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# Taste preference and psychopathology

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## **Abstract**

**Objective:** Excessive food intake has been linked to many factors including taste preference and the presence of psychopathology. The purpose of this study was to investigate the association between sweet and salty taste preference and psychopathology in patients with severe obesity.

**Methods:** A consecutive series of patients applying for bariatric surgery was recruited for the study. Taste preference was self-reported. Psychopathology was assessed using the revised version of the Minnesota Multiphasic Personality Inventory-2 (MMPI-2). 190 patients were included in the study.

**Results:** In comparison with patients who had salty taste preference, patients with sweet taste preference had significantly higher elevations on the depression (OD: 4.090,  $p=0.010$ ) and the hysteria (OD: 2.951,  $p=0.026$ ) clinical scales of the MMPI-2.

**Conclusion:** The results suggest the presence of an association between taste preference and psychopathology. The findings may be of interest for clinicians who are involved in the treatment of obesity. In particular, they may wish to pay increased attention to patients with sweet taste preference or who have a strong attraction for both sweet and salty foods, in order to detect psychopathology and to adapt the treatment.

**Key words:** taste preference; obesity; psychopathology; MMPI-2; depression; obesity surgery.

## Introduction

Taste preference (TP) <sup>1-5</sup> and psychopathology <sup>6,7</sup> are among the many factors that have been linked to the development of obesity.

TP has been linked to both food intake and psychopathology. Several studies examining the association between TP, eating regulation and weight suggest that preference for sweet fatty foods in non-obese stressed emotional eaters leads to an increase in eating <sup>8</sup> and that sweet TP correlates positively with body weight <sup>9</sup>.

Studies examining the association between TP and psychopathology, point to a relationship between craving for sweet food and psychopathology. In particular, sweet TP has been linked to depression in an experimental study conducted by Willner with animal and human models <sup>10</sup>. Mennella et al. found an association in children between TP for sweet foods and a family history of alcoholism and depression <sup>11</sup>. In contrast, Scinska et al studied a nonclinical population and did not found an association between sweet TP and depressive symptoms measured with the Beck Depression Inventory <sup>12</sup>.

TP in obese patients has also been associated with personality traits in a study by Elfhag et al <sup>13</sup>. Using the Swedish universities Scales of Personality, the authors assessed 60 obese patients and found that sweet TP was linked to higher levels of neuroticism.

On the whole, there is however little evidence up to now for an association between TP and psychopathology in obesity and it is not clear whether any specific TP is associated with a higher degree of psychopathology.

The aim of the present study was to further investigate the association between TP and psychopathology in subjects with severe obesity. It rests on the hypothesis that obese patients with sweet TP more frequently present with psychopathology, especially depression.

## Method

### Participants

The present study involved a consecutive series of obese patients applying for gastric bypass surgery in the Multidisciplinary Obesity Unit of the Hospital Centre of Luxembourg between July 2007 and December 2008. To be included in the study, patients had to sign a written informed consent form. The Research and Ethic National Committee of Luxembourg approved the study. 197 patients agreed to participate. 7 patients were excluded because of extreme values on the MMPI

validity scales: L (lie scale) >80, F (infrequency scale) >90 and K (defensiveness scale) > 70. Finally 190 participants were included (144 women and 46 men).

### **Instruments**

The preference for sweet or salty foods was determined by asking patients directly two questions concerning their TP: Do you often have a craving for sweets foods? Do you often have a craving for salty foods?

Psychopathology was assessed with the revised version of the MMPI-2<sup>14</sup>. The MMPI-2 is a 567-item self-report questionnaire comprising 10 clinical scales with in addition several validity scales. In the MMPI-2, a T score of 50 represents the population average, with a standard deviation of 10. The cut-off point defining clinically significant psychopathology is 65.

### **Statistical analyses**

Participants were subdivided into 4 groups according to their TP: sweet, salty, sweet and salty and no TP.

The scores of the 10 MMPI-2 clinical scales were analyzed as dichotomized variables using logistic regression. For each scale, patients with “high”, i.e. clinically significant T scores ( $\geq 66$ ) were compared with patients with “low” T scores ( $\leq 55$ ). Patients with “intermediate” T scores (56 to 65) were excluded from the analyses in order to have contrasting values without interference of borderline values. After adjustment for gender, age, BMI and years of education, logistic regression analyses were applied to compare patients with sweet taste preference to patients with salty taste preference. Two-tailed statistical tests were used and a level of  $p < 0.05$  was considered statistically significant. Data were analyzed with PASW Statistics 18 (IBM, SPSS Belux, Brussels, Belgium).

## **Results**

### **Sample Characteristics**

190 participants were included in the study and 4 groups of TP were assessed: 49 patients (25.8%) with sweet TP only, 53 (27.9%) with salty TP only, 49 (25.8%) with a craving for both sweet and salty foods and 39 (20.5%) with no TP.

Mean age was  $38.3 \pm 10.5$  years (range: 18 to 63), mean years of education was  $11.8 \pm 3.2$  years. 64.2 % of the subjects were married or cohabiting. 4.2 % were unemployed. Mean BMI was  $43.1 \pm 6.3$ .

There were significant differences between the 4 groups regarding gender, but there were no significant differences with regard to age, BMI, marital status, years of education and work situation (Table I).

**Table I. Taste preferences and demographic variables**

	No preference	sweet N=42	salt N=43	Sweet and salt	p-value
Women N(%)	21 (11.1)	43 (22.6)	43 (22.6)	37 (19.5)	0.002 <sup>a*</sup>
Age (m +sd)	38.3 ± 10.1	38.4 ± 11.1	39.6 ± 10.4	38.8 ± 10.3	0.930 <sup>b</sup>
BMI (m +sd)	42.6 ± 5.0	43.0 ± 6.9	44.0 ± 7.1	42.4 ± 5.9	0.610 <sup>b</sup>
Years of education (m +sd)	11.7 ± 2.6	12.0 ± 3.4	11.7 ± 3.0	11.9 ± 3.5	0.869 <sup>b</sup>
Marital status: married or cohabiting N(%)	30 (15.8)	30 (15.8)	32 (16.8)	30 (15.8)	0.326 <sup>a</sup>
Unemployed N(%)	2 (1.1)	1 (0.5)	4 (2.1)	1 (1.1%)	0.317 <sup>a</sup>

<sup>a</sup>P-values were obtained with Chi-square test

<sup>b</sup>with Kruskal Wallis test

\*All taste preferences were compared to no preference (logistic model). A significant difference was observed (p<0.05)

### **Psychopathological characteristics of the four groups of taste preference**

There were no significant correlations between the BMI and any of the 10 clinical scales of the MMPI-2.

The comparison between the four groups of TP, adjusted for gender, age, BMI and years of education with regard to the MMPI-2 scores used as dichotomous variables (i.e. “high” versus “low” scores) revealed significant odds ratios for the depression and hysteria clinical scales of the MMPI-2. Patients who had a preference for sweet foods were more likely to have “high” scores of depression and hysteria than patients who preferred salty foods (table II).

**Table II. Logistic regression of taste preference (sweet vs salty) and MMPI-2 scores**

(low=0-55 vs high=65-100)\*

		NP	SW	S	SW&S	Odds ratio	95 % CI *	p value
Hypochondriasis	Low (%)	53.8	41.7	52.8	31.4			
	High (%)	46.2	58.3	47.2	68.6	1.743	0.657-4.625	0.264
Depression	Low (%)	62.5	35.5	65.1	48.4			
	High (%)	37.5	64.5	34.9	51.6	4.090	1.410-11.861	0.010
Hysteria	Low (%)	54.5	43.2	65.1	39.4			
	High (%)	45.5	56.8	34.9	60.6	2.951	1.138-7.651	0.026
Psychopathic deviate	Low (%)	72.7	58.6	79.5	53.1			
	High (%)	27.3	41.4	20.5	46.9	3.008	0.999-9.060	0.050
Masculinity- Femininity	Low (%)	100	94.7	97.6	87.2			
	High (%)	0	5.3	2.4	12.8	3.586	0.670-19.190	0.136

		NP	SW	S	SW&S	Odds ratio	95 % CI *	p value
Paranoia	Low (%)	68.2	55.3	65.9	54.8	1.629	0.613-4.328	0.327
	High (%)	31.8	44.7	34.1	45.2			
Psychasthenia	Low (%)	63	64.9	73.9	57.6	1.592	0.590-4.301	0.359
	High (%)	37	35.1	26.1	42.4			
Schizophrenia	Low (%)	78.1	74.3	78.4	64.5	2.926	0.432-4.386	0.589
	High (%)	21.9	25.7	21.6	35.5			
Hypomania	Low (%)	92	91.9	90.2	82.9	0.729	0.147-3.617	0.699
	High (%)	8	8.1	9.8	17.1			
Social introversion	Low (%)	70.4	71.4	76.7	68.4	1.380	0.484-3.930	0.547
	High (%)	29.6	28.6	23.3	31.6			

(\*) All values are adjusted for gender, age, BMI and years of education

CI: Confidence interval; NP: no preference; SW: sweet preference; S: salt preference; SW&S: sweet and salt preference

## Discussion

The results of this study suggest that obese patients with sweet TP are at higher risk for pathological levels of depression and hysteria than obese patients who prefer salty food. These results are in accordance with two previous studies. Kampov-Polevoy et al observed that individuals with a strong sweet TP were more likely to report mood-altering effect than individuals showing no preference for sweet solutions <sup>15</sup> and Christensen et al have reported that participants in a non-clinical population had a tendency to consume sweet foods after a sad event <sup>16</sup>

In our study, depression was assessed with the Minnesota Multiphasic Personality Inventory-2 (MMPI-2) <sup>14</sup>. The MMPI-2 is the most widely used and researched instrument of adult psychopathology. In particular, it has been used in several studies to assess obese populations <sup>17-21</sup>.

Obesity and depression may in fact share a common underlying mechanism involving a dysfunction in brain serotonin activity and sweet taste could be involved as a stimulant of serotonin activity. According to Pagoto <sup>22</sup>, a reduction in serotonin activity could lead to overeating in obese patients. The authors investigated the effect of acute depletion of tryptophan in lean and obese subjects and found an increase in sweet calorie intake in obese subjects along with an increase in depressed mood.

In a study by Elfahg et al<sup>13</sup>, the authors compared sweet TP with fat TP whereas we compared sweet taste with salty TP.<sup>13</sup>. Although, Elfahg et al assessed personality traits and not psychopathology, their results nonetheless lend support to those obtained in our own study. The authors found a relation between sweet TP and neurotic personality traits such as neuroticism. Since neuroticism is related

to feelings of anxiety and depressive mood, those results are in concordance with those obtained in our study.

Our study suggests a higher risk of psychopathology in severe obese patients with a sweet TP compared to those with a salty TP. Patients with sweet TP have higher scores on the depression and hysteria clinical scales of the MMPI-2. We did not find any significant differences concerning the 8 other clinical scales of the MMPI-2.

The present study has several limitations. First, our sample was restricted to patients with severe obesity who applied for bariatric surgery. As such, the results cannot be extrapolated to other types of obese patients (the patients in our study were physically and psychosocially more disabled than less obese patients). Second, the proportion of women in our sample was much higher than that of men. This fact could have affected the results since it has been shown that obese women have more psychological problems than obese men <sup>23</sup>. Third, we excluded from the analyses patients who had intermediate scores on the clinical scales of the MMPI-2, and we compared only the extreme groups. Fourth, we assessed TP using simple direct questions (i.e. we did not use any scale such as a visual analogue scale).

The strength of this study is that we compared and included 4 groups of TP (sweet, salty, both preference and no preference) and we used the MMPI-2, which is an instrument not limited to assess current symptomatology, but which also assesses more permanent characteristics.

Our results may be of importance to all clinicians working in the field of obesity. Clinicians should be aware of the fact that sweet TP may be a risk factor for psychopathology in obese patients. In particular, they should not restrict their advice and care to nutritional concerns but also pay close attention to psychopathology, in particular to depression <sup>5</sup>.

On the whole, our results may contribute to a better understanding of the relationship between TP, obesity and psychopathology. Additional studies are needed to confirm and complement our results.

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## Disclosure

All authors declare no conflict of interest.

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The authors alone are responsible for the views expressed in this publication; GA, MV and CP are staff members of Public Research Center for Health- Luxembourg (Centre de Recherche Public de la Santé- Luxembourg) and they do not necessarily represent the decisions, policy or views of the CRP-Santé.

