Supplementary Table 1 - Overview of the ongoing clinical trials (CTs), available CDG *in vitro* and *in vivo* models and biomarkers and dietary supplementation strategies, being tested and used in these disorders. NA – Not available.

	ALG1-CDG Chitobiosyldiphospho-dolichol β-mannosyltransferase	**ALG6-CDG α-1,3-glucosyltransferase**	**ALG13-CDG UDP-GlcNAc transferase**	**ATP6AP1-CDG Accessory subunit of the vacuolar (V)-ATPase protein pump**	**CAD-CDG Tri-functional protein (ATase, CPSase, ATCase and DHOase)**	**CCDC115-CDG Coiled-coil domain-Containing protein 115**
CTs	Interventional NCT02955264	Interventional NCT02955264	NA		NA	NA
***In vitro* models**	*S. cerevisiae alg1* mutant (K57-6C strain) [24,34,41]	*S. cerevisiae alg6* mutant [87,88]	*S. cerevisiae* "Tet-Off " strain (pYGL047W::kanR-tet07-TATA URA3::CMV-tTA MATa his3-1 leu2-0 met15-0) [281]	*S. cerevisiae* (*voa1::H vma21QQ* strain) [97]	*CAD*-deficient CHO-G9C [100]	*S. cerevisiae* strains: HY13 (vma22Δ::LEU2) KHY34 (vma22Δ::LEU2 pep4-3) KHY38 (vma22Δ::URA3) KHY39 (vma22Δ::URA3 pep4-3) [105]
	S. cerevisiae alg1 mutant (PRY56 strain) [31]	MI8-5 *Alg6*$^{-/-}$ [89]				HeLa (*CCDC115* knockdown using CRISPR/Cas9) [106]
***In vivo* models**	NA	NA	NA	Zebrafish (*Atp6ap1b*$^{a82/a82}$,*Atp6ap1b* knockdown) [98]	*C. elegans pyr-1(cu8)* mutant [85]	NA
					D. melanogaster Rudimentary mutant [86]	

Supplementary Table 2 – continued.

	ALG1-CDG Chitobiosyldiphospho-dolichol β-mannosyltransferase	**ALG6-CDG α-1,3-glucosyltransferase**	**ALG13-CDG UDP-GlcNAc transferase**	**ATP6AP1-CDG Accessory subunit of the vacuolar (V)-ATPase protein pump**	**CAD-CDG Tri-functional protein (ATase, CPSase, ATCase and DHOase)**	**CCDC115-CDG Coiled-coil domain-Containing protein 115**
***In vivo* models**	NA	NA	NA	Chimeric Mouse (w/ *Atp6ap1* reduced expression) [99]	Zebrafish *Perplexed* (*plx*^{a52}) mutant [87] Zebrafish Transgenic *Tg(p2xr3.2:gfp)*^{sl23} mutant [88]	NA
Biomarkers	$GlcNAc_2$-PP-dolichol [31]	Dolichol-linked $Man_9GlcNAc_2$ [177]	GlcNAc-PP-dolichol	NA	NA	NA
	N-tetrasaccharide (Neu_5Ac_2,6Gal_1,4-GlcNAc_1,4GlcNAc) [34,178]	AGA [166]	ICAM-1 [190]			
		β-trace protein [180,189]				
Dietery therapy	Man suppl [178]	NA	Gal suppl [190]	NA	Uridine suppl [69,100]	Iron suppl [106]
Transplantation	NA	NA	NA	Liver transplantation (approved therapy in Europe)	NA	Liver transplantation (approved therapy in Europe) [224]

Supplementary Table 3 - continued.

	ALG1-CDG Chitobiosyldiphospho-dolichol β-mannosyltransferase	**ALG6-CDG α-1,3-glucosyltransferase**	**ALG13-CDG UDP-GlcNAc transferase**	**ATP6AP1-CDG Accessory subunit of the vacuolar (V)-ATPase protein pump**	**CAD-CDG Tri-functional protein (ATase, CPSase, ATCase and DHOase)**	**CCDC115-CDG Coiled-coil domain-Containing protein 115**
Gene therapy	NA	NA	NA	NA	NA	NA
Antisense therapy	NA	NA	NA	NA	NA	NA
PCs	NA	NA	NA	NA	NA	NA
Others	NPCRS [255,256]	NPCRS [255,256]	NPCRS [255,256]	NPCRS [255,256]	NPCRS [255,256]	NPCRS [255,256]
	DOLK-CDG Dolichol kinase	**GNE-CDG UDP-GlcNAc 2-epimerase/ ManNAc kinase**	**ISPD-CDG Isoprenoid synthase domain-containing protein**	**MAGT1-CDG Magnesium transporter 1**	**MPI-CDG Mannose-6-phosphate isomerase**	**NANS-CDG CMP-N-acetylneuraminic acid synthetase**
CTs	NA	Interventional NCT02346461 NCT01634750 NCT01517880	NA	NA	NA	SA trial approved but discontinued due unfavorable results in GNE-CDG

