

Supplementary Materials

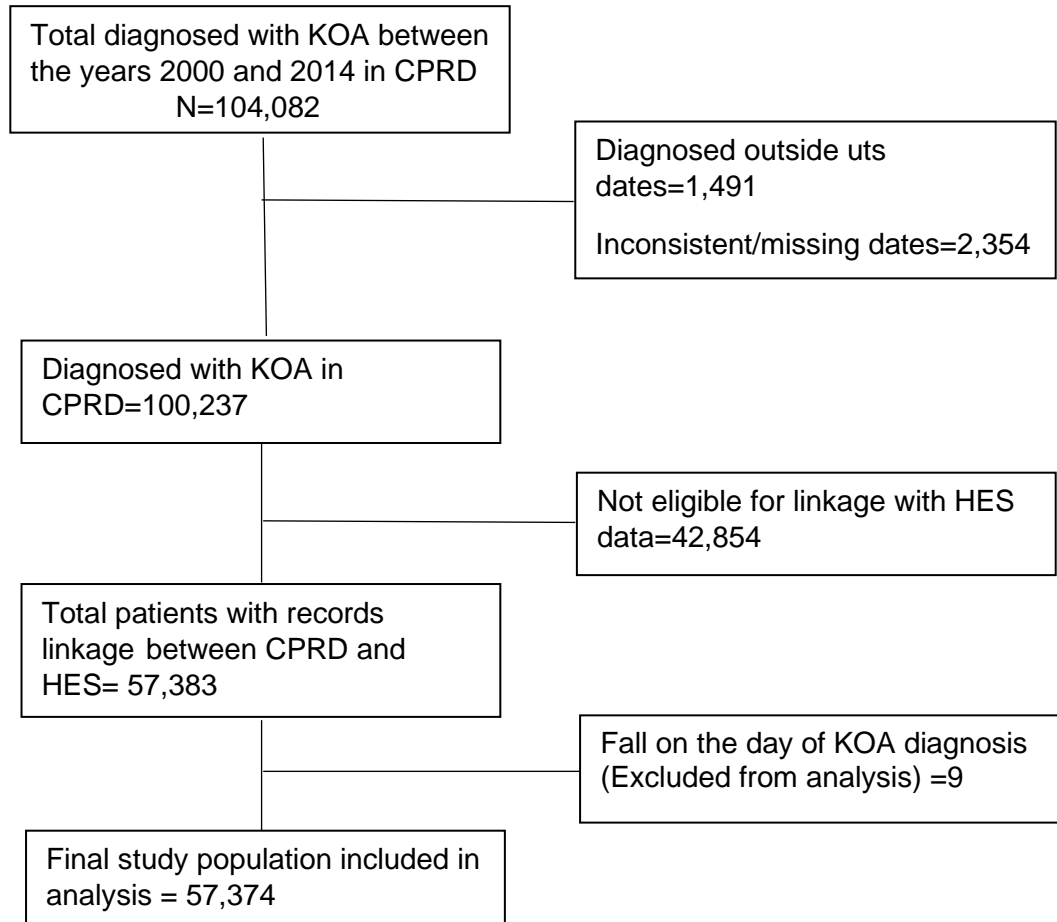
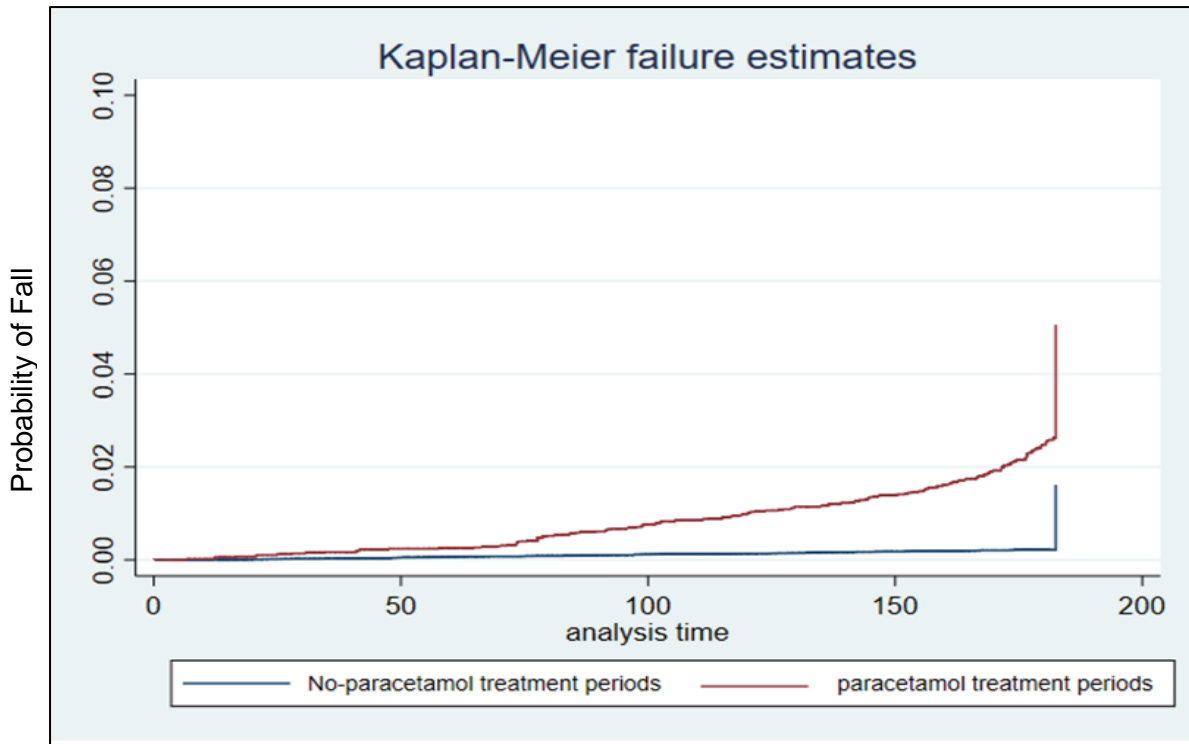