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# DTI of the Visual Pathway in Cerebral Lesions

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## **Abstract**

Diffusion tensor imaging (DTI) can be used to localise the visual pathway (VP). In the service of the neurosurgery we have been working since the beginning of this year to develop a protocol which is suitable for the every day clinical routine to show the tracts of the white matter. Many lesions of the brain concern the white matter. Up to date it is still difficult to portray the visual pathway. Many centers all around the world are actually trying to localize the visual pathway, yet it is still used for the research. The application of the DTI-data for surgical interventions remains still a rarity. We believe that using this technique it would reduce the intraoperative risk and improve the postoperative outcome. From the beginning of this year we have been able to localize the visual pathway in 14 patients with different illnesses and we performed also postoperative controls. Using this new technique we were able to minimize the intraoperative risk in our patients.

## **Keywords**

Diffusion tensor imaging; Fibertracking; High grade glioma; Homonymous hemianopsia; Tractography; Visual pathway

## **Abbreviations**

DTI: Diffusion Tensor Imaging, VP: Visual Pathway, WMT: White Matter Tracts, LGN: Left Geniculate Nucleus, EPI: Echo-Planar-Imaging, FACT: FiberAssignment by Continuous Tracking, ROI: Region of Interest, ALA: Aminolevulinic Acid

## Introduction

Diffusion tensor imaging (DTI) is a recently devised technique that permits the non-invasive three-dimensional visualization of white matter tracts (WMT) in vivo<sup>1</sup>. It uses the differences in water molecule diffusion patterns along axon bundles throughout the brain<sup>2,3</sup>. Tract localization might help the neurosurgeon to protect important fibers in eloquent regions<sup>4</sup>. DTI is mainly used for research purposes. Although there are some centers in which it is used for surgery too, in particular for the corticospinal tract, it is not part of the daily routine for the majority of neurosurgeons<sup>5,6</sup>.

The optic radiation carries visual information from the left geniculate nucleus (LGN) to the visual cortex. It was first described by Louis Pierre Gratiolet in 1856. Infiltration or destruction of the visual pathway can be induced by lesions or by the neurosurgeons who try to remove these lesions adjacent to the visual cortex. Avoiding these injuries is difficult as the visual pathway is not visible under the naked eye or under the microscope. DTI has the potential of guiding the neurosurgeon through the white matter in order to avoid the injuries which would result in a deficit of the visual field.

We report of 14 patients who have undergone surgery because of intracerebral lesions like glioblastomas, lymphomas, cavernomas or metastasis adjacent to the visual pathway (VP). There were seven women and seven men. Two of the patients have had already postoperative controls. The average age of the patients was 58,5.

## Materials and Methods

Our aim was to have a procedure which could be easily used in every day clinical routine to demonstrate the different tracts of the white matter and their relation to a lesion in an eloquent region. Using this procedure we were able to show the main parts of the VP and their proximity to the tumor for neurosurgical intervention. Our purpose was to delineate and thereby protect eloquent areas during neurosurgery.

For the protocol, a MRI-scan was acquired on a 3T General Electric SignaHDxt Scanner pre-operatively. We used a standard high-res 3D T1 scan for intraoperative navigation and a T2 weighted anatomical scan. Additionally we performed a DTI-sequence. The parameters used for the DTI-sequence were a square FOV of 200 mm, an acquisition matrix of 96 x 96 and a slice thickness of 2 mm, yielding nearly isotropic voxels of approximately 2 x 2 x 2 mm<sup>3</sup>. The scan was carried out in the axial flow using 32 gradient directions and one B0-image, utilizing Echo-Planar-Imaging (EPI) and ASSET parallel imaging, with an asset factor of 2.0. Additional MRI scan acquisition time was less than nine minutes. From our point of view this is the maximal acceptable additional time for daily routine. However, the limited time frame enforces trade-offs in the image quality.

We processed the DTI data on a standard commercial workstation (StealthViz, Medtronic Inc., USA). This software uses a straightforward fiber tracking approach known as fiber assignment by continuous tracking (FACT). FACT is based on the propagation of lines between regions of interest (ROIs) defined by the operator<sup>3,7</sup>. Parameters for the tractographies were a maximum angle of 45°, an FA Start Value of 0,10 and an ADC Stop Value of 0,20.

First we localized and segmented the optic chiasm in the T2 images to create a 3D model using it as starting ROI. In another step we localized the LGN on both hemispheres. We could show how the fibers ran from the optic chiasm to the LGN. Then we traced the fibers from the expected location of the LGN to the visual cortex, in order to visualize their relation to the tumor. Depending on where the lesion was situated the visual pathway was interrupted completely, it was split in some directions or it was pushed simply aside. These results were reproducible on different days. Cortical lesions like tumor are often surrounded by an edema which makes the task even more difficult because it can change the course of the visual pathway additionally. The surrounding edema was thus separately carved out using T2-weighted images. This allowed us to detect fibers ending in the edematous part of the occipital lobe when the visual cortex was invaded by edema. This created a challenge. Technical limitations in the used fiber tracking software do not allow the definition of intersecting 3D model ROIs. E.g. it was not possible to define a ROI modeling the primary visual cortex and a ROI modeling the extent of the edema because such ROIs would intersect in the presented case. To work around this limitation we used a simple box shaped ROI including the intact visual cortex and that part of it which was tangent to the edema. Box shaped ROIs are technically independent from the more complex 3D models. We computed the tractography using this box as target ROI. As a result, all fibers terminated in the visual cortex. The process described above, with the MRI T1, T2 and DTI sequences and fiber reconstruction was repeated on the first post-operative day. Later controls are planned to show the development.

## Results

Using DTI we were able to identify the main fibers of the VP from the optic chiasm through the LGN to their termination in the visual cortex. With the images and reconstruction tools we were able to choose the most advantageous entry point for a keyhole technique surgical intervention. Intra-operatively the tumors were further delineated with 5-ALA<sup>8</sup> if there was a suspicion of glioblastoma.

Ophthalmologic controls after surgery were made and they were compared to the results before surgery.

## Discussion

New technology in the localization and delineation of intracerebral tumors support progress in neurosurgical interventions. DTI is one such recently devised non-invasive MRI technique enabling the visualization of the white matter tracts in vivo. It is based on the concept of anisotropic water diffusion in myelinated fibers.

To date, it has principally been used for research into neurologic and psychiatric disorders such as amyotrophic lateral sclerosis,<sup>9</sup> multiple sclerosis, Alzheimer's disease,<sup>10</sup> Parkinson disease,<sup>11</sup> and schizophrenia. It is not a standard procedure for surgery until now. Although there are some centres which have shown particularly the corticospinal tract, results for the optical tract are still rare. This technique might prove also interesting from a neurosurgical point of view. Optimal identification and delineation of functional brain tissue would allow for greater confidence in resection while avoiding unnecessary damage<sup>12</sup>. Cerebral tumors can alter white matter tracts in three different ways: by mass displacement, by tract invasion and by disruption of tract fibers<sup>13</sup>. Edema may play an additional role in aggravating the situation<sup>14</sup>.

Recent studies have shown that it is possible to reconstruct WMTs despite this<sup>1,15</sup>.

DTI-tractography cannot, as yet, compete with the resolution achieved by direct fiber dissection in preserved human brains or chemical tract-tracing methods in animals. It may also potentially suffer from incongruence with anatomic images<sup>7</sup>. However, to date it has successfully been used to limit or avoid complications in tumor neurosurgery by pre-operative identification of tracts such as the corticospinal tract, the superior longitudinal fasciculus and the inferior fronto-occipital fasciculus<sup>4,16</sup>, letting the afore-mentioned authors conclude that this new technique might help neurosurgeons apply safer approaches in eloquent areas adjacent or invaded by a tumor.

Relatively long scan times might hamper DTI-utilization for daily routine<sup>4-6</sup>. Data integration during operation as well as the brain shift during surgery also remain limitations to more general usability<sup>17</sup>.

We present 14 patients in whom a specific approach to a suspected lesion in the visual pathway using DTI and neuronavigation allowed successful resection. DTI based tractography was especially used in order to depict the position of the main fibers of VP. This knowledge helped in modifying the surgical approach in order to preserve as many of the fibers as possible. Technical limitations of the used software, which lacks the capability to define intersecting ROIs, could be overcome using simple box shaped ROIs. As it has already been outlined above, box shaped ROIs are technically independent from the more complex 3D models. It allowed us to show parts of the VP ending in the non-edematous part of the visual cortex as

well as in the edematous part of it. During the whole procedure we never cropped any fibers nor did we use any exclusion masks. Also, our protocol would be easy in implementation in clinical routine with extra scanning time for performance of DTI-sequences measuring only 8.58 minutes.

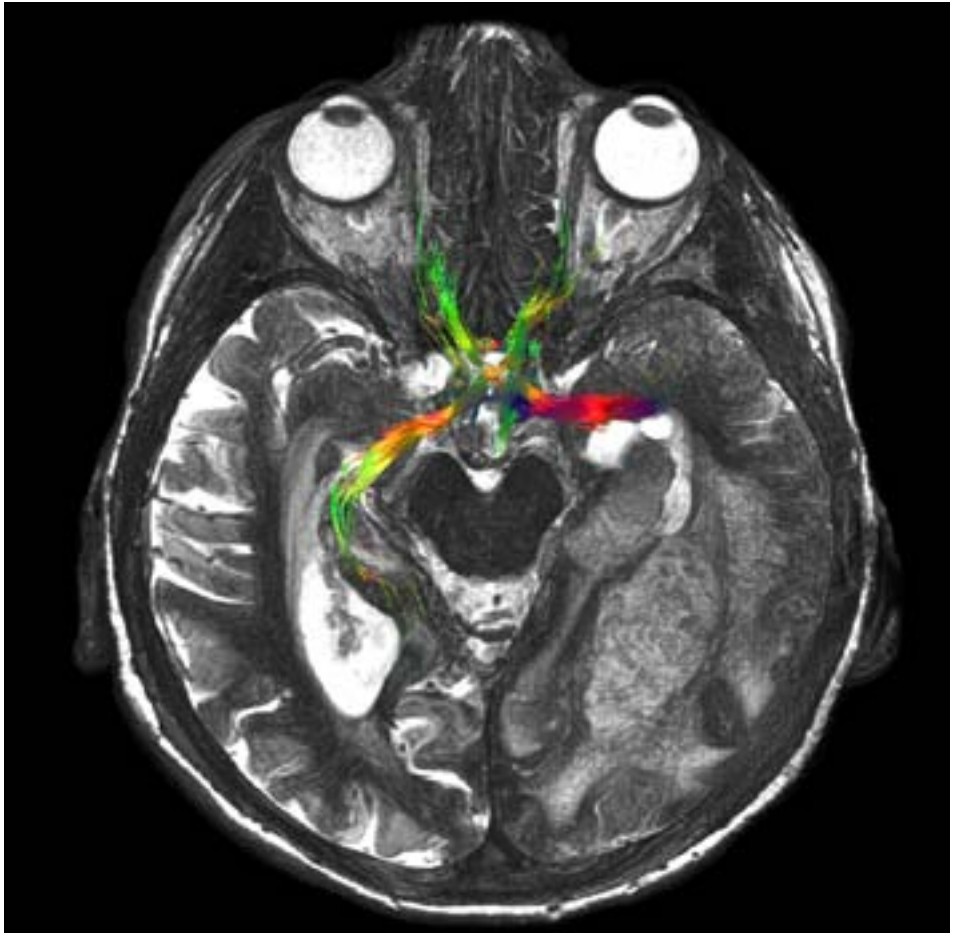
## Conclusion

Using DTI in neurosurgery might help the surgeon remove the tumor without harming adjacent eloquent areas of the brain. From our point of view it has the potential of becoming a standard procedure before surgery where the visual pathway might be compromised.

