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PUBLIC HEALTH | RESEARCH ARTICLE

Upper limb disorders among biomedical laboratory workers using pipettes

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Abstract: Laboratory workers engaged with biomedical work often process series of specimens by repetitive or static manual activities. The widespread use of stamp pipettes has in particular been suspected to entail upper-limb disorders. Our primary aim was to test, if cumulated pipette work is associated with self-reported and clinically examined upper-limb disorders. Additionally we explored, if non-pipette repetitive or static laboratory tasks are associated with upper-limb complaints. We also explored, if use of electrically driven pipettes (reducing the forces needed to activate the pipette) are in lesser degree associated with upper limb complaints than manually driven pipettes. In all, 1,398 female laboratory technicians at two workplaces were included in a questionnaire survey. Among 1,202 respondents, 167 cases with significant upper-limb symptoms and 134 controls without participated in a case-control study. Amount of pipette work (especially when cumulated over the last 2 years) was associated with symptoms in dominant upper limb, especially in the hand/wrist and thumb, and with impingement syndrome and muscle pain in dominant shoulder. Use of electrical pipettes did not modify this association. The non-pipette tasks were at highest vaguely related to upper-limb symptoms. In biomedical laboratory work, intensive pipette use seems to constitute a dominating major ergonomic problem.


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Jonas Winkel Holm is a medical doctor at Department of Occupational Medicine, University Hospital Holbæk. His research interests are occupational musculoskeletal disorders, primarily focusing on the relation between repetitive and physically demanding work and, on the other side, neck and upper limb disorders. Apart from studies in different occupational settings, the author has also been engaged in a twin study.

PUBLIC INTEREST STATEMENT

In medical and pharmaceutical laboratories, several tasks involve static postures and repetitive manual movements. This might trigger disorders in the upper limbs (the hands, arms and shoulders). A prominent example is the frequent use of pipettes in laboratories. Pipettes are hand-held instruments used to suck up and dispense small amounts of liquids.

In order to investigate, if frequent pipette use increases the risk of pain and disorders in the upper limbs, we examined laboratory workers at two large workplaces (a medical and a pharmaceutical).

Indeed, laboratory workers with frequent pipette use more often had pain and disorders in the arm handling the pipette than workers with less (or no) pipette use.

To deal with this ergonomic problem in laboratories, an important measure is to reduce the pipette work for the individual laboratory worker when planning the flow of work. In this respect, one should also consider introduction of robotic technology.

Subjects: Disability; Occupational Health and Safety; Occupational & Environmental Medicine; Occupational Health & Safety; Rheumatology

Keywords: industrial ergonomics; anatomy; health risks; musculoskeletal disorders; upper limb disorders

1. Introduction

In modern biomedical laboratories, biological and chemical hazards are normally well controlled, but wat about the *ergonomics* of this work? Often, large series of samples are processed, demanding precise and repetitive upper limb movements. These tasks are regularly performed under narrow and restricted working conditions, in biosafety cabinets etc. (Björksten, Almby, & Jansson, 1994; Kilroy & Dockrell, 2000; Park & Buchholz, 2013; Ramadan & Ferreira, 2006).

The widespread use of pipettes in biomedical laboratory work has especially been suspected to pose a risk of upper limb disorders. Pipettes are hand-held instruments used to dispense small, exact quantities of liquids.

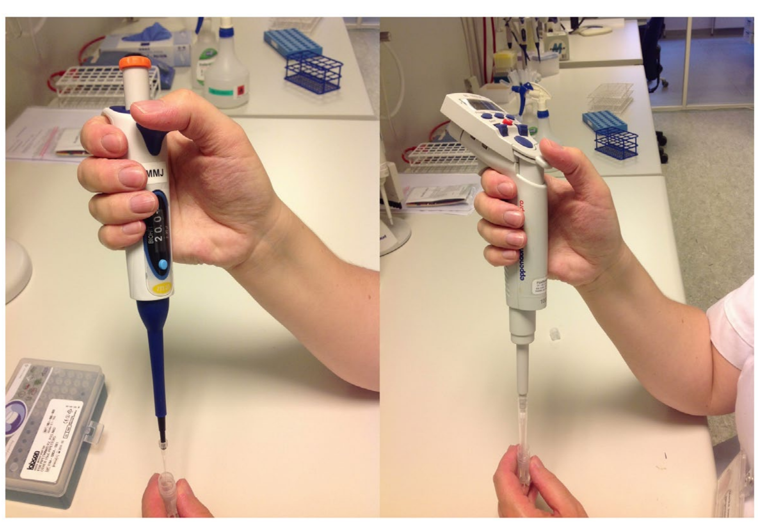
Nowadays' laboratory pipettes are mechanized stamp pipettes which normally have a dagger-like "thumb-push" design (Figure 1), leaving it to the thumb to activate the pipette functions by pressing buttons at the pipette top. Often, this is often repetitively during prolonged periods.

In the traditional stamp pipettes, which are still often in use, the pipette stamp is driven by manual force by loading and unloading a spring in the pipette cabinet (Figure 1, left picture). Electrical pipettes have however been increasingly frequent since the 1990s. In these pipettes, the pipette functions (or most of them) are driven by an inbuilt electromotor (Figure 1, right picture) which decreases the pressure needed to activate the pipette buttons.

From the 1980s, case studies emerged reporting musculoskeletal upper limb disorders among intensive pipette users (Baker & Cooper, 1998; Heath, 1998; Minuk, Waggoner, Hoofnagle, Hanson, & Pappas, 1982; Roullet & Castaigne, 1982; Vergouwen & Vermeulen, 2007). In the 1990s, two cross-sectional questionnaire studies investigated the relationship between pipette work and upper limb complaints (Björksten et al., 1994; David & Buckle, 1997). In both studies, pipette users more often had upper limb complaints than non-users, and intensive pipette users even more often had upper limb complaints than less intensive pipette users. These two pioneer studies, however, only sparsely included possible confounders: Other repetitive or static laboratory tasks besides pipette work were not included as possible confounders (or supplementary exposures). The studies moreover only investigated *complaints*, not clinically established musculoskeletal disorders. Finally, they only

Figure 1. Thumb-push pipettes.

The pipettes are held in a "daggert" grip, and the different pipette functions are mainly elicited by the thumb (i.e. aspiration and dispensing of fluid, emptying pipette cabinet, ejecting the pipette tip). The pipette is either *manually* driven (left picture) by or *electrically driven* (right picture).



preliminary explored if an exposure-response relation exists between the amount of pipette work and upper limb complaints.

