# **Industrial Injuries Advisory Council Information note**

# Osteoarthritis of the knee and work in the construction industry

#### May 2016

### **Background**

- 1. Osteoarthritis (OA) of the knee is a common disease in the general population, especially at older ages. It has been estimated that over 4 million people in England are affected, while in the UK almost a quarter of people aged 75 or over have sought treatment for the disease.<sup>1</sup>
- 2. Knee OA is characterised by destruction of the cartilage surrounding the knee joints and various alterations to the bone and the joint space between bones. Its main symptoms include knee pain, knee swelling, stiffness and reduced mobility. It can be a significant cause of disability, such that some 85,900 knee joint replacement operations were performed in Britain in 2013.<sup>1</sup>
- 3. Well recognised non-occupational risk factors for disease occurrence include advancing age, obesity, trauma around the knee (including previous cartilage injury and knee surgery), and various destructive joint diseases. OA of the knee is commoner in women and sometimes has a genetic component.
- 4. In addition, a growing body of research evidence indicates that the disease is more frequent in people whose occupations entail hard, repetitive, physically demanding use of the knee joints. Relevant observations include reports by Manninen *et al.* (2002), Felson *et al.* (1991), Sandmark *et al.* (2000), Sandmark (2000), Kivimaki *et al.* (1992), Schouten (1992), Anderson and Felson (1998), Coggon *et al.* (2000), Lau *et al.* (2000), Dawson *et al.* (2003), Vingård *et al.* (1991, 1992), Cooper *et al.* (1994), Seidler *et al.* (2008), Jensen (2005) and Jensen *et al.* (2000). Reviews of the evidence can be found in Palmer (2012) and in two earlier reports of the Council (Cm 7440, 2008; Cm 7964, 2010).
- 5. Knee OA is recognised for benefit under the Industrial Injuries Disablement Benefit (IIDB) Scheme as Prescribed Disease (PD) A14. However, prescription has proved possible so far only in two occupational circumstances: a) work underground in a coal mine (for at least 10 years in aggregate in certain specified jobs and timeframes); and b) work wholly or mainly fitting or laying carpets or floors (for at least 20 years in aggregate).
- 6. Many other occupations are suspected *a priori* of being at heightened risk of knee OA, notably those in the construction industry, and in 2015 the Council received a representation to add the occupation of "joiner" to the terms appearing in PD A14. This information note outlines the considerations and challenges behind prescription for PD A14; it also describes the history of the prescription, the evidence

<sup>&</sup>lt;sup>1</sup> Arthritis Research UK. Key facts about arthritis: Arthritis in the UK – facts and statistics. http://www.arthritisresearchuk.org/arthritis-information/data-and-statistics.aspx

gathered so far on knee OA and work in construction, and the Council's position on the scope for extending the prescription's terms.

This report contains technical terms, the meanings of which are explained in a concluding glossary

### **Conditions of prescription**

- 7. The Social Security Contributions and Benefits Act 1992 states that the Secretary of State may prescribe a disease where he is satisfied that the disease: "a) ought to be treated, having regard to its causes and incidence and any other relevant considerations, as a risk of the occupation and not as a risk common to all persons; and b) is such that, in the absence of special circumstances, the attribution of particular cases to the nature of employment can be established or presumed with reasonable certainty." In other words, a disease may only be prescribed if there is a recognised risk to workers in an occupation, and the link between disease and occupation can be established or reasonably presumed in individual cases. This is the framework the Industrial Injuries Advisory Council (IIAC) must observe when weighing the grounds for prescription.
- 8. For some diseases attribution to occupation is relatively straightforward. If, for example, the disease rarely occurs outside work (e.g. mesothelioma) or has distinctive clinical features when caused by work (e.g. occupational asthma), then attribution to employment can be established or presumed with reasonable certainty simply from the clinical picture and the occupational history. However, for other diseases, including knee OA, there are no special features that allow individual claims to be attributed like this. Instead, attribution depends on evidence that the disease is more frequent in people with that type of work. The threshold normally applied by the Council, as explained in other reports, requires reasonably robust evidence that a given work exposure or activity more than doubles the risk of disease. Broadly speaking, this corresponds to the probability that an individual claimant's disease is more likely than not to have arisen from their occupational exposure (i.e. it is attributable on the balance of probabilities).

