growth factor formulation
Intervention: Method of their characterization	Mesenchymal stem cells (MSCs)- conditioned growth factor formulation. Source of human growth factors is mesenchymal stem cells (MSCs) derived from adipose tissue. Medium containing growth factors secreted by this population of stem cells has demonstrated efficacy in promoting hair regrowth5; alteration of matrix metalloproteinase (MMP) expression in dermal fibroblasts that have been exposed to ultraviolet radiation (UVR)6; and modulating endothelial cell, fibroblast, and keratinocyte migration.
Intervention: Route of administration	Topical
Intervention: Dose	Dose not mentioned. The test products were applied twice daily for

	a period of three months.
Intervention: Dose - If the trial has taken multiple doses, then which dose values has been used for MA	Included only in systematic review, not included in meta-analysis
Efficacy Outcomes reported with time points	Improvement in facial wrinkling, percentage improvement in rhytids, skin texture, and skin firmness, safety.
Safety Outcomes reported with time points- Serious AEs	Not mentioned
Safety Outcomes reported with time points- Other Adverse Events	Not mentioned

8. Study	**Zhou et al. 2016[8]**
Study type	Parallel, randomized, blinded, placebo- controlled clinical trial.
Number of participants	38
Countries, setting and Funding	China, Funded by the Key Project of National Natural Science Foundation of China
Duration of study Follow up (post intervention)	4 weeks, 8 weeks and two years after treatment.
Subgroup analysis within study	
Inclusion criteria	18 to 60 years of age, had received surgical placement of an expander on the face, neck, anterior chest wall, abdominal wall or back that had been inflated to volumes of 80 to 600 cm^3. All patients had deterioration in expanded skin texture and thin/papery skin overlying the expander that did not improve after a 2 weeks' suspension of expansion, had elevated pressures in the tissue expander for at least 2 weeks, and needed further skin expansion to complete reconstruction.
Exclusion criteria	History of severe illnesses, including any cancers, hepatitis, coronary artery disease, arteriosclerosis, diabetes, obesity (BMI > 30), anemia, myelodysplastic syndromes, and a history of bone marrow transplantation. Patients with risk factors for tissue necrosis such as steroid use and smoking within the previous 6 months.
Recruitment/selection of patients	38 patients were randomized as 19 to study group, 19 to control group
Intervention: Source and Type of stem cells	Autologous bone marrow mononuclear cells (MNCs)
Comparator	Saline intradermal injection

Intervention: Method of their characterization	Autologous bone marrow mononuclear cell (MNC) were isolated using density gradient centrifugation (COBE 2991 Cell Processor, Gambro BCT, Lakewood, CO). An automated haemocytometer was used to confirm uniform cell counts in each MNC preparation; nucleated cell viability was assessed using trypan blue exclusion. The cell suspension including a total of 2.4–12.5 × 10^7 cells was adjusted to a final volume of 6–20 ml with saline. The flow cytometry analysis showed that MNCs samples contained an average of 2.37% CD34 cells, 0.92% CD90 cells, 3.51% CD105 cells and 0.95% CD133 cells. Approximately 0.1 ml cell suspension was injected intradermally into per cm^2 expanded skin via a 27-gauge needle (approximately 0.5–1 × 10^6 cells/cm^2).
Intervention: Route of administration	Intradermal injection
Intervention: Dose	The cell suspension including a total of 2.4–12.5 × 10^7 cells was adjusted to a final volume of 6–20 ml with saline. Approximately 0.1 ml cell suspension was injected intradermally. An equal volume of saline was injected in the control group.
Intervention: Dose - If the trial has taken multiple doses, then which dose values has been used for MA	Included only in systematic review, not included in meta-analysis
Efficacy Outcomes reported with time points	Outcomes were assessed at baseline (immediately before treatment) and 4 weeks, 8 weeks and two years after treatment. The primary end point was the absolute change in the expansion index measured at 4 weeks and 8 weeks after treatment. Secondary end points were changes in skin surface area, thickness and texture at 8 weeks versus baseline. Safety evaluations were conducted at two years.
Safety Outcomes reported with time points- Serious AEs	No serious adverse events occurred.
Safety Outcomes reported with time points- Other Adverse Events	During the study, one patient in the MNC group had their expander damaged via puncture during routine inflation. Temporary ecchymosis within the injected treatment area was observed in all patients in both groups.

9. Study	**Claudio-da-silva et al. 2009[9]**
Study type	Qualitative and prospective study
Number of participants	15
Countries, setting and Funding	Brazil, Hospital, No information
Duration of study Follow up	Monthly upto 1 year

(post intervention)	
Subgroup analysis within study	-
Inclusion criteria	Female volunteers with facial rhytides
Exclusion criteria	Not available
Recruitment/selection of patients	15 were randomized into HA-4, MSC-6, HA+MSC-5
Intervention: Source and Type of stem cells	Autologous MSC from adipose tissue
Comparator	Only hyaluronic acid (HA) group
Intervention: Method of their characterization	MSC group, MSC plus hyaluronic acid (HA) group. The Mesenchymal cells were grown in Dulbecco's Modified Eagles culture medium Medium (DMEM; LGC, Cotia, SP) supplemented with 10% fetal bovine serum (Cultilab, Campinas, SP, and antibiotics (100 U/ml of sodium penicillin and 100 mg/mL of streptomycin) and kept in an oven at 37°C with 5% CO_2 for up to a week.
Intervention: Route of administration	Intradermal injection
Intervention: Dose	-
Intervention: Dose - If the trial has taken multiple doses, then which dose values has been used for MA	Included only in systematic review, not included in meta-analysis
Efficacy Outcomes reported with time points	Immediate filling effect, filling of deep grooves, improvement in skin tone and reduction in expression lines.
Safety Outcomes reported with time points- Serious AEs	No adverse events were reported.
Safety Outcomes reported with time points- Other Adverse Events	No adverse events.

10. Study	**Butt et al. 2019[10]**
Study type	Randomised control trial
Number of participants	22
Countries, setting and Funding	Pakistan, Tissue Engineering and Regenerative Medicine Laboratory, Department of Biomedical Sciences & Department of Dermatology, King Edward Medical University/Mayo Hospital Lahore Funding: King Edward Medical University, Lahore, Pakistan
Duration of study Follow up	6 months

(post intervention)	
Subgroup analysis within study	-
Inclusion criteria	Male and female patients with androgenetic alopecia 15 y or older, Active hair loss within last 12 months, Hamilton score III to VI in male patients and Ludwig score I-III in female patients Patients receiving fitness certificate from fitness committee
Exclusion criteria	Patients with inflammation, infection, malignancy, allergic disease, autoimmune disease, pregnancy, and on current anticoagulant therapy. Patient on chemotherapy during the last 5 yr
Recruitment/selection of patients	22 (11 in SVF+ PRP and 11 in SVF)
Intervention: Source and Type of stem cells	Adipose tissue-derived SVF
Comparator	2 sessions of PRP injection at 4 weeks interval.
Intervention: Method of their characterization	Adipose tissue-derived SVF mixed with PRP (3 mL at 20 µL/100 000 cells). 2 sessions at 4 weeks interval. Adipose tissue was collected by tumescent. After sterilization of the skin surface, a tumescent solution (0.9% saline, lidocaine, epinephrine) was infiltrated into donor sites. Fat was harvested using a handheld cannula (3 mm) under sterilized conditions. Adipose tissue was processed within 2 hours under sterilized conditions to obtain SVF. Briefly, adipose tissue was washed repeatedly (3-5×) with an equal volume of phosphate buffer saline. Adipose tissue was then digested by adding an equal volume of collagenase type IV for 30 minutes at 37°C with periodic agitation. The digested tissue was passed through a 70 µm strainer and centrifuged at 650 g for 15 minutes, the supernatant was discarded, and SVF was obtained as a cell pellet mixed in 5 mL of PBS and centrifuged at 650 g for 5 minutes.
Intervention: Route of administration	Intra-dermal injections
Intervention: Dose	3 ml of PRP
Intervention: Dose - If the trial has taken multiple doses, then which dose values has been used for MA	Same as intervention dose
Efficacy Outcomes reported with time points	Hair Density
Safety Outcomes reported with time points- Serious AEs	No SAEs
Safety Outcomes reported	-

with time points- Other Adverse Events	

11. Study	**Gan et al. 2023[11]**
Study type	Randomised control trial
Number of participants	50
Countries, setting and Funding	China, not mentioned, National Natural Science Foundation of China (Grant No.81772104, No.81701929, No.81971889, No.81902013, No.82003085), the Natural Science Foundation of Guangdong Province (Grant No.2017A030310120, Grant No.2019A1515012170, 2020A1515010565), Guangdong Basic and Applied Basic Research Foundation (Grant No.2020A1515010565)
Duration of study Follow up (post intervention)	9 months
Subgroup analysis within study	Hair diameter as per treatment area
Inclusion criteria	The patients were 25-45 years old, with an average age of 32 ± 1.24 years. These included 25 female patients and 25 male patients, all of whom were Chinese. The Norwood grade for male hair loss was II-V, and the Ludwig grade for female hair loss was I-III
Exclusion criteria	Using medications or supplements, including finasteride, dutasteride, ketoconazole, minoxidil or any other hormonal products, that can affect hair growth; Patients with severe systemic diseases, immune diseases, endocrine diseases and nervous system diseases; Patients with head skin infection, allergic disease and malignant tumor.
Recruitment/selection of patients	Fifty patients received autologous healthy hair follicle MSC suspension injections. The average cell volume of each patient was $1x\ 10^{6.}$ All patients completed a 9-month follow-up period.
Intervention: Source and Type of stem cells	Autologous hair Follicle Mesenchymal Stem Cells (HF-MSCs)
Comparator	NS
Intervention: Method of their characterization	The obtained healthy human occipital hair follicles were placed under a stereoscope, excess adipose tissue was removed, and hair bulbs were isolated by micro-dissection. The treated hair follicle tissue was digested with 0.1% dispase for 15 min, and the dermal and epidermal components were separated by blowing. Next, 0.2% collagenase was added, digested at 37°C, and blown every 10 min. After observing that the dermal sheath (DS) was completely digested into single cells and dermal papillae (DP) spheres were

	separated from the hair bulb, digestion was stopped with an equal volume of normal saline. The enzyme solution was removed by centrifugation. After resuspension in normal saline, the suspensions were allowed to stand until the hair shaft sank to the bottom of the centrifuge tube. The supernatant containing DS single cells and DP spheres was obtained and repeated 2-3 times. After centrifugation, the cells were resuspended in normal saline to obtain the final HF-MSC suspension
Intervention: Route of administration	Scalp injection
Intervention: Dose	$1x10^5$ cells
Intervention: Dose - If the trial has taken multiple doses, then which dose values has been used for MA	Same as intervention dose
Efficacy Outcomes reported with time points	Mean diameter, proportion of terminal hair, cumulative hair diameter,
Safety Outcomes reported with time points- Serious AEs	No serious adverse reactions
Safety Outcomes reported with time points- Other Adverse Events	Some patients had slight redness, erythosis or mild swelling at the injection site within 24h after injection, disappeared after 24h. None of the patients experienced obvious infection. Erythosis or other adverse reactions.