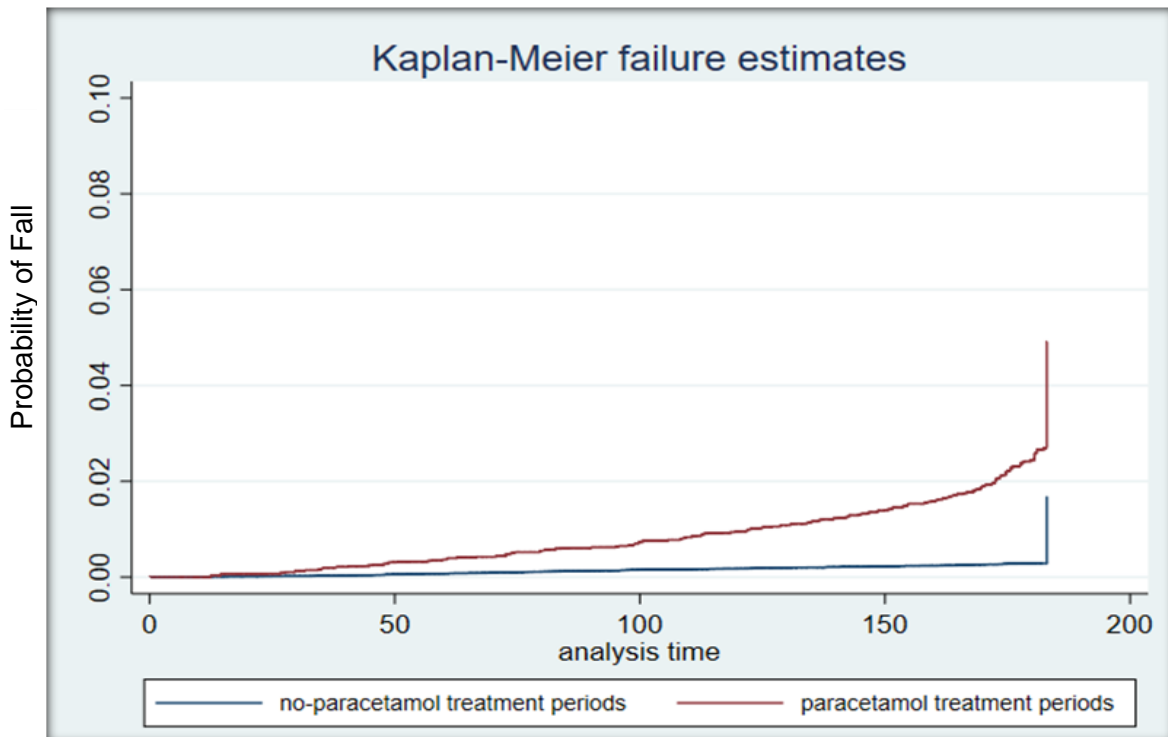
Figure S1 Selection of Study Population



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2 **Figure S2** Kaplan-Meier failure estimates for current use of paracetamol within the first six
 3 months of KOA diagnosis

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6 **Figure S3** Kaplan-Meier failure estimates for current use of paracetamol within the second
 7 six months of KOA diagnosis

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1 **Table S1** - Knee osteoarthritis diagnosis codes applied in cohort selection process

Knee osteoarthritis diagnosis codes applied in cohort selection		
21159	N05z600	Osteoarthritis NOS;of the lower leg
33479	N054600	Oligoarticular osteoarthritis; unspecified; of lower leg
34804	N051600	Localised; primary osteoarthritis of the lower leg
24079	Nyu2511	Primary gonarthrosis
24146	N051B00	Primary gonarthrosis, bilateral
665	N05z611	Knee osteoarthritis NOS
1296	N053611	Patellofemoral osteoarthritis
2487	N05zL00	Osteoarthritis NOS, of knee

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Table S2- Read Codes of Falls

Read Code	Code Description
16D..00	FALLS
16D1.00	RECURRENT FALLS
R200.12	[D] GERIATRIC FALL
TC...00	ACCIDENTAL FALLS
TC...11	FALL - ACCIDENTAL
TC0..00	FALL ON OR FROM STAIRS OR STEPS
TC00.00	FALL ON OR FROM ESCALATOR
TC00000	FALL ON ESCALATOR
TC01.00	FALL ON OR FROM STAIRS
TC01000	FALL ON STAIRS
TC01100	FALL FROM STAIRS
TC01z00	FALL ON OR FROM STAIRS NOS
TC02.00	FALL ON OR FROM STEPS
TC02000	FALL ON STEPS
TC02100	FALL FROM STEPS
TC02z00	FALL ON OR FROM STEPS NOS
TC0z.00	FALL ON OR FROM STAIRS OR STEPS NOS
TC1..00	FALL ON OR FROM LADDERS OR SCAFFOLDING
TC10.00	FALL FROM LADDER
TC11.00	FALL FROM SCAFFOLDING
TC2..00	FALL FROM OR OUT OF BUILDING OR OTHER STRUCTURE
TC20.00	FALL FROM BALCONY
TC21.00	FALL FROM BRIDGE
TC22.00	FALL FROM BUILDING
TC27.00	FALL FROM WALL
TC28.00	FALL FROM WINDOW
TC29.00	FALL THROUGH ROOF
TC2z.00	FALL FROM OR OUT OF BUILDING OR OTHER STRUCTURE NOS
TC3..00	FALL INTO HOLE OR OTHER OPENING IN SURFACE
TC30.00	ACCIDENT CAUSED BY DIVING OR JUMPING INTO WATER
TC31.00	ACCIDENTAL FALL INTO WELL
TC32.00	ACCIDENTAL FALL INTO MANHOLE
TC32000	ACCIDENTAL FALL INTO MANHOLE, UNSPECIFIED
TC3y.00	FALL INTO OTHER HOLE OR OTHER OPENING IN SURFACE
TC3y100	FALL INTO DOCK
TC3y200	FALL INTO HOLE
TC3y300	FALL INTO PIT
TC3y400	FALL INTO QUARRY
TC3y600	FALL INTO TANK
Read Code	Code Description