# The history of prescription for PD A14 in carpet and floor layers and miners

- 9. In the case of carpet and floor layers the criteria in paragraph 8 were met, as set out in Cm 7964. Early studies from the US (Thun *et al.*, 1987) and Finland (Kivimaki *et al.*, 1992) had methodological limitations and these found only a moderate elevation in risk.
- 10. However, three cross-sectional reports from Denmark (Jensen *et al.*, 2000; Jensen, 2005; Rytter *et al.*, 2009a), all of which considered only subjects with no prior knee injury, indicated a more than doubling of risk among older workers with a long employment history, with evidence supporting a dose-response relationship. Further studies from Sweden (Vingård *et al.*, 1992; Järvholm *et al.*, 2008) found a markedly higher rate of disability pensioning in carpet and floor layers (23-fold) and a 4.7- fold increased risk of surgical treatment in this occupational group. A more than doubled risk of cartilage tears was also found among the Danish floor layers (Rytter *et al.*, 2009b). Several reports on work activity in carpet and floor layers confirmed their high and sustained daily exposure to occupational kneeling and squatting (Jensen *et al.*, 2000; Kivimaki *et al.* 1992; Jensen *et al.*, 2010), which are recognised to be risk factors for knee OA in the general population (e.g. Coggon *et al.*, 2000; Cooper *et al.*, 1994; Anderson and Felson, 1998).

- 11. Thus, in 2010, knee OA (PD A14) was recognised for prescription in carpet and floor layers (Cm 7964).
- 12. In the case of underground coal miners, less direct evidence on risk was available than for carpet and floor layers. However, well-conducted studies by Lawrence (1955), in British coal miners, and a study of German miners by Greinemann (1997), pointed to a more doubling risk of knee OA given sufficiently long exposure. Additionally, several studies indicated a higher risk of meniscal injury in miners (e.g. Sharrard and Liddell, 1962); and the Council identified ample indirect evidence in the general population of increased risks arising from activities that would have been commonplace and extreme in underground miners prior to the advent of mechanisation in pits. The combination of limited direct evidence in miners and a large amount of indirect evidence, on risks by the activities typical of miners, made the argument for recognition under the Scheme.
- 13. Consequently, in 2008, knee OA was recognised for prescription in underground miners (Cm 7440).

### Earlier Council reviews of knee osteoarthritis in the construction industry

- 14. In the lead-up to its 2010 report, the Council sought evidence on whether the terms of PD A14 could encompass a broader range of construction trades than just carpet and floor layers. A detailed literature review was conducted, covering published research on knee OA and physical activities in construction trades. Since the industry includes a wide range of individual occupations, to ensure a comprehensive search and to ascertain findings in the finest level of detail available, a master list of job titles was established based on information supplied by the Health and Safety Executive (HSE) and the Construction Skills Network. The search was supplemented by a report on musculoskeletal problems in bricklayers, carpenters and plasterers commissioned for the HSE and by consultation with experts in the field. A separate search on physical exposures in construction was augmented by consulting an ergonomist from the HSE and relevant trades unions, and the Council issued a call for evidence in the medical and scientific press.
- 15. This review identified several reports relating to construction trades, as summarised in Cm 7964. Vingård *et al.* (1991) conducted a high quality prospective cohort study of 35-75 year-olds from Sweden in 1981-3. A comparison was made of hospital admission rates by occupation in construction trades and a panel of other blue-collar jobs deemed to involve low physical work effort. Linkage was achieved between subjects' hospital discharge records for knee OA and their occupational titles at the national censuses of 1960 and 1970. Risks were only slightly elevated in male construction workers (relative risk (RR) 1.36).
- 16. By contrast, in several other studies of knee OA in builders, construction workers and labourers, RRs were more than doubled. Thus, for example, in a Swedish case-control study of hospital treatment for knee OA by Sandmark *et al.* (2000), RRs were 3.1 times higher in construction workers; in a case-control study of disability pensioning for OA knee by Vingård *et al.* (1992), RRs were 5.1 times higher in construction workers; and in a second Swedish case-control study of surgery for