Supplementary Table 4 - continued.

	DOLK-CDG Dolichol kinase	**GNE-CDG UDP-GlcNAc 2-epimerase/ ManNAc kinase**	**ISPD-CDG Isoprenoid synthase domain-containing protein**	**MAGT1-CDG Magnesium transporter 1**	**MPI-CDG Mannose-6-phosphate isomerase**	**NANS-CDG CMP-N-acetylneuraminic acid synthetase**
CTs	-	Interventional NCT01830972 NCT02377921 NCT02736188 NCT02731690 NCT01359319 NCT00195637 NCT01236898 NCT02196909	-	-	-	-
		Observational NCT01784679 NCT01902940 NCT01417533				
In vitro models	*S. cerevisiae Sec59* mutant [18,29]	CHO *Gne*-deficient *Lec3* mutant [19,26,28,107,108]	HEK293 *Ispd* knockout [68]	*S. cerevisiae Alr1Δ* strain [90]	HT-29 *Mpi* knockdown [59]	NA
		HEK293 (D176V-*Gne*, V572L-*Gne* and *Gne* knockdown) [39,109]				
		BJA-B K20 (D176V-*Gne* and M712L-*Gne)* [110,111,206,207]				
		HL60-I [110,111]	HAP1 *Ispd* knockout [150]	HEK293 *Magt1* knock down [90]		
		Sf9 M712T-*Gne* [40]				
		Gne$^{-/-}$ mice ESC [74,112,113,115]				

Supplementary Table 5 - continued.

	DOLK-CDG Dolichol kinase	**GNE-CDG UDP-GlcNAc 2-epimerase/ ManNAc kinase**	**ISPD-CDG Isoprenoid synthase domain-containing protein**	**MAGT1-CDG Magnesium transporter 1**	**MPI-CDG Mannose-6-phosphate isomerase**	**NANS-CDG CMP-N-acetylneuraminic acid synthetase**
***In vivo* models**	NA	Mouse (*Gne*$^{-/-}$, *Gne*$^{+/-}$) [74,116]	Mouse (*Ispd*$^{L79*/L79*}$) [151]	Zebrafish (*Magt1* knock-out) [90] NA	Mouse (*Mpi*$^{Y255C/Y255C}$) [72]	Zebrafish model (*nansa* and *nansb* knockdown) [122]
		Mouse (*Gne*$^{M712T/M712T}$) [76,81,117]				
		Mouse (Gne$^{(-/-)}$ h*GNE*D176V-Tg) [118,119]	Mouse (Knock-out) [152]		Mouse (Mpi$^{-/-}$) [91]	
		Mouse (*Gne*$^{V572L/V572L}$) [76,81,117]				
		Mouse (Transgenic FVBN-GNR-R263L) [120]	Zebrafish (Knock-out) [153]		Zebrafish (w/ 13% of *mpi* activity) [92]	
		Zebrafish (*gne* knock-out) [121]				
Biomarkers	NA	GM3 and GD3 gangliosides [181,182]	NA	NA	N-tetrasaccharide (Neu$_5$Ac_2,6Gal_1,4-GlcNAc_1,4GlcNAc [178]	NA
		NCAM [116,183]			AGA [166]	
		Thomsen-Friedenreich (T)-antigen [184]			ICAM-I [174,175]	

Supplementary Table 6 - continued.