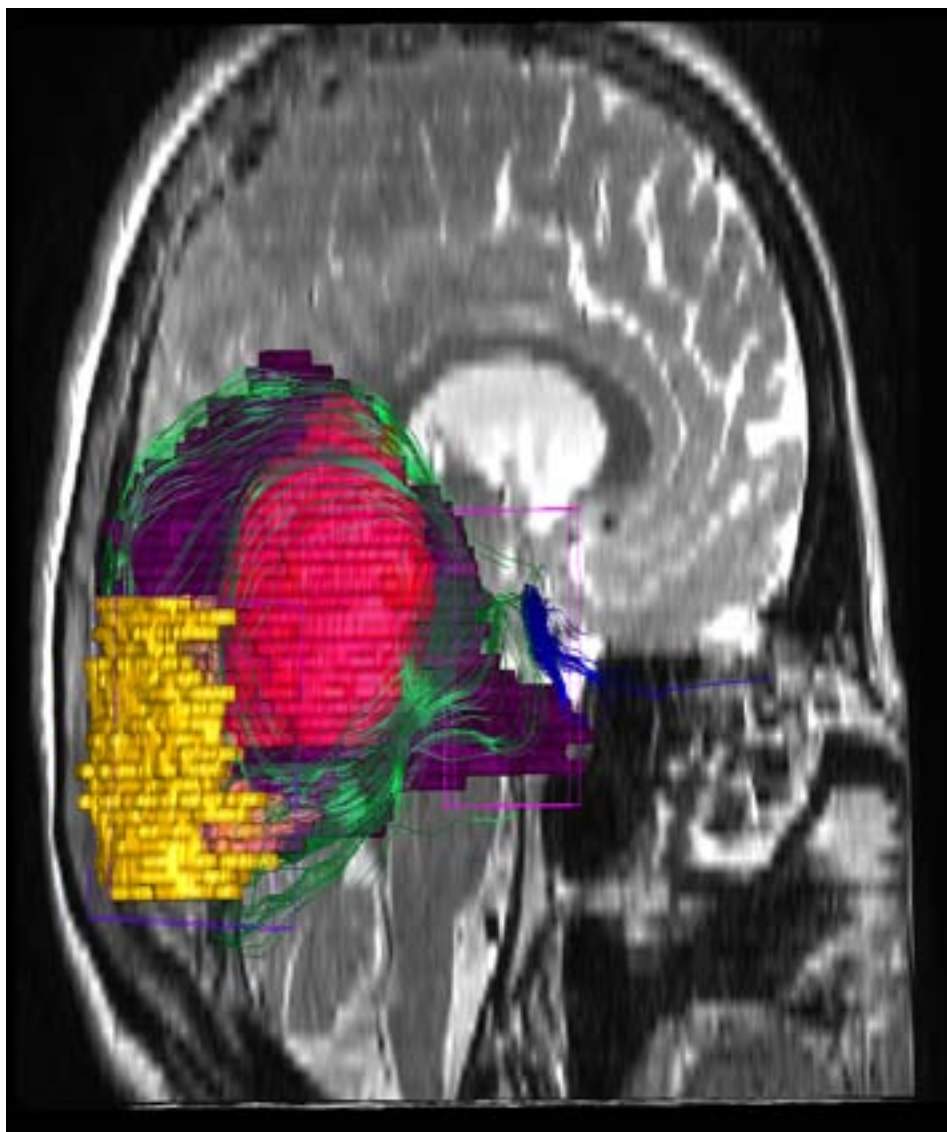
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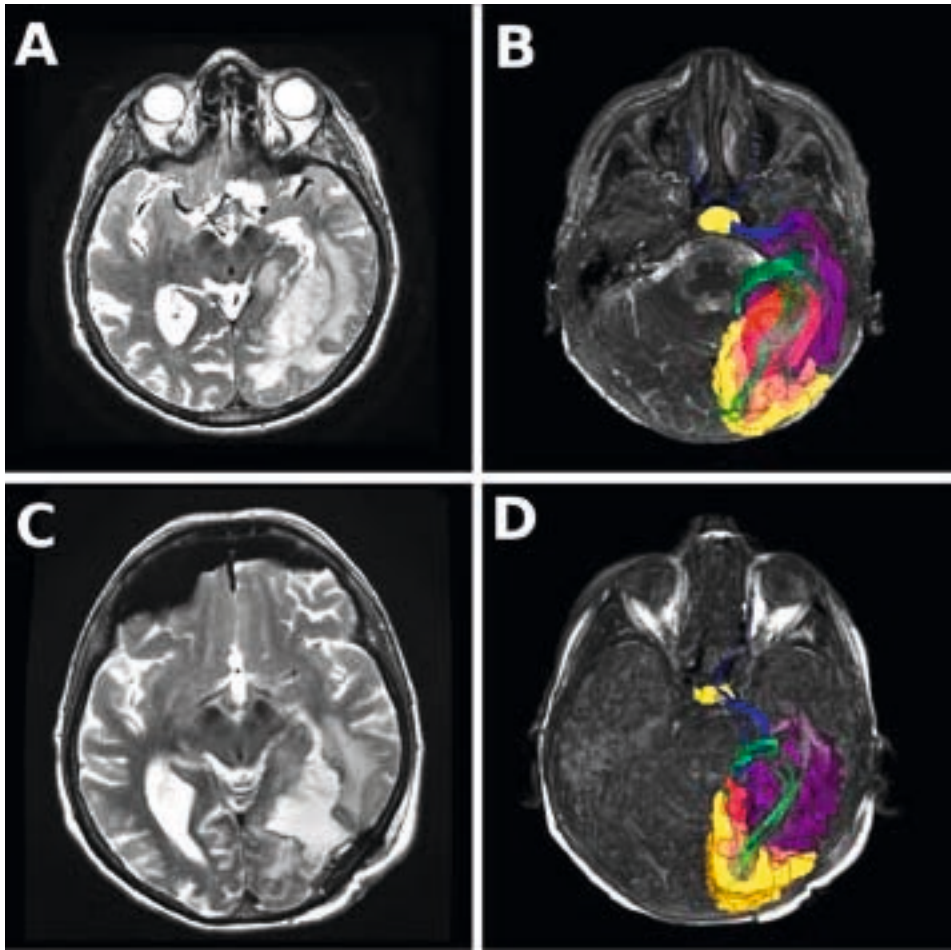
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**MRI Axial:** Interruption of the visual pathway on the left side.



**MRI Sagittal** : Tumor (red), Edema (purple), Visual cortex (gold), Opticradiatio (green), Optic tract (blue).

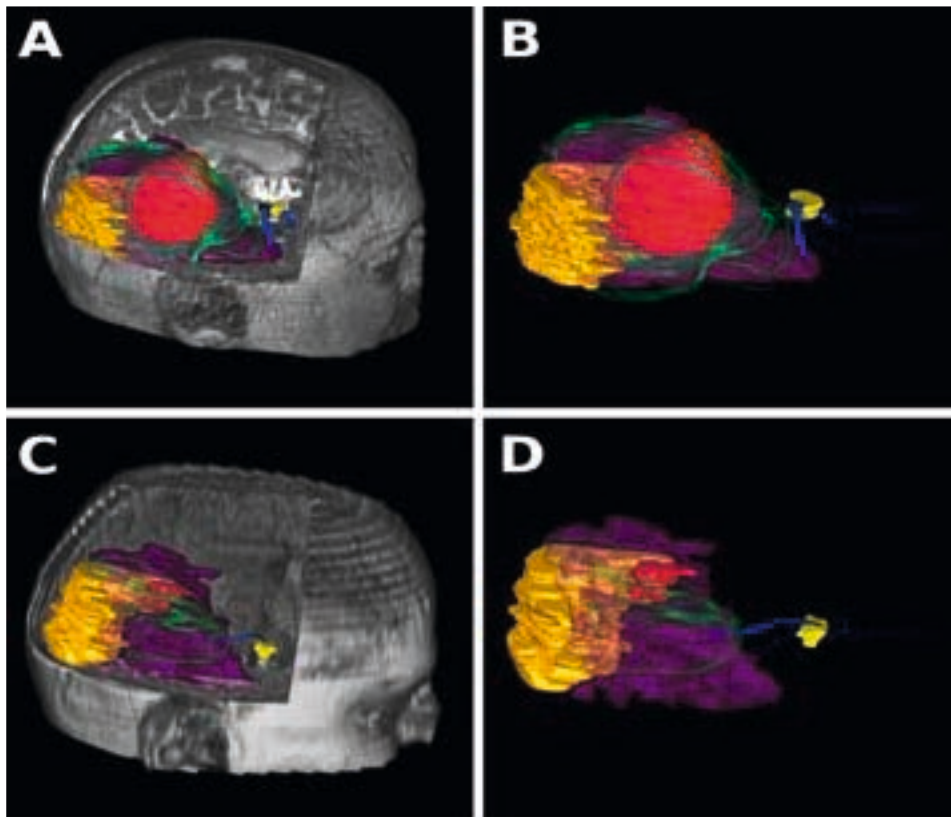


**MRI Axial : A and B before surgery :**

Tumor (red), Edema (purple), Visual cortex (gold), Opticradiatio (green), Optic tract (blue), Opticchiasm (yellow).

**MRI Axial : C and D after surgery :**

Tumor (red), Edema (purple), Visual cortex (gold), Opticradiatio (green), Optic tract (blue), Opticchiasm (yellow).



**MRI Sagittal : A and B before surgery :**

Tumor (red), Edema (purple), Visual cortex (gold), Opticradiatio (green), Optic tract (blue), Opticchiasm (yellow).

**MRI Sagittal : C and D after surgery :**

Tumor (red), Edema (purple), Visual cortex (gold), Opticradiatio (green), Optic tract (blue), Opticchiasm (yellow).

# Risk Factors and Disease Prevalence in 3331 Personal Check-ups Performed in Preventive Medicine Between 2006 and 2011. Cross-sectional and Follow-up Study

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## Abstract

### Introduction:

The present data results from a retrospective analysis of 3331 check-ups made in the preventive medicine department of the “ZithaKlinik”, named “ZithaGesondheitsZentrum”. These check-ups are done for the employee’s of several firm’s and institutions. According to gender and age, several tests and examinations are performed and the results are given to the person’s general practitioner or another doctor of his choice. We will present a global synthesis of all the results but also a follow-up study of persons having performed 2 check-ups or more over a 5-year period.

### Population:

In the cross-sectional part, the analysis is done on 3331 individual check-ups (1447 woman, 1884 men). The average age is 50.3 years +/- 11.4.

In the follow-up study, 478 persons (191 women, 287 men) had at least 2 (maximum 5) check-ups in the 5-year period of our observation. Initial age was 54.1 +/- 10.9 years for woman and 51.4 +/- 11.4 for men, respectively 56.4 +/- 10.9 and 53.7 +/- 11.2 at their last check-up.

### Results:

An alarming number of persons present with a weight or obesity problem (according to age ranging from 22.0% overweight and 7.3% obese from 18-29 years, respectively 37.5% and 11.3% from 30-49 years, finally 44.0% and 20.6% in the range 50-69 years).

Associated risk factors and pathologies (Hypertension, Dyslipidemia, NASH, diabetes type 2 and complete metabolic syndromes) are extremely frequent and getting more so with growing age.

Furthermore, physical activity is insufficient in grossly 2/3 of the studied population.

The only positive point is a tendency of decreasing tobacco use in all age groups.

The follow-up study is frustrating because most of the examined criteria get worse in-between check-ups instead of getting better with changes in lifestyle in an informed population.

### **Conclusions:**

Asymptomatic diseases or risk factors for non-communicable diseases are extremely frequent in the population examined. The follow-up data shows that huge parts of this group are not sufficiently conscientious of their problems to act up and change their life-style or seek adapted pharmacological prevention.

Absolute number of risk factors (prevalence) or pathologies rise evidently with age but incidence (newly discovered pathologies after a first, second or a record of 21 check-ups with our services) rises less. Life-style changes are rare or insufficient to change the pathological value back to normal or therapeutically range.

Even with several biases (retrospective design, selection bias, ...) our study puts similar problems forward in the population as ORISCAV.

The astonishing (better than national records) results in tobacco use is probably due to a selection of more health-oriented patients and of a higher socio-educative-economic level.

Alcohol abuse was very low but probably due to inadequate screening methods.

A better health promotion advocating healthier living must be associated with better communication and new motivational tools.

Therapeutical education for patients with chronic non-communicable diseases will be the challenge of the near future as their prevalences increase due to ageing of the population and worse individual lifestyles. In this task, efforts must be made on the personal level (health-team with the individual patient) but also on the national level (legal frame work for patient education by multi-professional teams as they exist already in neighbour states).

**Key words:** Risk Faktors, Population, Epidemiology, Non-communicable diseases, Pathologies,

# Prévalence de pathologies et de facteurs de risques dépistés dans 3331 bilans de médecine préventive entre 2006 et 2011: une étude transversale et longitudinale

## Introduction :

Les résultats de cette étude retrospective proviennent des rapports de bilans de santé en médecine préventive dans le département du « ZithaGesondheidsZentrum » de la « ZithaKlinik ». Ces bilans sont effectués à la demande de certaines firmes ou institutions dans le cadre de leurs efforts de promotion de santé au travail. En fonction de l'âge et du sexe, plusieurs examens et tests sont effectués et les résultats communiqués à la personne elle-même, à son médecin praticien ou tout autre médecin de son choix. La partie transversale présentera les résultats globaux, la partie longitudinale est une sous-analyse de personnes ayant effectué au moins 2 check-ups sur la période de 5 ans.

## Population :

La partie tranversale analyse 3331 bilans de santé, 1447 femmes, 1884 hommes avec un âge moyen de 50.3 +/- 11.4 ans.

Dans la partie longitudinale ont été inclus 478 personnes (191 femmes et 287 hommes) qui ont effectué au moins 2 (maximum 5) bilans dans la période de 5 ans analysée. Leur âge lors du bilan initial était de 54,1 +/- 10,9 ans pour les femmes et 56,4 +/- 11,4 ans pour les hommes respectivement 56,4 +/- 10,9 et 53,7 +/- 11,2 ans lors du dernier bilan de santé.

