

# EPITHELIAL TUMOURS OF HEAD AND NECK

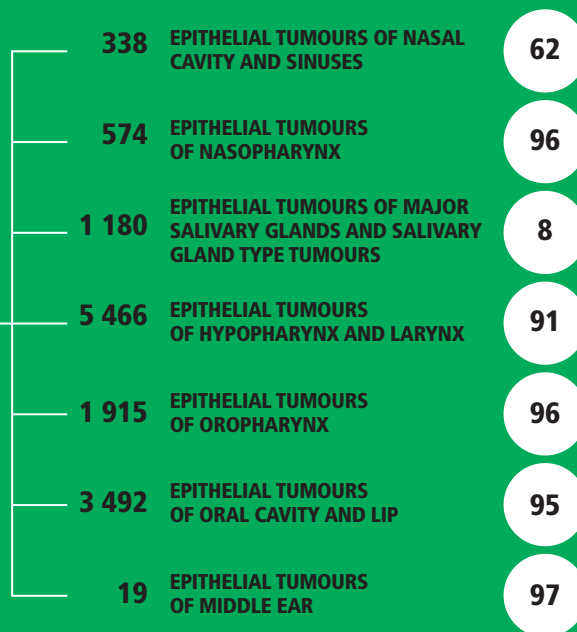
# 93%

OF HEAD AND NECK TUMOURS ARE RARE EPITHELIAL TUMOURS

## INCIDENCE

# 12 984

ESTIMATED NEW CASES ITALY, 2015



**62** % OF RARE EPITHELIAL TUMOURS OUT OF ALL TUMOURS IN EACH SITE

62

96

8

91

96

95

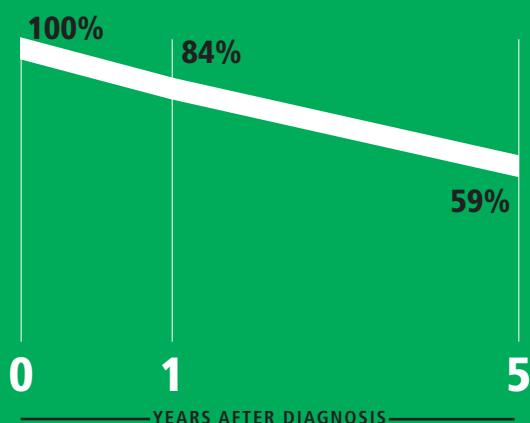
97

## PREVALENCE

# 116 200

ESTIMATED PREVALENT CASES ITALY, 2010

## SURVIVAL



# INCIDENCE



**EPITHELIAL TUMOURS OF HEAD AND NECK.** Crude incidence (rate per 100,000/year) and 95% confidence interval (95% CI), observed cases and proportion of rare cancers on all (common + rare) cancers by site. Rates with 95% CI by sex and age. Estimated new cases at 2015 in Italy.