Thus, the aims of the present study were:

- To investigate, if an exposure-response relation exists between the *amount of pipette work* and, on the other side, (a) *complaints* and (b) *clinically examined* musculoskeletal disorders in the upper limbs.
- Preliminary to explore, if *other* “non-pipette” repetitive or static biomedical laboratory *tasks* are associated with upper limb complaints.
- Preliminary to explore, if use of *electrical pipettes* are in lesser degree associated with upper limb complaints than use of manually driven pipettes.

In two large workplaces with various biomedical laboratory activities, we conducted a case-control study, nested in a cross-sectional questionnaire study forming the study base.

2. Material and methods

2.1. Design, selection of subjects

The study was carried out at two large enterprises with diverse biomedical laboratory activities, a large pharmaceutical company, and a public enterprise. At the pharmaceutical company many branches of biomedical research and development of pharmaceutical products are performed. The public enterprise is engaged with surveillance, diagnosis and research within infectious, autoimmune, congenital and genetic disorders.

All female laboratory technicians employed at these workplaces were invited to participate during the winter 1997–1998. As often seen in biomedical laboratories, the corresponding group of males was very small (7% of the study base of both sexes). Moreover, male technicians were often engaged with tasks in the “background” (in relation to the analytical work with samples), for instances, in the animal stables. Male technicians were therefore excluded.

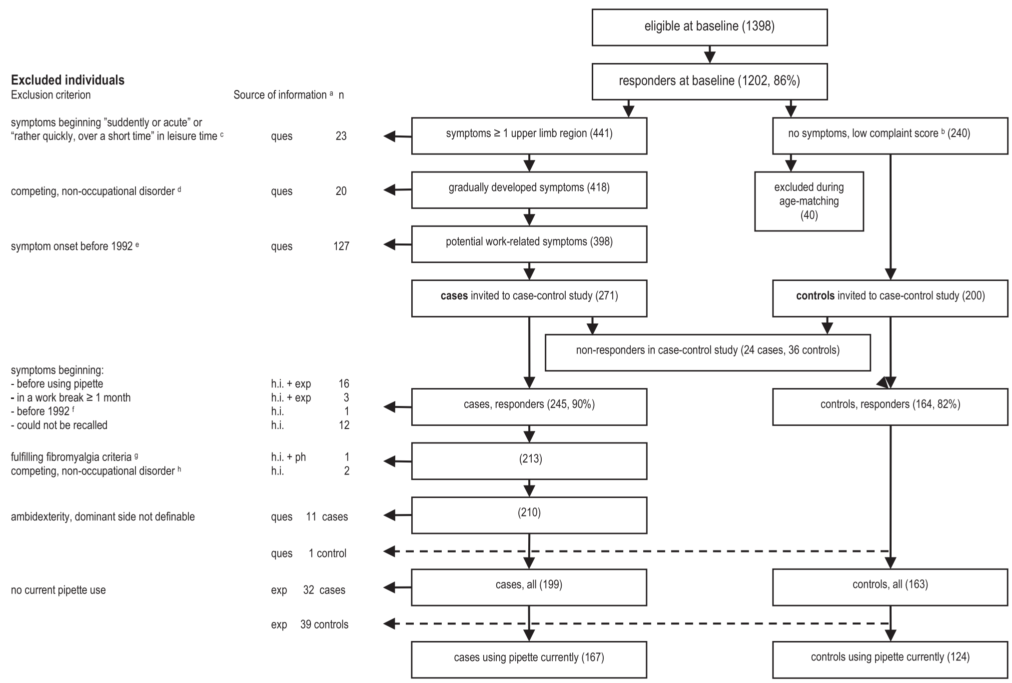
In all, 1,398 technicians were mailed a questionnaire at their home address. In all, 1,202 technicians (86%) filled out the questionnaire, and constituted the study base behind the case-control study. Details of the selection process are shown in Figure 2.

After the questionnaire study, cases with significant *symptoms* (cf. the subsection “Outcomes” below), along with their controls without *symptoms*, were included in the case-control study. This was conducted at the two workplaces during working hours in the winter 1997–1998, for practical reasons consecutively at the workplaces.

Cases-to-be were drawn among participants of the questionnaire study with *symptoms* from one or more upper limb regions. Hereafter, a list of exclusion criteria were applied based on information from the questionnaire (cf. Figure 2). Of 271 cases-to-be invited to the case-control study, 245 participated (90%). However, additional exclusion criteria were applied, combining information from the different parts of the case-control study proper, leaving 210 cases-to-be. It was, however, a posteriori decided that the terms “dominant” and “non-dominant” upper limb were preferable to “right” and “left”, a conversion which excluded genuine both-handed individuals. Thus, 199 cases finally remained in the case-control-study.

However, the final models investigating the effect of pipette work were only performed among *current* pipette users; these included 167 cases.

Figure 2. Flow-chart illustrating the establishment of the case-control population.



[a]ques: questionnaire, h.i.: health interview, exp: exposure interview, phys: Physical examination. [b]Defined as (1) a complaint score < 6 (range 0–36) in each of the nine anatomic regions, and (2) a combined complaint score for all regions < 12 (range 0–324). [c]Since the focus of the study was *gradually* developed *occupational* disorders. [d]Reporting to suffer from presumably serious competing, non-occupational disorders, e.g. rheumatoid arthritis, other rheumatologic disorders, "fibromyalgia", cervical disc herniation and whiplash syndrome. [e]The intention was to ensure detailed exposure assessments for at least 2 years before symptom development for each participant, considering the fact that the detailed part of the exposure interviews covered the period from 1990 onwards. Individuals who did leave this question blank or stated a span of years crossing the year of 1992 were also invited to the case-control study, where the question of symptom onset was further elaborated. [f]Even though stating otherwise in the questionnaire. [g]According to Wolfe et al. (1990). [h]1 individual with whiplash syndrome, 1 with cervical disc herniation.

Controls were drawn from questionnaire respondents with no or minor complaints in all eight upper limb regions *and* the neck (Figure 2). Among these, controls were drawn frequency-matched with the cases within ten-year age groups, but otherwise randomly. Of 200 eligible controls, 164 participated in the study (82%). One both-handed control was excluded a posteriori, leaving 163 controls for the case-control-study. The final models regarding the effect of pipette work were, as mentioned, only performed among current pipette users, hereof 124 controls.

