

Manual for the Pituitary Disease-Specific Module

Contents

1.0 Time-points to create an outcome (return)	2
1.2 General follow-up ('wait-and-scan' policy)	2
1.3 Tumour treatment during follow-up.....	4
1.3.1 Medical/surgical/radiotherapy tumour treatment.....	4
1.3.2 Multiple treatment modalities	5
1.3.3 Treatment within six months after diagnosis	5
2.0 Overview of tabs to be filled in per outcome	6
3.0 Instructions for Pituitary Tumour Module Tabs	7
3.1 Tab: Basic disease module	7
3.2 Tab: Manifestations and secreted hormones.....	7
3.3 Tab: Imaging – Tumour behaviour assessed by post-treatment imaging.....	8
3.4 Tab: Radiation	8
3.5 Tab: Genetics	8
3.6 Tab: Medical therapy	9
3.7 Tab: Surgical outcomes.....	9

Outcome = a dataset at a certain timepoint during the follow-up of the patient, could also be referred to as 'return'.

1.0 Time-points to create an outcome (return)

1.2 General follow-up ('wait-and-scan' policy)

- Create an outcome at the time of diagnosis (before the start of any treatment)
- Create a new outcome 2, 4, 5, 10, 15, 20 etc. years after diagnosis, unless there is progression* or a treatment (other than endocrine replacement) is initiated (see below).

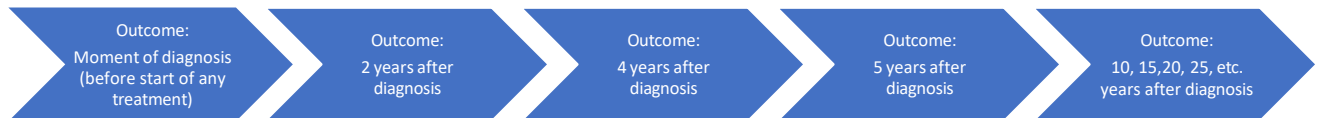


Figure 1 - General follow-up in case of no progression

*In case of progression that is not followed by treatment, create an extra outcome at the time of progression (Figure 2a and 2b).



Figure 2a – Example of general follow-up in case of progression not followed by treatment (3 years after diagnosis)



Figure 2b - Example of general follow-up in case of progression not followed by treatment (6/7/8/9 years after diagnosis)

- For each return, specify the moment during the disease process. For the return of the General follow-up, please select 'General follow-up' from the drop-down menu after the questions 'Specify which return is going to be made'.

Assessment date	1900-01-01
Specify which return is going to be made	General follow-up
General follow-up	General follow-up
What is the follow-up status of the patient?	Medical tumour treatment
	Surgical tumour treatment
	Radiotherapy treatment
Who is the clinical lead	

Then, select the specific return, for example 'Time of diagnosis', or '2 years after diagnosis', from the drop-down menu after the question 'General follow-up'.

Assessment date	<input type="text" value="1900-01-01"/>
Specify which return is going to be made	<input type="text" value="General follow-up"/>
General follow-up	<input type="text" value="- Select -"/>
What is the follow-up status of the patient?	<input type="text" value="- Select -"/>
Who is the clinical lead for the pituitary tumour care?	<input type="text" value="Time of diagnosis"/>
Has the patient started a transition process?	<input type="text" value="2 years after diagnosis"/>
	<input type="text" value="4 years after diagnosis"/>
	<input type="text" value="5 years after diagnosis"/>
	<input type="text" value="10 years after diagnosis"/>

1.3 Tumour treatment during follow-up

! Beware: **medical tumour treatment** is directed towards **growth/volume reduction** (e.g. such as with dopamine agonists, somatostatin analogues, or temozolamide) or treatment of hormonal excess (such as metyrapone, somatostatin analogues). Endocrine replacement therapies in case of hypopituitarism is **NOT** considered tumour treatment.

1.3.1 Medical/surgical/radiotherapy tumour treatment

- Create an outcome at the time of diagnosis (before the start of any treatment), see also paragraph 1.2 General follow-up.
- Create a new outcome before the start of treatment if the outcome at the time of diagnosis was more than 6 months ago. If the start of the treatment or surgery is within six months after diagnosis, you can combine these two outcomes, by selecting 'Medical/Surgical/Radiotherapy treatment' and 'Time of diagnosis = pre-medical/surgical/radiotherapy intervention' (see 1.3.3)
- Create a new outcome 6 months (3-9) after (initiating) medical/surgical/radiotherapy treatment.
- Subsequently, fall back into the outcomes of the general follow-up (see paragraph 1.2), unless there is progression or a new treatment
- If a new treatment is initiated, create a new outcome right before the treatment and 6 months after treatment.