	AIRTUM POOL (period of diagnosis 2000-2010)														ITALY
	RATE	95% CI	OBSERVED CASES (No.)	RARE EPITHELIAL CANCERS BY SITE (%)	SEX				AGE						ESTIMATED NEW CASES 2015
					MALE		FEMALE		0-54 yrs		55-64 yrs		65+ yrs		
					RATE	95% CI	RATE	95% CI	RATE	95% CI	RATE	95% CI	RATE	95% CI	
<b>EPITHELIAL TUMOURS OF HEAD AND NECK</b>	<b>19.46</b>	<b>19.28-19.65</b>	<b>43 163</b>	<b>93%</b>	<b>31.20</b>	<b>30.87-31.54</b>	<b>8.47</b>	<b>8.30-8.64</b>	<b>5.57</b>	<b>5.45-5.69</b>	<b>42.36</b>	<b>41.59-43.14</b>	<b>52.83</b>	<b>52.15-53.52</b>	<b>12 984</b>
<b>EPITHELIAL TUMOURS OF NASAL CAVITY AND SINUSES</b>	<b>0.50</b>	<b>0.47-0.53</b>	<b>1 114</b>	<b>62%</b>	<b>0.67</b>	<b>0.63-0.73</b>	<b>0.34</b>	<b>0.31-0.38</b>	<b>0.14</b>	<b>0.12-0.16</b>	<b>0.86</b>	<b>0.75-0.98</b>	<b>1.54</b>	<b>1.42-1.66</b>	<b>338</b>
Squamous cell carcinoma with variants of nasal cavity and sinuses	0.34	0.31-0.36	749		0.45	0.41-0.49	0.23	0.20-0.26	0.08	0.07-0.10	0.57	0.49-0.67	1.07	0.97-1.17	227
Lymphoepithelial carcinoma of nasal cavity and sinuses	<0.01	0.00-0.01	7		NE	–	NE	–	NE	–	NE	–	NE	–	2
Undifferentiated carcinoma of nasal cavity and sinuses	0.04	0.03-0.04	80		0.05	0.04-0.07	0.02	0.01-0.03	0.02	0.01-0.03	0.08	0.05-0.12	0.07	0.05-0.10	24
Intestinal type adenocarcinoma of nasal cavity and sinuses	0.02	0.02-0.03	47		0.04	0.03-0.05	<0.01	0.00-0.01	<0.01	0.00-0.01	0.04	0.02-0.07	0.06	0.04-0.09	14
<b>EPITHELIAL TUMOURS OF NASOPHARYNX</b>	<b>0.88</b>	<b>0.85-0.92</b>	<b>1 961</b>	<b>96%</b>	<b>1.34</b>	<b>1.27-1.41</b>	<b>0.46</b>	<b>0.42-0.50</b>	<b>0.59</b>	<b>0.55-0.63</b>	<b>1.72</b>	<b>1.57-1.89</b>	<b>1.38</b>	<b>1.28-1.50</b>	<b>574</b>
Squamous cell carcinoma with variants of nasopharynx	0.67	0.64-0.71	1 489		1.03	0.97-1.09	0.34	0.30-0.37	0.45	0.42-0.49	1.35	1.22-1.50	1.00	0.91-1.09	435
Papillary adenocarcinoma of nasopharynx	<0.01	0.00-0.00	1		NE	–	NE	–	NE	–	NE	–	NE	–	0*
<b>EPITHELIAL TUMOURS OF MAJOR SALIVARY GLANDS AND SALIVARY GLAND TYPE TUMOURS</b>	<b>1.77</b>	<b>1.71-1.82</b>	<b>3 921</b>	<b>8%</b>	<b>2.09</b>	<b>2.00-2.18</b>	<b>1.47</b>	<b>1.40-1.54</b>	<b>0.66</b>	<b>0.62-0.70</b>	<b>2.71</b>	<b>2.52-2.91</b>	<b>4.99</b>	<b>4.78-5.20</b>	<b>1 180</b>
Epithelial tumours of major salivary glands	1.23	1.18-1.28	2 726		1.43	1.36-1.50	1.04	0.98-1.10	0.44	0.40-0.47	1.78	1.62-1.94	3.60	3.43-3.78	829