In the case-control study, the participants underwent an exposure interview, a physical examination and a health interview:

2.2. Exposure assessment. The exposure interviews

Ergonomic assessments were made on the workplaces in autumn 1997, before the case-control study. First, experienced occupational therapists from the two workplaces and the first author identified 16 ergonomically distinctive (and reasonably frequent) "generic" laboratory tasks by workplace walk-troughs (cf. Table 2). The intention was to obtain a priori suppositions about which lab tasks might be "potential harmful" with respect to musculoskeletal disorders of the upper limbs (incl. the shoulders). Hereafter, the first author ergonomically assessed each of the 16 tasks, as performed by at least four workers. Tasks assessed to involve prolonged repetitive or static strain on the upper limbs were regarded as "potential harmful". In borderline situations, also manual force and non-neutral joint movements/postures were assessed, using the principles of the Moore Strain Index (Steven Moore & Garg, 1995). This resulted in 10 tasks categorized "potentially harmful" (cf. Table 2 including footnotes) such as "work with culture (Petri) dishes" and "putting on and removal of lids and caps", while 6 tasks, such as "paper work and talking" and "setting up, clearing up, cleaning", were not.

Later, in the case-control study, the participants' *individual* laboratory work histories were assessed by exposure interviews, structured upon these 16 tasks. The interviews were performed by five occupational therapists experienced with the laboratory occupation, and covered rather detailed laboratory work during the preceding approximately 7.5 years (from 1990 to the interview). First, the participant's laboratory work history was divided into one or more "job periods", defined as time windows (of at least 3 months duration) with broadly unchanged work content. For each job period, starting with the present one, the participant was asked to estimate her average time consumption for each task. (For pipette work, e.g.: "How much do you think you have been working with pipette, on average, in the time period from (start of job period) to (end of job period)").

Finally, supplementary questions addressed pipette use: On the period from 1990 and forth questions were asked about use of electrical vs. manual pipettes (cf. Figure 1), as percentage of total "pipette time". On the period *before* 1990 questions were asked about the total time span with pipette use (years), and the average amount of pipette use during this period (hours/week). The interviewers were blinded to the participants' health status.

From these assessments, exposure variables were computed for the 10 "potential harmful" tasks. First, a *pipette* exposure parameter was chosen. Some "candidates" were listed in the form of cumulated parameters as well as current amount of pipette work (Table 1).

All exposure parameters were associated with case-control status, but cumulated amount of pipette work during the last 2 years presented the largest explanatory power in this respect, assessed by the partial correlation coefficient *R*. We therefore chose this as pipette exposure parameter. (cf. Table 1; the 9 "non-pipette" potential harmful lab tasks were parameterized analogously).

In order to explore, if use of electrical pipettes were differently related to upper limb complaints than manually driven pipettes, we computed the additional parameter (for pipette users): "Proportion of electrical pipette use", as percentage of the individual's total pipette use during the last 2 years.

Table 1. Different pipette exposure parameters. Bivariate distribution among cases and controls

	Cases (n = 167) median	Interquartile range	Controls (n = 124) median	Interquartile range	Z statistic[a]
Current amount of pipette work (h/week)	5.00	2.00–9.00	2.75	1.00–5.00	−3,29**
Average amount of pipette work (h/week):					
During the last 1 year	5.00	2.00–9.00	2.50	1.00–5.00	−3,74***
During the last 2 years	4.93	2.00–8.00	2.50	1.01–5.00	−3,82***
During the last 3 years	4.52	2.00–7.53	2.50	1.28–5.00	−3,81***
During the last 4 years	4.30	2.00–7.50	2.50	1.24–4.98	−3,81***
During the last 5 years	4.03	1.98–7.50	2.50	1.18–5.00	−3,71***
During the last 7 years	3.59	1.92–7.34	2.49	1.13–4.99	−3,51**
Lifetime amount of pipette work (hours)	4,878	2,504–10,142	3,916	1,478–7,935	−2,12*

[a]*Applying* Mann-Whitney U test.

*$p \leq 0.05$ comparing cases with controls.

**$p \leq 0.01$ comparing cases with controls.

***$p \leq 0.001$, comparing cases with controls.

2.3. Outcomes

2.3.1. Upper limb symptoms

Complaints from the upper limbs, derived from the questionnaire, formed the main outcomes. The participants reported complaints from eight anatomic regions, four in both upper limbs: (1) the shoulder (and upper arm), (2) the elbow, (3) the hand and wrist, and (4) the thumb/thenar separately. For each anatomic region, the participants were asked to rank symptom intensity and limitation of daily activities resulting from the complaints on a numeric box scale ranging from 0 (no complaints) to 9 (as bad as could be). This symptom-recording instrument was a slightly modified, Danish version of the Chronic Pain Grade questionnaire (CPG) (Von Korff, Ormel, Keefe, & Dworkin, 1992). The modification was a broadening of the outcome definition from merely pain to "complaints (pain and discomfort)". Four questions were asked for each anatomic region: (1) the worst and (2) the average complaint level in the past 3 months, (3) the impairment of daily activities (at work or in leisure time) during the same period, and finally (4) the average complaint level in the past 7 days. The scores of these items were summarized to a complaint score for each anatomic region (range: 0–36).

Complaints from a particular upper limb region likely to have clinical significance were defined by a complaint score ≥ 12 (Kaergaard, Andersen, Rasmussen, & Mikkelsen, 2000). The resulting dichotomous outcomes were simply termed *symptoms* (or not) in the upper limb region in question.

Participants reporting *symptoms* in an upper limb region were directed to supplementary questions developed for the study, inquiring if the symptoms began (1) "quite suddenly, acute during an accident (a sprain, a blow, a fracture etc.)" (2) "rather quickly, over a short period of time", or (3) "slowly and gradually". If the respondent chose the second answer, she was directed to three response categories, questioning if the complaints started (1) in leisure time, (2) at work, or (3) if this could not be decided. Furthermore, the participant was asked to state (approximately) which year the symptoms began in the upper limb region in question.

Few participants reported symptoms in the *non-dominant* elbow, wrist/hand and thumb; therefore, these outcomes were combined as "symptoms in the distal, non-dominant upper limb".

2.3.2. Clinically established disorders

These outcomes derived from a combination of information from the questionnaire and from physical examinations of cases and controls. The examinations were carried out by the first author, focusing on the upper limbs, including the neck and shoulder girdle. It comprised investigation of palpation tenderness, active/passive range of motion, and some common provocative clinical tests, cf. Table 5 (Beighton, Solomon, & Soskolne, 1973; Finkelstein, 1930; Hawkins & Kennedy, 1980; Kaergaard et al., 2000; Ranney, 1997; Toomingas, 1998; Travell & Simons, 1983; Waris et al., 1979). The first author noted the findings in an examination form, and was blinded as regard the participants' work situation and health status.

Based on the physical examination, 14 clinically established disorders or "diagnoses" of more or less tentative nature were defined by predetermined criteria, consisting of (1) physical signs, following common accepted guidelines (Andersen & Gaardboe, 1993; Kaergaard et al., 2000; Waris et al., 1979) and (2) reporting of symptoms in the same anatomic region (Table 5).