12. Study	**Lee et al. 2020[12]**
Study type	Double-blinded, randomized, and placebo-controlled
Number of participants	30
Countries, setting and Funding	Korea, Dermatology Department (Yonsei College of Medicine, Severence Hospital, Seoul, Korea), Yonsei University College of Medicine faculty research grant
Duration of study Follow up (post intervention)	At 4, 8, and 12 weeks of interrvention
Subgroup analysis within study	-
Inclusion criteria	Patients with male pattern hair loss or female pattern hair loss
Exclusion criteria	Patients who had used any products or medications that could influence hair growth during the 4 weeks before the study were excluded from the study
Recruitment/selection of patients	30 in total: 15 in experimental and 15 in control group
Intervention: Source and Type of stem cells	Commercial adipose derived MSC

Comparator	Normal saline
Intervention: Method of their characterization	Human adipose derived mesenchymal stem cells - conditioned media (ADSC-CM) is a conditioned medium from the culture of human ADSCs that are obtained from healthy donors who provide written informed consent and satisfy donor eligibility tests. ADSCs were cultured with hydrogel for 72 hours in serum-free DMEM/F12 (WELGENE, Inc., Gyeongsan-si, Republic of Korea) supplemented with EGF (R&D Systems, Inc.) and bFGF (R&D Systems, Inc., Minneapolis, MN). Then, the culture medium was collected. The collected total culture media were filtered using 0.22-mm filters. To produce the final product, a solution with Cu-tripeptide, pyridoxine hydrochloride, panthenol, and biotin was prepared in water for injection, and stem cell conditioned medium was added to the solution.
Intervention: Route of administration	Topical application
Intervention: Dose	Not mentioned. once per week for 12 consecutive weeks
Intervention: Dose - If the trial has taken multiple doses, then which dose values has been used for MA	Same as intervention dose
Efficacy Outcomes reported with time points	Hair Density, Treatment assessment score,
Safety Outcomes reported with time points- Serious AEs	Not mentioned
Safety Outcomes reported with time points- Other Adverse Events	No adverse effects

13. Study	**Tak et al. 2020[13]**
Study type	Randomized, double-blind, placebo-controlled clinical trial
Number of participants	38
Countries, setting and Funding	South Korea, a tertiary hospital in Yangsan, South Korea, No information available
Duration of study Follow up (post intervention)	Upto 16 weeks after treatment
Subgroup analysis within study	-
Inclusion criteria	18 and 59 yers, diagnosed with AGA with at least M2, C2, or U1 basic type and V1 or specific type of AGA. Additionally, they maintained a consistent hair style and did not receive any other

	hair care throughout the 16-week study period.
Exclusion criteria	Intake of medications or supplements, including finasteride, dutasteride, steroids, vasodilators, anticonvulsants, beta-receptor blockers, cell death agents, bronchodilators, diuretics, spironolactone, cimetidine, diazoxide, cyclosporine, ketoconazole, or any other hormonal products, that can affect hair growth in the preceding 30 days Surgical history for hair loss suchas hair transplantation or scalp reduction; Treatment history of hyperthyroidism or hypothyroidism; Currently pregnant or planning conception within the next 6 months or currently breastfeeding; Drug history of topical steroids, hair growth solution, or hair restorers to the scalp in the preceding month; Uncontrolled blood pressure (BP) and blood glucose levels, infectious skin diseases, or psychiatric disorders in the preceding 6 months; Aspartate aminotransferase (AST) or alanine aminotransferase (ALT) serum levels >80 mg/dL or creatinine (Cr) level >1.5 mg/dL; and Allergic to the ingredients in this study's interventions
Recruitment/selection of patients	38 patients were randomized as 19 in experimental and 19 in control
Intervention: Source and Type of stem cells	Allogenic adipose-derived stem cells conditioned media
Comparator	Placebo (distilled water)
Intervention: Method of their characterization	Prior to collecting the adipose tissue, the donors were tested for the presence of the hepatitis B virus, hepatitis C virus, human immunodeficiency virus, human T-cell lymphotropic virus, Epstein-Barr virus, cytomegalovirus, parvovirus B19, and Treponema pallidum. Prior to disrupting the ADSCs ultrasonically, they were dispersed in distilled water. The ADSC cell membrane could be disrupted using a low frequency of ultrasound wave. The ADSCs were observed under a microscope to ensure complete lysis. Thereafter, the cell membrane debris was removed using centrifugation and successive filtration steps. Finally, we obtained Adipose-derived stem cell constituent extract (ADSC-CE) enriched with stem cell proteins, which was used for stem cell therapy
Intervention: Route of administration	Topical application
Intervention: Dose	A total of 130 mL of test material was prepared in a bottle to both groups. Topical solution for stem cell group had 1% ADSC-CE in distilled water, and that for control group contained distilled water

	alone
Intervention: Dose - If the trial has taken multiple doses, then which dose values has been used for MA	Same as intervention dose
Efficacy Outcomes reported with time points	Hair Density, Hair Diameter, Treatment Assesment Score
Safety Outcomes reported with time points- Serious AEs	No SAEs
Safety Outcomes reported with time points- Other Adverse Events	

14. Study	**Gentile et al. 2020[14]**
Study type	Placebo controlled, randomized, evaluator-blinded, half-head group study
Number of participants	27
Countries, setting and Funding	Italy, not mentioned No information available
Duration of study Follow up (post intervention)	Till 58 weeks after last treatment
Subgroup analysis within study	-
Inclusion criteria	This investigation enlisted 27 patients, of whom 17 males showed AGA grades 2–5 as controlled by the Norwood–Hamilton (NH) scale and 10 females showed AGA grades 1-2 as dictated by the Ludwig (L) scale.
Exclusion criteria	Immunosuppression and cancer, sepsis, and the utilization of pharmacological therapeutics targeting on AGA (finasteride, similar drugs, and/or antiandrogens) in the earlier year. Localized exclusion criteria included the utilization of topical medicines for AGA (lotions as minoxidil, prostaglandin analogs, retinoids, or corticosteroids) in the earlier year.
Recruitment/selection of patients	This investigation enlisted 27 patients, of whom 17 males showed AGA grades 2–5 as controlled by the Norwood–Hamilton (NH) scale and 10 females showed AGA grades 1-2 as dictated by the Ludwig (L) scale.
Intervention: Source and Type of stem cells	Autologous, human hair follicle mesenchymal stem cells (HF-MSCs)
Comparator	Placebo infusions (saline solution NaCl 0.9%)
Intervention: Method of their characterization	Autologous micrografts of HFSCs from scalp tissue were injected in three sessions spaced 45 days apart. To obtain autologous

	micrografts through a mechanical fragmentation of different biological tissues (epidermis, dermal, fat tissue, hair, bulb area, and bulge area) and requires different steps of execution. The first step is harvesting of the scalp tissues (30–50 fragments depending on the size of the area to treat) with punch biopsy (2 mm diameter) , storing in saline solution, and cutting the fragments into strips of 2.0×2.0 mm, resulting in collection and disaggregation of the strips (group of 3 fragments each time) sterilely through a manual splitting performed by multiple incisions with scalpel number 11 in 1.2 mL of saline (NaCl 0.9%) for each 3 fragments with the aim of sorting a cell group having a diameter of 80–120 μm. The second step is collecting the suspension obtained; an average 20ml for 50 fragments was disaggregated and fragmented, in two 10 mL Luer-Lock syringes, and centrifuged for 3 minutes at 3000 RPM ;1.5 mL of the supernatant was removed from each syringe, and 9 ml of the micrograft's suspension was obtained; two syringes containing 4.5 ml of the micrograft's suspension were positioned in a mesotherapy gun.
Intervention: Route of administration	Interfollicular infusions
Intervention: Dose	9 ml of the micrograft's suspension s (0.2 mL/cm^2)
Intervention: Dose - If the trial has taken multiple doses, then which dose values has been used for MA	Same as intervention dose
Efficacy Outcomes reported with time points	Hair regrowth, histological evaluation of follicle quantity, safety
Safety Outcomes reported with time points- Serious AEs	No information
Safety Outcomes reported with time points- Other Adverse Events	No information

15. Study	**Han et al. 2019[15]**
Study type	Double-blind, placebo-controlled clinical trial
Number of participants	30
Countries, setting and Funding	Korea, not mentioned, No information available
Duration of study Follow up (post intervention)	Upto 16 weeks after treatment
Subgroup analysis within	-

study	
Inclusion criteria	This study included physically and mentally healthy adults aged 20~60 with a diagnosis of mild-to-moderate patterned hair loss (men: modified Norwood-Hamilton classification types II, IIa, IIv, IIIa, or IIIv and women
Exclusion criteria	Patients with a history of any skin or scalp disorders, endocrine abnormalities, or systemic diseases associated with liver dysfunction were excluded from this study. To prevent the effect of other treatment on our results, we excluded patients who had previously received other treatments for androgenetic alopecia, including those who received finasteride, topical hair restoration agents, or surgical treatments such as hair transplants and scalp reduction. Pregnant and nursing women were also excluded.
Recruitment/selection of patients	Patients were categorized using stratified permuted block randomization, the randomization table for which was generated by a statistician using an allocation code.
Comparator	Placebo tonic contained alcohol without any conditioned medium.
Intervention: Source and Type of stem cells	Human Umbilical cord blood (hUCB)-MSC-derived conditioned medium.
Intervention: Method of their characterization	Human Umbilical Cord Blood Mesenchymal Stem Cell. Mononuclear cells derived from cord blood were isolated by centrifugation and were washed several times to remove any remaining foreign bodies. These cells were cultured as a monolayer at an appropriate density. The cultured spindle-shaped mesenchymal cells formed homogeneous colonies, and these cells were allowed to proliferate until a sufficient number of cells could be acquired during passaging.
Intervention: Route of administration	Topical on scalp
Intervention: Dose	10% dilution solution of hUCB-MSC-derived conditioned medium.
Intervention: Dose - If the trial has taken multiple doses, then which dose values has been used for MA	Same as intervention dose
Efficacy Outcomes reported with time points	Hair density, thickness of hair, hair growth rate
Safety Outcomes reported with time points- Serious AEs	No severe adverse reactions were reported.
Safety Outcomes reported with time points- Other Adverse Events	-