## Résultats :

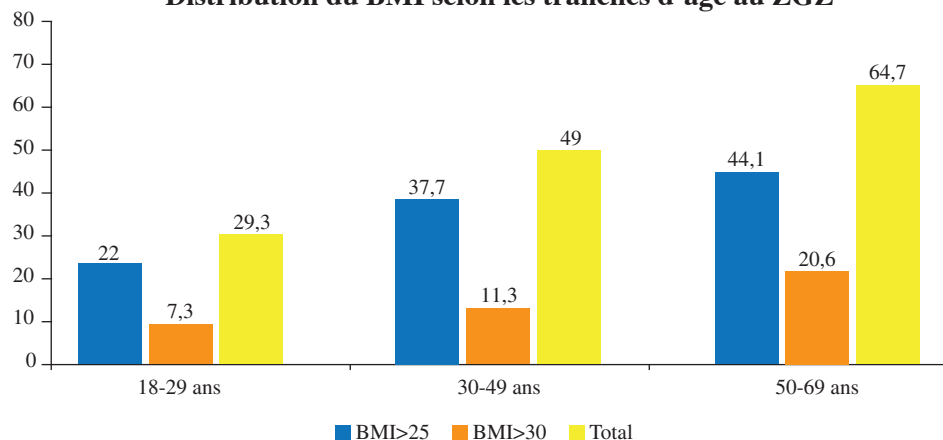
Un nombre alarmant de personnes présente un problème de surcharge pondérale ou d'obésité franche (selon la tranche d'âge allant de 22 % de surcharge pondérale et de 7,3 % d'obésité pour les personnes de 18 à 29 ans, respectivement 37,5 % et 11,3 % pour les 30 à 49 ans, finalement 44 % et 22 6 % pour les personnes âgées de 50 à 69 ans).

Cross-sectional study	F	H
Nombre de personnes	<b>1447</b>	<b>1884</b>
Âge moyen	50,4 +/- 11,9	50,3 +/- 11,0
Poids moyen	67,1 +/- 12,9	84,3 +/- 13,0
Taille moyenne	1,644 +/- 0,07	1,780 +/- 0,07
BMI moyen	25,1 +/- 4,9	26,8 +/- 3,8
Tour de taille moyen cm	84,4 +/- 11,7	97,0 +/- 10,5
> 80cm > 94cm %	<b>58,4%</b>	<b>60,4%</b>
Body fat % moyen	33,4 +/- 7,3	25,8 +/- 5,8
> norme %	<b>62,9%</b>	<b>56,4%</b>
BMI>25	29,2%	49,7%
BMI>30	14,5%	17,1%
<b>Total</b>	<b>43,7%</b>	<b>66,8%</b>

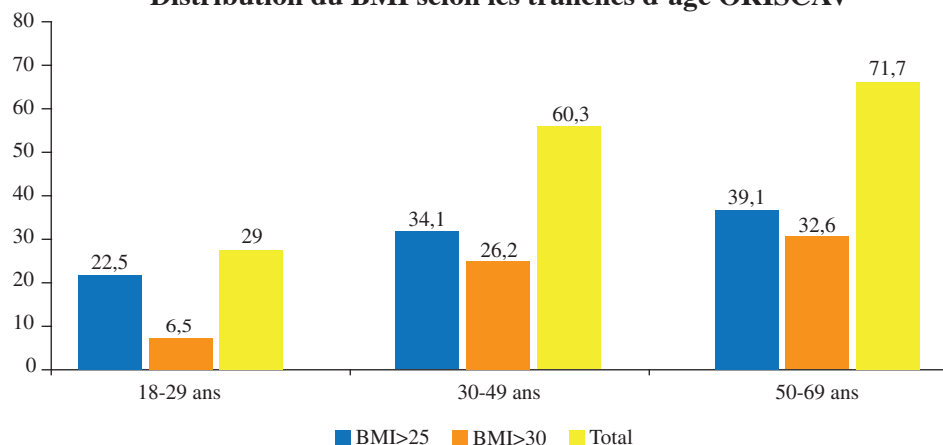
Tableau 1 : données démographiques de base globaux : Les normes pour les tours de taille ont été choisis de façon stricte, <80 cm pour les femmes et <94cm pour les hommes pour dépister au plus tôt les tendances à une surcharge de type androïde. Les normes pour l'excès de masse grasse proviennent des indications du fabricant de l'impédancemètre et sont indiqués dans l'annexe 1.

Le BMI est plus souvent supérieur à la norme pour les hommes (tableau 1) par rapport aux femmes, mais en prenant le critère de la présence de graisse abdominale (périmètre de la taille) avec leurs normes respectives pour les femmes (<80cm) et les hommes (<94cm) on remarque que les femmes présentent aussi fréquemment que les hommes un excès pondéral de répartition androïde (graphique C).

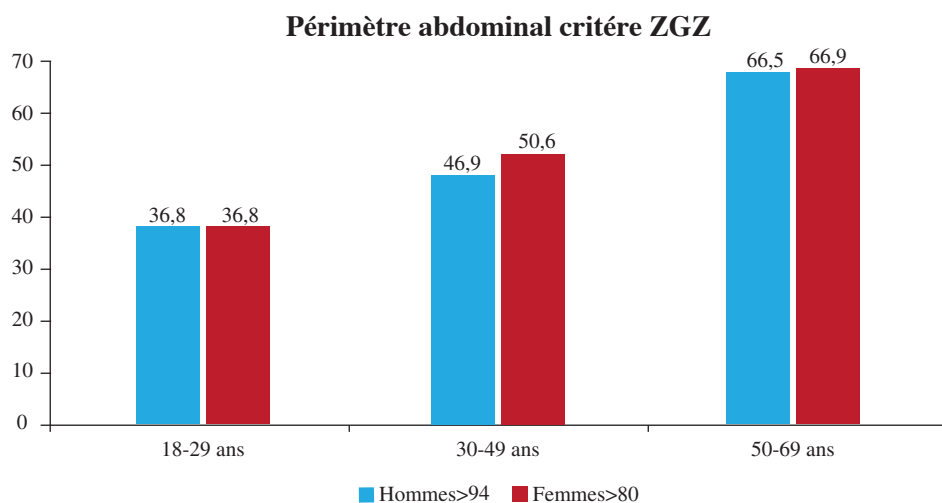
**Distribution du BMI selon les tranches d'âge au ZGZ**



**Distribution du BMI selon les tranches d'âge ORISCAV**

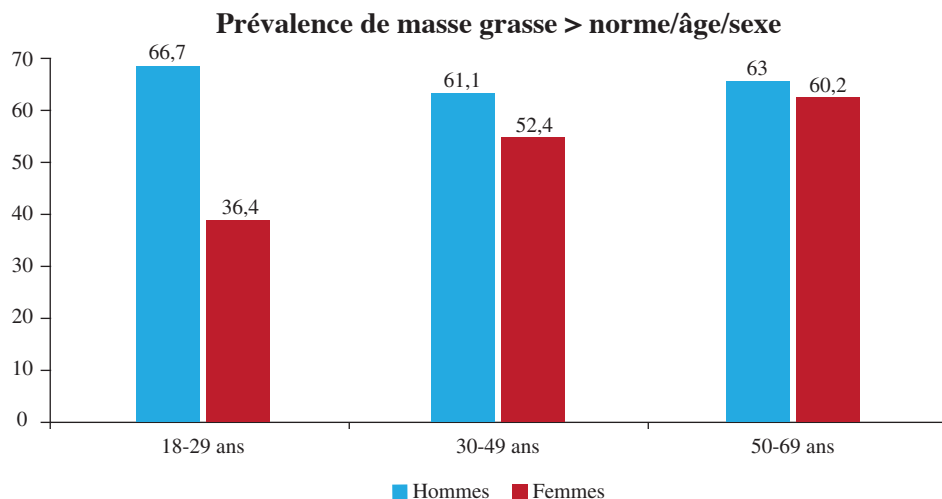


Graphiques A et B : Distribution du BMI selon les tranches d'âge dans la population ZGZ et dans la population ORISCAV.



Graphique C : Pourcentage de personnes ayant un périmètre abdominal supérieur à la norme pour leur sexe respectif.

En prenant comme critère l'excès de masse grasse mesurée par impédancemétrie (toujours avec des normes pour les femmes et hommes en fonction des tranches d'âge, cf annexe 1) on peut voir que les femmes excèdent les hommes avec un excès de masse grasse plus fréquente (graphique D). Ensemble avec un BMI moindre que les hommes ceci ne peut que s'expliquer par une masse musculaire amoindrie, avec comme conséquence une réduction de métabolisme de base et un risque de prise de masse grasse supplémentaire.



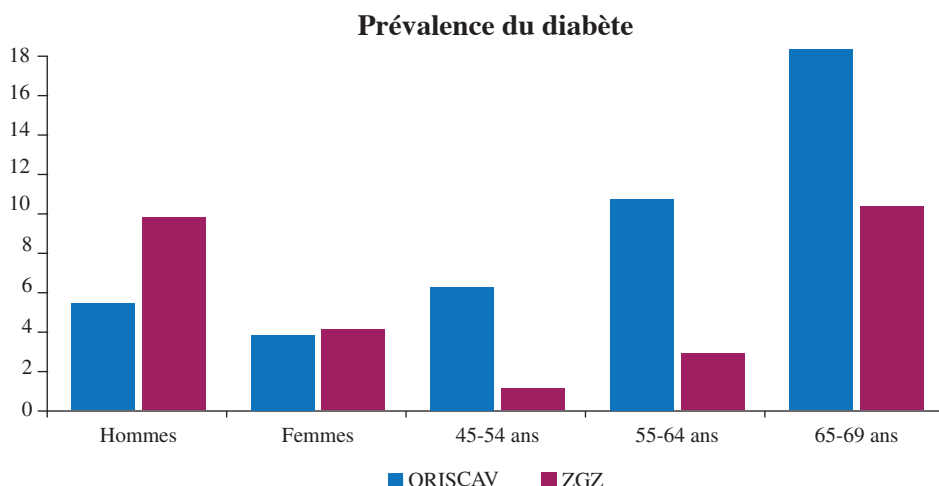
Graphique D : Pourcentage de personnes ayant une masse grasse supérieure à la norme pour leur sexe et tranche d'âge respectif. Les normes du fabricant de l'impédancemètre se trouvent dans l'annexe 1.

De plus le manque d'activité physique est très fréquent allant d'environ 1/3 des personnes jeunes jusqu'à deux tiers des personnes plus âgées (tableau 2 ; les chiffres en italiques signifient qu'un nombre insuffisant de données a été retrouvé/examinés).

<b>Cross-sectional study prevalence</b>	<b>&lt;30</b>	<b>30-50</b>	<b>&gt;50</b>
Nombre de personnes	<b>116</b>	<b>1407</b>	<b>1606</b>
HTA %	12.5	17.3	43.8
Diabète %	0.9	2.7	10.1
Tabagisme %	14.9	16.2	16.0
Cholestérol %	<b>5.2</b>	<b>18.7</b>	<b>44.0</b>
Hyperuricémie %	4.3	5.6	10.3
LP(a) %	0	33.3	28.3
Homocystéinémie > N %	15.8	27.7	26.1
Manque d'AP %	<b>35.5</b>	<b>45.5</b>	<b>51.6</b>
Prob. Cardio %	1.7	4.9	10.9
Prob. Gyneco %	3.4	8.9	9.4
Prob. Alcool %	1.0	3.1	5.8
Prob. Gastro-entéro %	4.3	22.4	30.5
Stress %	6.0	6.5	6.2
Prob. Dos %	2.6	4.2	4.9
Migraines %	1.7	1.6	1.4
Cutané %	11.0	15.2	11.8
Endocrino %	9.8	8.8	12.1
Prob. Urologique %	1.0	5.0	12.3
<b>Prévalence moyenne</b>	<b>1,56 +/- 1,3</b>	<b>2,73 +/- 1,9</b>	<b>4,0 +/- 2,2</b>
<b>Incidence moyenne</b>	<b>0,94 +/- 0,9</b>	<b>1,54 +/- 1,1</b>	<b>1,9 +/- 1,3</b>

Tableau 2 : prévalence de certaines maladies et facteurs de risques en fonction des tranches d'âges. La prévalence moyenne signifie le nombre de présence de pathologies existantes. L'incidence moyenne signifie le nombre de pathologies nouvellement identifiés par ce bilan de santé. P. ex. : un patient atteint de diabète de type 2 et d'obésité à qui on trouve une nouvelle HTA aura une prévalence de 3 et une incidence de 1.