2.4. The health interview

After the physical examination, the first author performed a brief, structured health interview of cases, breaking the blinding in this final step of the study. The primary aim was to encircle the period in which the symptoms first appeared. The participant was also asked if a physician had diagnosed the symptoms, which could perhaps constitute a non-occupational "competing" disorder, cf. Figure 2.

2.5. Potential confounders

Deriving from the questionnaire, several variables were considered potential confounders: The occupational psychosocial dimensions of the extended demand-control model (job decision latitude/control, job demands, and social support) were each represented by 2 or 3 items with 4 or 5 response categories, extracted from the Whitehall-II version of the job content questionnaire (Karasek & Theorell, 1990). For each dimension, sum scores were constructed from the item scores. General mental well-being was represented by the mental health and vitality dimensions in the SF-36 (Short Form questionnaire, 36 items) (Ware & Sherbourne, 1992). The two dimensions were combined to a common sum score (9 items, 6 response alternatives). Self-reported type A behaviour was assessed by 3 items with 5 response categories, combined to a sum score (Hägg, Suurküla, & Kilbom, 1990). Moreover, the total duration of vocational education was assessed, and considered a proxy for social class. Physical activity in leisure time was represented by a single question with four response categories (North et al., 1993), and present smoking was also included. Furthermore, the newly developed question "Have you within the last 3 months used pain-killers (including pain-killers for headache) for other pain than pain in hands, arms, shoulders or neck" was considered a proxy for general level of pain perception and/or pain-related behaviour, and regarded a potential confounder. The response categories were "daily", "one to several times a week", "one to several times a month" and "more seldom or never".

Finally, deriving from the physical examination, body height, body mass index and upper limb hypermobility were included as confounder variables.

From Tables 2 and 3 the final parameterisation of the confounder variables appears. As no exposure-response relations could be stated a priori for these, the parameterisation of covariates was decided by preliminary analyses "optimizing" the association of each variable with the symptom outcomes.

2.6. Data analysis

In bivariate analyses, the Mann-Whitney U test was applied to numerical variables, as no parameter approximated a Gaussian distribution; for dichotomous variables, χ^2-test was used. In the multivariate models for the symptom outcomes (including case-control status), prevalence odds ratios (OR) and their 95% confidence intervals (95%-CI) were calculated from the maximum likelihood estimates of the coefficients and their standard errors, using logistic regression with log likelihood-ratio testing. The method of successive backward elimination of the least significant variable was applied. For each outcome, two partial models were initially made, respectively, for (a) non-occupational/general parameters and (b) occupational parameters. Entry and exit criteria for the variables in these models were significance levels on respectively $p \le 0.10$ and $p \le 0.20$. Variables remaining in the two partial models were fused in a combined model, and again backward elimination was applied (with entry and exit criteria for the variables on, respectively, $p \le 0.05$ and $p \le 0.10$.).

Since the case-control study was performed as separate sub-studies on the two workplaces, the selection of age-matched controls was also restricted by workplace - in effect an additional matching factor besides the age matching (ten-year age groups). These matching factors were introduced in all partial and combined models (and if rejected, reintroduced in the final models). The acceptability of the final models was supported by the Hosmer-Lemeshow test generating insignificant χ^2 values (Hosmer & Lemeshow, 1989).

Reported *p*-values are two-sided, and probability levels of $p \le 0.05$ were regarded statistically significant. As statistical software was used SPSS for Windows version 8.0.2.

3. Results

As regards occupational characteristics (Table 2), cases tended to report higher amount of current pipette work than controls, and higher amount of “putting on and removal of lids and caps”. Moreover, cases reported lower job control and social support, and higher job demands than controls.

Table 2. Occupational characteristics of cases and controls

	Cases				Controls				
	n	%	Median	IQR	*n*	%	Mean	IQR	*p*-value
Subjects	199				163				–
Working at the State Serum Institute		34				37			ns
Potential harmful laboratory tasks (hours/week)									
Pipette work			3.0	1.0–7.5			1.7	0.3–5.0	***
Computer work			5.0	2.5–10.0			5.0	2.0–10.0	ns
Work with culture (Petri) dishes			0.0	0.0–1.0			0.0	0.0–0.5	ns
Putting on and removal of lids and caps			1.0	0.3–1.5			0.5	0.0–1.0	*
Microscopy			0.0	0.0–0.5			0.0	0.0–0.5	ns
Loading and unloading machines			0.5				0.5	0.0–0.5	ns
Operations, injections, blood samples on animals			0.0	0.0–0.0			0.0	0.0–0.0	
Use of manual whirl mixer (vortex mixer)[a]			0.0	0.0–0.5			0.0	0.0–0.5	*
Use of manual diluter (dispenser)[b]			0.0	0.0–0.0			0.0	0.0–0.0	ns
Other work with cells and tissue[c]			0.0	0.0–0.0			0.0	0.0–0.0	ns
Other repetitive or static laboratory work[d]			0.0	0.0–1.5			0.0	0.0–1.0	ns
Psychosocial characteristics									
Low job control[e]		55				23			***
High job demands[e]		50				30			***
Low job support[e]		53				37			**

Notes: IQR: Interquartile range, ns = not significant.

[a]Electromotor-driven, vibrating device used to mix small quantities of liquids.

[b]Small, hand-held apparatus used to dilute small quantities of liquids with water.

[c]Painting and fixing tissue samples etc.

[d]Different more infrequently performed repetitive or static lab tasks combined (filtration with syringe, work with microtome etc.). The following six lab tasks were not assessed as “potential harmful”: “setting up, clearing up, cleaning”, “paper work and talking”, “breaks”, “pouring and filling up”, “weighting” and “other work with animals than operations, injections and taking blood samples”.

[e]sum score below or above median (Here presented dichotomously for clarity. In multivariate analyses, the parameter was treated as a continuous variable based on the sum score).

*$p \leq 0.05$.

**$p \leq 0.01$.

***$p \leq 0.001$.

The length of the working week (not shown in table) was comparable between cases and controls, respectively 37.6 (4.1) h/week and 37.5 (4.3) h/week (mean (SD)).