16 (A) Study	Legiawati et al. 2023[16]
Study type	Double-blind, randomized clinical trial
Number of participants	37
Countries, setting and Funding	Indonesia, Dermato-venereology outpatient clinic of Dr. Cipto Mangunkusumo Hospital, National Research and Innovation Agency of Indonesia/Badan Riset dan Inovasi Nasional (BRIN)
Duration of study Follow up (post intervention)	Evaluated every 2 week during 6 weeks of intervention
Subgroup analysis within study	-
Inclusion criteria	Male AGA patients between the ages of 25 and 59 years old whose clinical presentation met Hamilton-Norwood criteria grades II to VI. Cessation of anti-androgens and minoxidil treatment for at least 1 month was mandatory
Exclusion criteria	Patients with hair loss other than AGA Patients receiving 5-alpha reductase inhibitor therapy; Patients who had received growth factor treatment platelet-rich plasma or microneedling) for at least 6 months prior to the study; History of hypertrophic scars or blood clotting disorders.
Recruitment/selection of patients	37 patients were randomized into group A and B. In group A, scalp of 17 patients were divided into intervention side and control side
Intervention: Source and Type of stem cells	Allogenic adipose-derived stem cells conditioned media (ADSCs-CM)
Comparator	0.9% NaCl with Minoxidil
Intervention: Method of their characterization	Non-concentrated ADSC-CM with minoxidil. ADSC-CM used in this study was allogeneic, formed by the culture of human mesenchymal stem cells (MSC). These mesenchymal stem cells originated from adipose tissue which has been screened previously for infectious pathogens. After successful isolation of MSCs, these stem cells were multiplied in a normoxic condition until it reached the fifth passage, with a culture confluence of at least 80%. The conditioned media were then obtained by removing the stem cells.
Intervention: Route of administration	Intradermal injection
Intervention: Dose	2ml of Concentrated ADSCs-CM or Control in both sides. Over 6 weeks, this regimen was administered intradermally every 2 weeks
Intervention: Dose - If the trial has taken multiple doses, then which dose values has been used for MA	Same as intervention dose

Efficacy Outcomes reported with time points	Hair count, hair dnsity, vellus rate, terminal rate, mean thickness, total follicular units and patient satisfaction score.
Safety Outcomes reported with time points- Serious AEs	
Safety Outcomes reported with time points- Other Adverse Events	Most patients complained of mild local irritation, itchiness, and folliculitis during minoxidil treatment. One participant developed contact dermatitis after 2 weeks of minoxidil usage. Pain, itchiness, and redness around the treatment area were the most reported post-injection side effects.

16(B) Study	**Legiawati et al. 2023[16]**
Study type	Double-blind, randomized clinical trial
Number of participants	37
Countries, setting and Funding	Indonesia, Dermato-venereology outpatient clinic of Dr. Cipto Mangunkusumo Hospital, National Research and Innovation Agency of Indonesia/ Badan Riset dan Inovasi Nasional (BRIN)
Duration of study Follow up (post intervention)	Evaluated every 2 week during 6 weeks of intervention
Subgroup analysis within study	-
Inclusion criteria	Male AGA patients between the ages of 25 and 59 years old whose clinical presentation met Hamilton-Norwood criteria grades II to VI. Cessation of anti-androgens and minoxidil treatment for at least 1 month was mandatory.
Exclusion criteria	• Patients with hair loss other than AGA • Patients receiving 5-alpha reductase inhibitor therapy; • Patients who had received growth factor treatment platelet-rich plasma or microneedling) for at least 6 months prior to the study; • History of hypertrophic scars or blood clotting disorders.
Recruitment/selection of patients	37 patients were randomized into group A and B. In group B, scalp of 20 patient were divided into intervention side and control side
Intervention: Source and Type of stem cells	Allogenic adipose-derived stem cells conditioned media (ADSCs-CM).
Comparator	0.9% NaCl with Minoxidil
Intervention: Method of their characterization	Concentrated ADSCs-CM with minoxidil. ADSCs-CM used in this study was allogeneic, formed by the culture of human mesenchymal stem cells (MSCs). These mesenchymal stem cells originated from adipose tissue which has been screened previously for infectious pathogens. After successful isolation of MSCs, these stem cells were multiplied in a normoxic condition until it reached the fifth passage,

	with a culture confluence of at least 80%. The conditioned media were then obtained by removing the stem cells.
Intervention: Route of administration	Intradermal injection
Intervention: Dose	2ml of non-concentrated ADSCs-CM or Control in both sides. Over 6 weeks, this regimen was administered intradermally every 2 weeks
Intervention: Dose - If the trial has taken multiple doses, then which dose values has been used for MA	Same as intervention dose
Efficacy Outcomes reported with time points	Hair count, hair dnsity, vellus rate, terminal rate, mean thickness, total follicular units and patient satisfaction score.
Safety Outcomes reported with time points- Serious AEs	
Safety Outcomes reported with time points- Other Adverse Events	Most patients complained of mild local irritation, itchiness, and folliculitis during minoxidil treatment. One participant developed contact dermatitis after 2 weeks of minoxidil usage. Pain, itchiness, and redness around the treatment area were the most reported post-injection side effects.

17. Study	**Tsuboi et al. 2020[17]**
Study type	Double blinded RCT
Number of participants	65
Countries, setting and Funding	Japan, 2 centers in Japan Shiseido Co., Ltd., Japan
Duration of study Follow up (post intervention)	Upto 12 months after injection
Subgroup analysis within study	-
Inclusion criteria	Eligible men and women were older than 20 years, with male pattern hair loss in men classified as type III-vertex, IV, V, and VI using the Norwood Hamilton classification and female pattern hair loss in women classified as grades 3 through 6 based on the Shiseido classification
Exclusion criteria	Subjects who used topical or systemic drugs that stimulate hair growths-1) within the past 3 months; who were pregnant or hoping to become pregnant, or were breast-feeding; who were taking any medications for systemic diseases that might influence hair growth; who were diagnosed with cancer; who had undergone hair loss unrelated to PHL within the past 3 months; who had hair transplants within the past 24 months; who had more than 10%

	gray hair at the hair loss area
Recruitment/selection of patients	50 men and 15 women with mean age 52.0±6.7 and 48.0±7.3 respectively.
Intervention: Source and Type of stem cells	Autologous, dermal sheath cup (DSC) cells
Comparator	Placebo
Intervention: Method of their characterization	Autologous, dermal sheath cup (DSC) cells. A 6 mm diameter occipital scalp skin tissue biopsy was collected from each subject and was transported to the Shiseido Cell Processing and Expansion Center (SPEC). Hair follicles were isolated from each biopsy and DSCs were dissected under a stereomicroscope as described previously. s-2) Isolated DSCs were transferred into culture plates and were incubated at 37°C and 5% CO_2 in the culture medium for cell expansion. After the completion of the cultures, the DSC cells for each subject were suspended in cryopreservation liquid and the concentration was adjusted to 7.5×10^6/mL (High-dose), 1.5×10^6/mL (Med.-dose) and 3.0×10^5/mL (Low-dose), blinded by randomized codes for injection, then frozen in vial tubes and stored in liquid nitrogen until shipped to the hospital. Alkaline phosphatase (ALP) activity of cultured DSC cells was used as an identity and/or potency marker for DSC cells and was measured using a BCIP/NBT Liquid Substrate System (Sigma-Aldrich JAPAN).
Intervention: Route of administration	Injection to the hair loss areas
Intervention: Dose	Three concentrations of DSC cell suspensions (7.5×10^6, 1.5×10^6, and 3.0×10^5 cells) and a placebo (each in a volume of 1 mL) were injected separately into 4 randomly allocated injection sites in each patient.
Intervention: Dose - If the trial has taken multiple doses, then which dose values has been used for MA	7.5×10^6
Efficacy Outcomes reported with time points	Total hair density, cumulative hair diameter
Safety Outcomes reported with time points- Serious AEs	No serious adverse events
Safety Outcomes reported with time points- Other Adverse Events	Mild adverse events, such as erythema, swelling, purpura, and small hemorrhages, at the injection site were observed in 14 cases.

18. Study	**Abouzaid et al. 2021[18]**

Study type	Prospective, open-label single center, randomized control clincal trial
Number of participants	100
Countries, setting and Funding	Egypt, Alexandria University, Alexandria, Egypt, No information
Duration of study Follow up (post intervention)	Upto 6 months based on recovery of the individual
Subgroup analysis within study	-
Inclusion criteria	Newly admitted burn patients aged between 14 and 45 years, any gender, stable general condition, total body surface area (TBSA) affected between 10% and 25%, with the depth of the superficial or deep dermal burns.
Exclusion criteria	Age groups beyond the designated for the study (< 14 or > 45 years), burns with TBSA < 10% or > 25%, burns with loss of subcutaneous fat, fascia, muscles and bones, inhalational burn, and burns in genitalia, perineum, and peri-anal areas and co-morbidity (ies) that might affect wound healing or eligibility for an esthesia and surgery such as diabetes mellites, vascular in sufficiency, known immunological diseases, renal or hepatic failure, cardiac diseases, cerebrovascular events
Recruitment/selection of patients	100 patients were randomized into Group A, study group (50) and Group B, control group (50).
Intervention: Source and Type of stem cells	Autologous fat
Intervention: Method of their characterization	Group A consisted of 50 patients treated with a single injection of autologous fat grafting in the affected area along with topical nanofat application, and then the wounds were dressed with nanofat. For stem cell isolation and characterization, nanofat samples were washed in an equal volume of PBS supplemented with 1% Penicillin/Streptomycin (3 washes). 0.1% collagenase type I was dissolved in an equal volume of the sample [(Sigma-Aldrich, C0103), 1% bovine serum albumin (BSA, Caisson) in PBS] was added to the adipose solution.
Intervention: Route of administration	Injection of autologous fat grafting in the affected area along with topical nanofat application, and then the wounds were dressed with nanofat
Intervention: Dose	1 cc fat over 10 cm long line
Intervention: Dose - If the trial has taken multiple doses, then which dose values has been used for MA	-

Efficacy Outcomes reported with time points	Area percentage of collagen, Days of hospitalization, Frequency of visits to OPD, Area of epithelization, Hypopigmentation, Hyperpigmentation, contractures, Hypertrophic Scar
Safety Outcomes reported with time points- Serious AEs	Not mentioned
Safety Outcomes reported with time points- Other Adverse Events	Not mentioned

19. Study	**Abou Eitta et al. 2019[19]**
Study type	Split face comparative study
Number of participants	10
Countries, setting and Funding	Egypt, Department of Dermatology and Venereology outpatient clinic, Faculty of Medicine, Alexandria University, Center of Excellence for Research in Regenerative Medicine and its Application, CERRMA, (STDF funded) is acknowledged for providing all needed equipment for the processing and char acterization of the adipose tissue derived stem cells under com plete sterile conditions
Duration of study Follow up (post intervention)	3 months
Subgroup analysis within study	-
Inclusion criteria	Bilateral involvement of both halves of the face with post-acne scarring
Exclusion criteria	Active acne lesions, treatment by systemic retinoid in the last 12 months, skin infection at the site of injection, dark skin types (V, VI), whether the patient received any treatment for scars, pregnancy, lactation in females, history of skin diseases, and history of previous complication of laser therapy and blood dyscriasis.
Recruitment/selection of patients	Ten patients were recruited from the Department of Dermatology and Venereology outpatient clinic, Faculty of Medicine, Alexandria University, from April 2017 to September 2018 and subjected to split-face treatment after approving the study and signing a written consent.
Intervention: Source and Type of stem cells	Adipose, Autologous
Intervention: Method of their characterization	Autologous adipose tissue-derived adult stem cells (AT-ASCs) on right side. SVF was isolated from lipoaspirate obtained from several regions of the body including abdominal regions, thighs, and buttocks.