Les facteurs de risque et pathologies associées (hypertension artérielle, dyslipidémies, NASH, diabète de type 2 ou syndrome métabolique complet) sont très fréquents et augmentent avec l'âge (graphique E). Le seul point positif est la tendance à l'arrêt du tabac dans toutes les tranches d'âge (tableau 2).



Graphique E : Prévalence de diabète (type 1 mais principalement de type 2, souvent non précisée) dans la population et selon certaines tranches d'âge, comparé avec certaines données publiées d'ORISCAV.

Dans l'étude longitudinale nous devons constater une augmentation de la fréquence de présence de la plupart des pathologies et facteurs de risque entre les différents bilans de santé au lieu de s'améliorer suite à un changement de style de vie ou de thérapie dans cette population informée (tableau 3).

Suivi longitudinal	Initial	Final	Initial	Final
	F	F	H	H
Nombre de personnes	<b>191</b>	<b>191</b>	<b>287</b>	<b>287</b>
Âge moyen	54,1 +/- 10,9	56,4 +/-10,9	51,4 +/- 11,4	53,7 +/- 11,2
Poids moyen	66,1 +/- 12,9	67,1 +/-13,4	84,0 +/- 12,6	83,9 +/- 12,5
<b>Taille moyenne</b>	<b>1,641 +/- 0,067</b>	<b>1,635 +/- 0,067</b>	<b>1,785 +/- 0,076</b>	<b>1,777 +/- 0,077</b>
BMI moyen	24,3 +/- 5,3	25,5 +/- 5,2	26,5 +/- 3,8	27,0 +/- 3,9
Tour de taille moyen cm	88,3 +/- 11,3	83,7 +/- 11,0	97,4 +/- 10,0	96,9 +/- 10,6
> 80cm > 94cm %	73.0	55.9	66.7	59.5
Body fat % moyen	33,4 +/- 6,1	32,5 +/- 7,5	25,8 +/- 6,8	25,6 +/- 5,6
> norme %	52.3	53.8	48.7	51.4
BMI>25	32.8	29.4	50.6	50.7
BMI>30	10.9	13.9	14.7	17.6
<b>Total</b>	<b>43.7</b>	<b>43.3</b>	<b>65.3</b>	<b>68.3</b>

Tableau 3 : données démographiques de base pour l'étude longitudinale : Les normes pour les tours de taille ont été choisis de façon stricte, <80 cm pour les femmes et <94cm pour les hommes pour dépister au plus tôt les tendances à une

surcharge de type androïde. Les normes pour l'excès de masse grasse proviennent des indications du fabricant de l'impédancemètre et sont indiqués dans l'annexe 1.

## Discussion

En présence d'un nombre augmentant de personnes atteint d'un syndrome métabolique cette étude met clairement en évidence la problématique de dépistage précoce de l'obésité. Le seul critère de BMI n'est pas satisfaisant (le jeune sportif peut se retrouver avec un BMI > 25, mais avec une masse grasse normale ou basse et une femme sédentaire peut très bien présenter un BMI à 24,8 mais avec un périmètre de taille de 88cm et une masse grasse augmenté de 50 % par rapport à la norme pour sa tranche d'âge).

Globalement il nous semble que des critères ou limites assez strictes permettent une mise en garde précoce. Il semble de plus en plus logique qu'il est plus facile de garder un poids atteint et des habitudes de vie que d'attendre que la problématique soit devenue plus grave pour essayer de traiter une obésité de grade II et de faire perdre un grand nombre de kilos durablement.

Dans l'étude de follow-up, on peut constater une certaine stabilité de poids malgré que le métabolisme de base chute d'environ 1 % par année de vie (entre les âges de 20 et 70 ans). Mais comme la taille réduit également (tableau 3 les chiffres en italiques signifient qu'un nombre insuffisant de données a été retrouvé/examinés) le BMI augmente même légèrement. Ceci vaut pour la masse grasse en absolue et en % supérieur à la norme vraisemblablement même si cela ne ressort pas des chiffres (le nombre de mesures initiales étant faibles, une comparaison n'est pas possible).

A part le tabagisme, aucune des fréquences de facteurs de risques ou de maladies n'a pu être diminuée (tableau 4) ce qui montre bien que les maladies asymptomatiques dont la correction dépend des habitudes de vie sont difficilement « traitables ».

Suivi longitudinal	Initial	Final	Initial	Final
	F	F	H	H
Nombre de personnes	<b>191</b>	<b>191</b>	<b>287</b>	<b>287</b>
HTA	17.3	24.5	28.7	38.6
Diabète	4.7	5.3	9.8	9.8
Tabagisme	<b>13.0</b>	<b>11.6</b>	<b>13.6</b>	<b>12.2</b>
Cholestérol	24.6	30.4	32.2	28.5
Hyperuricémie	1.0	1.1	6.3	10.8
Manque d'AP	<b>41.5</b>	<b>57.7</b>	<b>37.5</b>	<b>57.6</b>
Prob. Cardio	5.8	6.8	9.1	12.9
Prob. Gyneco	20.9	26.3		

Suivi longitudinal	Initial	Final	Initial	Final
	F	F	H	H
Prob. Alcool	2.2	4.2	2.6	4.5
Prob. Gastro-entéro	19.4	18.9	23.8	26.1
Stress	4.2	6.8	3.1	5.9
Prob. Dos	6.3	3.2	2.8	3.8
Migraines	3.1	1.6	0.7	1.0
Cutané		7.6		16.2
Endocrino		18.5		4.5
Prob. Urologique		4.2		21.0
Prévalence moyenne		3,21 +/- 2,0		3,83 +/- 2,1
Incidence moyenne		1,35 +/- 1,0		1,45 +/- 1,0

Tableau 4 : prévalence de certaines maladies et facteurs de risques en fonction des tranches d'âges. La prévalence moyenne signifie le nombre de présence de pathologies existantes. L'incidence moyenne signifie le nombre de pathologies nouvellement identifiées par ce bilan de santé. P. ex. : un patient atteint de diabète de type 2 et d'obésité à qui on trouve une nouvelle HTA aura une prévalence de 3 et une incidence de 1.

Cette distinction entre prévalence et incidence n'était pas encore systématiquement fait en 2006 et 2007 en début de l'étude de même que la recherche de certaines pathologies.

La seule différence significative de pathologies par rapport à la population ORISCAV est la plus grande prévalence de dyslipidémie dans cette dernière. Ceci est dû à des critères différents (normes NCEP pour ORISCAV et seuil de significativité clinique/thérapeutique pour le groupe ZGZ) utilisés pour les 2 études.

Dans l'étude ORISCAV il y a une meilleure représentativité des différentes couches socio-économiques et néanmoins les résultats sont comparables.

L'avantage de la présente analyse est qu'il y a des données de suivie actuellement non disponibles pour ORISCAV.

## Conclusion

Les maladies asymptomatiques ou les facteurs de risque pour ces maladies sont fréquents dans la population étudiée. Les données de l'étude longitudinale montre qu'un grand nombre de personnes n'est pas suffisamment conscient de ses problèmes de santé pour changer le style de vie et/ou pour adhérer à une prévention pharmacologique. Le nombre absolu de maladie ou de facteur de risque (prévalence) augmente avec l'âge, mais l'incidence (le nombre de deux nouvelles pathologies dépistées après une première, deuxième ou après un record de 21 bilans de santé avec nos services) augmente moins vite. Les changements de style de vie sont rares ou insuffisants pour changer les valeurs pathologiques vers des résultats anormaux ou pour atteindre les zones souhaitables selon les recommandations internationales.

Malgré certains biais (analyse rétrospective, biais de sélection, ...) notre étude montre les problèmes de santé publique similaires à la population de l'étude ORISCAV.

La faible prévalence de tabagisme (taux inférieur au taux de nationaux) est probablement due à un biais de sélection de patients orientés vers la santé avec un niveau socio-éducatif et économique plus élevé. L'abus d'alcool était peu fréquent mais probablement dû à une méthode de dépistage inadéquate.

Une promotion de santé pour une vie plus saine devra trouver de meilleurs outils de communication et de nouvelles techniques motivationnelles.

L'éducation thérapeutique de personnes avec un risque de maladies chroniques sera le défi du futur proche car la prévalence de ces maladies augmente avec le vieillissement de la population et les habitudes de vie qui se dégradent. Cette tâche devra se décliner au niveau individuel (équipes multi-disciplinaires face à une personne active pour sa santé) mais aussi au niveau de la population générale (législation pour l'éducation thérapeutique de la personne et du patient comme elle existe déjà dans les pays voisins).

Age	Hommes	Femmes
20-29 ans	11,8-19,9 %	18,5-25,2 %
30-39 ans	15,3-22,1 %	20,3-27,0 %
40-49 ans	18,0-24 %	23,4-30,1 %
50-60 ans	19,8-25,6 %	26,6-33,1 %
> 60 ans	20,2-26,2 %	22,7-34,0 %

Annexe 1: Zones de masse grasse normale dans une population normale selon le sexe et les tranches d'âges (indication du fabricant de l'impédancemètre).

## Références

La situation épidémiologique des facteurs de risque cardio-vasculaire potentiellement modifiables chez les adultes résidant au Luxembourg, en 2007-2008

Ala'a Alkerwi, Nicolas Sauvageot, Anne Nau, Guy Weber, Agnès Columbeau, Jean Beissel, Charles Delagardelle, Sophie Couffignal, Marie-Lise Lair

Résultats de l'étude ORISCAV-LUX « Observation des Risques et de la Santé Cardio-vasculaire au Luxembourg »



# Transpatellar access for intramedullary stabilisation of the tibia

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## **Abstract**

Postoperative deformities of the knee and sequaelae after intraarticular surgery can interfere with a standard parapatellar approach for intramedullary stabilisation of the tibia. Even the suprapatellar approach can be rendered impossible.

For these rare indications we describe the patella osteotomy and transpatellar approach.

**Keywords:** Tibial fracture, transpatellar, intramedullary

## **Introduction:**

The majority of tibial shaft fractures can be stabilised by intramedullary fixation; numerous techniques for this purpose have been described. When the extensor apparatus is intact and the flexion capacity largely normal, the parapatellar or the transpatellar access is used. Both access routes are well established and show no significant differences in terms of anterior knee pain syndrome or function <sup>6</sup>. Diaphyseal fractures and the majority of proximal metaphyseal fractures can be stabilised using these access approaches. The parapatellar access can if required be extended towards cranial, but then requires more extensive detachment of the supporting ligaments. The retropatellar portal, among others, has been described as a means of avoiding this intervention. The knee joint can remain in an extended position; the otherwise unavoidable dislocation of the proximal fragment in flexion is thereby avoided. This access method is therefore a major addition to the available range of options, especially for proximal metaphyseal fractures. This exclusively percutaneous procedure, however, may involve relevant injury of the anterior internal knee structures. There are however situations in which previous surgical interventions or infections have led to fibrosis of the internal joint cavity and have abolished flexion capacity. In such a constellation, neither conventional parapatellar or transpatellar stabilisation nor retropatellar stabilisation is possible

without damaging the extensor apparatus. These are generally rare indications but even in emergency situations appropriate intramedullary stabilisation should be ensured when alternative methods of stabilisation are ruled out. Transpatellar access is suitable for these rare indications. This access method was originally presented by UE Wehrli <sup>7</sup> for primary knee endoprosthetics.

We now present the indication and technique of transpatellar access for these individual cases.

### **Patients:**

The indication for transpatellar access for intramedullary stabilisation is limited and has so far been performed twice at this clinic.

**Patient Z.** suffered an open fracture of the left lower leg in 1985 which was treated with an external fixation. Bone consolidation ensued, but for the last 15 years there has been chronic osteomyelitis with fistulation. The patient had previously refused restorative treatment. In December 2009 he suffered a pathological fracture (**Fig. 1**). On admission the patient weighed 140 kg, indulged in continuous nicotine abuse and had a diabetic metabolic situation. The microbiological analysis primarily and for the first surgical procedures showed infection with *Corynebacteria*, *Actinomycetes* and anaerobic peptostreptococci (**Fig. 2**). Remediation was achieved in numerous surgical revision procedures with resection of the infected bone (**Fig. 3**), vacuum therapy and finally plastic coverage with gastrocnemius and hemisoleus. Segment transport could not be achieved over the complete distance as the proximal scar tissue led to a deviation in the transport segment (**Fig. 4**). Because of the multiple previous operations, the edematous induration of the leg and the plastic coverage (**Fig. 5**), percutaneous plate osteosynthesis was ruled out. We therefore opted for intramedullary stabilisation using the transpatellar approach (**Fig. 6 and Fig. 7A and B**).