Table 3. Non-occupational and general characteristics of cases and controls

	Cases				Controls				
	n	%	Median	IQR	*n*	%	Median	IQR	*p*-value
Subjects	199				163				–
Age (years)			39	32–49			41	33–41	ns
Height ≥ 175 cm		9				14			ns
Height < 160 cm		11				6			ns
High upper limb hypermobility score[a]		10				8			ns
Length of vocational education (years)			2.9	0.8			2.8	0.8	ns
Low physical activity[b]		61				46			**
Body mass index[c]									ns
<20 kg/m² (underweight)		13				10			ns
20–30 kg/m²		80				87			ns
>30 kg/m² (obesity)		7				3			ns
Smoking > 10 g tobacco/day		23				15			ns
Low degree of mental well-being[d]		49				26			***
High degree of Type A behaviour[e]		37				20			***
Use of pain-killers for other reason than upper limb or neck pain									***[f]
less than monthly		36				63			
at least monthly		48				33			
weekly or daily		17				4			

Notes: IQR: Interquartile range, ns = not significant.

[a]Upper limb hypermobility score > 2 (range: 0–6).

[b]Defined as: "sedentary lifestyle or light physical activity"; i.e. maximum 4 h light physical activity/week *and* less than 2 h more strenuous physical activity/week) (as opposed to "moderate to heavy physical activity/week" i.e. physical activity beyond the described limits).

[c]When comparing the prevalence of underweight between cases and controls (with X^2-test), obese individuals were excluded (and vice versa when obesity was examined).

[d]i.e. sum score below median (Here presented dichotomously for clarity; in multivariate analyses, the parameter was treated as a continuous variable based on the sum score).

[e]i.e. sum score above upper quartile; the same parameterization was used in multivariate analyses.

[f]X^2-test for trend was applied.

**$p \leq 0.01$.

***$p \leq 0.001$.

Moreover, nearly all cases, in contrast to controls, were either present or previous pipette users (97% of cases vs. 88% of controls, $p = 0.01$, not in table), and cases were a little more often than controls current pipette users (84% vs. 76%, $p = 0.06$).

Concerning non-occupational/general characteristics (Table 3), cases more often than controls reported low physical activity in leisure time, low general mental well-being, high level of "Type A" behaviour, and use of "pain-killers for other pain than upper limb and neck pain".

Among the potential harmful lab tasks, only amount of pipette work remained in the final models (Table 4), being positively associated with case status and symptoms in all dominant upper limb regions (and insignificantly also with symptoms in non-dominant shoulder). Somewhat unexpectedly, one potential harmful task was *negatively* associated with some of the outcomes, namely "work with culture dishes". Low job control and high job demands (but not social support) were risk factors for all symptom outcomes.

Not shown in Table 4 is the fact that the unadjusted risk estimates of pipette work and the other lab tasks were very similar to the final, adjusted estimates. As regards specifically the psychosocial work dimensions, the in- or exclusion of these in the multivariate models left the risk estimates of pipette work (and the other lab tasks) essentially unchanged.

In order to assess more thoroughly the impact of the *non-pipette* potential harmful laboratory tasks, the final multivariate analyses were repeated in the full case-control population, including non-pipette users. The results in Table 4 were nearly unchanged (not shown), but supplementary

Table 4. Occupational risk factors of the symptom outcomes, multivariate associations[a]

	Status as case	Symptoms in dominant			Symptoms in non-dominant:		
		Shoulder	Elbow	Hand/wrist[b]	Thumb	Shoulder	Distal upper limb[c]
	(*n* = 167)	(*n* = 74)	(*n* = 57)	(*n* = 67)	(*n* = 47)	(*n* = 28)	(*n* = 30)
	OR (95%–CI)	OR (95%–CI)	OR (95%–CI)	OR (95%–CI)	OR (95%–CI)	OR (95%–CI)	OR (95%–CI)
Pipette work	1.15 (1.06–1.25)	1.13 (1.02–1.24)	1.12 (1.01–1.24)	1.20 (1.09–1.32)	1.25 (1.11–1.41)	1.12 (0.99–1.27)	1.07 (0.95–1.21)
Work with dilutor	–	–	–	–	–	1.54 (1.07–2.23)	–
Work with culture dishes	–	–	–	–	0.74 (0.58–0.94)	–	–
Low job control	1.85 (1.36–2.51)	2.41 (1.62–3.59)	1.88 (1.28–2.74)	1.61 (1.10–2.35)	1.89 (1.23–2.89)	2.24 (1.25–4.02)	2.87 (1.67–4.94)
High job demands	1.52 (1.14–2.02)	1.47 (1.02–2.12)	1.54 (1.07–2.23)	1.82 (1.25–2.66)	1.89 (1.26–2.85)	1.95 (1.10–3.43)	2.41 (1.44–4.03)

[a]Among current pipette users, the different outcome groups are compared with the control group ($n = 124$). All occupational and non-occupational parameters are introduced (cf. Tables 2 and 3) but only occupational parameters in the final models are shown.

[b]Including the thumb.

[c]The non-dominant elbow, hand/wrist and thumb combined.

potential harmful laboratory tasks emerged in the final models. Amount of "putting on/removal of lids and caps" appeared as a determinant of symptoms in the dominant thumb (OR 1.69, 95-% CI 1.12–2.54), and "other work with cells and tissue (e.g. painting/fixing tissue samples)" as a determinant of symptoms in non-dominant distal upper limb (OR 1.46, 95-% CI 1.08–1.97).

The final multivariate results as regarding pipette work are further unfolded in Figure 3.

In the highest exposure level (pipette work > 5 h/week) elevated risk estimates are seen in all dominant upper limb regions, most clearly for the hand/wrist and thumb. Some dose-response tendency is perhaps seen, but only with insignificant risk elevations for the intermediary exposure level, pipette work < 2–5 h/week. For the non-dominant upper limb, a somewhat resembling, but very vague picture is seen.

The parameter "proportion of electrical pipette use" was subsequently introduced in all final models, but was invariably rejected by the backward elimination process ($p > 0.15$ in every case).

Among current pipette users (Table 5), only two clinically established disorders were reasonably frequent, both located in the dominant shoulder region: "shoulder impingement syndrome" and "muscle pain in the shoulder girdle". These were also the only ones showing any association with amount of pipette work.

Figure 3. Amount of pipette work and symptoms in different upper limb regions, multivariate associations. Among current pipette users, the different symptom groups are compared with the control group. Amount of pipette work (average of the past 2 years) is parameterized in three exposure levels, divided by tertiles among current pipette users.