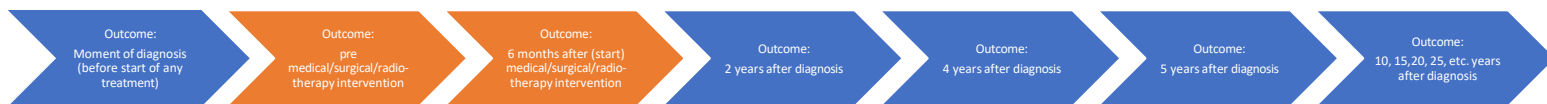


Figure 3 – Example of medical/surgical/radiotherapy treatment started within 2 years after diagnosis

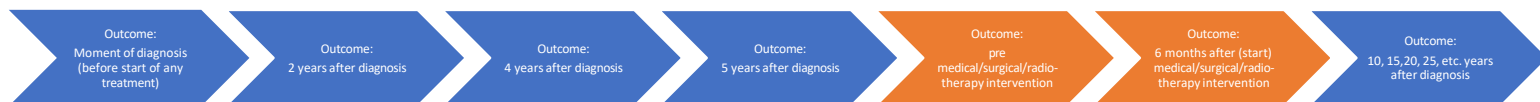


Figure 4 - Example of medical/surgical/radiotherapy treatment started 6/7/8/9 years after diagnosis

1.3.2 Multiple treatment modalities

In case a patient is treated with multiple modalities during their follow-up period, please make sure that you have created an outcome for the moment of diagnoses, 2, 4, 5, 10, 15 years etc. after diagnosis and add treatment specific outcomes (See Figure 5).

At the moment two modalities of treatment are given at the exact same time, these outcomes can be combined.



Figure 5 - Example of surgical therapy within 2 years after diagnosis followed by radiotherapy 3/4 years after diagnosis

1.3.3 Treatment within six months after diagnosis

In case the first treatment (medical/surgical or radiotherapy) has taken place within the first six months after diagnosis, there is an option to combine the first two outcomes. This is done to prevent a double work-load since these returns will most likely be the same.

1. Indicate the treatment from the drop-down menu after the question ‘Specify which return is going to be made’, for example ‘surgical tumour treatment’.

Specify which return is going to be made	General follow-up
General follow-up	General follow-up
What is the follow-up status of the patient?	Medical tumour treatment
Who is the clinical lead	Surgical tumour treatment
	Radiotherapy treatment

2. Select ‘Time of diagnosis = pre-surgical intervention’ from the drop-down menu after the question ‘Surgical tumour treatment’.

Specify which return is going to be made	Surgical tumour treatment
Surgical tumour treatment	- Select -
What is the follow-up status of the patient?	- Select -
Who is the clinical lead for the pituitary tumour care?	Time of diagnosis
Has the patient started a	Time of diagnosis = pre-surgical intervention
	Pre-surgical intervention
	6 months post-surgical

In case the status of the patient differs between the moment of diagnosis and the moment before a treatment, please create two separate returns.

2.0 Overview of tabs to be filled in per outcome

Table 1 - Overview of tabs to be filled in per outcome

	Basic disease module	Auxology parameters	Endocrine manifestations	Secreted hormones	Visual impairment	Imaging	Genetics	Histopathology	Radiation	Medical therapy	Surgical outcomes	VTE
Return												
General follow-up: time of diagnosis	X	X	X	X	X	X	X					**
General follow-up: x years after diagnosis	X	X	X	X	X	X	X	*	*	*	*	**
General follow-up: progression not followed by treatment	X	X	X	X	X	X	X					**
Medical tumour treatment: pre-medical intervention	X	X	X	X	X	X	X	*	*	*	*	**
Medical tumour treatment: 6 months after initiating medical intervention	X	X	X	X	X	X	X	*	*	X	*	**
Surgical tumour treatment: pre-surgical intervention	X	X	X	X	X	X	X	*	*	*	*	**
Surgical tumour treatment: 6 months post surgical intervention	X	X	X	X	X	X	X	X	*	*	X	**
Radiotherapy treatment: pre radiotherapy intervention	X	X	X	X	X	X	X	*	*	*	*	**
Radiotherapy treatment: 6 months post radiotherapy	X	X	X	X	X	X	X	*	X	*	*	**

* = only if applicable based on prior treatments, update assessment dates and outcomes

** = only if VTE occurred. Cushing Severity Index at every time point for patients with M. Cushing

3.0 Instructions for Pituitary Tumour Module Tabs

3.1 Tab: Basic disease module

- The return of 'Time of diagnosis' should be filled in before any treatment has been given. The variables 'Has the patient been on medical therapy?', 'Has the patient undergone pituitary tumour related surgery?', and 'Has the patient received radiotherapy as part of the pituitary tumour treatment', should ideally be answered with 'No'.