**Patient B.** had hemiparesis with asensitivity of the right leg following tubercular encephalitis. His medical history included a supradiacondylar femoral fracture

and tibial plateau fracture. These were consolidated but showed a patella baja, with almost direct contact between the tibial plateau and the distal patellar pole as well as patellofemoral arthrosis. On admission we diagnosed an almost non-dislocated diaphyseal fracture (**Fig. 8A and B**). Because of the asensitivity, conservative plaster cast treatment was not possible. The only alternatives were external fixation or percutaneous plate osteosynthesis. On admission, a hematoma was already apparent with impending full-skin necrosis. Because of the compromised soft-tissue situation on admission and the limited assessability during the course, we decided in favour of intramedullary stabilisation (**Fig. 9**). A secure intramedullary stabilisation (**Fig. 10 A and B**) could be achieved with primary healing of the approach.

### **Transpatellar access technique:**

With the knee joint in close to extension position, a median access is created over the patella. It must be remembered that the anterior arterial plexus consist of 2 layers. To prevent skin necrosis, dissection should therefore be performed on the movable layer, the galea aponeurotica of the patella <sup>5</sup>. After sharp dissection onto the patella, the quadriceps tendon is split for several centimetres along the longitudinal course of the fibres. The articular surface of the patella can be palpated. From the radial edge of the patella, 3 holes are now created with a 2.5 mm drill bit. To maintain the most parallel possible alignment, after drilling the first hole a Kirschner wire can be inserted as a guide. The osteotomy of the patella is done in median position; up to the middle of the diameter the oscillating saw can be used with continuous irrigation. The osteotomy is completed with a chisel to avoid damaging the patellofemoral cartilage. Splitting the patellar tendon is not necessary. The guide wire of the nail can now be placed without force under fluoroscopic control onto the anterior edge of the tibia in accordance with the recommendations for the system used. The further technique does not differ from the conventional technique. In the cases described, the osteosynthesis of the osteotomy was performed as a screw osteosynthesis or tension belt osteosynthesis.

### **Discussion**

The majority of proximal metaphyseal tibial fractures can be reliably stabilised through a parapatellar access. The temporary use of fixation or poller screws <sup>3</sup> may be necessary. Problem fractures that cannot be adressed with this technique can be stabilised using the a suprapatellar access. A trocar is placed through the quadriceps tendon, between the condyles and directed onto the anterior edge of the tibial head. The advantage of this procedure is the extended or close to extended position of the knee joint, allowing the fracture to be aligned along the longitudinal axis. The disadvantage of this technique is the limited visualisation of the anterior internal articular structures. Eastman <sup>1</sup> observed an injury of the medial meniscus in 12.5% of cases and of the medial joint surface in 6.25% of cases despite fluoroscopic control. A relevant increase in the retropatellar contact pressure was not found to occur in a cadaveric study <sup>2</sup>.

When this approach is not feasible a regular arthrotomy can be performed. However, the vascular and nerval structures should be considered.

With already compromised soft tissues a wide dissection might disrupt the arterial supply which consists of a network supplied from medial and lateral and extends in 2 layers <sup>5</sup>.

With respect to the nerve supply the superficial medial layer the knee joint is innervated by the infrapatellar branch of the saphenous nerve and the ventral cutaneous femoral branches. In the deeper layer branches of the obturator, tibial,

peroneal and saphenous nerves and branches of the quadriceps nerve innervate the articular capsule as nerve endings.

Therefore, an alternative approach that allows visualisation of the anterior structures of the plateau, circumvents a disturbance of blood flow and reduces neurological impairment might be of advantage.

This consideration and the possibility of damage to the proprioceptive and nociceptive apparatus were primary factors prompting the development of the transpatellar access as described by Wehrli et al. for primary endoprosthetics of the knee joint <sup>7</sup>.

In patient B. with an already compromised soft tissue situation after hemiparesis and previous operations a renewed arthrotomy is certainly capable of causing a significant impairment of blood flow within the patella.

A strictly median access therefore offers advantages compared to parapatellar arthrotomy both under the aspect of neural but also arterial supply. An impairment of patellofemoral kinematics following osteotomy can be ruled out on the basis of experimental data <sup>4</sup>.

After an atraumatic split of the cartilage and step-free osteosynthesis, complication-free healing can be expected. To this extent, in cases like those described above, extensive arthrotomy should be weighed against osteotomy. Because of the limited invasiveness, when correctly executed the transpatellar approach can represent a useful addition to the range of alternative access routes.

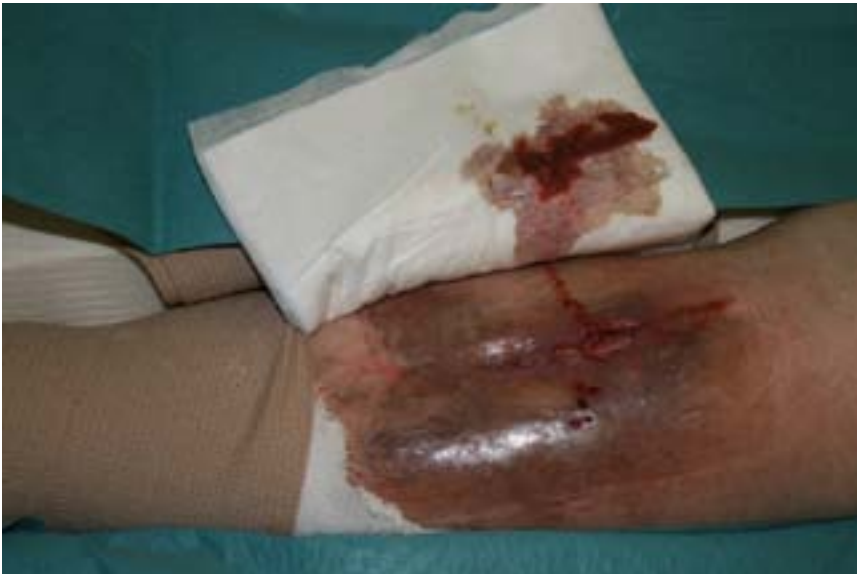
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## Illustrations



**Fig. 1 Pathological fracture of the tibia in chronically fistulating osteomyelitis**



**Fig. 2 Fistulating osteomyelitis of diaphyseal tibia for 15 years**



**Fig. 3 Treatment of osteomyelitis by segment resection, Debridement until germ-free. Intermittent stabilisation with a cement spacer by Masquelet technique with additional antibiotic treatment**



**Fig. 4 Incomplete segment transport. Because of the rigid scar tissue, a proximal connection was not possible. It was decided to change techniques with an intramedullary method.**



**Fig 5 Soft tissue situation after removal of external fixation and coverage of the soft tissue defect with split-thickness skin graft.**



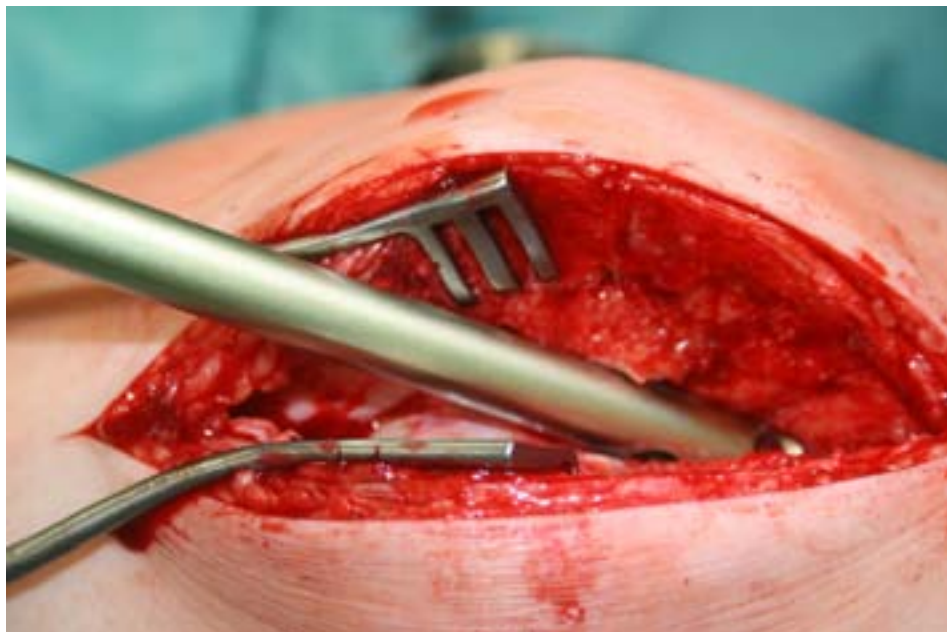
**Fig 6 Transpatellar access for intramedullary stabilisation**



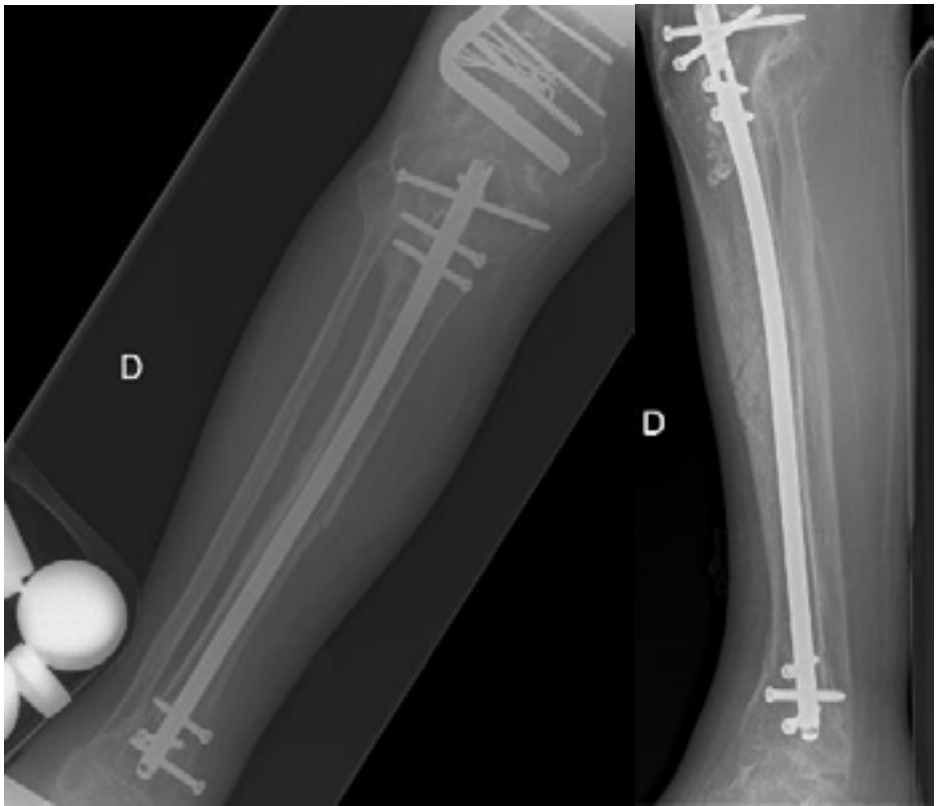
**Fig 7a and 7b Control after intramedullary stabilisation**



**Fig. 8a and 8b Rigid osteoarthritis and patella baja after fracture of the tibia head and diacondylar fracture of the distal femur preventing a standard intramedullary approach.**



**Fig. 9 Inline insertion of the nail in full extension of the knee.  
The osteotomised patella is retracted.**



**Fig. 10a and 10b Stabilisation of the non-displaced tibial fracture.**

# Investigation of an excess of *Salmonella* Enteritidis phage type 14b and MLVA type 4-7-3-13-10-2-2 in Luxembourg, Belgium and Germany during 2010

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## Abstract

We investigated an increase of human cases of *Salmonella* Enteritidis occurring from August until November 2010 in Belgium, Luxembourg and Germany involving an estimated three hundred laboratory confirmed cases. Molecular typing indicated that the increase in Luxembourg and Belgium was due a particular strain having phage type 14b, MLVA pattern 4-7-3-13-10-2-2 and fully susceptible to the Enternet panel of antibiotics. MLVA and phage typing were found to have similar discriminatory power on a collection of 40 Belgian and Luxembourg strains isolated during 2010. Epidemiological investigations in Luxembourg suggested eggs as a possible source for some cases, although supermarket eggs tested were negative. No other EU countries observed a substantial increase of cases, although three smaller outbreaks in Germany were also due to a strain with the same phage type and MLVA pattern. In 2010 the EU directive banning battery cages came into force in Germany followed by a dioxin food scare incident. Given that the EU Laying Hens Directive will come into force across all Member States in 2012, a closer monitoring of *Salmonella* contamination of imported eggs at retail and wholesale level is recommended.