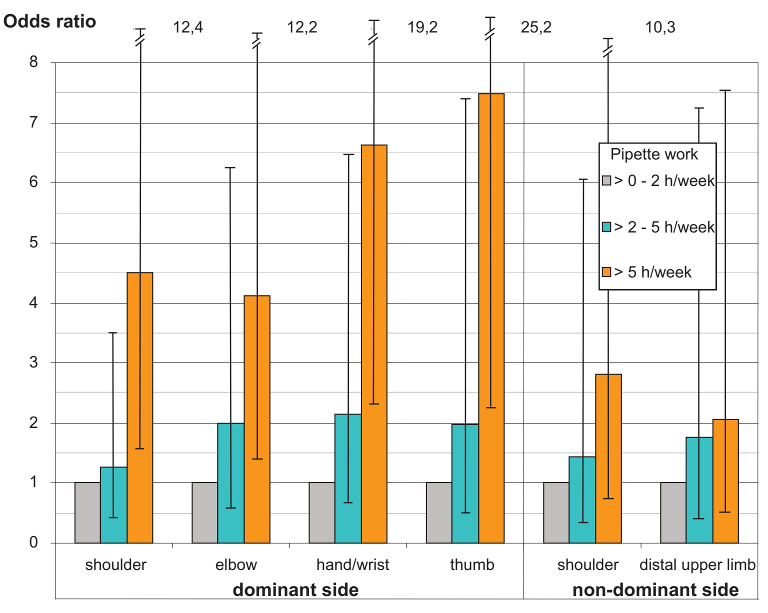


Table 5. Amount of pipette work and clinically established disorders in the dominant upper limb, bivariate associations[a]

Clinically established disorder	Total group	Amount of pipette work (h/week)			X^2-trend test	Diagnostic criteria
		>0–2	>2–5	>5		
	n = 291	*n* = 86	*n* = 92	*n* = 113		
	n (%)	*n* (%)	*n* (%)	*n* (%)	*p*-value	
Shoulder:						*Symptoms in dominant shoulder and following physical signs:*
Shoulder impingement syndrome	33 (11)	5 (6)	8 (9)	20 (18)	0.02 (7.2)	Positive painful arc sign *or* shoulder pain by any of following restricted movements: abduction or inwards/outwards rotation)
Muscle pain in shoulder girdle	86 (30)	18 (21)	26 (28)	42 (37)	0.04 (6.3)	Significant palpation tenderness (with pain reaction) in at least 2 of 5 muscle groups[b]
Acromioclavicular osteoarthritis, (possible)	14 (5)	4 (5)	1 (1)	9 (8)	0.22 (1.5)	Distinct pain in joint by compression of clavicula *or* by passive adduction and inward rotation in shoulder joint
Elbow:						*Symptoms in dominant elbow and following physical signs*:
Lateral epicondylitis	9 (3)	2 (2)	4 (4)	3 (3)	0.95 (0.0)	Palpation tenderness on lateral epicondyle *and* pain by restricted wrist extension
Hand/wrist (including thumb):						*Symptoms in dominant hand (incl. the thumb) and following physical signs:*
Tendinitis of wrist extensor tendons	18 (6)	6 (7)	7 (8)	5 (4)	0.43 (0.6)	Palpation tenderness on dorsal aspect of wrist *and* pain by restricted wrist extension on dorsal wrist side
Tendinitis of wrist flexor tendons	9 (3)	4 (5)	0 (0)	5 (4)	0.95 (0.0)	Palpation tenderness on ventral aspect of wrist *and* pain by restricted wrist flexion on ventral wrist side
Carpal tunnel syndrome (possible)	22 (8)	7 (8)	7 (8)	8 (7)	0.78 (0.1)	Positive Tinel's sign on ventral aspect of wrist (pain or paresthesia in at least one of the three radial fingers)
De Quervain's syndrome[c]	21 (7)	4 (5)	8 (9)	9 (8)	0.40 (0.7)	Positive Finkelsteins test[d] *and* palpation tenderness in Tabátiere
Osteoarthritis in the basal thumb joint (possible)	11 (4)	1 (1)	5 (5)	5 (4)	0.27 (1.2)	Positive "grind test": pain located at the joint by axial passive rotation of 1. finger with pressure in proximal direction

[a]Among current pipette users (*n* = 291). The following five infrequent disorders (with *n* < 9, i.e. prevalence < 3%) are not shown in the table: (1) bicipital tendinits (*n* = 2) defined as: positive Yergason test (pain in anterior aspect of shoulder by restricted supination of the forearm with elbow flexed in 90°) and palpation tenderness on caput longum m. (musculus) bicipitis, (2) shoulder capsulitis defined as: restricted passive outward rotation in shoulder joint (<70º) and passive outward rotation more restricted than inward rotation or abduction (3) medial epicondylitis (*n* = 0) defined as: palpation tenderness on medial epicondyle *and* pain by restricted wrist flexion, (4) tendinitis of thumb flexor tendons (*n* = 8) defined as: palpation tenderness on ventral aspect of wrist *and* pain on ventral aspect of wrist by restricted flexion of distal thumb joint, (5) cervical radiculitis (nerve root compression), defined as: positive foramen compression test, specified as: pain radiating from the neck to the arm when the cervical column is compressed, and the following passive movements of the neck are applied: maximal rotation and lateral flexion to the side of the arm, and maximal extension.

[b]i.e. the following five muscle groups: (1) paracervical neck musculature in C3 to C6 level, (2) m. trapezius, (3) m. levator scapulae, (4) m. supraspinatus and (5) mm. rhomboidei maj. et min.

[c]Tendinitis in m. abductor pollicis longus and /or in m. extensor pollicis brevis (with or without tenosynovial stenosis).

[d]Distinct pain with pain reaction in the Tabátiere by passive maximal ulnar deviation in wrist and with the four ulnar fingers flexed around flexed thumb.

4. Discussion

4.1. Main results

In this case-control study, increasing amount of pipette work, especially when cumulated over the past 2 years, was associated with increasing risk of symptoms in the dominant upper limb, most convincingly regarding the hand and wrist and the thumb. Increasing amount of pipette work was also associated with increased risk of having the shoulder disorders "shoulder impingement syndrome" and "muscle pain in the shoulder girdle", both at dominant side.

Nine non-pipette laboratory tasks were assessed, likely to inflict repetitive or static strain on the upper limbs, but neither of these was as consistently related to upper limb symptoms as pipette work.

4.2. Interpretation of results, accordance with previous literature

Our results are in accordance with the previous cross-sectional questionnaire studies investigating the topic (Björksten et al., 1994; David & Buckle, 1997). Thus, out of 128 female lab technicians using pipette, Björksten et al. (1994) reported elevated frequencies of right hand and shoulder ailments (with OR, respectively, 5.0 and 2.4) among technicians reporting more than 300 h of pipette work/year compared to technicians reporting less pipette work. (The exposure parameter was estimated as an average for all years of pipette use for each individual). When all 128 pipette-using technicians were compared with an external reference group (female state employees) a similar risk estimate contrast was found, with the highest risk among laboratory technicians.