	After sterilization of the (donor site) with povidone iodine 10%, local anesthesia was used to make a small incision through which an infiltration cannula (Tulip Field Bilevel Liposuction Infiltration Cannula, 2.4 mm 20 cm; Mount Vernon, WA, USA) was introduced then infiltration anesthesia was performed using the modified Klein's solution. After 15 minutes, a blunt-tipped cannula was introduced through the incision and connected to a 60-ml syringe; average collected volume was 50 ml. The cannula was then moved back and forth while gently drawing fat into the syringe and then lipo-aspirate was evacuated into asterile tube and immediately transferred to the stem cells laboratory.
Intervention: Route of administration	Intradermal injection
Intervention: Dose	Single injection of stem cells suspended in 1 ml phosphate buffered saline
Intervention: Dose - If the trial has taken multiple doses, then which dose values has been used for MA	-
Efficacy Outcomes reported with time points	Transepidermal water loss, Area of scar, skin hydration, degree of scar severity
Safety Outcomes reported with time points- Serious AEs	Not mentioned
Safety Outcomes reported with time points- Other Adverse Events	Not mentioned

20. Study	**Roohaninasab et al. 2023[20]**
Study type	A double-blind randomized controlled trial
Number of participants	10
Countries, setting and Funding	Iran, This research was supported by the Skin and Stem Cell Research Center, Tehran University of Medical Sciences
Duration of study Follow up (post intervention)	1 year
Subgroup analysis within study	-
Inclusion criteria	Patients with skin types 1 to 4 who had burn scars at more than one site that had been present for at least three months and were between 25 and 50 years of age.
Exclusion criteria	Exclusion criteria included laser treatment in the past three months,

	pregnancy and breastfeeding, coagulation and platelet disorders, use of anticoagulant medications, diabetes and connective tissue disease, active viral infections, history of malignancy, and use of chemotherapeutic agents
Recruitment/selection of patients	Two scar areas were randomly named A and B in each patient, and patients were given four sealed envelopes with the letters AS, AL, BS, and BL. The first letter represents the desired area, and the second letter indicates that the procedure can be performed. If the letter S is present, the SVF injection is performed along with the fractional CO_2 laser, and if the letter L is present, only the fractional CO_2 laser is injected along with normal saline as a placebo.
Intervention: Source and Type of stem cells	Adipose derived SVF, autologous
Intervention: Method of their characterization	CO_2 laser with SVF. First, 100 cc of fat was removed from the thigh area of each patient. The tissue was then washed with phosphate-buffered saline (PBS) (Miltenyi Biotec, Cologne, Germany) to remove red blood cells and leukocytes. The adipose tissue was digested with collagenase type I (Worthington Biochemical Corp, Lakewood, USA) for 20 min at 37°C to produce a collagenase solution with a concentration of 0.1%. Enzyme digestion was prevented by washing with DMEM 10% FBS (Invitrogen, Carlsbad, USA), and floating and lysed fat cells were discarded. SVF cells were pelleted by centrifugation at 500g for 10 min. The pellet was resuspended in PBS, and an erythrocyte lysis buffer (Sigma-Aldrich Corp, St. Louis, USA) was added and incubated at 37°C for 10 min. This cell suspension was centrifuged (500g, 5 min), and SVF cells were counted using an automatic cell counter.
Intervention: Route of administration	-
Intervention: Dose	Injection into burn scars
Intervention: Dose - If the trial has taken multiple doses, then which dose values has been used for MA	20×10^6 cells/mL from aspirated 100 cc of fat tissue
Efficacy Outcomes reported with time points	Transepidermal water loss, Epidermal thickness, hydration, Dermal thickness, Complete thickness, Vancuover scar scale, Erythema, Melanin, Viscoelasticity, Patient satisfaction
Safety Outcomes reported with time points- Serious AEs	Not mentioned
Safety Outcomes reported with time points- Other	Not mentioned

Adverse Events	

21. Study	**Fan et al. 2020[21]**
Study type	Double-blind, placebo-controlled, three arm RCT
Number of participants	90
Countries, setting and Funding	China, Affiliated Foshan Maternity & Child Healthcare Hospital, Southern Medical University. Funded by the Affiliated Foshan Maternity & Child Healthcare Hospital, Southern Medical University (FSFY20160501).
Duration of study Follow up (post intervention)	6 months
Subgroup analysis within study	Subgroup analysis was stratified according to gestational age and maternal age
Inclusion criteria	Primiparous women receiving elective cesarean delivery Ages between 21-35 years Gestation ages ≥37 weeks and < 42 weeks, Willing to give and sign an informed consent form and a photographic release form, Willing to comply with study dosing and complete the entire course of the study
Exclusion criteria	Any systemic uncontrolled disease, Recent or current cancer, History or presenting with a keloid formation, Wounds or local disease in treatment area, Planning any other cosmetic procedure to the study area during the study period, smoking, gel allergy.
Recruitment/selection of patients	Ninety primiparous singleton pregnant women undergoing elective cesarean section were randomly allocated to receive placebo, low-dose (3×10^6 cells), or high-dose (6×10^6 cells) transdermal hydrogel UC-MSCs on the surface of the skin incision.
Intervention: Source and Type of stem cells	Allogenic, Umbilical Cord Mesenchymal Stem Cells (UC-MSCs).
Intervention: Method of their characterization	The UC-MSCs were isolated from the umbilical cord of a healthy donor after informed consent by the method described above. Briefly, the umbilical cord tis- sue was washed with phosphate-buffered saline (PBS) and then minced into 1–2 mm^3 fragments. These tissue pieces were then incubated with 0.075% collagenase (Sigma, St Louis, MO, USA) for 30 min and then 0.125% trypsin (Gibco, Grand Island, NY, USA) for 30 min with gentle agitation at 37°C. Fetal bovine serum (FBS) (Hyclone, Logan, UT, USA) was added to neutralize the excess trypsin. The digested mixture was then passed through a 100-μm filter to obtain cell suspensions. The cells were plated at a density of 1×10^6 cells/cm^2 in non- coated T-25 or T-75 cell culture flasks. Growth medium consisted of Dulbecco's modified Eagle's medium with low glucose (DMEM-LG; Gibco) and 5% fetal bovine serum, supplemented with 10 ng/mL vascular endothelial growth factor (VEGF; Sigma), 10ng/mL

	epidermal growth factor (EGF; Sigma), 100 U penicillin/streptomycin (Sigma), and 2 mM L-glutamine (Gibco). Cell cultures were maintained in a humidified atmosphere with 5% CO_2 at 37 °C.
Intervention: Route of administration	Transdermal hydrogel was occupied immediately after skin incision suturing.
Intervention: Dose	Low-dose (3×10^6), high-dose (6×10^6), The participants received a total of six hydrogels on the surface of the skin incision, once a day.
Intervention: Dose - If the trial has taken multiple doses, then which dose values has been used for MA	High-dose (6×10^6)
Efficacy Outcomes reported with time points	Area of scar, Volume of scar, Vancuover scar scale, Pigmentation, Erythema, Patient satisfaction
Safety Outcomes reported with time points- Serious AEs	Not mentioned
Safety Outcomes reported with time points- Other Adverse Events	No adverse effects

22. Study	**Kwon et al. 2020[22]**
Study type	Prospective, Double-blind, split-face RCT
Number of participants	25
Countries, setting and Funding	South Korea, not funded
Duration of study Follow up (post intervention)	6 weeks (3 consecutive treatment with interval of 3 weeks)
Subgroup analysis within study	-
Inclusion criteria	Patients whose échelle d'évaluation clinique des cicatrices d'acné (ECCA) scores were 50 or higher were eligible for inclusion
Exclusion criteria	Patients whose échelle d'évaluation clinique des cicatrices d'acné (ECCA) scores were 50 or higher were eligible for inclusion
Recruitment/selection of patients	Twenty-five Korean subjects (18 men and 7 women, age range 19–54 years, 12 with Fitzpatrick skin type III and 13 with type IV) with atrophic acne scars were enrolled between October and November 2019.
Intervention: Source and Type of stem cells	Adipose-derived Stem Cell (ASC)-conditioned medium (CM), allogenic
Intervention: Method of their characterization	Adipose-derived Stem Cell Exosomes (ASCE) were prepared as gel solutions at 2 different doses for clinical application. To prepare the

	ASCE gel, ASCE were prepared at 9.78×10^{10} particles/ml (for the day of FCL treatment) or 1.63×10^{10} particles/ml (for days subsequent to FCL treatment) in a gel solution containing 30% ASCE.
Intervention: Route of administration	Topical
Intervention: Dose	All patients were treated with 1 ml of either ASCE gel or control gel on each half of the face according to random assignment just after finishing the laser treatment. For the next two consecutive days after each treatment, patients were instructed to apply each solution to the designated half of the face twice a day as described.
Intervention: Dose - If the trial has taken multiple doses, then which dose values has been used for MA	1 ml
Efficacy Outcomes reported with time points	Percentage change in ECCA score, percentage change in scar volume
Safety Outcomes reported with time points- Serious AEs	Not mentioned
Safety Outcomes reported with time points- Other Adverse Events	Various treatment-related side-effects, including post treatment pain, erythema, oedema, and dryness, were experienced on both ASCE and control sides