## Introduction

*Salmonella enterica* subsp. *enterica* serovar Enteritidis (*S. Enteritidis*) is currently the serovar associated with most cases of human salmonellosis in Europe <sup>1</sup>. In recent years though, many countries in Western Europe have witnessed a substantial decrease of *S. Enteritidis* cases compared to the late 1990s, most likely due to increased local use of vaccines in the poultry and egg production industries <sup>2-5</sup>. Against this decreasing trend, imported eggs are known to have caused substantial national outbreaks <sup>6, 7</sup>. Historically, epidemiological subtyping of *S. Enteritidis* has relied on phage typing, which is carried out by only a few reference laboratories in Europe, and often has limited discriminatory power <sup>8</sup>. In recent years, multiple-locus variable number tandem repeat analysis (MLVA) has emerged as a new typing technique for *S. Typhimurium* and *S. Enteritidis* with greater discriminatory power than pulsed-field gel electrophoresis (PFGE) <sup>9-17</sup>. Here we report the first microbiological investigation of a concurrent increase of cases of *S. Enteritidis* phage type 14b in Belgium and Luxembourg and a few outbreaks in Germany during late summer 2010 initially detected by MLVA typing.

## Methods

At the end of September 2010, an unusual increase of *Salmonella* Enteritidis with MLVA pattern 4-7-3-13-10-2-2 was detected by the *Salmonella* reference laboratory in Luxembourg who launched an international urgent enquiry (UI) on ECDC's Epidemic Intelligence Information System (EPIS) platform <sup>18</sup>. In response to the UI, the Belgian national reference laboratory reported an unusual increase of *S. Enteritidis* of phage type 14b during the same time period. The two reference laboratories immediately started a collaboration by exchanging strains and subtyping them according to locally used methods, that is phage typing in Belgium and MLVA typing in Luxembourg using standard protocols <sup>19, 20</sup>, respectively. Following the results of this Belgo-luxembourgish collaboration, the German reference centre also contributed to the investigation by providing recent and historic 14b strains for subtyping with MLVA.

In both Belgium and Luxembourg following isolation by medical microbiology laboratories, human *Salmonella* isolates are routinely sent to their respective national reference laboratories for serotyping and antibiotic resistance testing for surveillance purposes. In Belgium, a random sample of all *Salmonella* Enteritidis strains is submitted for phage typing: the volume of strains tested varies during the year with 5 strains test per week during weeks 1-24 and 48-53, 10 strains per week tested during weeks 25-29 and 42-47 and 20 strains tested during weeks 30-41. In Luxembourg, *S. Typhimurium*, its monophasic variant and *S. Enteritidis* are routinely typed by MLVA whereas other rarer serovars are typed by PFGE. MLVA nomenclature is based on loci SE1-SE2-SE3-SE5-SE6-SE8-SE9 and refers to the number of tandem repeats for each locus.

An outbreak investigation was conducted in Luxembourg by interviewing cases with the common MLVA type to find common food sources focusing on consumption of eggs or poultry. No epidemiological investigation was done in Belgium.

Statistical tests were conducted with Stata 10.1 (StataCorp LP, College Station, Texas, USA). Total cases of the implicated strain in Belgium were estimated by multiplying separately for each month from July to November, the proportion of cases with phage type 14b by the number of total cases with *S. Enteritidis* and then adding them up.

## Results

### Epidemic curves

Figure 1 shows the monthly distribution of laboratory confirmed *S. Enteritidis* cases in Luxembourg and Belgium during 2010 in comparison to 2009. For Belgium, it is clear that more cases of *Salmonella* Enteritidis were reported for the period August-September 2010 compared to the same period in 2009. For Luxembourg, the differences in observed cases was less marked. No excess of cases was observed in November and December.

Figure 2 shows that most of the increase of *S. Enteritidis* cases was due to either MLVA type 4-7-3-13-10-2-2 in Luxembourg or phage type 14b in Belgium, respectively.

Overall, 30 isolates of MLVA type 4-7-3-13-10-2-2 were observed in Luxembourg from July until November 2010 with the peak occurring mid September representing 59% of all *S. Enteritidis* cases during that period. The median age of cases with the implicated MLVA strain in Luxembourg was significantly higher than recent *S. Enteritidis* cases with different MLVA types during 2011 (36 vs 11 years,  $p=0.0342$  Wilcoxon rank-sum test). There was no spatial clustering within Luxembourg, with cases being widely dispersed in a manner approximately proportional to local population densities.

In Belgium, 47.1% of strains isolated in July-October had phage type 14b, compared to 5.6% in the period January-July ( $\chi^2$ -test,  $p<0.0001$ ). By extrapolation, we can estimate that approximately 250 laboratory confirmed cases of *S. Enteritidis* phage type 14b occurred between July and November 2010, with a peak in September 2010.

## **Outbreak investigation**

Interviews of cases contacted as part of the outbreak investigation in Luxembourg did not reveal a common food source. However, one of the cases with the outbreak strain reported that several friends and family also fell ill with gastro-enteritis following consumption of homemade pasta made with fresh table eggs. While the eggs used for the pasta were no longer available for testing, the person who prepared the meal indicated that she always bought the same type of eggs at the same supermarket. 8 batches of table eggs from a supermarket were tested for *Salmonella*, but all samples were negative.

## **Molecular analysis**

Overall, eight human strains from Luxembourg, 32 human strains from Belgium collected between May and November 2010 were analyzed with both phage typing and MLVA methods (see table 1). All strains were completely susceptible to the Enternet panel of antibiotics. MLVA yielded 11 different patterns and phage typing 10 different patterns (see table 1 and table 2) on this collection. Twenty isolates shared a common MLVA pattern 4-7-3-13-10-2-2 and phage type 14b. One strain with the outbreak MLVA pattern isolated earlier in May in Luxembourg had phage type 8 and one strain from Belgium isolated at the end of September had phage type 34b. Similarly, two Belgian strains having phage type 14b had different MLVA patterns.

At national level Germany did not report any increase of *S. Enteritis* during the latter half of 2010. Data from SurvStat at the RKI suggest a continual decreasing trend of reported SE cases from 2007 to 2010 (not shown). According to data available to the german national reference centre, PT 14b isolates are fairly rare and were responsible for 3 smaller outbreaks and one sporadic case during the latter half of 2010. In June an outbreak occurred in Mecklenburg-Western Pomerania involving six cases at a family party, in September an outbreak in Saxony involved 3 patients (1 death) in a nursing home and in October an outbreak in Bavaria involving 17 cases was probably due to contaminated potato salad. Strains from two outbreaks in Saxony and Bavaria shared the same MLVA pattern 4-7-3-13-10-2-2 also found in Belgium and Luxembourg suggesting that these episodes could be due to a common source.

One veterinary strain of phage type 14b isolated from an egg yolk obtained from a farm in Germany in 2005 had MLVA pattern 4-7-3-13-10-2-2, although it was resistant to sulfamerazine. One isolate from a spent hen (which is considered too old to lay eggs) obtained during August 2010 from a Belgian farm had phage type 14b and MLVA pattern 4-7-3-13-10-2-2.

## European collaboration

On 21<sup>st</sup> October 2010, the national reference laboratory in Luxembourg launched an urgent enquiry through the EPIS platform. EPIS is a communication platform tool, which allows risk assessment bodies to exchange non-structured and semi-structured information regarding current or emerging public health treats with a potential impact in the European Union. Its aim is to facilitate information sharing and to ensure coordination of actions epidemiologists and microbiologists working on food-borne diseases at the European level. Eight countries provided replies to the urgent enquiry, most of them negative. In addition to Belgium, only Estonia reported an increase in *S. Enteritidis* since week 34. The reported cases were associated to outbreaks in a kindergarten and a nursing home. The cases from the nursing home were suspected to be from contaminated egg consumption. Five strains from Estonia sent for typing to Luxembourg had MLVA profile 5-5-2-11-10-1-3 which is different to strain involved in the increase of cases in Belgium and Luxembourg.

## Discussion

To our knowledge this report is the first to describe an increase of *S. Enteritidis* which was initially detected using MLVA illustrating its potential as a useful real-time subtyping method for *S. Enteritidis*. Due to its high discriminatory power, MLVA typing is increasingly being used for epidemiological typing purposes of isolates of the *S. Typhimurium* complex. Our study shows that MLVA can also be used for typing *S. Enteritidis* in laboratories that have access to a capillary sequencer which greatly facilitates fragment analysis. On our collection of strains, MLVA had a similar discriminatory power than phage typing. However one of the disadvantages of MLVA typing is that not many public health laboratories are using this methodology yet and thus phage typing remains necessary to enable international comparisons.

Unfortunately we were not able to detect the strain responsible for the increase of cases observed in humans directly in any food product (including eggs). The epidemiological evidence from the outbreak investigation conducted in Luxembourg suggested that table eggs of a Belgian wholesale supplier could have been a possible source for some cases in Luxembourg. Indeed several large Belgian supermarket chains also operate throughout Luxembourg and it is likely that wholesale egg suppliers are shared by the two countries, which could explain the fact the increase of cases occurred mainly in these 2 countries. The molecular evidence also points towards eggs as the most likely source: the two non-human strains that had identical phage and MLVA type originated from egg yolk and a “spent” laying hen, respectively.

In Belgium, since 2006, four main phage types (PT4, PT21, PT6 and PT8) represented altogether about 70% of all the *Salmonella* Enteritidis phage types isolated from human and flocks. Even if a shift in the distribution of phage types was also observed after the vaccination campaign of the layer flocks (started in Belgium in 2004), the prevalence of phage type 14b remained very low ranging from 1% to 5% between 2006 until 2009 <sup>21</sup>.

More generally within Europe, phage type 14b has recently been reported to have caused a large outbreak in England in 2009 linked to a single egg production establishment in Spain <sup>7</sup> as well as causing meningitis and septicemia in a non-immunocompromised person as part of a larger outbreak in Ireland <sup>22</sup>. Earlier in the previous decade Spanish wholesale eggs were implicated in outbreaks of phage type 14b infections in the United Kingdom <sup>6,23</sup>. However, most Anglo-Irish 14b strains were reported to be resistant to nalidixic acid which is not the case for the strain responsible for our increase in cases. Another important source of phage type 14b infections in Northern Europe during the previous decade was consumption of chicken meat in travellers to Greece: the strains of Greek origin were susceptible to nalidixic acid <sup>24</sup>.

In Germany during 2010, three main phage types (PT4, PT8 and PT 21) were responsible for 25 (76%) of 33 typed SE outbreaks compared to 3 outbreaks (9%) due to PT14b.

Although we did find the implicated strain in a Belgian hen, the fact that these strains are rarely found in veterinary isolates and that the regional increase of cases was very limited in time supports the hypothesis that the eggs were imported from abroad, possibly due to regional shortage of locally produced eggs. Indeed 2010 was a rather eventful year for the regional egg production industry. Beginning on the 1<sup>st</sup> January 2010, German legislation came into force banning the use of battery cages two years earlier than required by the 1999/74 EU Hens directive. Also, german organic egg producers were affected by a dioxin scandal due to contaminated feed in May 2010 which forced discount supermarket chains Lidl and Aldi (which also have stores in Belgium and Luxembourg) to temporarily retract their whole stock of organic eggs <sup>19</sup>. Thus one might speculate that a combination of these could have led to a temporary increase of contaminated imported eggs in analogy to the increase observed in the Netherlands in 2003 as a side effect of the concurrent avian influenza outbreak <sup>25</sup>.

While we believe that eggs were the most likely source for the observed increase of *S. Enteritidis* cases in Luxembourg and Belgium, a much more substantial and costly effort by epidemiologists, microbiologists and veterinarians would be needed to take corrective actions. The prevalence of *Salmonella* in eggs is notoriously low, and a substantial number of contaminated eggs would need to be tested to obtain an isolate which can be typed and compared to human cases. Secondly the

timely sharing of strains/typing data between veterinary/human epidemiologists/microbiologists within and between countries remains still a problem. A combination of these factors means that all too often small or medium-size outbreaks involving several hundred salmonellosis cases of a common serovar can at best be detected, but not acted upon in a timely fashion such that the outbreak is likely to have resolved even without any public intervention. This unsatisfactory situation for public health can only improve if more financial resources are made available to national reference laboratories and epidemiologists to establish a real-time molecular integrated surveillance system of human, food, veterinary and environmental strains under one roof. Given that the EU Laying Hens Directive 1999/74 will come into force across all Member States in 2012, a closer monitoring of *Salmonella* contamination of imported eggs at retail & wholesale level is recommended.