Salivary gland type tumours of head and neck	0.54	0.51-0.57	1 195		0.66	0.61-0.71	0.43	0.39-0.46	0.22	0.20-0.24	0.93	0.82-1.05	1.39	1.28-1.50	351
<b>EPITHELIAL TUMOURS OF HYPOPHARYNX AND LARYNX</b>	<b>8.21</b>	<b>8.09-8.33</b>	<b>18 205</b>	<b>91%</b>	<b>15.28</b>	<b>15.05-15.52</b>	<b>1.58</b>	<b>1.51-1.66</b>	<b>1.81</b>	<b>1.74-1.88</b>	<b>19.98</b>	<b>19.45-20.52</b>	<b>22.82</b>	<b>22.38-23.27</b>	<b>5 466</b>
Squamous cell carcinoma with variants of hypopharynx	1.04	0.99-1.08	2 296		1.87	1.79-1.95	0.25	0.22-0.28	0.34	0.31-0.37	2.81	2.61-3.02	2.33	2.19-2.48	686
Squamous cell carcinoma with variants of larynx	7.17	7.06-7.29	15 909		13.41	13.19-13.63	1.33	1.27-1.40	1.47	1.41-1.54	17.17	16.68-17.67	20.49	20.07-20.92	4 780
<b>EPITHELIAL TUMOURS OF OROPHARYNX</b>	<b>2.89</b>	<b>2.82-2.96</b>	<b>6 410</b>	<b>96%</b>	<b>4.71</b>	<b>4.58-4.84</b>	<b>1.19</b>	<b>1.13-1.25</b>	<b>1.01</b>	<b>0.96-1.07</b>	<b>7.61</b>	<b>7.28-7.94</b>	<b>6.40</b>	<b>6.16-6.64</b>	<b>1 915</b>
Squamous cell carcinoma with variants of oropharynx	2.67	2.60-2.74	5 914		4.35	4.23-4.48	1.09	1.03-1.15	0.95	0.90-1.00	7.10	6.79-7.43	5.81	5.59-6.04	1 762
<b>EPITHELIAL TUMOURS OF ORAL CAVITY AND LIP</b>	<b>5.18</b>	<b>5.09-5.28</b>	<b>11 492</b>	<b>95%</b>	<b>7.08</b>	<b>6.92-7.24</b>	<b>3.41</b>	<b>3.30-3.52</b>	<b>1.37</b>	<b>1.31-1.43</b>	<b>9.45</b>	<b>9.09-9.82</b>	<b>15.60</b>	<b>15.24-15.98</b>	<b>3 492</b>
Squamous cell carcinoma with variants of oral cavity	3.76	3.68-3.84	8 330		4.88	4.75-5.02	2.70	2.61-2.80	1.16	1.10-1.21	7.57	7.25-7.91	10.29	9.99-10.60	2 499
Squamous cell carcinoma with variants of lip	1.10	1.06-1.14	2 437		1.77	1.69-1.85	0.47	0.43-0.51	0.12	0.10-0.14	1.38	1.25-1.53	4.28	4.08-4.47	765
<b>EPITHELIAL TUMOURS OF MIDDLE EAR</b>	<b>0.03</b>	<b>0.02-0.03</b>	<b>60</b>	<b>97%</b>	<b>0.03</b>	<b>0.02-0.05</b>	<b>0.02</b>	<b>0.01-0.03</b>	<b>&lt;0.01</b>	<b>0.00-0.01</b>	<b>0.04</b>	<b>0.02-0.07</b>	<b>0.10</b>	<b>0.07-0.13</b>	<b>19</b>
Squamous cell carcinoma with variants of middle ear	0.02	0.01-0.03	41		0.02	0.02-0.04	0.01	0.01-0.02	<0.01	0.00-0.01	0.03	0.01-0.05	0.07	0.05-0.10	13
Adenocarcinoma with variants of middle ear	<0.01	0.00-0.01	5		NE	–	NE	–	NE	–	NE	–	NE	–	1