TC3y600	FALL INTO TANK
TC3yz00	FALL INTO OTHER HOLE, UNSPECIFIED
TC3z.00	FALL INTO HOLE NOS
TC4..00	OTHER FALL FROM ONE LEVEL TO ANOTHER
TC40.00	FALL FROM PLAYGROUND EQUIPMENT
TC41.00	FALL FROM CLIFF
TC42.00	FALL FROM CHAIR OR BED
TC42000	FALL FROM CHAIR
TC42100	FALL FROM BED
TC42z00	FALL FROM CHAIR OR BED NOS
TC4y.00	OTHER FALL FROM ONE LEVEL TO ANOTHER
TC4y100	FALL FROM HAYSTACK
TC4y200	FALL FROM STATIONARY VEHICLE
TC4y300	FALL FROM TREE
TC4yz00	OTHER FALL FROM ONE LEVEL TO ANOTHER NOS
TC4z.00	FALL FROM ONE LEVEL TO ANOTHER NOS
TC5..00	FALL ON SAME LEVEL FROM SLIPPING, TRIPPING OR STUMBLING
TC50.00	FALL ON SAME LEVEL FROM SLIPPING
TC51.00	FALL ON SAME LEVEL FROM TRIPPING
TC52.00	FALL ON SAME LEVEL FROM STUMBLING
TC5z.00	FALL ON SAME LEVEL FROM SLIPPING, TRIPPING OR STUMBLING NOS
TC6..00	FALL ON SAME LEVEL- COLLISION/PUSH/SHOVE BY/WITH OTH PERSON
TC60.00	FALL ON SAME LEVEL FROM SPORTS CONTACT
TC60000	FALL ON SAME LEVEL FROM TACKLE IN SPORT
TC60y00	OTHER FALL IN SPORT
TC60z00	FALL ON SAME LEVEL FROM SPORTS CONTACT NOS
TC6y000	FALL ON SAME LEVEL FROM COLLISION WITH OTHER PERSON, UNSPEC
TC6y100	FALL ON SAME LEVEL FROM PUSHING BY OTHER PERSON, UNSPECIFIED
TC6y200	FALL ON SAME LEVEL FROM SHOIVING BY OTHER PERSON, UNSPECIFIED
TC6yz00	OTHER FALL ON SAME LEVEL- PUSH/SHOVE/COLLIDE-OTH PERSON NOS
TC6z.00	FALL ON SAME LEVEL- PUSH/SHOVE/COLLIDE - OTHER PERSON NOS
TCy..00	OTHER FALLS
TCy0.00	FALL FROM BUMP AGAINST OBJECT
TCyz.00	OTHER ACCIDENTAL FALL NOS
TCz..00	ACCIDENTAL FALLS NOS
U10..00	[X]FALLS
U100.00	[X]FALL ON SAME LEVEL INVOLVING ICE AND SNOW
Read Code	Code Description
U100000	[X]FALL ON SAME LEVEL INVOLVING ICE AND SNOW OCCURRN HOME