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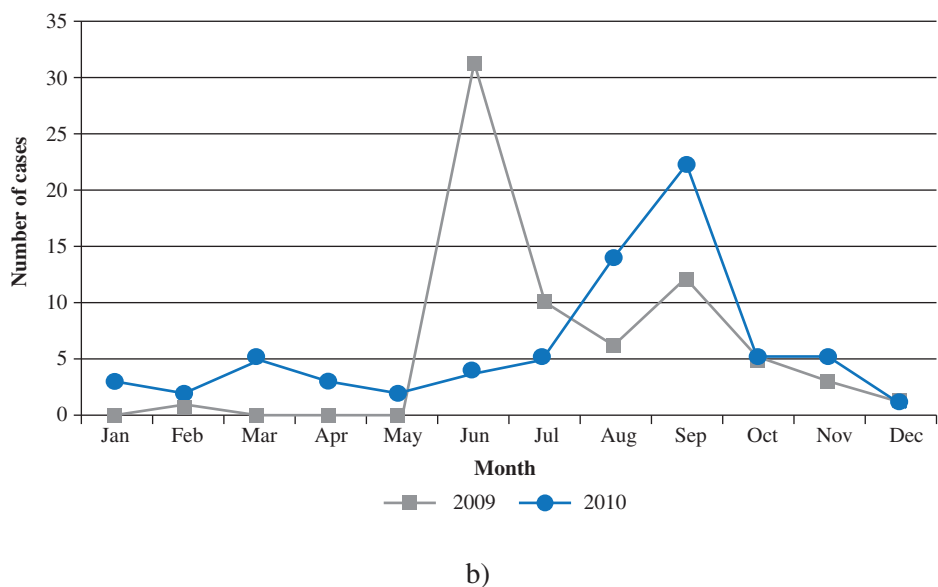
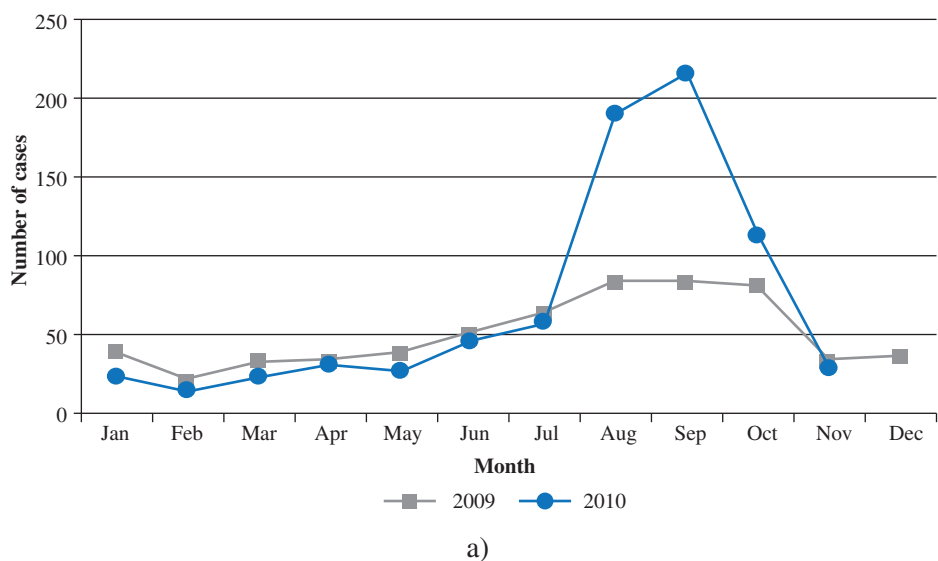
**Table 1:** Collection of *Salmonella* Enteritidis isolates submitted to phage and MLVA typing for this investigation. BE, LU, DE represents Belgium, Luxembourg & Germany, respectively, as the country of origin of strains in the column Strain ID.

Strain ID	Origin	MLVA type	Phage type	Date
BE10-01928	Human	4-7-3-10-10-2-2	14b	07/05/2010
BE10-02487	Human	5-5-2-9-10-1-3	14b	23/07/2010
BE10-02575	Human	4-7-3-13-10-2-2	14b	02/08/2010
BE10-02601	Human	5-5-2-9-10-1-3	14c	03/08/2010
BE10-02636	Human	4-7-3-14-10-2-2	8	30/07/2010
BE10-02760	Human	4-7-3-13-10-2-2	14b	11/08/2010
BE10-02785	Human	5-5-2-10-10-1-3	21c	09/08/2010
BE10-02897	Human	4-7-3-13-10-2-2	14b	16/08/2010
BE10-02966	Human	4-7-3-13-10-2-2	14b	22/08/2010
BE10-03023	Human	4-7-3-10-10-2-2	8	20/08/2010
BE10-03244	Human	4-5-2-10-10-1-3	6c	28/08/2010
BE10-03249	Human	4-7-3-11-10-2-2	8	29/08/2010
BE10-03288	Human	4-7-3-13-10-2-2	14b	31/08/2010
BE10-03685	Human	4-7-3-13-10-2-2	14b	14/09/2010
BE10-03742	Human	4-7-3-10-10-2-2	8	20/09/2010
BE10-03796	Human	4-7-3-13-10-2-2	14b	26/09/2010
BE10-03807	Human	4-7-3-13-10-2-2	14b	23/09/2010
BE10-03896	Human	4-7-3-13-10-2-2	14b	03/10/2010
BE10-03938	Human	4-7-3-14-10-2-2	8	28/09/2010
BE10-03970	Human	5-5-2-12-10-1-3	21c	02/10/2010
BE10-04002	Human	5-5-2-9-10-1-3	51	04/10/2010
BE10-04063	Human	4-7-3-13-10-2-2	34b	27/09/2010
BE10-04174	Human	5-5-2-10-10-1-3	6a	12/10/2010
BE10-04314	Human	4-7-3-13-10-2-2	14b	15/10/2010
BE10-04675	Human	4-7-3-13-10-2-2	14b	14/10/2010
BE10-04813	Human	4-5-2-10-10-1-3	1	08/11/2010
BE10-05008	Human	4-7-3-10-10-2-2	8	24/11/2010
BE10-05032	Human	4-7-3-13-10-2-2	14b	25/11/2010
BE10-05163	Human	5-5-2-12-10-1-3	21c	29/11/2010
BE10-05361	Human	6-8-3-10-10-2-2	8	07/12/2010
BE10-05458	Human	4-7-3-13-10-2-2	14b	12/10/2010
BE10-05489	Human	5-6-2-10-10-1-3	4b	17/12/2010
BE10-13706	Spent hen	4-7-3-10-10-1-3	14b	Aug-10
LU-C100636	Human	4-7-3-13-10-2-2	8	14/05/2010
LU-C101179	Human	4-7-3-13-10-2-2	14b	16/08/2010
LU-C101216	Human	4-7-3-13-10-2-2	14b	23/08/2010

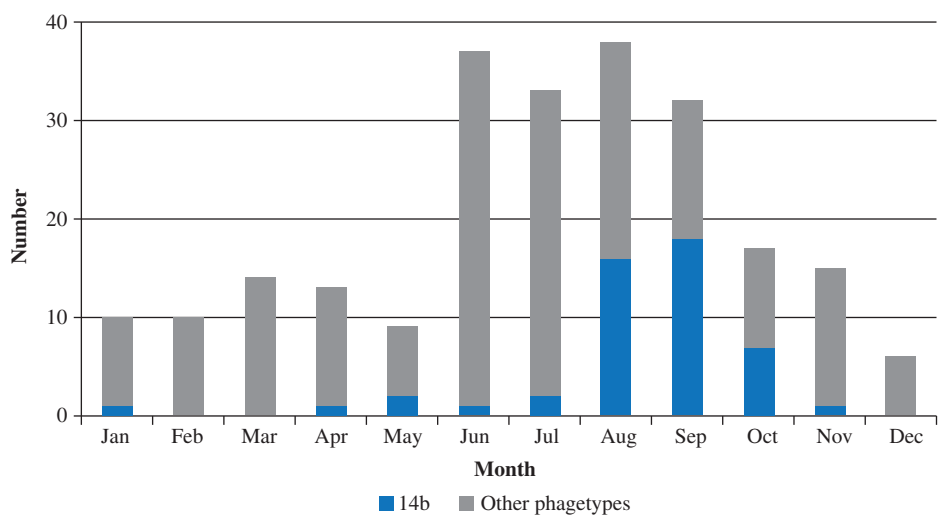
Strain ID	Origin	MLVA type	Phage type	Date
LU-C101396	Human	4-7-3-13-10-2-2	14b	17/09/2010
LU-C101398	Human	4-7-3-13-10-2-2	14b	17/09/2010
LU-C101417	Human	4-7-3-13-10-2-2	14b	22/09/2010
LU-C101442	Human	4-7-3-13-10-2-2	14b	27/09/2010
LU-C101507	Human	4-7-3-13-10-2-2	14b	11/10/2010
DE10-05696	Human	4-7-3-13-10-2-2	14b	21/10/2010
DE10-05694	Human	4-7-3-13-10-2-2	14b	21/10/2010
DE10-05003	Human	4-7-3-13-10-2-2	14b	20/09/2010
DE10-05002	Human	4-7-3-14-10-2-2	14b	20/09/2010
DE10-03033	Human	?-5-2-10-10-1-3	14b	29/06/2010
DE10-03032	Human	4-7-2-10-10-2-3	14b	29/06/2010
DE10-01568	Human	4-11-?-?-10-1-3	14b	25/03/2010
DE09-07460	Human	5-5-2-12-10-1-3	14b	10/11/2009
DE09-07459	Human	5-5-2-12-10-1-3	14b	10/11/2009
DE09-06700	Human	5-5-2-11-10-1-3	14b	12/10/2009
DE09-06699	Human	5-5-2-11-10-1-3	14b	12/10/2009
DE08-05834	Human	?-5-2-8-10-1-3	14b	03/09/2008
DE08-04340	Human	4-7-3-13-10-2-2	14b	21/07/2008
DE07-06550	Human	6-9-2-8-10-1-2	14b	28/09/2007
DE07-02979	Human	4-3-2-9-10-2-3	14b	05/06/2007
DE05-05956	Egg yolk	4-7-3-13-10-2-2	14b	30/08/2005

**Table 2:** Correspondence between phage and MLVA typing of human strains from Belgium and Luxembourg.

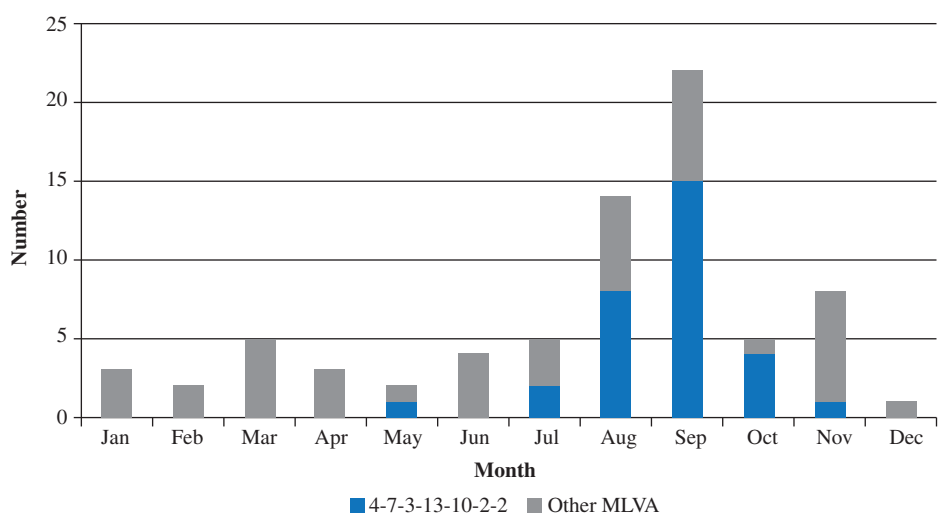
	Phage type										
MLVA type	1	4b	6a	6c	8	14b	14c	21c	34b	51	Total
4-5-2-10-10-1-3	1			1							2
4-7-3-10-10-2-2					3	1					4
4-7-3-11-10-2-2					1						1
4-7-3-13-10-2-2					1	20			1		22
4-7-3-14-10-2-2					2						2
5-5-2-10-10-1-3			1					1			2
5-5-2-12-10-1-3								2			2
5-5-2-9-10-1-3						1	1			1	3
5-6-2-10-10-1-3		1									1
6-8-3-10-10-2-2					1						1
Total	1	1	1	1	8	22	1	3	1	1	40



**Figure 1:** Monthly distribution of human *S. Enteritidis* cases reported to the respective national reference laboratories in 2009 and 2010 in a) Belgium and b) Luxembourg. The spike in June 2009 in Luxembourg represented a travel-related outbreak of tourists returning from Slovenia and Croatia.



a)



b)

**Figure 2:** Monthly distribution during 2010 of a) a random selection of human *S. Enteritidis* by phage type in Belgium b) all laboratory confirmed human *S. Enteritidis* in Luxembourg by MLVA pattern.