	DOLK-CDG Dolichol kinase	**GNE-CDG UDP-GlcNAc 2-epimerase/ ManNAc kinase**	**ISPD-CDG Isoprenoid synthase domain-containing protein**	**MAGT1-CDG Magnesium transporter 1**	**MPI-CDG Mannose-6-phosphate isomerase**	**NANS-CDG CMP-N-acetylneuraminic acid synthetase**
Diatery therapy	NA	ManNAc suppl [66,80–82,117]	Ribitol suppl [68,150]	Mg^{2+} suppl [63,215]	Man suppl [49,160–169]	SA suppl [122]
		ManN suppl [78,83]				
		SA suppl [78,82,83]				
		6′-sialyllactose suppl [82,84]				
		Ac_4ManNAc suppl [83,207]				
Transplantation	Heart transplantation [252,253]	NA	NA	Hematopoietic cell transplantation [215]	Liver transplantation (approved therapy in Europe) [171]	NA
Gene therapy	NA	AVV8 [61,243]	NA	NA	NA	NA
		AVV-TS [244]				
		GNE-lipoplex [28,246–248]				

Supplementary Table 7 – continued.

	DOLK-CDG Dolichol kinase	**GNE-CDG UDP-GlcNAc 2-epimerase/ ManNAc kinase**	**ISPD-CDG Isoprenoid synthase domain-containing protein**	**MAGT1-CDG Magnesium transporter 1**	**MPI-CDG Mannose-6-phosphate isomerase**	**NANS-CDG CMP-N-acetylneuraminic acid synthetase**
Antisense therapy	NA	NA	NA	NA	NA	NA
PCs	NA	NA	NA	NA	NA	NA
Others	NPCRS [255,256]	NPCRS [255,256]	NPCRS [255,256] GNEM-FAS [261] REMUDY [262,263]	NPCRS [255,256]	NPCRS [255,256]	NPCRS [255,256]
	PGM1-CDG Phosphoglucomutase 1	**PGM3-CDG Phosphoglucomutase 3**	**PIGA-CDG Phosphatidylinositol N-acetylglucosaminyltransferase (subunit A)**	**PIGM-CDG GPI α-1,4-mannosyltransferase I**	**PIGO-CDG GPI ethanolamine phosphate transferase 3**	**PMM2-CDG Phosphomannomutase 2**
CTs	Interventional NCT02955264	NA	NA	NA	NA	Interventional NCT03250728 2017-000810-44 Observational NCT03173300
***In vitro* models**	HeLa *Pgm1* and *LDB3* two hybrid system [123]	NA	hiPSC (hypomorphic PIGAc.1234C>T and *Piga* null [145]	Ramos517 cells *Pigm*-deficient [148] *S. cerevisiae* Gpi14-deficient [149]	CHO *Pigo*-deficient [35,37] HEK293 *Pigo* knockout [35]	iPSC (hypomorphic PMM2$^{422G>A/357C>A}$ and PMM2$^{422G>A/357C>A}$-iPSC with additional knockdown [93]

Supplementary Table 8 - continued.

	PGM1-CDG Phosphoglucomutase 1	**PGM3-CDG Phosphoglucomutase 3**	**PIGA-CDG Phosphatidylinositol N-acetylglucosaminyltransferase (subunit A)**	**PIGM-CDG GPI α-1,4-mannosyltransferase I**	**PIGO-CDG GPI ethanolamine phosphate transferase 3**	**PMM2-CDG Phosphomannomutase 2**
***In vivo* models**	NA	Mouse (*Pgm3*^{mld1}) [124]	Chimeric Mouse (*Piga*-deficient) [146]	NA	NA	Mouse (Knock-out) [75]
						Mouse (Pmm2$^{R137H/R137H}$) [77]
						Mouse (Pmm2$^{F118L/F118L}$) [77]
						Mouse (Pmm2$^{R137H/F118L}$) [77]
						Mouse (Pmm2 $^{R137H/F115L}$) [94]
						Zebrafish (Knock-out) [95]
		Mouse (*Pgm3*^{gt}) [124]	Mouse (Partial exon2 excision) [147]			Drosophila melanogaster (*pmm2*-null) [96]
						D.melanogaster (*pmm2* knockdown) [96]
						Xenopus laevis (*Pmm2*-null) [282]
Biomarkers	NA	NA	NA	NA	NA	N-tetrasaccharide (Neu$_5$Ac_2,6Gal_1,4-GlcNAc_1,4GlcNAc) [178]

Supplementary Table 9 - continued.