Has the patient been on medical therapy?	No
Has the patient undergone pituitary tumour related surgery?	No
Has the patient received radiotherapy as part of the pituitary tumour treatment?	No

3.2 Tab: Manifestations and secreted hormones

- To be filled in for every outcome to monitor hormone excess and pituitary function loss over time for all patients independent of their treatments.
- In case of remission of hormone secreting adenoma (e.g. Cushing) 'Cushing disease' in the 'Endocrine manifestations' tab stays selected and 'Main secreted hormone' needs to be changed to 'None'. In case of a recurrence 'ACTH' needs to be re-selected.

Assessment date	yyyy-mm-dd
Endocrine manifestations and clinical syndromes	<input type="checkbox"/> Acromegaly <input type="checkbox"/> Gigantism <input type="checkbox"/> Growth failure <input type="checkbox"/> Growth hormone deficiency <input type="checkbox"/> Infertility <input type="checkbox"/> Male hypogonadism <input type="checkbox"/> Female hypogonadism <input type="checkbox"/> Primary amenorrhoea <input type="checkbox"/> Secondary amenorrhoea <input type="checkbox"/> Precocious puberty <input type="checkbox"/> Galactorrhea <input type="checkbox"/> Secondary hypothyroidism <input type="checkbox"/> Thyrotoxicosis <input checked="" type="checkbox"/> Cushing disease <input type="checkbox"/> Hypocortisolism <input type="checkbox"/> Diabetes insipidus <input type="checkbox"/> Pituitary apoplexy <input type="checkbox"/> None <input type="checkbox"/> Other
Main secreted hormone	ACTH
Co-secreted hormones	<input type="checkbox"/> ACTH <input type="checkbox"/> GH <input type="checkbox"/> Prolactin <input type="checkbox"/> FSH <input type="checkbox"/> LH <input type="checkbox"/> TSH <input checked="" type="checkbox"/> None

Biochemically active M. Cushing with hypercortisolism

Assessment date ?

Endocrine manifestations and clinical syndromes ?

- Acromegaly
- Gigantism
- Growth failure
- Growth hormone deficiency
- Infertility
- Male hypogonadism
- Female hypogonadism
- Primary amenorrhoea
- Secondary amenorrhoea
- Precocious puberty
- Galactorrhea
- Secondary hypothyroidism
- Thyrotoxicosis
- Cushing disease
- Hypocortisolism
- Diabetes insipidus
- Pituitary apoplexy
- None
- Other

Assessment date ?

Main secreted hormone ?

Co-secreted hormones ?

- ACTH
- GH
- Prolactin
- FSH
- LH
- TSH
- None

M. Cushing in biochemical remission (without hypercortisolism, this could potentially be due to the use of medication such as metyrapone)

- In case of additional pituitary axis loss as a result of surgery, the additional pituitary axis loss must be selected in the 'Endocrine manifestations'.
- Please only select secretion of Prolactin in case this is thought to be produced by the adenoma itself and not due to the stalk effect.

3.3 Tab: Imaging – Tumour behaviour assessed by post-treatment imaging

- The items 'progression', 'increase of maximal tumour diameter' and 'increase of tumour volume' needs to be compared to the last MRI before treatment when filling in a 6 months post-intervention outcome and compared to the first post-intervention MRI if applicable or the MRI at diagnosis when filling in the general follow-up outcomes.

Tumour behaviour assessed by post-treatment imaging

Assessment Date ?

Age at Assessment Date

Is there a tumour progression?

Has the maximal tumour diameter assessed by post-treatment imaging increased?

Has the tumour volume assessed by post-treatment imaging increased?

Tumour remnant visible on MRI?

Which of the following standard therapies has been used in this patient? ?

- Medical therapy
- Surgical therapy
- Radiation therapy

Figure 6 – Fields abouts progression at the section of tumour behaviour assess by post-treatment imaging

3.4 Tab: Radiation

- 'Endocrine response' and 'tumour response' following radiation therapy have to be **compared to hormone levels (in case of functional adenomas) and imaging right before the initiation of radiation treatment**

3.5 Tab: Genetics

Fill in whenever possible, but **specifically in patients <30 years of age.**

3.6 Tab: Medical therapy

- 'Endocrine response' and 'tumour response' following radiation therapy have to be **compared to hormone levels (in case of functional adenomas) and imaging right before start of medical treatment**

3.7 Tab: Surgical outcomes

- Endocrine response following surgery has to be **compared to hormone levels right before surgery**
- Complications: please register all complications that have happened between the surgery and 3-6 months postoperatively. You can select 'transient' or indicate that a complication has been transient in case a complication has happened but is not present anymore at 3-6 months after surgery.

3.8 Tab: VTE

Venous thromboembolism (VTE) module

- Fill in IF VTE occurred