U100300	[X]FALL SAME LEVL INVOLV ICE/SNOW, OCC SPORT/ATHLET AREA
U100400	[X]FALL SAME LEVL INV ICE AND SNOW, OCC STREET / HIGHWAY
U100500	[X]FALL SAME LEVL INV ICE / SNOW, OCC TRADE / SERVICE AREA
U100z00	[X]FALL SAME LEVL INV ICE / SNOW, OCC AT UNSPECIFIED PLACE
U101.00	[X]FALL ON SAME LEVEL FROM SLIPPING, TRIPPING AND STUMBLING
U101000	[X]FALL SAME LEVL FRM SLIP TRIP + STUMB, OCCURRENCE AT HOME
U101100	[X]FALL SAME LEVEL FROM SLIP TRIP + STUMB OCC RESID INSTIT
U101200	[X]FALL SME LEVL SLP TRP+STMB OCC SCH, OTH INST/PUB ADM AREA
U101300	[X]FALL SME LEVL FRM SLIP TRIP+STUMB, OCC SPORT/ATHLET AREA
U101400	[X]FALL SAME LEVEL FROM SLIP TRIP+STUMB, OCC STREET/HIGHWAY
U101500	[X]FALL SME LVL FRM SLIP TRIP+STUMB, OCC TRADE/SERVICE AREA
U101600	[X]FALL SAME LEVEL, SLIP TRIP+STUMB OCC INDUST/CONSTRUCT AREA
U101700	[X]FALL SAME LEVEL FROM SLIP TRIP+STUMBLING, OCCUR ON FARM
U101y00	[X]FALL SAME LEVEL, SLIP TRIP+STUMB, OCC OTHER SPECIF PLACE
U101z00	[X]FALL SAME LEVL FRM SLIP TRIP+STUMBLING, OCC UNSPEC PLACE
U102.00	[X]FALL INVOLV ICE-SKATES SKIS ROLLER-SKATES OR SKATEBOARDS
U102000	[X]FALL INV ICE-SKATE SKIS ROLL-SKATE/SKATEBOARD, OCC HOME
U102300	[X]FALL INV ICE-SKT SKI ROL-SKT/SKBRD OCC SPORT/ATHLET AREA
U102400	[X]FALL INV ICE-SKAT SKI ROLL-SKAT/SKBRD OCC STREET/HIGHWAY
U102700	[X]FALL INV ICE-SKAT SKI ROLL-SKAT/SKATEBRD, OCCUR ON FARM
U102z00	[X]FALL INV ICE-SKAT SKI ROLL-SKAT/SKBRD OCC UNSPECIF PLACE
U103.00	[X]OTH FALL SAME LEVL DUE COLLISN/PUSHING BY ANOTHER PERSON
U103000	[X]OTH FALL SAME LEVL, COLLISN/PUSH BY ANOTH PERS, OCC HOME
U103300	[X]OTH FALL SME LEVL COL/PUSH ANOTH PERS OCC SPORT/ATHL AREA
U103y00	[X]OTH FALL SME LEVL COLL/PUSH ANOTH PER OCC OTH SPEC PLACE
U103z00	[X]OTH FALL SAME LEVL COLL/PUSH ANOTH PERS OCC UNSPEC PLACE
U104.00	[X]FALL WHILE BEING CARRIED OR SUPPORTED BY OTHER PERSONS
Read Code	Code Description
U104100	[X]FALL WHLE CARRIED/SUPPORTED OTH PERSONS OCC RESID INSTIT
U104600	[X]FALL WHLE CARR'D/SUPPRTD OTH PERS OCC INDUST/CONSTR AREA