23. Study	**Park et al. 2021[23]**
Study type	Split face, RCT
Number of participants	15
Countries, setting and Funding	South Korea, Anterogen Inc. Seoul, Korea
Duration of study Follow up (post intervention)	Upto 2 months
Subgroup analysis within study	-
Inclusion criteria	Healthy subjects aged 19 to 65 years and diagnosed with atrophic acne scars
Exclusion criteria	Preexisting skin conditions, with skin infections, retinoids intakes, those with photosensitive dermatoses and severe systemic disease, frequently smoking tobacco, with allergies to topical anesthetic cream, and those who were pregnant, or lactating have all been excluded.
Recruitment/selection of patients	For patients aged 19 to 65 years, the face was divided into left and right sides and then randomly assigned for topical application. Of the 15 subjects in total, 12 (80%) were male and three (20%) were

	female. The mean age of patients was 32.0 ± 8.5 years.
Comparator	Fractional eCO_2 laser followed by normal saline, later HA
Intervention: Source and Type of stem cells	Adipose, allogenic
Intervention: Method of their characterization	Human adipose derived stem cell-conditioned media (HSCM). Fractional eCO_2 laser followed by, 100% HSCM initially, then 80% HSCM with Hyaluronic acid (HA) for next 6 days, twice a day
Intervention: Route of administration	Topical
Intervention: Dose	-
Intervention: Dose - If the trial has taken multiple doses, then which dose values has been used for MA	Fractional eCO_2 laser followed by, 100% HSCM initially, followed by 80% HSCM with Hyaluronic acid (HA) for next 6 days
Efficacy Outcomes reported with time points	Volume of atrophic acne scar, volume of skin pores, erythema
Safety Outcomes reported with time points- Serious AEs	Not mentioned
Safety Outcomes reported with time points- Other Adverse Events	Not mentioned

viii. List of excluded studies:

Study	Exclusion reason
Ahmadi, A. R. and Atiee, G. and Chapman, B. and Reynolds, L. and Sun, J. and Cameron, A. M. and Wesson, R. N. and Burdick, J. F. and Sun, Z. 2023	wrong population
Arjunan, S. and Gan, S. U. and Choolani, M. and Raj, V. and Lim, J. and Biswas, A. and Bongso, A. and Fong, C. Y.2020	wrong population
Banlue, A. and Kaewmuangmoon, J. and Janebodin, K. and Tansriratanawong, K. 2023	wrong population
Basu, S. and Singh, V. 2023	wrong population
Braga, F. T. and Santos, A. C. and Bueno, P. C. and Silveira, R. C. and Santos, C. B. and Bastos, J. K. and Carvalho, E. C. 2015	wrong population
Busin, M. and Breda, C. and Bertolin, M. and Bovone, C. and Ponzin, D. and Ferrari, S. and Barbaro, V. and Elbadawy, H. M. 2016	wrong population
Charles-de-Sa, L. and de Amorim, N. F. G. and Dantas, D. and Han, J. V. and Amable, P. and Teixeira, M. V. T. and de Araujo, P. L. and Link, W. and Borojevich, R. and Rigotti, G. 2015	wrong population
El Kahky, H. and Diab, H. and Helal, H. A. 2017	wrong population
Falanga, V. and Grada, A. and Otero-Vinas, M. and Lin, X. and Yufit, T. and Fiore, D. and Carson, P. 2022	wrong population
Figueiredo, G. S. and Hogg, J. and Okonkwo, A. and Baylis, O. J. and Berry, M. and Ali, S. and Lako, M. and Figueiredo, F. C. 2023	wrong population
Fujiwara, O and Prasai, A and Perez-Bello, D and Ayadi, Ae and Petrov, Iy and Esenaliev, Ro and Petrov, Y and Herndon, Dn and Finnerty, Cc and Prough, Ds and et al. 2020	wrong population
Grada, A. and Otero-ViÃ±as, M. and Prieto-Castrillo, F. and Falanga, V. 2020	wrong population
GrÃ¸nhÃ¸j, C. and Jensen, D. H. and Vester-Glowinski, P. and Jensen, S. B. and Bardow, A. and Oliveri, R. S. and Fog, L. M. and Specht, L. and Thomsen, C. and Darkner, S. and Jensen, M. and MÃ¼ller, V. and Kiss, K. and Ag and er, T. and Andersen, E. and Fischer-Nielsen, A. and von Buchwald, C. 2018	wrong population
GÃ¼nter, C. I. and Bader, A. and Dornseifer, U. and Egert, S. and Dunda, S. and Grieb, G. and Wolter, T. and Pallua, N. and von Wild, T. and Siemers, F. and MailÃ¤nder, P. and Thamm, O. and Ernert, C. and Steen, M. and Sievers, R. and Reichert, B. and Rahmanian-Schwarz, A. and Schaller, H. and Hartmann, B. and Otte, M. and Kehl, V. and Ohmann, C. and Jelkmann, W. and Machens, H. G. 2013	wrong population
Han, Y. M. and Sheng, Y. Y. and Xu, F. and Qi, S. S. and Liu, X. J. and Hu, R. M. and Miao, Y. and Huang, G. Q. and Yang, Q. P. 2015	wrong population
Han, Y. M. and Sheng, Y. Y. and Xu, F. and Qi, S. S. and Liu, X. J. and Hu, R. M. and Miao, Y. and Yang, Q. P. 2014	wrong population
He, A. and Zheng, S. and Luan, W. and Wang, L. and Qian, L. and Qi, F. and Feng, Z. 2023	wrong population
Hu, Z. J. and Li, T. 2015	wrong population
Khanna, D and Mayes, Md and Simms, Rw and Steen, Vd and Cohen, S and Caldron, P and Martin, R and Kafaja, S and Shah, A and Shahouri, S and et al. 2016	wrong population
Kmiecik, J. and Kulus, M. J. and Popiel, J. and Cekiera, A. and Cegielski, M. 2021	wrong population

Kuroda, R. and Matsumoto, T. and Niikura, T. and Kawakami, Y. and Fukui, T. and Lee, S. Y. and Mifune, Y. and Kawamata, S. and Fukushima, M. and Asahara, T. and Kawamoto, A. and Kurosaka, M. 2014	wrong population
Lamo-Espinosa, J. M. and Mora, G. and Blanco, J. F. and Granero-MoltÃ³, F. and NuÃ±ez-CÃ³rdoba, J. M. and SÃ¡nchez-Echenique, C. and BondÃa, J. M. and Aquerreta, J. D. and Andreu, E. J. and Ornilla, E. and VillarÃ³n, E. M. and ValentÃ-AzcÃ¡rate, A. and SÃ¡nchez-Guijo, F. and CaÃ±izo, M. C. and ValentÃ-Nin, J. R. and PrÃ³sper, F. 2016	wrong population
Lavery, L. A. and Fulmer, J. and Shebetka, K. A. and Regulski, M. and Vayser, D. and Fried, D. and Kashefsky, H. and Owings, T. M. and Nadarajah, J. 2014	wrong population
Lavery, L. A. and Fulmer, J. and Shebetka, K. A. and Regulski, M. and Vayser, D. and Fried, D. and Kashefsky, H. and Owings, T. M. and Nadarajah, J. and Grant, D. and Lowhorn, M. and Hendrick, T. and Streja, D. and Friedl and er, G. and Goldman, D. and Budny, A. and Treadwell, T. and Ware, D. and Kerzner, M. and Gordon, I. 2014	wrong population
Li, Y. and Yan, B. and Wang, H. and Li, H. and Li, Q. and Zhao, D. and Chen, Y. and Zhang, Y. and Li, W. and Zhang, J. and Wang, S. and Shen, J. and Li, Y. and Guindi, E. and Zhao, Y. 2015	wrong population
MartÃnez, Ml and Escario, E and Poblet, E and SÃ¡nchez, D and BuchÃ³n, Ff and Izeta, A and Jimenez, F. 2016	wrong population
Marx, Re and Harrell, Db. 2014	wrong population
Marx, R. E. and Harrell, D. B. 2014	wrong population
Meneses, J. V. and Fortuna, V. and de Souza, E. S. and Daltro, G. C. and Meyer, R. and Minniti, C. P. and Borojevic, R. 2016	wrong population
Nakano, N. and Kubota, A. and Tokunaga, M. and Tokunaga, M. and Makino, T. and Takeuchi, S. and Takatsuka, Y. and Utsunomiya, A. 2014	wrong population
https://clinicaltrials.gov/show/NCT02033525. 2014	wrong population
https://clinicaltrials.gov/show/NCT02226848. 2014	wrong population
https://clinicaltrials.gov/show/NCT02034669. 2014	wrong population
Pattayadeekul, T. and Pawcsuntorn, T. and Nararatwanchai, T. 2022	wrong population
Pedrotti, E. and Passilongo, M. and Fasolo, A. and Nubile, M. and Parisi, G. and Mastropasqua, R. and Ficial, S. and Bertolin, M. and Di Iorio, E. and Ponzin, D. and Marchini, G. 2015	wrong population
Rateb, A. A. and Mohammed, F. N. and Sayed, K. S. and Hegazy, R. A. and Al Agha, R. R. and Rashed, L. A. and Sayed, S. S. 2015	wrong population
Rezaei Yazdi, F. and Ghahary, A. and Mirdoraghi, M. and Sarvnaz, H. and Asgardoon, M. H. and Rastegar, T. and Malek, F. and Abbasi Moayyer, T. and Ghaffari Dafchahi, K. and Takzaree, N. 2021	wrong population
Sharma, N. and Lathi, S. S. and Sehra, S. V. and Agarwal, T. and Sinha, R. and Titiyal, J. S. and Velp and ian, T. and T and on, R. and Vajpayee, R. B. 2015	wrong population
Sibilla, Mg and Zollino, I and Zamboni, M and Tessari, M and Malagoni, Am and Campioni, D and Zamboni, P. 2018	wrong population
Silva, A. and Sampaio, R. and Fern and es, R. and Pinto, E. 2014	wrong population
Srivastava, R. N. and Dwivedi, M. K. and Bhagat, A. K. and Raj, L. 2019	wrong population
Svanberg, A. and Ã–hrn, K. and BirgegÃ¥rd, G. 2015	wrong population
Szabo, C. and Brunyanszki, A. and Erdelyi, K. and Olah, G. and Coletta, C. and Yanagi, K. and Szczesny, B. and Herndon, D. 2014	wrong population