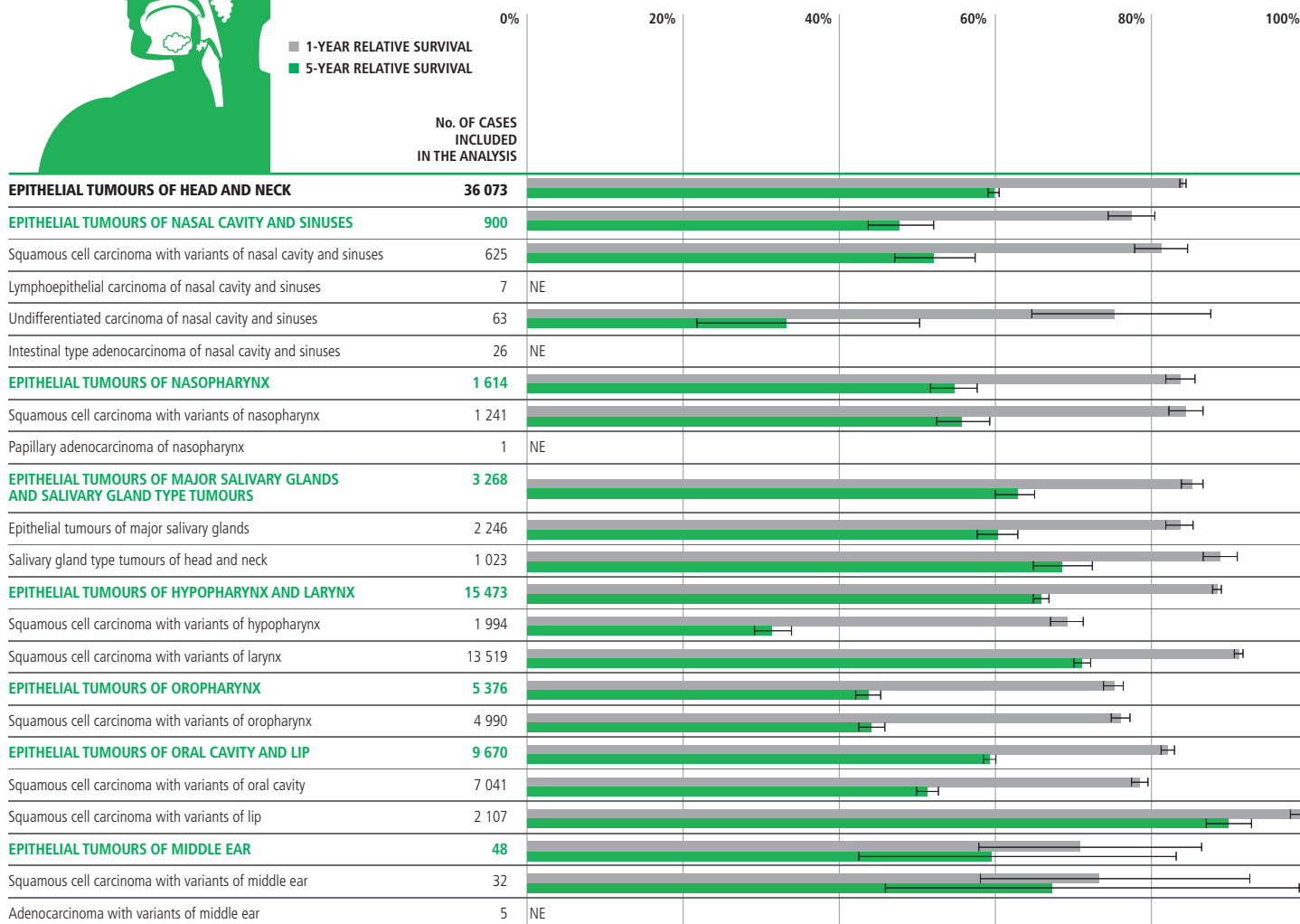
NE: not estimable because 15 or less incident cases were observed