	PGM1-CDG Phosphoglucomutase 1	**PGM3-CDG Phosphoglucomutase 3**	**PIGA-CDG Phosphatidylinositol N-acetylglucosaminyltransferase (subunit A)**	**PIGM-CDG GPI α-1,4-mannosyltransferase I**	**PIGO-CDG GPI ethanolamine phosphate transferase 3**	**PMM2-CDG Phosphomannomutase 2**
Biomarkers	NA	NA	NA	NA	NA	Band 3 and glycophorin A [185]
						Glycosphingolipids (Gb3, GM2, GD3 and GD1a) [186]
						AGA [166]
						ICAM-I [174,175]
						α_1-acid glycoprotein [155,187]
						Ceruloplasmin [155,187]
						α_1-antichymotrypsin [155,187]
						α_1B-glycoprotein [155,187]
						TSH and TF_4 [4,188]
						β-trace protein [180,189]
Dietery therapy	Gal suppl [65,208,209]	GlcNAc Suppl [67]	Ketogenic diet [216]	Sodium Phenylbutyrate suppl [57]	Vitamine B6 suppl [220]	Man (Man-1-P) suppl http://glycomine.com/ [46,47,52,77,194,202]
	Uridine suppl [209,210]					
	Glucose IV administration [211]					Glc starvation [194]

Supplementary Table 10 - continued.

	PGM1-CDG Phosphoglucomutase 1	PGM3-CDG Phosphoglucomutase 3	PIGA-CDG Phosphatidylinositol N-acetylglucosaminyltransferase (subunit A)	PIGM-CDG GPI α-1,4-mannosyltransferase I	PIGO-CDG GPI ethanolamine phosphate transferase 3	PMM2-CDG Phosphomannomutase 2
Transplantation	Heart transplantation [65]	Hematopoietic cell transplantation [42]	NA	NA	NA	NA
Gene therapy	NA	NA	NA	NA	NA	NA
Antisense therapy	NA	NA	NA	NA	NA	AMO (c.640-15479C>T) [239]
PCs	NA	NA	NA	NA	NA	1-(3-chlorophenyl)-3-3-bis(pyridine-2-yl)urea [231]
Others	NPCRS [255,256] TPCRS [260]	NPCRS [255,256]	NPCRS [255,256]	NPCRS [255,256]	NPCRS [255,256]	Metformin [200] MPI inhibitors [59,237] NPCRS [255–258] ICARS [257,258]

Supplementary Table 11 - continued.

	SLC35A1-CDG CMP-sialic acid transporter	**SLC35A2-CDG UDP-galactose transporter**	**SLC35C1-CDG GDP-fucose transporter**	**SLC39A8-CDG Solute carrier family 39 (zinc transporter), member 8**	**SRD5A3-CDG Steroid 5α-reductase type 3**	**TMEM165-CDG Transmembrane protein 165**
CTs	NA	NA	NA	Interventional NCT02955264 Mn^{2+} trial (registered)	Interventional NCT02955264	Interventional NCT02955264
***In vitro* models**	CHO *Lec 2* mutants [17,25,26,38,125]	CHO *Lec8* mutant [33]	CHO *Slc35c1* knockout [130]	NA	*S.cerevisiae Dfg10-100* [140]	*S. cerevisiae Gdt1Δ* [30,141,142]
	CHO MAR-11 mutant [126]	CHO *Lec8* mutant [33]	CHO *Slc35c1* knockout derived from MAR-11 mutants [128,129]			HEK293 *TMEM165* knockout and knockdown [36,142]
	HAP1 *Slc35a1* knockout [32]		ESC *Slc35c1* knockout [131]			HeLa *TMEM165* knockdown [142]
***In vivo* models**	NA	*C. elegans Srf-1* mutants [127]	Mouse (*Slc35c1*$^{-/-}$) [132,133]	Mouse (Slc39a8$^{(neo/neo)}$) [138,139]	Mouse (*Srd5a3*$^{Gt/Gt}$) [140]	Zebrafish (*tmem165*$^{-/-}$) [143]
			Zebrafish (*slytherin*) [135,136]			
			Zebrafish (Slc35c1 overexpression) [137]	Mouse (Slc39a8$^{-/-}$) [85]		
Biomarkers	NA	NA	NA	NA	NA	NA

Supplementary Table 12 - continued.