Tang, H-Y and Ma, H and Lu, M and Ling, H-J. 2013	wrong population
Tedesco, M and Bellei, B and Garelli, V and Caputo, S and Latini, A and Giuliani, M and Cota, C and Chichierchia, G and Romani, C and Foddai, Ml and et al. 2020	wrong population
Wang, X. and Chen, J. 2015	wrong population
Wang, X. P. 2012	wrong population
Wang, Z. and Hu, Y. and Wang, X. and Chen, Y. and Wu, D. and Ji, H. and Yu, C. and Fang, J. and Pan, C. and Wang, L. and Wang, S. and Guo, Y. and Lu, Y. and Wu, D. and Ren, F. and Zhu, H. and Shi, Y. 2023	wrong population
Wgealla, M. M. A. M. A. and Liang, H. and Chen, R. and Xie, Y. and Li, F. and Qin, M. and Zhang, X. 2022	wrong population
Zhong, F. L. and Li, X. X. and He, W. J. 2013	wrong population
Zollino, I and Campioni, D and Sibilla, Mg and Tessari, M and Malagoni, Am and Zamboni, P. 2019	wrong population
Abstracts from 2nd European Congress on Endometriosis. 2013	wrong population
10th International Hereditary Hemorrhagic Telangiectasia Scientific Conference. 2013	wrong population
36th Annual Conference on Shock. 2013	wrong population
Poster Abstracts, American Academy of Dermatology 72nd Annual Meeting. 2014	wrong population
Canadian Stroke Conference 2015	wrong population
LSC - 2020 - Characterizing lung resident mesenchymal stem cells in idiopathic pulmonary fibrosis patients. 2020	wrong population
Stem Cell Treatment for Diabetic Foot Ulcers: A Meta-analysis of Randomized Clinical Trials. 2023	wrong population
Arjunan, S. and Gan, S. U. and Choolani, M. and Raj, V. and Lim, J. and Biswas, A. and Bongso, A. and Fong, C. Y. 2020	wrong study design
Ding, J. Y. and Chen, M. J. and Wu, L. F. and Shu, G. F. and Fang, S. J. and Li, Z. Y. and Chu, X. R. and Li, X. K. and Wang, Z. G. and Ji, J. S. 2023	wrong study design
El-Khalawany, M. and Rageh, M. A. and Elnokrashy, I. and Ibrahim, S. M. A. 2023	wrong study design
Feldman, D. S. and McCauley, J. F. 2018	wrong study design
Garay, R. P. 2023	wrong study design
Greil, R. and Psenak, O. 2007	wrong study design
Han, Y. M. and Sheng, Y. Y. and Xu, F. and Qi, S. S. and Liu, X. J. and Hu, R. M. and Miao, Y. and Yang, Q. P. 2014	wrong study design
Karakol, P. and Bozkurt, M. 2021	wrong study design
Liang, Z. J. and Lu, X. and Li, D. Q. and Liang, Y. D. and Zhu, D. D. and Wu, F. X. and Yi, X. L. and He, N. and Huang, Y. Q. and Tang, C. and Li, H. M. 2018	wrong study design
Lu, J. and Ding, Y. and Yi, X. and Zheng, J. 2016	wrong study design
Ma, J. and Yan, X. and Lin, Y. and Tan, Q. 2020	wrong study design
Meng, X. and Gao, X. and Chen, X. and Yu, J. 2021	wrong study design
Mokdara, K. and Tangkijngamvong, N. and Pongprutthipan, M. and Koaykul, C. 2023	wrong study design
Nakano, N. and Kubota, A. and Tokunaga, M. and Tokunaga, M. and Makino, T. and Takeuchi, S. and Takatsuka, Y. and Utsunomiya, A. 2014	wrong study design

Nangâ€™ole, W. F. and Omu, A. and Ogengâ€™o, J. A. and Agak, G. W. 2022	wrong study design
Niebergall-Roth, E. and Frank, N. Y. and Ganss, C. and Frank, M. H. and Kluth, M. A. 2022	wrong study design
Oh, H. A. and Kwak, J. and Kim, B. J. and Jin, H. J. and Park, W. S. and Choi, S. J. and Oh, W. and Um, S. 2020	wrong study design
Panero, A. J. and Hirahara, A. M. and Andersen, W. J. and Rothenberg, J. and Fierro, F. 2019	wrong study design
PliszczyÅ„ski, J. and Nita, M. and Kowalewski, C. and WoÅºniak, K. and Eljaszewicz, A. and Moniuszko, M. and KamiÅ„ski, A. and Åšladowski, D. and Zimek, Z. and Majewski, S. and Kosieradzki, M. and Fiedor, P. 2020	wrong study design
Rateb, A. A. and Mohammed, F. N. and Sayed, K. S. and Hegazy, R. A. and Al Agha, R. R. and Rashed, L. A. and Sayed, S. S. 2015	wrong study design
Robbins, M. E. 2008	wrong study design
Shim, J. H. 2015	wrong study design
Tanha, S. and Vakilinezhad, M. and Javar, H. A. 2018	wrong study design
Vu, D. M. and Nguyen, V. T. and Nguyen, T. H. and Do, P. T. X. and Dao, H. H. and Hai, D. X. and Le, N. T. and Nguyen, X. H. and Than, U. T. T. 2022	wrong study design
Yam, G. H. and Yang, T. and Geary, M. L. and Santra, M. and Funderburgh, M. and Rubin, E. and Du, Y. and Sahel, J. A. and Jhanji, V. and Funderburgh, J. L. 2023	wrong study design
Yeni, B. 2019	wrong study design
Yusharyahya, Sn and Ven, Japranata V and Sitohang, Ibs and Legiawati, L and Novianto, E and Suseno, Ls and Rachmani, K. 2023	wrong study design
Zhang, M. L. 2008	wrong study design
El Kahky, H. and Diab, H. and Helal, H. A. 2017	wrong study design
Fukuoka, H. and Suga, H. 2015	wrong study design
https://trialsearch.who.int/Trial2.aspx?TrialID=IRCT20200127046282N27. 2023	wrong study design
Kmiecik, J. and Kulus, M. J. and Popiel, J. and Cekiera, A. and Cegielski, M. 2021	wrong study design
Nangâ€™ole, W. F. and Omu, A. and Ogengâ€™o, J. A. and Agak, G. W. 2022	wrong study design
Schulman, C. I. and Namias, N. and Pizano, L. and Rodriguez-Menocal, L. and Aickara, D. and Guzman, W. and C and anedo, A. and Mar and a, E. and Beirn, A. and McBride, J. D. and Badiavas, E. V. 2022	wrong study design
Vu, D. M. and Nguyen, V. T. and Nguyen, T. H. and Do, P. T. X. and Dao, H. H. and Hai, D. X. and Le, N. T. and Nguyen, X. H. and Than, U. T. T. 2022	wrong study design
Irish Endocrine Society 39th Annual Meeting. 2014	wrong study design
13th Biennial Congress of the European Association of Oral Medicine, EAOM 2016	wrong study design
25th European Congress of Perinatal Medicine Abstracts. 2016	wrong study design
Global Spine Congress 2018, GSC 2018	wrong study design
ICS 2020 LAS VEGAS SCIENTIFIC PROGRAMME	wrong study design
Abbas, O. L. and Ã–zatik, O. and GÃ¶nen, Z. B. and Ã–ÄŸÃ¼t, S. and Ã–zatik, F. Y. and SalkÄ±n, H. and Musmul, A. 2019	wrong study design
Abd El All, H. S. and Abd El Kareem, G. F. and El Maged, R. A. and Ayada, M. M. 2009	wrong study design
Abdal-hay, A. and Barakat, N. A. M. and Lim, J. K. 2013	wrong study design

Adlerz, K. and Lembong, J. and Olsen, T. and Rowley, J. and Ahsan, T. 2019	wrong study design
Adlerz, K. and Trempel, M. and Rowley, J. A. and Ahsan, T. 2019	wrong study design
Adlerz, K. and Trempel, M. and Wang, D. and Kirian, R. D. and Rowley, J. A. and Ahsan, T. 2019	wrong study design
Aghajanova, L. and Houshdaran, S. and Balayan, S. and Manvelyan, E. and Irwin, J. C. and Huddleston, H. G. and Giudice, L. C. 2018	wrong study design
Ahmed, A. S. and Chavarria, J. and Brenneman, T. and Johnson, K. and Antonsen, E. and Rosenfeld, S. 2016	wrong study design
Ahn, Y. and Kim, Y. S. and Hong, M. H. and Song, C. H. and Jeong, M. H. and Cho, J. G. and Park, J. C. and Kang, J. C. 2009	wrong study design
Aho, O. M. and Lehenkari, P. and Ristiniemi, J. and Lehtonen, S. and Risteli, J. and LeskelaÌˆ, H. V. 2013	wrong study design
Aiba, S. and Uddin, Z. and Nakagawa, S. and Sugawara, S. and Rikiishi, H. and Kumagai, K. and Tagami, H.	wrong study design
Aiba-Kojima, E. and Tsuno, N. H. and Inoue, K. and Matsumoto, D. and Shigeura, T. and Sato, T. and Suga, H. and Kato, H. and Nagase, T. and Gonda, K. and Koshima, I. and Takahashi, K. and Yoshimura, K. 2002	wrong study design
Akimoto, M. and Hashimoto, H. and Shigemoto, M. and Maeda, A. and Yamashita, K. 2005	wrong study design
Al Fessi, R. and Rizqiawan, A. and Chairani, E. and Pratiwi, E. S. and Purwati and Pramono, C. 2018	wrong study design
Al-Mousawi, A. M. and Jeschke, M. G. and Herndon, D. N. 2020	wrong study design
Alamein, M. A. and Stephens, S. and Liu, Q. and Skabo, S. and Warnke, P. H. 2013	wrong study design
Alamgeer, M. and Brown, T. J. and Briggs, P. and Midolo, P. and Markman, B. and Marini, K. and Banakh, I. and Watkins, D. N. and Ganju, V. 2013	wrong study design
Alessio, N. and Pipino, C. and Mandatori, D. and Di Tomo, P. and Ferone, A. and Marchiso, M. and Melone, M. A. B. and Peluso, G. and Pandolfi, A. and Galderisi, U. 2018	wrong study design
Alessio, N. and Stellavato, A. and Squillaro, T. and Del Gaudio, S. and Di Bernardo, G. and Peluso, G. and De Rosa, M. and Schiraldi, C. and Galderisi, U. 2018	wrong study design
Alexander, B. D. and Dodds Ashley, E. S. and Addison, R. M. and Alspaugh, J. A. and Chao, N. J. and Perfect, J. R. 2006	wrong study design
Alharbi, Z. and OplÃ¤nder, C. and Almakadi, S. and Fritz, A. and Vogt, M. and Pallua, N. 2013	wrong study design
Alhawarat, F. M. and Hammad, H. M. and Hijjawi, M. S. and Sharab, A. S. and Abuarqoub, D. A. and Al Shhab, M. A. and Zihlif, M. A. 2019	wrong study design
Ali, M. and Kwak, S. H. and Byeon, J. Y. and Choi, H. J. 2023	wrong study design
Ali, M. R. W. and Mustafa, M. and BÃ¥rdsen, A. and Bletsa, A. 2019	wrong study design
Alijotas-Reig, J. and FernÃ¡ndez-Figueras, M. T. and Puig, L. 2013	wrong study design
Alkabie, S. and Boileau, A. J. 2016	wrong study design
Alluri, R. and Jakus, A. and Bougioukli, S. and Pannell, W. and Sugiyama, O. and Tang, A. and Shah, R. and Lieberman, J. R. 2018	wrong study design
Almeida, L. D. F. and Babo, P. S. and Silva, C. R. and Rodrigues, M. T. and Hebling, J. and Reis, R. L. and Gomes, M. E. 2018	wrong study design
Alper, J. 2009	wrong study design