U105.00	[X]FALL INVOLVING WHEELCHAIR
U105100	[X]FALL INVOLVNG WHEELCHAIR OCCURRENCE RESIDENTIAL INSTIT'N
U105500	[X]FALL INVOLVNG WHEELCHAIR OCCURRNCE AT TRADE/SERVICE AREA
U106.00	[X]FALL INVOLVING BED
U106000	[X]FALL INVOLVING BED, OCCURRENCE AT HOME
U106100	[X]FALL INVOLVING BED OCCURRENCE IN RESIDENTIAL INSTITUTION
U107.00	[X]FALL INVOLVING CHAIR
U107000	[X]FALL INVOLVING CHAIR, OCCURRENCE AT HOME
U107200	[X]FALL INVLV CHAIR OCC AT SCHOOL OTH INSTIT/PUB ADMIN AREA
U107600	[X]FALL INVOLVING CHAIR OCCURRENCE AT INDUST/CONSTRUCT AREA
U107z00	[X]FALL INVOLVING CHAIR, OCCURRENCE AT UNSPECIFIED PLACE
U108.00	[X]FALL INVOLVING OTHER FURNITURE
U108000	[X]FALL INVOLVING OTHER FURNITURE, OCCURRENCE AT HOME
U108100	[X]FALL INVOLV OTHER FURNITURE OCCURRN RESIDENT INSTITUT'N
U108600	[X]FALL INVOLV OTH FURNITRE OCCURRNCE AT INDUST/CONSTR AREA
U109.00	[X]FALL INVOLVING PLAYGROUND EQUIPMENT
U109000	[X]FALL INVOLVING PLAYGROUND EQUIPMENT, OCCURRENCE AT HOME
U109200	[X]FALL INV PLAYGRND EQUIP OCC SCH OTH INST/PUB ADMIN AREA
U109z00	[X]FALL INVOLV PLAYGRND EQUIPM OCCURRNCE AT UNSPECIF PLACE
U10A.00	[X]FALL ON AND FROM STAIRS AND STEPS
U10A000	[X]FALL ON AND FROM STAIRS AND STEPS, OCCURRENCE AT HOME
U10A100	[X]FALL ON + FROM STAIR + STEP OCCURRNCE RESIDENT INSTIT'N
U10A500	[X]FALL ON + FROM STAIR + STEP OCCURRN AT TRADE/SERVICE AREA
U10A511	[X]FALL ON OR FROM ESCALATOR
U10Ay00	[X]FALL ON + FROM STAIR + STEP OCCURRN AT OTH SPECIF PLACE
U10Az00	[X]FALL ON + FROM STAIR + STEP OCCURRNCE AT UNSPECIF PLACE
U10B.00	[X]FALL ON/FROM LADDER
U10B000	[X]FALL ON AND FROM LADDER, OCCURRENCE AT HOME
U10By00	[X]FALL ON+FROM LADDER, OCCURRENCE AT OTHER SPECIFIED PLACE
Read Code	Code Description
U10C600	[X]FALL ON+FROM SCAFFOLD OCCURRN ATIndustr/CONSTRUCTN AREA