knee OA by Holmberg *et al.* (2004), risks were elevated 3.7-fold in men in "building and construction" for 11-30 years vs. <1 year although by only 1.6-fold for >30 years vs. <1 year of such experience. Lindberg and Montgomery (1987), in a cross-sectional survey of older labourers from Malmo, Sweden (average employment 32 years), reported that radiographic OA was more common than in white-collar workers and men from the general population (3.9% vs. 1.4% to 1.6%, Prevalence Ratio >2.4). In a German case-control study, odds of knee OA were elevated 2.1-fold in male construction workers vs. other men, but findings were not statistically significant (Seidler *et al.*, 2008).

- 17. Unfortunately the job titles "construction worker", "builder" and "labourer" cover a multiplicity of trades, some perhaps conferring a doubling of risk of knee OA, but others certainly not. The Council felt unable to recommend prescription for builders, labourers, or construction workers defined generally and as a class, without more evidence as to the occupation(s) at risk, and the level(s) and type(s) of risk-conferring activity.
- 18. Information by more specific definitions of occupation was strictly limited at that time. In one of a few such reports, Järvholm *et al.* (2008) compared hospitalisation rates for surgically treated OA of the knee in a large cohort of male Swedish construction workers aged 15-67 years, identified through an occupational health programme. A registry-based comparison was made with a baseline of various white-collar jobs. Table 1 is an extract of the main findings. The elevated risks in floor layers were particularly noteworthy, but a doubling of risk was seen across a range of occupations, including asphalt workers, plumbers, rock workers, sheet metal workers and woodworkers.

Table 1: Relative risk (RR) of surgical treatment for knee OA in Swedish construction workers (vs. white collar occupations). Adapted from Järvholm et al. (2008) with kind permission.

Occupation	RR	(95% CI)
Asphalt workers	2.81	(1.11-7.13)
Bricklayers	2.14	(1.08-4.25)
Floor layers	4.72	(1.80-12.33)
Plumbers	2.29	(1.19-4.43)
Rock workers	2.59	(1.18-5.69)
Sheet metal workers	2.60	(1.06-6.37)
Woodworkers	2.02	(1.11-3.69)
Drivers	2.01	(0.89-4.53)
Concrete workers	1.80	(1.00-3.25)
Electricians	1.18	(0.53-2.59)
Painters	1.44	(0.70-2.95)

- 19. There were few other observations, however, with which to compare Järvholm's findings. However, in apparent contrast to the higher risk in woodworkers, carpenters were treated as a control group in two Danish reports and were thereby found to have a substantially lower prevalence of knee OA than floor and carpet layers (Jensen *et al.*, 2000; Jensen, 2005).
- 20. Painters were treated as a control group in the study by Kivimaki *et al.* (1992) and were found to have only a limited risk of OA. They were also regarded as controls in a study by Wickstrom *et al.* (1983) that compared X-rays of their knees with those of male concrete reinforcement workers: Wickstrom *et al.* found both groups to have similar disease rates, despite marked differences in physical workload.
- 21. Finally, the German study by Seidler *et al.* (2008) reported a more than five-fold higher risk in a group which combined plasterers, insulators, glaziers, construction carpenters and upholsterers. No risk estimates were published for each of these occupations separately, however.
- 22. Following the approach that was adopted in prescribing for coal miners in 2008 (paragraph 12), the Council explored the case for combining indirect evidence on risk of knee OA by physical activity with direct evidence on risk by occupational title. However, only limited evidence was available on the extent of exposure to kneestraining physical activity within different construction trades. More fundamental from the viewpoint of prescription was the lack of direct evidence on risks of knee OA by

job title, other than for carpet fitters and floor and carpet layers. In the absence of more convincing direct evidence on doubling of risk, the Council decided against extrapolation.

23. However, the Council has remained open to the possibility of extending the terms of PD A14. When then, in 2015, it received a representation to add the occupation of "joiner" to this prescription, the opportunity was taken re-appraise the evidence base.