Alzoghaibi, M. A. 2013	wrong study design
Amann, E. M. and GroÃŸ, A. and Rojewski, M. T. and Kestler, H. A. and Kalbitz, M. and Brenner, R. E. and Huber-Lang, M. and Schrezenmeier, H. 2019	wrong study design
Amorim, S. and Martins, A. and Neves, N. M. and Pires, R. A. and Reis, R. L. 2013	wrong study design
Anbar, B. and Verboket, R. and Schaible, A. and Kontradowitz, K. and Marzi, I. and Henrich, D. 2019	wrong study design
Anderson, J. J. and Boone, J. J. and Hansen, M. and Brady, C. and Gough, A. and Swayzee, Z. 2014	wrong study design
Andia, I. and Abate, M. 2014	wrong study design
Andreassi, M. and Bilenchi, R. 2019	wrong study design
Angele, M. K. and Frantz, M. C. and Chaudry, I. H. 2006	wrong study design
Angele, P. and MÃ¼ller, R. and Schumann, D. and Englert, C. and Zellner, J. and Johnstone, B. and Yoo, J. and Hammer, J. and Fierlbeck, J. and Angele, M. K. and Nerlich, M. and Kujat, R. 2009	wrong study design
Ansary, M. and Gabr, H. and Osama, A. and Anany, H. and Gad, A. 2013	wrong study design
Butt, G and Hussain, I and Ahmad, Fj and Choudhery, Ms. 2020	wrong intervention
Dâ€™Andrea, M. and Perrotta, A. and Ferrillo, M. and Cantelli, M. and Donnarumma, M. and Fabbrocini, G. 2019	wrong intervention
Donaparthi, N. and Chopra, A. 2016	wrong intervention
Elizondo, J. 2017	wrong intervention
GÃ¼nter, C. I. and Bader, A. and Dornseifer, U. and Egert, S. and Dunda, S. and Grieb, G. and Wolter, T. and Pallua, N. and von Wild, T. and Siemers, F. and MailÃ¤nder, P. and Thamm, O. and Ernert, C. and Steen, M. and Sievers, R. and Reichert, B. and Rahmanian-Schwarz, A. and Schaller, H. and Hartmann, B. and Otte, M. and Kehl, V. and Ohmann, C. and Jelkmann, W. and Machens, H. G. 2013	wrong intervention
Kadoya, K and Makino, Et and Jiang, Li and Bachelor, M and Chung, R and Tan, P and Cheng, T and Naughton, Gk and Mehta, Rc 2017	wrong intervention
https://clinicaltrials.gov/show/NCT03013049. 2016	wrong intervention
Osama, Ab and Ahdallah, Ek and Ali, Ekm and Mamdouh, Na. 2020	wrong intervention
PliszczyÅ„ski, J. and Nita, M. and Kowalewski, C. and WoÅºniak, K. and Eljaszewicz, A. and Moniuszko, M. and KamiÅ„ski, A. and Åšladowski, D. and Zimek, Z. and Majewski, S. and Kosieradzki, M. and Fiedor, P. 2020	wrong intervention
Ramirez, J. I. and Maguina, P. 2016	wrong intervention
Razmi, M. and Parsad, D. and Kumaran, S. 2016	wrong intervention
Sabirov, U. Yu and Azimova, F. V. and Toirov, B. A. and Muminova, S. R. 2020	wrong intervention
Tan, P. C. and Chao, P. C. and Cheng, C. and Chen, C. H. and Huang, R. L. and Zhou, S. B. and Xie, Y. and Li, Q. F. 2021	wrong intervention
Tedesco, M and Bellei, B and Garelli, V and Caputo, S and Latini, A and Giuliani, M and Cota, C and Chichierchia, G and Romani, C and Foddai, Ml and et al. 2020	wrong intervention
Vashisht, Kr and Arava, Sk and Tembhre, Mk and Parihar, As and Sharma, Vk and Das, Bk and Sreenivas, V and Sethuraman, G and Gupta, S. 2020	wrong intervention
Zhang, Dm and Hong, Ws and Fu, Lf and Wei, Xd and Xu, Ae. 2014	wrong intervention
Abaroa, F. and Reyes, K. and Barrera, D. and CastelÃ¡n, E. and Montemayor, B.	wrong intervention

and Izabal, G. and PÃ©rez, I. and Moreno, A. 2016	
Abate, M. and Salini, V. and Schiavone, C. and Andia, I. 2017	wrong intervention
Abramenko, I. V. and Bilous, N. I. and Chumak, S. A. and Loganovsky, K. M. 2017	wrong intervention
Addo, E. K. and Allman, S. J. and Arunkumar, R. and Gorka, J. E. and Harrison, D. Y. and Varner, M. W. and Bernstein, P. S. 2023	wrong intervention
Adds, P. J. and Hunt, C. J. and Dart, J. K. G. 2001	wrong intervention
Advani, A. and Elson, P. and Hsi, E. D. and Davis, R. and Kalaycio, M. and Sobecks, R. and Copelan, E. and Duong, H. K. and Foster, B. and Rush, M. L. and Farhat, L. and Sekeres, M. A. 2012	wrong intervention
Ahmed, N. S. and Ghatak, S. and El Masry, M. S. and Gnyawali, S. C. and Roy, S. and Amer, M. and Everts, H. and Sen, C. K. and Khanna, S. 2017	wrong intervention
Alemohammad, H. and Motafakkerazad, R. and Asadzadeh, Z. and Farsad, N. and Hemmat, N. and Najafzadeh, B. and Vasefifar, P. and Baradaran, B. 2022	wrong intervention
AlGhamdi, K. M. and Khurrum, H. and TaÃ¯eb, A. and Ezzedine, K. 2012	wrong intervention
Alten, J. A. and Benner, K. and Green, K. and Toole, B. and Tofil, N. M. and Winkler, M. K. 2009	wrong intervention
Alyousef, Aa and Divakar, Dd and Muzaheed. 2017	wrong intervention
Gennai, A. and Zambelli, A. and Repaci, E. and Quarto, R. and Baldelli, I. and Fraternali, G. and Bernardini, F. P. 2017	no comparator
Ichihashi, M. and Tanaka, M. and Iizuka, T. and Totsuka, H. and Tominaga, E. and Hitomi, Y. and Ando, H. and Nishikata, T. and Mizutani, K. I. 2023	no comparator
Kamishima, T. and Hirabe, C. and Ohnishi, T. and Taguchi, J. and Myint, K. Z. Y. and Koga, S. 2023	no comparator
Makino, E. and Tan, P. and Mehta, R. 2018	no comparator
Mathen, C. and Dsouza, W. 2022	no comparator
Schulman, Ci and C and anedo, A and Rodriguez-Menocal, L and Guzman, W and McBride, J and Pizano, L and Namias, N and Orozco, O and Badiavas, Ev. 2018	no comparator
Bhat, S. and Amirthalingam, M. and Ballambat, S. P. and Bhupasandra Vasudev, M. and Gupta, P. K. and Padya, B. S. and Mutalik, S. and Seetharam, R. N. 2022	no comparator
ClÃ©, D. V. and Catto, L. F. B. and Gutierrez-Rodrigues, F. and Donaires, F. S. and Pinto, A. L. and Santana, B. A. and Darrigo, L. G. and Valera, E. T. and Koenigkam-Santos, M. and Baddini-Martinez, J. and Young, N. S. and Martinez, E. Z. and Calado, R. T. 2023	no comparator
Czarnecka, A. and Odziomek, A. and Murzyn, M. and Dubis, J. and BagÅ‚aj-Oleszczuk, M. and Hyncewicz-GwÃ³Åºdźº, A. 2021	no comparator
Kesper, C. and Heinzelmann, J. and Viestenz, A. and Hammer, T. and Foja, S. and Stein, M. and Viestenz, A. 2023	no comparator
MartÃnez-SantamarÃa, L. and Maseda, R. and SacedÃ³n, R. and De Arriba, M. C. and Jimenez, E. and GarcÃa, M. and ChacÃ³n, E. and SuÃ¡rez-Sancho, S. and Fernandez-Bello, I. and Carretero, M. and YaÃ±ez, R. and Lwin, S. M. and Martinez-Queipo, M. and Liu, L. and Mee, J. and De Paz, R. and Borobia, A. and FernÃ¡ndez-Santos, M. E. and Butta, N. and Yuste, V. and McGrath, J. A. and Del RÃo, M. and Vicente, A. and De Lucas, R. and EscÃ¡mez, M. J. 2020	no comparator
Sun, L. and Wang, D. and Zhang, H. and Liang, J. and Feng, X. 2010	no comparator
Rashidghamat, E. and Kadiyirire, T. and Ayis, S. and Petrof, G. and Liu, L. and	no comparator