Comparable findings were reported by David and Buckle (1997). When comparing 48 laboratory employees with more than 220 pipette hours during the past year with 32 laboratory employees with less (but some) pipette use, elevated risks of ailments in the elbows was found (OR = 3.2, right and left side were combined) and hand/wrist (OR = 2.8). When the combined group of 80 pipette users was compared with 85 laboratory employees without pipette use (scientists, secretaries etc.) they found a similar risk estimate contrast, with highest risk among pipette-users. This study, however, suffered from a low response rate (55%). In both previous studies, moreover, the confounder control was rather impartial, e.g. as concerns other lab tasks than pipette work and psychosocial dimensions.

In the present study, the cumulated amount of pipette use during the past 2 years slightly exceeded the other pipette exposure parameters in being associated with upper limb symptoms. However, this finding is probably of less interest, considering the small differences in this respect. Moreover, the different pipette exposure parameters were rather strongly interrelated (Spearman's ρ varying between 0.65 and 0.99 amongst current pipette users).

In the dominant hand/wrist, not at least the thumb, we found high risks of symptoms among the highest exposure group, >5 h of pipette work/week or approximately >1 h/work day. The association is probably causal, since the ordinary "thumb-push" pipette implies several inherent ergonomic problems: Thus, this pipette leaves the job to the thumb to activate the pipette functions (or most of them) by pressing buttons at the top of the pipette barrel. This is normally performed *repetitively*, and often involves high push forces. As concerns manually driven pipettes, activation forces between 4 and 41 Newton (i.e. 0.4–4.2 kpond) have been described (the highest values typically when ejecting the pipette tip or emptying the pipette cabinet) (Asundi, Bach, & Rempel, 2005; Fredriksson, 1995; Lee & Jiang, 1999; Lichty, Janowitz, & Rempel, 2011; Lu, James, Lowe, Barrero, & Kong, 2008). To compare, the maximal voluntary thumb flexion power among 10 women has been measured to 77 Newton (7.9 kpond) (Fredriksson, 1995).

Using the ordinary thumb-push, "dagger-designed" pipette however also implies *static* muscular strain on the thumb. Thus, the thumb must serve both as pipette *activator* and as grip *stabilizer*, allowing the fine, well-controlled movements of the pipette's tip and stamp while securing a steady base for the fine movements (Asundi et al., 2005; Fredriksson, 1995; Rempel, Janowitz, Alexandre, Lee, & Rempel, 2011; Wu, Sinsel, Zhao, Anss, & Buczek, 2015; Wu et al., 2012). Moreover, since the pipette handle is normally rather slender, the thumb must often assume an awkward "resting" position in extension and inward rotation, resulting in unstable joint juxtaposition (Fredriksson, 1995; Lintula & Nevala, 2006).

In the search for ergonomic improvements, electrical pipettes have as mentioned been introduced. Indeed, electrical pipettes have more easily activated pipette functions than manually driven pipettes, but generally, their weight is higher, and they share the "dagger" design exposing the thumb, as well as the other described ergonomic problems, with their manual counterparts (Lichty et al., 2011). In our study, the lack of explanatory power of the parameter "proportion of electrical pipette" neither suggest the shift towards electrical pipettes to be of crucial ergonomic importance. During recent years, attempts have been made to design new "non-dagger" pipettes, but while these endeavours hold some promises, they are still preliminary (Lee & Jiang, 1999; Lichty et al., 2011).

In our study, amount of pipette work was in modest degree also associated with symptoms in the dominant elbow, upper arm and shoulder, and with "muscle pain in the neck-shoulder girdle" and "shoulder impingement syndrome" in the dominant shoulder. These findings are probably also caused by the repetitive and static nature of pipette work (Andersen et al., 2003; Lee & Jiang, 1999; Lu et al., 2008; Ranney, Wells, & Moore,1995; van Rijn, Huisstede, Koes, & Burdorf, 2010; Silverstein, Fine, & Armstrong, 1986). Thus, during pipette use, the pipette-handling upper limb normally moves the pipette *repetitively* between different vessels. In addition, *static* strain on the upper limbs, primarily on the (normally dominant) "pipette" shoulder, arises from different sources. As mentioned, pipette work is regularly performed under narrow working conditions (biosafety cabinets etc.), a situation aggravated by the lengthiness of most pipettes (Fredriksson, 1995; Lee & Jiang, 1999; Lichty et al., 2011; Lintula & Nevala, 2006; Lu et al., 2008; Sormunen & Nevala, 2013). Such circumstances during pipette use often force the "pipette shoulder" in some degree of prolonged abduction or flexion (Lee & Jiang, 1999; Lu et al., 2008). Hereto, the precise pipette movements necessitate the shoulder girdle as a fixed "working platform", further increasing the static strain on the pipette shoulder (Laursen, Jensen, & Sjøgaard, 1998; Lee & Jiang, 1999; Park & Buchholz, 2013; Rempel et al., 2011) and aggravating the tendency to pain in the shoulder (Jensen et al., 1998).

Somewhat surprising, the amount of pipette work was not associated with clinically established disorders in the dominant thumb or hand/wrist, only with the two mentioned shoulder disorders (Armstrong, 1986; Moore, 1997; Silverstein et al., 1986). One can probably suggest that regular, clinically established disorders, especially in the "pipette thumb" (such as de Quervain's disease) practically preclude pipette use and causes a "healthy worker"-effect.

Two non-pipette "potential harmful" lab tasks appeared as determinants for some outcomes. Thus, "putting on and removal of lids and caps" was associated with symptoms in the dominant thumb—which is exactly the finger normally used repetitively during that task. It is less obvious why "other work with cells and tissue" (e.g. painting and fixing tissue samples) was associated with symptoms in distal *non-dominant* upper limb. However, some degree of "mass significance" eliciting Type 1 errors is plausible due to the relatively many (10) "potential harmful" lab tasks. As regards the non-pipette "potential harmful" tasks, neither Type 2 errors can be ruled out due to limited statistical power, as most of these tasks were relatively infrequent at the workplaces.

As regards the occupational variables, also some of the *psychosocial* work dimensions (low job demands and low job control) were rather important determinants for upper limb symptoms in the final models, as seen in many other occupational settings (Ariëns et al., 2001; Karasek & Theorell, 1990). The fact that the risk estimates for pipette work in our study were essentially unchanged, whether these psychosocial factors were included or not in the multivariate models, indicates that the effect of pipette work is not mediated by psychosocial work factors.

4.3. Strengths and limitations

The main *strengths* of the study are perhaps our effort to identify a relevant pipette exposure parameter, and our introduction of clinically established disorders. Hereto, we broadened the study scope by considering non-pipette "potential harmful" lab tasks as potential supplementary exposures and confounders.