# Updated review of knee osteoarthritis in the construction industry

- 24. The literature search which informed the Council's report *Osteoarthritis of the knee in carpet fitters and carpet and floor layers* (Cm 7964, 2010) was updated initially in 2012 (Palmer, 2012) and subsequently by the Council's scientific advisor to April 2016. In 2015-16, the HSE and relevant trades unions were contacted and a general call for evidence was issued in the medical and scientific press.
- 25. A Council member also corresponded with the authors of original research reports, to establish whether data existed to allow risks of knee OA to be established in finer granularity than published by occupational title rather than by industry label.
- 26. Finally, to explore again the feasibility of combining direct evidence on risk by occupational title with indirect evidence on risk of knee OA by physical activity, the various literature searches and personal consultations and calls for evidence were extended to update the Council's previous assessment and to establish if possible the likely levels of exposure to knee-straining activities in different construction trades (relative, for example, to those in carpet and floor laying). During this process, a Council member contacted research colleagues from Denmark active in the field of job-exposure assessment and sought evidence on national surveys of working conditions.

#### Direct evidence on risks by job title

- 27. An initial literature search for the Council focussing specifically on OA knee in joiners and woodworkers did not identify new research evidence.
- 28. More generally, two papers were identified in floor layers, which tended to support the current terms of prescription for this occupational group (Jensen *et al.*, 2012a, Jensen *et al.* 2012b), and two reports offering estimates of risk in other contexts (Andersen *et al.*, 2012, Apold *et al.*, 2014).
- 29. Andersen *et al.* (2012) used registry data for the whole Danish working population between 1981 and 2006 to identify hip and knee OA during 1996-2006. "Construction workers" were found to be at significantly increased risk of knee OA, but with odds ratios (ORs) increased overall by only 27-37%. In further analyses by cumulative years of employment, however, risks were roughly doubled in construction workers with over 10 years of exposure (for men, OR 1.96; for women, 2.06). Current terms of prescription for knee OA in floor layers were also confirmed (OR 2.27 in those employed more than 10 years).

- 30. In Norway, Apold *et al.* (2014) assessed risks of knee replacement for primary OA in over 300,000 participants from national health screenings followed prospectively over 12 years, with linkage to the Norwegian Arthroplasty Register. Strong associations were found with obesity, while men reporting intensive physical activity at work had a relative risk of 2.4 (versus those with sedentary activity at work), and women were at similar risk. "Intensive" physical activity at work was defined as "heavy manual labour e.g. forestry worker, dockworkers, farmworker, ditch digger". Risks in those with intensive physical activity were higher than those with intermediate or moderate activity, a group which included construction workers but combined them with cashiers, office workers, machinery workers, foremen and mailmen).
- 31. Correspondence with the authors of six reports (mentioned in paragraphs 16, 21, 29 and 30) established that in general the published risk estimates in construction workers, builders and labourers could not be disaggregated to establish risks by a given job title.
- 32. A partial exception was the report by Seidler *et al.*, further information from which was published in an erratum (Journal of Occupational Medicine and Toxicology 2012, 7:21) (Table 2). However, the authors confirmed that risks in Table 2 could not be distinguished in, say, carpenters separately from plastic workers, or painters separately from varnishers, or plasterers separately from the several trades analysed together. A challenge, evident in Table 2, was that finer granularity led to analyses being based on small numbers (e.g. only 16 labourers in all). There was wide statistical uncertainty, such that effects of chance were difficult to discount; several of the nine risk estimates in Table 2 were more than doubled, but only one of these was statistically significant.