U10D.00	[X]FALL FROM, OUT OF OR THROUGH BUILDING OR STRUCTURE
U10D000	[X]FALL FROM OUT OF/THROUGH BUILDING/STRUCTUR OCCURN HOME

U10D300	[X]FALL FRM OUT/THRO BLDNG/STRUCT OCC AT SPORT/ATHLET AREA
U10D600	[X]FALL FROM OUT/THRO BUILDNG/STRUCT OCC INDUST/CONSTR AREA
U10E.00	[X]FALL FROM TREE
U10E000	[X]FALL FROM TREE, OCCURRENCE AT HOME
U10Ez00	[X]FALL FROM TREE, OCCURRENCE AT UNSPECIFIED PLACE
U10F000	[X]FALL FROM CLIFF, OCCURRENCE AT HOME
U10F300	[X]FALL FROM CLIFF, OCCURRENCE AT SPORTS AND ATHLETICS AREA
U10G.00	[X]DIV'G/JUMP'G INTO WATER CAUS INJ OTH THAN DROWN'G/SUBM'N
U10G300	[X]DIV/JMP WATR CAUS INJ OTH THN DRWN/SUBM, SPRT/ATHLET AREA
U10G600	[X]DIV/JMP WATR CAUS INJ OTH THN DRWN/SUBM OCC INDUS AREA
U10H.00	[X]OTHER FALL FROM ONE LEVEL TO ANOTHER
U10H000	[X]OTHER FALL FROM ONE LEVEL TO ANOTHER, OCCURRENCE AT HOME
U10H200	[X]OTHR FALL FRM ONE LEVEL TO ANOTHR, SCH INST/PUB ADM AREA
U10H300	[X]OTHR FALL FROM ONE LEVEL TO ANOTHR OCC SPORT/ATHLET AREA
U10H400	[X]OTHR FALL FROM ONE LEVEL TO ANOTHR OCCURRN STREET/H'WAY
U10H500	[X]OTHER FALL FRM ONE LEVEL TO ANOTHR OCC AT TRDE/SERV AREA
U10Hy00	[X]OTHER FALL FRM ONE LEVL TO ANOTHR OCC AT OTH SPECIF PLCE
U10Hz00	[X]OTHR FALL FRM ONE LEVEL TO ANOTHR OCCURRN AT UNSPEC PLCE
U10J.00	[X]OTHER FALL ON SAME LEVEL
U10J000	[X]OTHER FALL ON SAME LEVEL, OCCURRENCE AT HOME
U10J300	[X]OTHER FALL ON SAME LEVEL OCCURRN AT SPORTS/ATHLETIC AREA
U10J600	[X]OTHER FALL ON SAME LEVL, OCCURRN AT INDUST/CONSTRUCT AREA
U10z.00	[X]UNSPECIFIED FALL
U10z000	[X]UNSPECIFIED FALL, OCCURRENCE AT HOME
U10z100	[X]UNSPECIFIED FALL, OCCURRENCE IN RESIDENTIAL INSTITUTION
U10z300	[X]UNSPECIFIED FALL, OCCURRENCE AT SPORTS / ATHLETICS AREA
U10z600	[X]UNSPECIFIED FALL OCCURRN AT INDUSTRIAL/CONSTRUCTION AREA
U10zz00	[X]UNSPECIFIED FALL, OCCURRENCE AT UNSPECIFIED PLACE