\*One case every 3 years is expected

## SURVIVAL



**EPITHELIAL TUMOURS OF HEAD AND NECK.** One and 5-year relative survival. Error bars are 95% confidence interval. Cohort approach (complete analysis), period of diagnosis 2000-2008.



NE: not estimable because 30 or less incident cases were observed

# PREVALENCE



**EPITHELIAL TUMOURS OF HEAD AND NECK.** Observed prevalence (proportion per 100,00 and 95% confidence interval - 95% CI) by duration ( $\leq 2$ , 2-5,  $\leq 15$  years) prior to prevalence date (1<sup>st</sup> January 2007), and complete prevalence. Estimated prevalent cases in 2010 in Italy.

	AIRTUM POOL								ITALY
	OBSERVED PREVALENCE BY DURATION						COMPLETE PREVALENCE		ESTIMATED PREVALENT CASES 2010
	$\leq 2$ YEARS		2-5 YEARS		$\leq 15$ YEARS		PROPORTION	95% CI	
	PROPORTION	95% CI	PROPORTION	95% CI	PROPORTION	95% CI			
<b>EPITHELIAL TUMOURS OF HEAD AND NECK</b>	<b>34.22</b>	<b>33.00-35.47</b>	<b>37.10</b>	<b>35.83-38.40</b>	<b>144.25</b>	<b>141.73-146.79</b>	<b>200.86</b>	<b>197.23-204.50</b>	
<b>EPITHELIAL TUMOURS OF NASAL CAVITY AND SINUSES</b>	<b>0.75</b>	<b>0.58-0.95</b>	<b>0.75</b>	<b>0.58-0.95</b>	<b>2.74</b>	<b>2.40-3.11</b>	<b>3.71</b>	<b>3.23-4.18</b>	<b>2 129</b>
Squamous cell carcinoma with variants of nasal cavity and sinuses	0.53	0.39-0.71	0.63	0.48-0.82	2.17	1.88-2.51	2.97	2.54-3.40	1 706
Lymphoepithelial carcinoma of nasal cavity and sinuses	0.01	0.00-0.06	NE	–	0.01	0.00-0.06	NE	–	NE
Undifferentiated carcinoma of nasal cavity and sinuses	0.07	0.03-0.15	0.03	0.01-0.10	0.14	0.07-0.24	0.20	0.08-0.32	110
Intestinal type adenocarcinoma of nasal cavity and sinuses	0.01	0.00-0.06	0.01	0.00-0.06	0.05	0.01-0.12	0.09	0.00-0.17	48
<b>EPITHELIAL TUMOURS OF NASOPHARYNX</b>	<b>1.30</b>	<b>1.07-1.56</b>	<b>1.31</b>	<b>1.08-1.58</b>	<b>4.78</b>	<b>4.34-5.27</b>	<b>6.69</b>	<b>6.04-7.34</b>	<b>3 903</b>
Squamous cell carcinoma with variants of nasopharynx	1.01	0.81-1.25	1.12	0.91-1.36	3.71	3.32-4.14	4.90	4.36-5.44	2 866
Papillary adenocarcinoma of nasopharynx	NE	–	NE	–	NE	–	NE	–	NE
<b>EPITHELIAL TUMOURS OF MAJOR SALIVARY GLANDS AND SALIVARY GLAND TYPE TUMOURS</b>	<b>3.29</b>	<b>2.92-3.69</b>	<b>3.57</b>	<b>3.18-3.99</b>	<b>13.69</b>	<b>12.92-14.49</b>	<b>21.44</b>	<b>20.21-22.67</b>	<b>12 466</b>
Epithelial tumours of major salivary glands	2.18	1.88-2.52	2.24	1.93-2.57	8.85	8.24-9.50	14.54	13.49-15.59	8 464
Salivary gland type tumours of head and neck	1.10	0.89-1.35	1.33	1.10-1.60	4.84	4.39-5.32	7.19	6.49-7.90	4 184
<b>EPITHELIAL TUMOURS OF HYPOPHARYNX AND LARYNX</b>	<b>14.88</b>	<b>14.08-15.71</b>	<b>17.23</b>	<b>16.37-18.13</b>	<b>70.43</b>	<b>68.68-72.22</b>	<b>98.31</b>	<b>95.74-100.89</b>	<b>56 626</b>
Squamous cell carcinoma with variants of hypopharynx	1.49	1.25-1.77	1.00	0.80-1.24	4.31	3.89-4.77	5.15	4.62-5.68	2 964
Squamous cell carcinoma with variants of larynx	13.39	12.63-14.18	16.24	15.41-17.11	66.18	64.48-67.91	93.16	90.65-95.68	53 662
<b>EPITHELIAL TUMOURS OF OROPHARYNX</b>	<b>4.60</b>	<b>4.16-5.08</b>	<b>4.33</b>	<b>3.90-4.79</b>	<b>15.68</b>	<b>14.86-16.54</b>	<b>19.10</b>	<b>18.06-20.15</b>	<b>11 070</b>
Squamous cell carcinoma with variants of oropharynx	4.34	3.91-4.80	4.18	3.76-4.63	14.95	14.15-15.78	18.19	17.17-19.21	10 543
<b>EPITHELIAL TUMOURS OF ORAL CAVITY AND LIP</b>	<b>9.47</b>	<b>8.83-10.14</b>	<b>9.96</b>	<b>9.30-10.64</b>	<b>38.09</b>	<b>36.80-39.41</b>	<b>51.34</b>	<b>49.52-53.15</b>	<b>29 842</b>
Squamous cell carcinoma with variants of oral cavity	6.83	6.29-7.40	6.68	6.15-7.24	24.45	23.43-25.51	31.15	29.78-32.52	18 075
Squamous cell carcinoma with variants of lip	2.30	1.99-2.64	2.98	2.63-3.37	12.15	11.43-12.91	16.66	15.65-17.68	9 726
<b>EPITHELIAL TUMOURS OF MIDDLE EAR</b>	<b>0.05</b>	<b>0.01-0.12</b>	<b>0.05</b>	<b>0.01-0.12</b>	<b>0.17</b>	<b>0.10-0.28</b>	<b>0.28</b>	<b>0.14-0.42</b>	<b>163</b>
Squamous cell carcinoma with variants of middle ear	0.03	0.01-0.10	0.01	0.00-0.06	0.07	0.03-0.15	0.12	0.02-0.21	69
Adenocarcinoma with variants of middle ear	0.01	0.00-0.06	0.01	0.00-0.06	0.06	0.02-0.13	0.07	0.01-0.13	40