Table 2: Osteoarthritis of the knee – risks by service occupation and years of employment (adapted from Seidler et al., 2012)

	OR (95%CI) (number in trade)		
	1-10 years	>10 years	
Construction (structural & civil engineering)	2.3 (0.7-6.9)	1.7 (0.4-7.1)	
	(n=23)	(n=13)	
Plasterers, insulators, glaziers, terazzo	0.6 (0.2-2.4)	3.7 (0.9-15.2)	
workers, construction carpenters, roofers,	(n=13)	(n=14)	
upholsterers			
Woodworkers and plastic workers	2.3 (0.6-8.1)	3.3 (0.7-16.0)	
(carpenters, cabinet makers, wooden or	(n=15)	(n=10)	
plastic models makers, wood-frame			
construction)			
Painters, varnishers	1.3 (0.3-6.3)	9.6 (1.2-77.9)	
	(n=11)	(n=13)	
Labourers	2.7 (0.8-9.1)	-	
	(n=16)		

OR – odds ratio; CI – confidence interval; n = number

Knee-straining activities in construction workers

33. Other correspondence with a specialist from Denmark (Dr Jane Frølund Thomsen, personal communication) identified a recent report by Rubak *et al.* (2014) on patterns of lower limb exposure by job title. Access was granted to the raw dataset, which listed construction jobs believed (by an average of expert consensus) to involve kneeling to an extent that would put them in the top 10% for all jobs across all industries in Denmark (Table 3). In the table the estimates have been compared with those for floor layers. No other trade was believed to be as heavily exposed, but plumbers, pipe-fitters, thatchers and paviours were considered to kneel for 66% to 71% of the time that floor layers did. A few other occupations were estimated to kneel for 31% to 51% of that time, as detailed in Table 3.

34. Also identified with Dr Frølund Thomsen's help, was an annual survey of self-reported working conditions across a large randomly selected sample of workers in Denmark.<sup>2</sup> Table 4 records occupations where more than 50% of respondents estimated that they had spent at least one-quarter of the work time squatting or kneeling (perhaps 2 hours/day) in 2014. Those reporting such exposures comprised painters, "masons, plumbers and others" (probably plumbers and bricklayers), carpenters and joiners, electricians and mechanics. However, these self-reported estimates were compatible with the expert ratings in Table 3 only for plumbers, and higher than for woodworkers, electricians and painters.

<sup>2</sup> <a href="http://www.arbejdsmiljoforskning.dk/da/arbejdsmiljoedata/arbejdsmiljoe-og-helbred-20/arbejdsmiljoeet-i-tal/sammenligning-af-jobgrupper/diagram?question=NA HUGKNMIN 1 4

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Table 3: Occupations in the top 10% of all for kneeling in Denmark (Rubak et al., 2014, adapted with kind permission)

HEG heading	International occupational title	Kneeling hrs/day	% of floor layer's time
Wood working, craftmanship	joiner	1.5	43%
-	apprentice, joiner		
	joiner, construction		
	boatbuilder, wood		
	carpenter,		
	erector, green house		
	housebuilder, non-traditional materials		
	shipwright, metal		
	maker, model/wooden		
	cabinetmaker		
	builder, model		
	assembler, furniture/wood & related		
	finisher, furniture		
	hand, carpenter		
Roofers	roofer	1.6	46%
	roofer, composite material		
Floor layers	parquetry worker	3.5	(100%)
	floor layer, parquetry		
	floor-layer, carpet		
Insulations workers	insulation worker	1.8	51%
	hand, insulation worker		
Plumbers and pipe fitters/layers	fitter, pipe/gas	2.3	66%
, ,	plumber		
	fitter, pipe		
	layer, pipe		
	boilersmith		
Thatchers	thatcher	2.4	70%
Paviours	paviour	2.5	71%
	hand, paviour		
Bricklayers and stonemasons	stonemason, construction	1.5	43%

	layer, tile		
	bricklayer, construction		
Workers in drainage	layer, drain	1.3	37%
and sewage	worker, sewer		
	sewer contractor		
Electricians and fitters	fitter, pipe/ventilation	1.1	31%
of ventilation	electrician, building/electrical installation		
	electrician, building repairs		
	electrician		
Painters and wallpaper hangers	painter-decorator, wallpapering	1.1	31%
	painter, ship's hull		
	apprentice, painter		
	painter, building		
	wallpaper hanger		
	painter, house		
	painter-decorator, wallpapering		
	handyman, building maintenance		
Workers in road and building	land clearer	1.1	31%
construction	labourer, maintenance/roads		
	hand, contractor (labour)		
	labourer, construction		
	hand, building site		
	labourer, construction/buildings		
Sheet metal workers,	coach-builder	1.2	34%
working with metal for vehicles	maker, metal sheet		
	sheet-metal worker, vehicles		
	beater, vehicle panel		
	sheet metal worker, vehicles		
	machine-operator, planing metal		