	SLC35A1-CDG CMP-sialic acid transporter	SLC35A2-CDG UDP-galactose transporter	SLC35C1-CDG GDP-fucose transporter	SLC39A8-CDG Solute carrier family 39 (zinc transporter), member 8	SRD5A3-CDG Steroid 5α-reductase type 3	TMEM165-CDG Transmembrane protein 165
Diatery therapy	SA, ManNAc or the fetuin suppl (all w/o beneficial effects) [71]	Gal suppl [33,221]	Fuc suppl [23,27,50,51,53,132,136,222]	Mn^{2+} suppl [226,228] Uridine suppl [226,227] Gal suppl [226,227]	NA	Mn^{2+} suppl [70,142] Gal suppl [70]
Transplantation	NA	NA	NA	NA	NA	NA
Gene therapy	NA	NA	NA	NA	NA	NA
Antisense therapy	NA	NA	NA	NA	NA	AMO (c.792+182G>A) [238]
PCs	NA	NA	NA	NA	NA	NA

Supplementary Table 13 – continued.

	SLC35A1-CDG CMP-sialic acid transporter	**SLC35A2-CDG UDP-galactose transporter**	**SLC35C1-CDG GDP-fucose transporter**	**SLC39A8-CDG Solute carrier family 39 (zinc transporter), member 8**	**SRD5A3-CDG Steroid 5α-reductase type 3**	**TMEM165-CDG Transmembrane protein 165**
Others	NPCRS [255,256]	NPCRS [255,256]	NPCRS [255,256]	NPCRS [255,256]	NPCRS [255,256]	NPCRS [255,256]

Supplementary Table 14 – continued.

	TMEM199-CDG Transmembrane protein 199						
CTs	NA	***In vivo* models**	NA	**Antisense therapy**	NA	**PCs**	NA
***In vitro* models**	DJY62/DJY102 (pep4–3 vma12 Δ::LEU2) DJY63 (vma12 Δ::LEU2) [105,144]	**Trans-plantation**	NA	**Biomarkers**	NA	**Others**	NPCRS [255,256]
	HeLa cell line (TMEM199 knowdown by CRISPR/Cas9) [106]	**Gene therapy**	NA	**Diatery therapy**	Iron supp [106]		

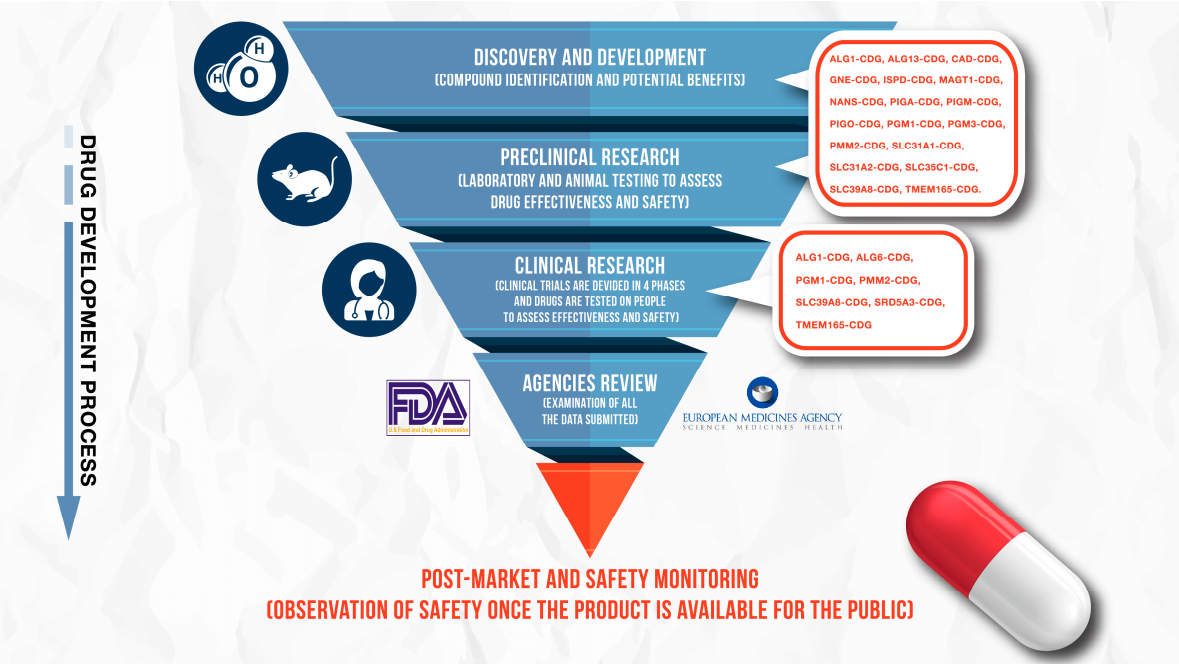

Figure S1 – Drug development process overview.