NE: not estimable in observed prevalence if no cases were observed within  $\leq 2$ , 2-5,  $\leq 15$  years prior to prevalence date, in complete prevalence if the 15-year prevalence is NE

According to the RARECARE project,<sup>1</sup> this group includes cancers originating from body sites that are very close to each other. Given the heterogeneous types of tissues and organs included in the head and neck, aetiology and pathogenesis are extremely different. However, head and neck cancers, as defined here, include only epithelial cancers originating from the oral cavity, nasal cavity and sinuses, nasopharynx, salivary glands, pharynx, and larynx (these two latter are sometimes grouped with trachea and lung cancers in other publications). This is because the list of rare cancers proposed by the RARECARE project<sup>1</sup> separates epithelial and non-epithelial tumours in addition to combining topographies and morphologies to define a specific tumour. Thus, non-epithelial tumours, such as sarcomas, neuroendocrine tumours, and lymphomas of the head and neck, are not included and will be described in the sarcoma, neuroendocrine tumours, and lymphoma grouping.

The definition of rare cancer is based on the incidence of a specific tumour in the European population. According to the European RARECAREnet database ([www.rarecarenet.eu](http://www.rarecarenet.eu)), all head and neck cancers have an incidence that is lower than 6 per 100,000 and are rare. Thus, even though in Italy some head and neck cancer types (such as larynx cancers) have an incidence >6 per 100,000, they are considered rare cancers because the definition is based on the European and not on the country-specific incidence rate.

Epithelial head and neck tumours comprise the following:

- **epithelial tumours of nasal cavity and sinuses** (squamous cell carcinomas, lymphoepithelial carcinoma, undifferentiated carcinoma, intestinal type adenocarcinoma);
- **epithelial tumours of nasopharynx** (squamous cell carcinomas, papillary adenocarcinoma);
- **epithelial tumours of major salivary glands and salivary gland type tumours** (epithelial tumours of major salivary glands, salivary gland type tumours of head and neck);
- **epithelial tumours of hypopharynx** (squamous cell carcinomas);
- **epithelial tumours of larynx** (squamous cell carcinomas);
- **epithelial tumours of oropharynx** (squamous cell carcinomas);
- **epithelial tumours of oral cavity and lip** (squamous cell carcinomas);
- **epithelial tumours of middle ear** (squamous cell carcinomas, adenocarcinomas).

## WHAT DO WE KNOW ABOUT THESE CANCERS?

Head and neck squamous cell carcinoma is the 6<sup>th</sup> most prevalent type of cancer worldwide and arises in the mucosa of the upper aerodigestive tract.<sup>2</sup> Incidence shows large variations across Europe and between sexes.<sup>1</sup> In Italy, incidence is higher in the Northern regions and the risk is much higher in men than women. These differences reflect differences in the diffusion of the main risk factors: smoking, alcohol, viruses (Human Papilloma virus – HPV, Epstein-Barr virus – EBV) and occupational exposures. Smoking and alcohol consumption are strong risk factors for larynx and oro-hypopharynx cancers,<sup>3</sup> intestinal-type carcinomas of the nasal cavity and ethmoid cancers have a high attributable fraction due to occupational exposure to wood, leather, dusts, and formaldehyde.<sup>4</sup> Nasopharynx carcinomas are related to EBV infection, while oropharynx carcinomas are related to HPV type 16 infection.<sup>4</sup> Even though most of the known risk factors are more frequent in

males than in females, incidence is much higher in males than expected based on the prevalence of the listed risk factors.<sup>4</sup> Prognosis is very different depending on disease site, and in some cases aetiology (HPV-related cancers have better prognosis if appropriately treated).<sup>1</sup>

Primary treatment varies with the anatomic site and stage of disease. For most early cancers, surgical resection is the cornerstone of treatment. However, for certain anatomic sites such as tonsils, base of tongue and floor of the mouth, as well as for all locally advanced cancers, radiotherapy is used, either alone or combined with surgery. Chemotherapy may be used in addition to radiotherapy. Nasopharynx carcinoma is sensitive to both radiation therapy and chemotherapy. The responsiveness of nasopharyngeal carcinoma to both radiotherapy and chemotherapy distinguishes it from other head and neck cancers, which are typically insensitive to chemotherapy.<sup>5</sup>

Because tumours of different localisations are managed differently, epidemiological data reflecting clinically relevant tumour grouping are essential.