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3 Table S3- ICD10 Codes of Falls

ICD-10 Code	Description
W01	Fall on same level from slipping, tripping and stumbling
W02	Fall involving ice-skates, skis, roller-skates or skateboards

W03	Other fall on same level due to collision with, or pushing by, another person
W04	Fall while being carried or supported by other persons
W05	Fall involving wheelchair
W06	Fall involving bed
W07	Fall involving chair
W08	Fall involving other furniture
W09	Fall involving playground equipment
W10	Fall on and from stairs and steps
W11	Fall on and from ladder
W12	Fall on and from scaffolding
W13	Fall from, out of or through building or structure
W14	Fall from tree
W15	Fall from cliff
W16	Diving or jumping into water causing injury other than drowning or submersion
W17	Other fall from one level to another
W18	Other fall on same level
W19	Unspecified fall

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1 **Table S4 Drug classes and individual drugs included in the study***

Antidepressants	AEDs	Opioids	NSAIDs
Amitriptyline	Phenobarbital	Morphine	Celecoxib
Imipramine	Ethosuximide	Oxycodone	Rofecoxib
Clomipramine	Phenytoin	Fentanyl**	Etodolac
Lofepramine	Primidone	Tramadol	Meloxicam
Fluoxetine	Levetiracetam	Buprenorphine***	Tenoxicam
Paroxetine	Tiagabine	Tapentadol	Etoricoxib
Citalopram	Lamotrigine	Pethidine	Nemisulide
Isocarboxazide	Gabapentin	Hydromorphone	Piroxicam
Phenelzine	Felbamate	Codeine	Diclofenac
Agomelatin	Oxcarbazepine	Dihydrocodeine	Ibuprofen
Trazodone	Valproic acid	Dextropropoxyphene	Ketoprofen
Nefazodone	Carbamazepine		Dexibuprofen
Venlafaxine	Clonazepam		Dexketoprofen
Nortriptyline	Vigabatrin		Fenbufen
Doxepin	Pregabalin		Tiaprofenic acid
Dosulepin	Lacosamide		Acementacine
Amoxapine	Rufinamide		Tolmetin
Escitalopram	Zonisamide		Indomethacin
Sertraline	Retigabine		Nabumetone
Fluvoxamine			Aceclofenac
Meclobemide			Mefenamic acid
Tranlycypromine			Phenylbutazone
Mirtazapine			Fenoprofen
Reboxetine			Flurbiprofen
Mianserine			Naproxen
Duloxetine			Ketorolac
AEDs: Anti-epileptic drugs, NSAIDs: Non-Steroidal Anti-Inflammatory Drugs			
*Oral forms were included unless specified otherwise ** transdermal and transmucosal ***sublingual and transdermal			

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