Animal models	Liver transplant	Heart transplantation	N-acetyl-D-mannosamine (ManNAC)
Yeast	Heart transplant	Transplantation	Mannosamine (ManN)
Drosophila melanogaster	Bone marrow transplant	Stem cell transplantation	Ribitol
Zebrafish	Transplant	Oral supplementation	Magnesium (Mg2+)
Mouse	Pharmacological chaperones	Mannose	N-Acetyl glucosamine (GlcNAc)
Rat	Chaperones	Galactose	Phenylbutyrate
Clinical trials	Antisense therapy	Fucose	Guanosine diphosphate
Therapies	Man-1-P	Sialic Acid	Uridine-5'-Diphosphate
C.elegans	Man-1-P therapy	Manganese	L-Aspartic acid
Therapy	Splicing	Uridine	L-Glutamine
Therapeutic strategies	Induced pluripotent stem cells	Metformin	Famotidine
Therapeutic options	Biomarkers	Acetazolamide	Phosphoric acid

IN COMBINATION WITH

Congenital disorders of glycosylation	ALG1	ALG1-CDG	ALG6
ALG6-CDG	ALG12	ALG12-CDG	ALG13
ALG13-CDG	ATP6VAP1	ATP6VAP1-CDG	CAD
Carbohydrate deficient glycoprotein syndrome	CAD-CDG	CCDC115	CCDC115-CDG
COG5	COG5-CDG	DOLK	DOLK-CDG
GNE	GNE-CDG	ISPD	ISPD-CDG
MAGT1	MAGT1-CDG	MPI	MPI-CDG
NANS	NANS-CDG	PGM1	PGM1-CDG
PGM3	PGM3-CDG	PIGM	PIGM-CDG
PMM2	PMM2-CDG	SL39A8	SL39A8-CDG
SLC35A2	SLC35A2-CDG	SLC35C1	SLC35C1-CDG
SRD5A3	SRD5A3-CDG	TMEM165	TMEM165-CDG
PIGA	PIGA-CDG	PIGO	PIGO-CDG

Figure S2 – List of all keywords used for this systematic literature review.

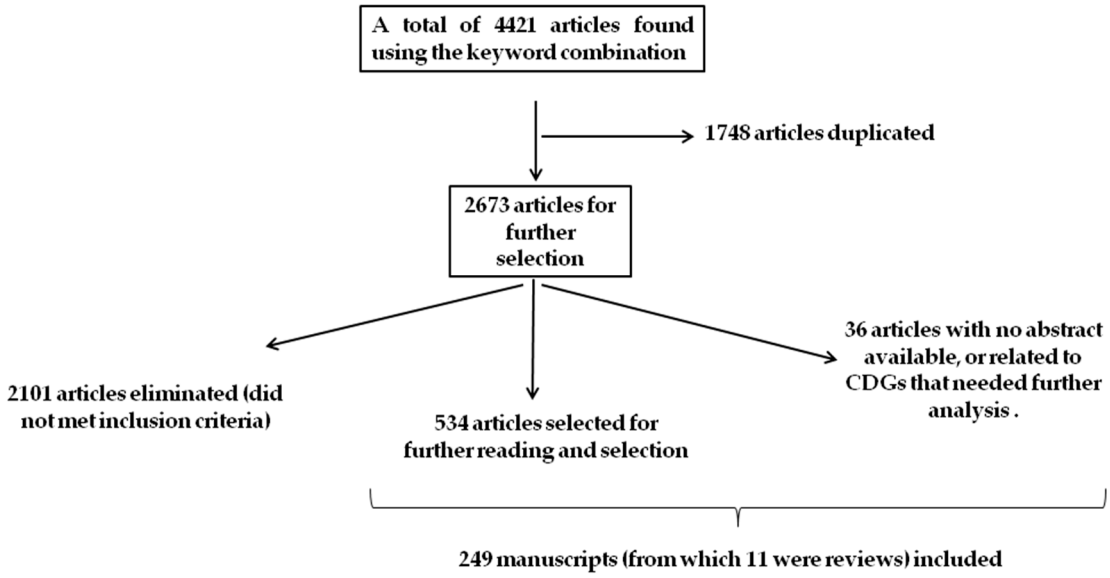

Figure S3 – Diagram of the inclusion/elimination process used for manuscript selection.