On the other side, well-known *limitations* derive from the cross-sectional study design (Hennekens & Buring, 1987; Rothman & Greenland, 1998). This erases the temporal sequence of cause and effect, mixes etiologic and prognostic factors, and tends to introduce "healthy worker" effect.

However, the temporal sequence between case and effect was presumably partially "restored" by our exclusion of individuals reporting symptoms *before* commencing pipette use (or who could not recollect this matter).

The "healthy worker" effect has undoubtedly played a role. However, both workplaces had been maintaining an active rehabilitation policy during many years before the study, focusing on keeping injured technicians employed. Besides, our precaution to perform the final analyses among only *current* pipette users was partly serving the same purpose, as we excluded individuals who had ceased pipette use (perhaps for health-related reasons). By restricting the final analyses to the *current* pipette users, we also aimed at securing another condition essential for the case-control design, namely that cases and controls derive from the same population. Thus, the fact that the controls had *some* degree of current pipette work probably has served to diminish the "peculiarity" of controls as compared with the cases. Our decision of age-matching the controls with the cases should be seen in the same light.

The self-reported exposure parameters imply a risk of information bias (Hennekens & Buring, 1987; Rothman & Greenland, 1998). Participants with symptoms can be liable to overestimate their exposure (Leijon, Wiktorin, Härenstam, Karlqvist, & MOA Research Group, 2002; Viikari-Juntura et al., 1996). Partly, this can originate from the participants' anticipation of causality between exposure and outcome. This was probably to some degree counterbalanced by our presentation of the study as a *general* investigation of disorders in the locomotive apparatus among laboratory technicians, not focusing on pipette work. As regards the exposure assessments in the study, it should be underlined that the exposure interviews were carried out by occupational therapists familiar with the occupation (Wiktorin et al., 1999) and that the exposure interviews were firmly structured. We used plain exposure questions, addressing well-known laboratory tasks, instead of more generic and "abstract" postures or movements (Fallentin et al., 2001; Moore, Rucker, & Knox, 2001; Wiktorin, Hjelm, Winkel, & Köster, 1996; Wiktorin et al., 1999).

Self-reported symptom outcomes also involves a risk of information bias. We used CPG, a symptom questionnaire instrument that has shown indications of validity in different populations (Von Korff et al., 1992). Strictly speaking, we used a slightly modified Danish version of the CPG, which in a previous study demonstrated a fine test-retest reliability (Brauer, Thomsen, Loft, & Mikkelsen, 2003). Reliability is however—as well as validity—specific to the population in question.

When defining potential clinically relevant symptoms, we choose a cut point of which has proved sensitive in identifying individuals with clinically detectable shoulder disorders (Kaergaard et al., 2000). Hereto, we supplemented the symptom outcomes with more objective clinical outcomes.

The study participation is rather fine, both in the initial cross-sectional questionnaire study (86%) and in the case-control study (87%). However, the latter study was "nested" in the former, and an "effective" over-all participation in the case-control study can be estimated approximately by multiplying these two participation frequencies. This makes 75%. Being an acceptable value, it does not rule out some selection bias.

The definition of (especially) cases was somewhat elaborate, which contributed to the fact that a relatively small part of the study base was included in the case-control-study (*n* = 362 or 30% of the 1,202 individuals, in the final models even fewer). In order to characterize the many individuals not included in the case-control-study (*n* = 731), we compared these in supplemental analyses with the 362 included (bivariate analyses, analogously with Tables 2 and 3—however, for the non-included group we did not have information on the lab tasks, neither on anthropometrics and hypermobility). The non-included group was generally a little younger than the included group (respectively, the mean (with SD) was 39.3 (9.6) and 40.8 (9.7) years). This undoubtedly reflected another tendency seen, namely, that cases with *significant* symptoms—and therefore their age-matched controls too—tended to be older than "neither cases-nor-controls". The latter was a group largely consisting of technicians with minor, *non-significant* symptoms. This however hardly afflicts the representativity of the case-control-population.

Nevertheless, the outlined sources of selection and information bias can create spurious associations. Counteracting this, however, important forces tend to drag the results towards the null-hypothesis, namely inaccuracy of exposure and outcome parameters (non-differential misclassification), and perhaps the healthy worker effect too.

The fact that our study dated back to 1997–1998 clearly is a limitation, considering the possibility of ergonomic improvements since. To alleviate this, the first author performed additional walk-troughs on the workplaces autumn 2015, reevaluating the laboratory tasks ergonomically. The most obvious ergonomic change since 1997–1998 was increased automatization, involving robot technology supplanting *some of,* especially, the pipette work and the work with cell culture dishes. This imply that fewer laboratory technicians are currently "at risk" ergonomically than before. However, as regards the many non-automatized lacunas of laboratory work, we generally only noted minor ergonomic changes. This however had one possible exception: We observed that electrical pipettes had become increasingly frequent at the expense of the manually driven pipettes. Nevertheless, this ergonomic change is, as described above, hardly of crucial importance.

The psychosocial work environment was not formally reevaluated during the walk-troughs in 2015, but the general impression was that the job demands (not at least the work pace) had increased. Furthermore, the automatization had led to an ongoing reduction of the laboratory staff, and some technicians mentioned a decrease in (the feeling of) job security. All in all, it is likely that the importance of psychosocial factors in laboratory work nowadays have increased, relative the physical-ergonomic factors.

Overall, we think that the transferability of our results to present-day biomedical laboratory work is acceptable. In this connection, one should also keep in mind that disorders of the locomotive apparatus generally often take prolonged courses and not seldom have arisen in a somewhat "outdated" work environment. In addition, according to the author's experience, many biomedical workplaces, not at least smaller ones, have not implemented the same degree of automatization than the large workplaces involved in this study.

4.4. Implication of findings, conclusions

Our findings support that in biomedical laboratory work, especially pipette use pose an ergonomic problem, even though a longitudinal study might provide more valid results. One should seek to reduce prolonged, intensive pipette use by further automation or job organisation. Moreover, the postural ergonomics surrounding pipette use and other laboratory tasks should be optimized, e.g. when designing cabinetry, lab benches etc. Also, resistance training for the neck and shoulder should be considered (Zebis et al., 2011). Finally, the efforts of redesigning the traditional "dagger" pipette design should continue.

Practitioner summary

Biomedical laboratory workers frequently perform repetitive or static activities. In a cross-sectional case–control study, cumulated amount of pipette work was associated with symptoms in dominant upper limb, and impingement syndrome and muscle pain in dominant shoulder. Intensive pipette use seems to constitute a major ergonomic problem in biomedical laboratories.

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Competing Interests

The authors declare no competing interest.

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