Pullabhatla, V. and Ainali, C. and Guy, A. and Aristodemou, S. and McMillan, J. R. and Ozoemena, L. and Mee, J. and Pramanik, R. and Saxena, A. and Nuamah, R. and de Rinaldis, E. and Serrano, S. and Maurin, C. and Martinez-Queipo, M. and Lwin, S. M. and Ilic, D. and Martinez, A. and Dazzi, F. and Slaper-Cortenbach, I. and Westinga, K. and Zeddies, S. and van den Broek, M. and Onoufriadis, A. and Mellerio, J. E. and McGrath, J. A. 2020	
Audet, R. G. and Diller, R. B. and Dominguez, D. and Bardsley, T. A. and Kellar, R. S. 2019	wrong outcome
Banlue, A. and Kaewmuangmoon, J. and Janebodin, K. and Tansriratanawong, K. 2023	wrong outcome
Figueiredo, G. S. and Hogg, J. and Okonkwo, A. and Baylis, O. J. and Berry, M. and Ali, S. and Lako, M. and Figueiredo, F. C. 2023	wrong outcome
Frias, F. and Matos, B. and Jarnalo, M. and Freitas-Ribeiro, S. and Reis, R. L. and Pirraco, R. P. and Horta, R. 2023	wrong outcome
Wgealla, M. M. A. M. A. and Liang, H. and Chen, R. and Xie, Y. and Li, F. and Qin, M. and Zhang, X. 2022	wrong outcome
Bai, K. H. and Hu, C. and Li, Q. Q. and Wang, F. 2019	wrong outcome
Bai, M. and Wang, H. and Liu, J. and Liu, J. 2022	wrong outcome
Bai, X. Z. and Hu, D. H. and Bai, L. and Liu, Y. and Su, Y. J. and Tang, C. W. 2012	wrong outcome
Bajouri, A. and Dayani, D. and Taj Sharghi, A. and Karimi, S. and Niknejadi, M. and Bidgoli, K. M. and Madani, H. and Kakroodi, F. A. and Blourieh, T. and Mardpour, S. and Jaroughi, N. and Aghdami, N. and Ataie-Fashtami, L. and Shafiyan, S. and Vosough, M. 2023	all group stem cells
Rahmadewi, R and Retha, R and Pitasari, Da and Kusumastanto, Va and Ardhaninggar, Aaa and Citrashanty, I and Sari, M and Umborowati, Ma and Prakoeswa, Crs. 2020	all group stem cells
Yusharyahya, Sn and Ven, Japranata V and Sitohang, Ibs and Legiawati, L and Novianto, E and Suseno, Ls and Rachmani, K. 2023	all group stem cells
Dabiri, G. and Heiner, D. and Falanga, V. 2013	no comparator
Dixit, P. and Donnelly, H. and Edamatsu, M. and Galvin, I. and Bunton, R. and Katare, R. 2015	all group stem cells
Dolp, R. and Eylert, G. and Auger, C. and Aijaz, A. and Chen, Y. A. and Amini-Nik, S. and Parousis, A. and Datu, A. K. and Jeschke, M. G. 2021	all group stem cells
Brockmann, I. and Ehrenpfordt, J. and Sturmheit, T. and Brandenburger, M. and Kruse, C. and Zille, M. and Rose, D. and Boltze, J. 2018	wrong study design
Buonocore, D. and Nobile, V. and Michelotti, A. and Marzatico, F. 2013	no comparator
Burgos-Alonso, N. and Lobato, I. and Hernandez, I. and Sebastian, K. S. and Rodriguez, B. and Grandes, G. and Andia, I. 2017	wrong intervention

REFERENCES:

1. Lee HJ, Lee EG, Kang S, Sung JH, Chung HM, Kim DH. Efficacy of Microneedling Plus Human Stem Cell Conditioned Medium for Skin Rejuvenation: A Randomized, Controlled, Blinded Split-Face Study. Ann Dermatol. 2014;26(5):584.
2. Liang X, Li J, Yan Y, Xu Y, Wang X, Wu H, Liu Y, Li L and Zhuo F. Efficacy of Microneedling Combined With Local Application of Human Umbilical Cord-Derived Mesenchymal Stem Cells Conditioned Media in Skin Brightness and Rejuvenation: A Randomized Controlled Split-Face Study. Front Med [Internet]. 2022 [cited 2023 Nov 30];9.
3. Widianingsih NPS, Setyaningrum T, Prakoeswa CRS. The efficacy and safety of fractional erbium yag laser combined with topical amniotic membrane stem cell (AMSC) metabolite product for facial rejuvenation: A controlled, split-face study. Dermatol Rep [Internet]. 2019 Mar 29
4. Prakoeswa CRS, Pratiwi FD, Herwanto N, Citrashanty I, Indramaya DM, Murtiastutik D, Sukanto H, Rantam FA. The effects of amniotic membrane stem cell-conditioned medium on photoaging. J Dermatolog Treat. 2019 Aug;30(5):478-482.
5. Charles-de-Sá L, Gontijo-de-Amorim N, Sbarbati A, Benati D, Bernardi P, Borojevic R, Carias RBV, Rigotti G. Photoaging Skin Therapy with PRP and ADSC: A Comparative Study. Stem Cells Int. 2020 Jul 16;2020:2032359.
6. Park, G., Kwon, H.H., Seok, J., Yang, S.H., Lee, J., Park, B., Shin, E., & Park, K. Efficacy of combined treatment with human adipose tissue stem cell-derived exosome-containing solution and microneedling for facial skin aging: A 12-week prospective, randomized, split-face study. J Cosmet Dermatol. 2023; 22:3418-3426.
7. Wu DC, Goldman MP. A Prospective, Randomized, Double-blind, Split-face Clinical Trial Comparing the Efficacy of Two Topical Human Growth Factors for the Rejuvenation of the Aging Face. J Clin Aesthetic Dermatol. 2017 May;10(5):31–5.
8. Zhou SB, Zhang GY, Xie Y, Zan T, Gan YK, Yao CA, Chiang CA, Wang J, Liu K, Li H, Zhou J, Yang M, Gu B, Xie F, Pu LQ, Magee WP 3rd, Li QF. Autologous Stem Cell Transplantation Promotes Mechanical Stretch Induced Skin Regeneration: A Randomized Phase I/II Clinical Trial. EBioMedicine. 2016 Nov;13:356-364.
9. Claudio-da-Silva C, Baptista LS, Carias RBV, Menezes Neto HDC, Borojevic R. Cultura autóloga de células-tronco mesenquimais de tecido adiposo para o tratamento de rítides faciais. Rev Colégio Bras Cir. 2009 Aug;36(4):288–91.
10. Butt G, Hussain I, Ahmad FJ, Choudhery MS. Stromal vascular fraction-enriched platelet-rich plasma therapy reverses the effects of androgenetic alopecia. J Cosmet Dermatol. 2020 May;19(5):1078–85.
11. Gan Y, Du L, Wang H, Li K, Fan Z, Sun P, Zhang J, Hu Z, Miao Y. A Clinical Trial of Treating Androgenic Alopecia with Mesenchymal Stem Cell Suspension Derived from Autologous Hair Follicle. Plast Reconstr Surg. 2024 Sep 1;154(3):444e-450e.
12. Lee YI, Kim J, Kim J, Park S, Lee JH. The Effect of Conditioned Media From Human Adipocyte-Derived Mesenchymal Stem Cells on Androgenetic Alopecia After Nonablative Fractional Laser Treatment. Dermatol Surg. 2020 Dec;46(12):1698–704.

13. Tak YJ, Lee SY, Cho AR, Kim YS. A randomized, double-blind, vehicle-controlled clinical study of hair regeneration using adipose-derived stem cell constituent extract in androgenetic alopecia. Stem Cells Transl Med. 2020 Aug 1;9(8):839–49.
14. Gentile P, Scioli MG, Cervelli V, Orlandi A, Garcovich S. Autologous Micrografts from Scalp Tissue: Trichoscopic and Long-Term Clinical Evaluation in Male and Female Androgenetic Alopecia. BioMed Res Int. 2020 Jan 28; 2020:1–10.
15. Han HS, Park KY, Ko EJ, Kim BJ. Efficacy of a Hair Tonic Containing Human Umbilical Cord Blood Mesenchymal Stem Cell-derived Conditioned Media in patients with Androgenetic Alopecia. Korean J Dermatol. 2019;57(5):251-257.
16. Legiawati L, Suseno LS, Sitohang IBS, Yusharyahya SN, Pawitan JA, Liem IK, et al. Combination of adipose-derived stem cell conditioned media and minoxidil for hair regrowth in male androgenetic alopecia: a randomized, double-blind clinical trial. Stem Cell Res Ther. 2023 Aug 21;14(1):210.
17. Tsuboi R, Niiyama S, Irisawa R, Harada K, Nakazawa Y, Kishimoto J. Autologous cell–based therapy for male and female pattern hair loss using dermal sheath cup cells: A randomized placebo-controlled double-blinded dose-finding clinical study. J Am Acad Dermatol. 2020 Jul;83(1):109–16.
18. Abouzaid AM, El Mokadem ME, Aboubakr AK, Kassem MA, Al Shora AK, Solaiman A. Effect of autologous fat transfer in acute burn wound management: A randomized controlled study. Burns. 2022 Sep;48(6):1368–85.
19. Abou Eitta RS, Ismail AA, Abdelmaksoud RA, Ghezlan NA, Mehanna RA. Evaluation of autologous adipose-derived stem cells vs. fractional carbon dioxide laser in the treatment of post acne scars: a split-face study. Int J Dermatol. 2019 Oct;58(10):1212–22.
20. Roohaninasab M, Khodadad F, Sadeghzadeh-Bazargan A, Atefi N, Zare S, Jafarzadeh A, Rahimi ST, Nouri M, Nilforoushzadeh MA, Behrangi E, Goodarzi A. Efficacy of fractional CO_2 laser in combination with stromal vascular fraction (SVF) compared with fractional CO_2 laser alone in the treatment of burn scars: a randomized controlled clinical trial. Stem Cell Res Ther. 2023 Sep 23;14(1):269.
21. Fan D, Zeng M, Xia Q, Wu S, Ye S, Rao J, Lin D, Zhang H, Ma H, Han Z, Guo X, Liu Z. Efficacy and safety of umbilical cord mesenchymal stem cells in treatment of cesarean section skin scars: a randomized clinical trial. Stem Cell Res Ther. 2020 Jun 25;11(1):244.
22. Kwon HH, Yang SH, Lee J, Park BC, Park KY, Jung JY, Bae Y, Park GH. Combination Treatment with Human Adipose Tissue Stem Cell-derived Exosomes and Fractional CO2 Laser for Acne Scars: A 12-week Prospective, Double-blind, Randomized, Split-face Study. Acta Derm Venereol. 2020 Nov 4;100(18): adv00310.
23. Park CS, Park JH, Kim CR, Lee JH. Objective analysis of volume restoration in atrophic acne scars and skin pores: a split study using human stem cell-conditioned media. J Dermatolog Treat. 2021 Feb;32(1):73-77.
24. G. Monil, M. Snehal, Krishna C. Veligandla, R. Rahul, D. Gauri, K. Bhavesh, and S. Snehal. 2023. Epidemiology and Treatment Aspects of Hair Loss in India – A Cross-Sectional, Multicentre, Database Study (HAILO). Asian Journal of Research in Dermatological Science 6 (1):22–32.
25. Krupa Shankar D, Chakravarthi M, Shilpakar R. Male androgenetic alopecia: population-based study in 1,005 subjects. Int J Trichology. 2009 Jul;1(2):131-3.

26. Żwierełło W, Piorun K, Skórka-Majewicz M, Maruszewska A, Antoniewski J, Gutowska I. Burns: Classification, Pathophysiology, and Treatment: A Review. Int J Mol Sci. 2023 Feb 13;24(4):3749.
27. Li D, Fan S, Zhao H, Song J, Li W, Xu X. Global, regional and national burden of skin and subcutaneous diseases: a systematic analysis of the Global Burden of Disease Study 2021. Int Health. 2026 Mar 3;18(2):183-196.