HEG - Homogeneous Exposure Groups

Table 4: National Institute of Occupational Health: Working in Denmark 2012-2020 – Occupations: % who squat or kneel at least 1/4 of the time during 2014

			95% Confidence Interval	
Occupation	%	No. of persons	Lower limit	Upper limit
Painters	85.1	77	76.4	91.6
Masons, plumbers and others	78.7	145	72.3	84.2
Carpenters and Joiners	74.4	144	67.2	80.7
Electricians	61.2	181	54.7	67.4
Car mechanics	55.8	177	48.5	63.0

- 35. It should be noted that the data in Tables 3 and 4 are based on opinions rather than measurements. In Table 3 they were independent of the respondent, but based on the views of only a small panel of experts. Although Table 4 was derived from a large study sample, estimates by job title were based still on relatively small numbers of workers in a given trade (e.g. 77 painters). Use of them would require the Council to assume similar working conditions in Britain as in Denmark.
- 36. Checks were also made for information on levels of knee-straining activity in the HSE's Workplace Health and Safety Survey (WHASS) programme and the European Working Conditions Survey, (EWCS) but no additional information was obtained on representative exposures within the construction industry.

Risks of knee osteoarthritis by duration of kneeling and squatting – general population findings

37. Finally, the general literature contains reports of risks by duration of self-reported kneeling or squatting. Some evidence suggests that kneeling and squatting may double risks after 30 minutes to 2 hours/day (Palmer, 2012), but contradictory estimates exist, including ones that discount risks at this level of exposure and others that indicate a higher duration, such as 3 hours/day. Studies have varied considerably in their quality in a research area that is prone to potential biases (described in Palmer, 2012). This creates some uncertainty in defining *a priori* the levels of exposure that would support prescription.

#### Summary and assessment of the evidence

38. As in 2008, 2010 and 2012, when the Council previously reviewed the terms of PD A14, there remains a relative shortage of direct evidence on risks of knee OA by job title. Such evidence as exists tends to point potentially to a qualifying level of risk among "construction" workers when defined very broadly, but gives only limited evidence on risks by more closely defined job titles within the industry. New reports have added a few more data points to a growing research database but have not changed this position.

- 39. By contrast, there is now a large established general evidence base on risks of knee OA by occupational activity. However, such reports of activity are subjective; self-reported; harder to corroborate in a claims environment than time spent in a defined occupation; and subject to some uncertainty regarding the levels and types of exposure that would double risks of the disease. Many different metrics have been applied in research studies, most of which would be impractical to use in a high-volume low-cost benefits assessment system.
- 40. For OA knee in underground miners, prescription proved possible despite a relative lack of direct evidence on doubling of risks in miners and notwithstanding the problems of prescription defined by occupational activity (paragraph 39) because a combination of direct and indirect evidence was brought to bear (paragraph 12). Such an approach was sought here, to overcome the challenges faced in prescribing for the disease in construction workers. In practice, however, a further present limitation is that representative levels of exposure to knee-straining activity are still not at all well described in British construction workers. Despite a literature review, calls for evidence and consultation with experts, the Council managed only to identify some subjective and not wholly consistent estimates of exposure for workers from Denmark. (In that country no working group was identified as being exposed as heavily to kneeling and squatting as were carpet and floor layers; but several construction trades were identified as being at the 'heavy' end of exposure. Uncertainties exist in extrapolating from work practices in Denmark to those in the UK, but Tables 3 and 4 suggest possible 'candidate' trades for which further data relevant to the UK would be of special interest in future to receive.)

#### Conclusions

- 41. For the reasons set out above the Council remains unable to recommend extending the prescription for knee OA to encompass additional trades within the construction industry.
- 42. However, the Council remains committed periodically to updating its appraisal of the evidence base on work and knee OA. It would be pleased at any time to receive new evidence, both on risks of the disease by occupational title and on representative information on exposures to knee-straining activity by occupational title in Britain. Both types of evidence may in future serve to strengthen the arguments for extending the terms of PD A14.