## THE EPIDEMIOLOGICAL DATA IN ITALY

### Incidence

The majority of cases of head and neck cancers in Italy (incidence table, p. 34) arise from the larynx (37%), followed by the oral cavity (19%), oropharynx (15%), salivary glands (6%), lip (6%), hypopharynx (5%), nasopharynx (5%), salivary gland type tumours of head and neck (3%), nasal cavity and sinuses (3%), and finally by the very rare cancers of the middle ear (0.1%). For all sites, males have a higher risk than females: from 10-fold for larynx to 1.4-fold for salivary glands. The incidence rate (IR) increases with age for all cancer sites, with the exception of the nasopharynx, where the age-specific IR shows a plateau from intermediate age upward (data not shown). In children, head and neck cancers are extremely rare and are mostly epithelial tumours of the major salivary glands, squamous cell carcinoma of nasopharynx and oral cavity (data not shown). These results are similar to those observed in Europe in the RARECAREnet database ([www.rarecarenet.eu](http://www.rarecarenet.eu)), with the exception of tumours of nasopharynx and larynx which have a higher incidence in Italy than in Europe. This is most likely due to the different distribution of the previously listed risk factors.

### Survival

Five-year overall relative survival (RS) is 59%. Five-year RS ranges from 31% for squamous cell carcinoma of the hypopharynx to 89% for squamous cell carcinoma of the lip. Between these extremes, 5-year RS for squamous cell carcinoma of the larynx is 71%, for salivary gland type tumours it is 68%, and for squamous cell carcinoma of the middle ear it is 67% (based on 32 cases only). Squamous cell carcinomas of all other sites have similar 5-year RS (about 50%). Undifferentiated carcinoma of the nasal cavity and sinuses has a 5-year RS of 33%, based on 63 cases (survival figure, p. 35). Differences in survival among sites reflect the availability of effective surgical and radiotherapy treatments, responsiveness of the major histotypes to chemotherapy, and stage at diagnosis: some cancers give symptoms at a very early stage (oropharynx) and others remain asymptomatic until advanced stage (nasopharynx).<sup>4</sup> Five-year RS rates are similar to those observed in Europe in the

RARECAREnet database, with the exception of 5-year RS of larynx cancer, which in Europe is slightly lower than in Italy (61% vs. 71%, respectively). Five-year RS rates in Europe differ between geographic areas and countries, ranging (excluding larynx cancer) from 46.5% in Northern Europe to 28% in Eastern Europe,<sup>6</sup> probably reflecting different mix of head and neck sites and aetiologies, as well as different access to adequate treatment.

## Prevalence

Around 116,000 persons were estimated to be living with a diagnosis of head and neck epithelial tumours in 2010. About 32,000 cases had survived more than 15 years after diagnosis.

Squamous cell carcinoma with variants of larynx are the most frequent (46% of all prevalent cases), followed by squamous cell carcinoma with variants of oral cavity (16%), squamous cell carcinoma with variants of oropharynx (10%), squamous cell carcinoma with variants of lip (8%), epithelial tumours of major salivary glands (7%), salivary gland type tumours of head and neck (4%), epithelial tumours of nasopharynx (3%), squamous cell carcinoma with variants of hypopharynx (3%), epithelial tumours of nasal cavity and sinuses (2%), and finally epithelial tumours of middle ear (0.1%).

These results may be different from previous AIRTUM-published figures of incidence and prevalence, due to different selections of topographical and morphological codes. For Head and Neck group, this

monograph includes only epithelial cancers (which account for most cancers of head and neck) and salivary gland types of head and neck cancer are not included within each site but in a distinct group, «salivary gland type tumours of head and neck». Because of this, incidence and prevalence estimates will be slightly lower for most head and neck sites. In addition, for larynx, oropharynx, and oral cavity, prevalence estimates are slightly higher compared to AIRTUM published data on prevalence because the methodology used to calculate complete prevalence is different (for more details, see «Materials and Methods», pp. 14-21).

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## REFERENCES

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