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### **Glossary**

# Types of study

**Case control study:** A study which compares people who have a given disease (cases) with people who do not (non-cases, also called controls) in terms of exposure to one or more risk factors of interest. Have cases been exposed more than non-cases? The outcome is expressed as an **Odds Ratio**, a form of **Relative Risk**.

**Cohort study**: A study which follows those with an exposure of interest (usually over a period of years), and compares their incidence of disease or mortality with a second group, who are unexposed or exposed at a lower level. Is the incidence rate higher in the exposed/more exposed workers than the unexposed/less exposed group? Sometimes the cohort is followed forwards in time ('prospective' cohort study), but sometimes the experience of the cohort is reconstructed from historic records ('retrospective' or 'historic' cohort study). The ratio of risk in the exposed relative to the unexposed can be expressed in various ways, such as a **Relative Risk**, or **Standardised Mortality Ratio**.

**Cross-sectional study**: A study which classified people at a point in time as having a given disease (or characteristic) or not (controls), and then compares them in terms of exposure to one or more risk factors of interest. Is disease more frequent in those with exposure than in those without? The outcome can be expressed as an **Odds Ratio**, **Prevalence Ratio** or **Relative Risk**.

#### **Measures of association**

**Statistical significance and P values:** Statistical significance refers to the probability that a result as large as that observed, or more extreme still, could have arisen simply by chance. The smaller the probability, the less likely it is that the findings arise by chance and the more likely they are to be 'true'. A 'statistically significant' result is one for which the chance alone probability is suitably small, as judged by reference to a pre-defined cut-point. (Conventionally, this is often less than 5% (P<0.05)).

**Relative Risk (RR):** A measure of the strength of association between exposure and disease. RR is the ratio of the risk of disease in one group to that in another. Often the first group is exposed and the second unexposed or less exposed. *A value greater than 1.0 indicates a positive association between exposure and disease.* (This may be causal, or have other explanations, such as bias, chance or **confounding.**)

**Odds Ratio (OR)**: A measure of the strength of association between exposure and disease. It is the odds of exposure in those with disease relative to the odds of exposure in those without disease, expressed as a ratio. For rare exposures, odds and risks are numerically very similar, so the OR can be thought of as a **Relative Risk**. A value greater than 1.0 indicates a positive association between exposure and disease. (This may be causal, or have other explanations, such as bias, chance or **confounding**.)

## Other epidemiological terms

Confidence Interval (CI): The Relative Risk reported in a study is only an estimate of the true value in the underlying population; a different sample may give a somewhat different estimate. The CI defines a plausible range in which the true population value lies, given the extent of statistical uncertainty in the data. The commonly chosen 95%CIs give a range in which there is a 95% chance that the true value will be found (in the absence of bias and confounding). Small studies generate much uncertainty and a wide range, whereas very large studies provide a narrower band of compatible values.

**Confounding:** Arises when the association between exposure and disease is explained in whole or part by a third factor (confounder), itself a cause of the disease, that occurs to a different extent in the groups being compared.

For example, smoking is a cause of lung cancer and tends to be more common in blue-collar jobs. An apparent association between work in the job and lung cancer could arise because of differences in smoking habit, rather than a noxious work agent.

Studies often try to mitigate the effects of ('control for') confounding in various ways such as: restriction (e.g. only studying smokers); matching (analyzing groups with similar smoking habits); stratification (considering the findings separately for smokers and non-smokers); and mathematical modelling (statistical adjustment).

## **Experts consulted**

The Council wishes to thank the following researchers for their assistance with review inquiries:

Dr Jane Frølund Thomsen, Bispebjerg University Hospital, Copenhagen, Denmark Professor Eva Vingård, Uppsala University, Uppsala, Sweden Professor Helene Sandmark, Mälardalen University, Sweden Professor Andreas Seidler, Technical University of Dresden, Dresden, Germany Dr Sara Holmberg, Research and Development Centre, Kronoberg County Council, Växjö, Sweden Susan Andersen, University of Southern Denmark, Odense, Denmark